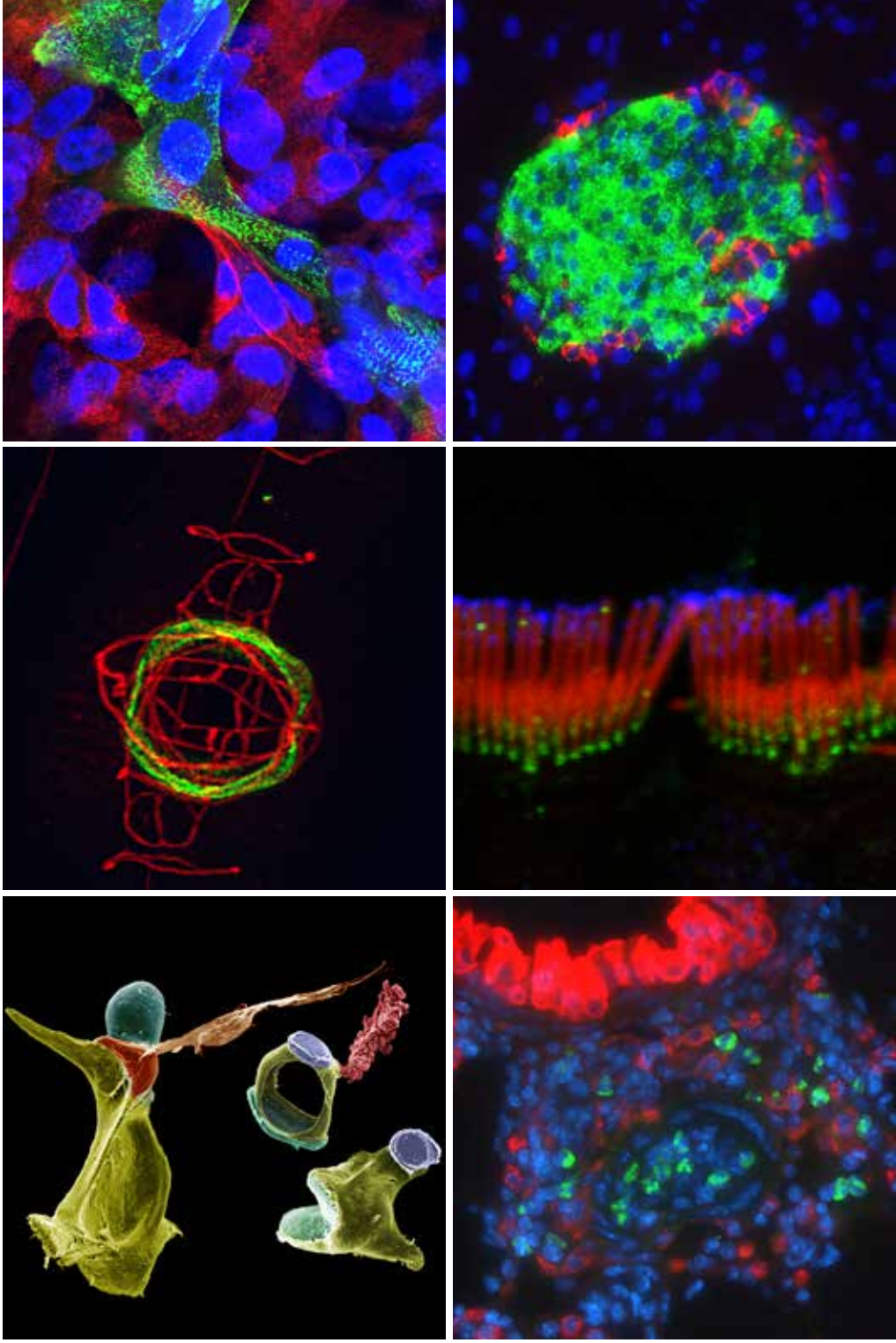


TEL AVIV UNIVERSITY
Pursuing the Unknown

Sackler Faculty of Medicine

Preclinical Research 2018

TEL AVIV UNIVERSITY

Sections

Cover images (from bottom left, clockwise):

Image 1: Human embryonic stem cell derived cardiomyocytes stained with fluorescent antibodies. The cardiac marker alpha-actinin (green), calcium channel modulator, Ahnak1 (red) – Shimrit Oz, Nathan Dascal.

Image 2: Islet of Langerhans containing insulin-producing beta-cells (green) and glucagon-producing alpha-cells (red) – Daria Baer, Limor Landsman.

Image 3: β-catenin in *C. elegans* vulva – Michal Caspi, Limor Broday, Rina Rosin-Arbesfeld.

Image 4: Stereocilia of a sensory outer hair cell from a mouse inner ear – Shaked Shivatzki, Karen Avraham.

Image 5: Electron scanning micrograph of middle ear ossicles from a mouse ear stained with pseudo colors – Shaked Shivatski, Karen Avraham.

Image 6: Resistin-like molecule alpha (red), eosinophil major basic protein (green) and DAPI (blue) staining of asthmatic mice – Danielle Karo-Atar, Ariel Munitz.

Editor: Prof. Karen Avraham
Graphic design: Michal Semo Kovetz, TAU Graphic Design Studio
February 2018

The Sackler Faculty of Medicine

The Sackler Faculty of Medicine is Israel's largest medical research and training complex. The Sackler Faculty of Medicine of Tel Aviv University (TAU) was founded in 1964 following the generous contributions of renowned U.S. doctors and philanthropists Raymond, and the late Mortimer and Arthur Sackler. Research at the Sackler Faculty of Medicine is multidisciplinary, as scientists and clinicians combine efforts in basic and translational research. Research is conducted in the laboratories on the TAU campus, and in the clinical facilities affiliated to the Faculty. The Faculty of Medicine includes the Sackler School of Medicine, the School of Health Professions, the School of Public Health, and the School of Dental Medicine. Education takes place in all these schools and in the Graduate School of Medicine, School of Continuing Medical Education, the New York State American Program and the B.Sc. Program in Medical Life Sciences. This network of preclinical and clinical teams helps realize the ultimate goals of the research: the basic understanding of human pathophysiology and the prevention, diagnosis and treatment of disease. The research of Preclinical faculty members from the Sackler School of Medicine are featured in this research brochure.

The Faculty of Medicine engages in joint teaching and research programs with nearly every faculty at TAU, including the Wise Faculty of Life Sciences, the Sagol School of Neuroscience, the Edmond J. Safra Bioinformatics Center, the TAU Center for Nanoscience and Nanotechnology, and the Edmond J. Safra Center for Ethics, and multi-nationally with schools, hospitals and research centers throughout the world. The Sackler faculty is known for research in the following areas: cancer biology, stem cells, diabetes, neurodegenerative diseases, infectious diseases and genetic diseases, including but not imited to Alzheimer's disease, Parkinson's disease and HIV/AIDS. Physicians in 181 Sacker affiliated departments and institutes in 17 hospitals hold academic appointments at TAU. The Gitter-Smolarz Life Sciences and Medicine Library serves students and staff and is the center of a consortium of 15 hospital libraries.

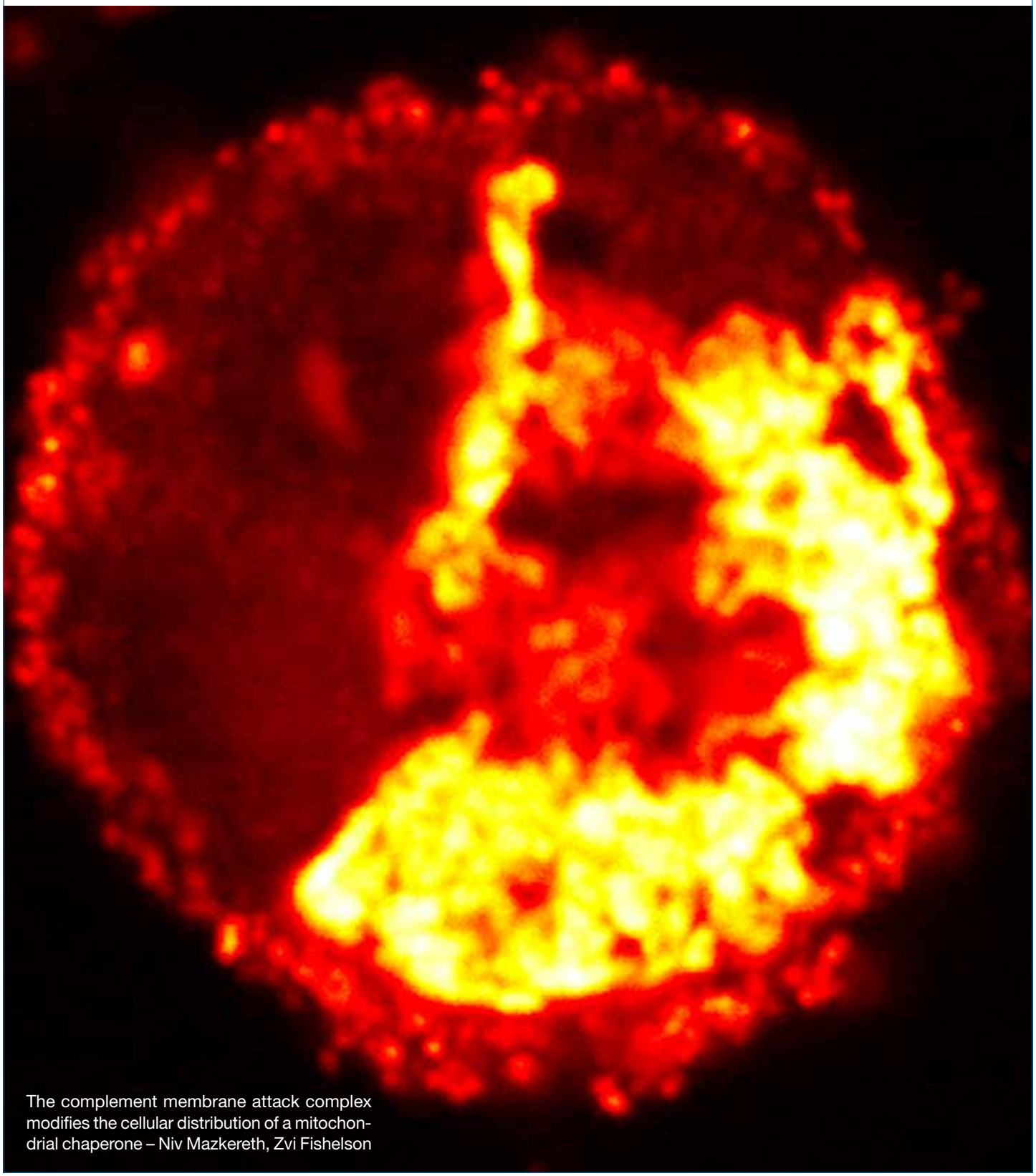
The student body is made up of 750 Israeli students enrolled in the 6-year M.D. degree program, 300 American and Canadian students enrolled in a 4-year M.D. program chartered by the State of New York and accredited by the State of Israel, and a 4-year program for Israeli students for the M.D. degree, with 260 students. Approximately 200 students study dental medicine in a six-year program where they are awarded the D.M.D. degree and another 2,000 students are enrolled in the health professions programs where they will earn degrees in Communications Disorders, Nursing, Physical Therapy and Occupational Therapy. Sackler's Graduate School for Advanced Studies trains approximately 800 masters and doctoral level students in the biomedical disciplines, with a special emphasis on a multidisciplinary approach and application of fundamental knowledge to important biomedical problems.

The Sackler Faculty of Medicine is led by the Dean, Professor Ehud Grossman; Vice Deans Prof. Karen Avraham, Prof. Iris Barshack, Prof. Moshe Phillip, Prof. Anat Lowenstein, Prof. Meir Lahav, Prof. Ami Fishman, and Assistant to the Dean, Ms. Michal Gilboa.

TEL AVIV UNIVERSITY

Table of Contents

Cancer and Molecular Therapies



The complement membrane attack complex modifies the cellular distribution of a mitochondrial chaperone – Niv Mazkereth, Zvi Fishelson

Dr. Yaron Carmi, Ph.D.

Department of Pathology
Sackler School of Medicine
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: yaron.carmi@gmail.com

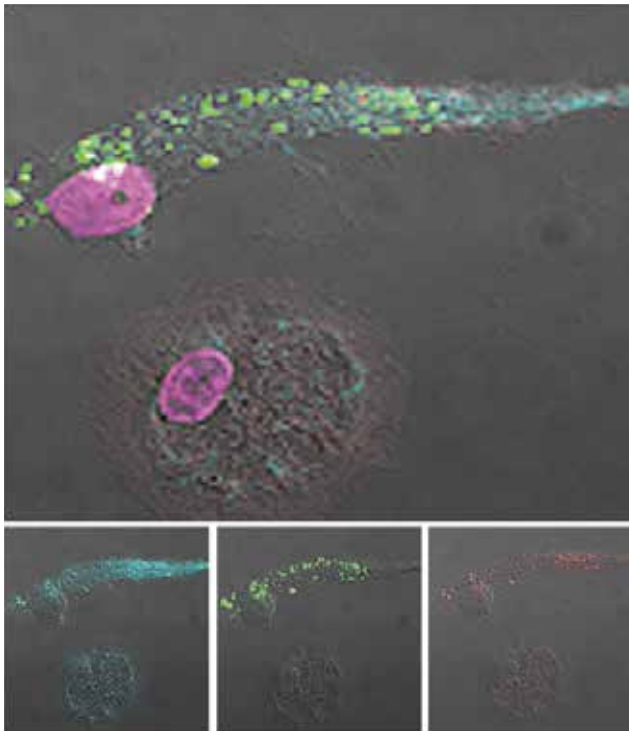
Cellular and Molecular Mechanisms of Antigen-Restricted Tumor Immunity

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

The goal of our work is to provide a detailed understanding of the mechanisms, signals and molecular pathways that regulate discriminating self from non-self and give rise to tumor-specific cytotoxic T cell immunity. Our specific aims are to address the following: 1) What are the cellular and molecular elements that enable the immune system to recognize subtle antigenic variations from self to initiate a cytotoxic immune response? 2) How is the specificity of the induced immune response determined? In other words, what is the process by which the presentation of diverse antigens by DC is reduced to activation of specific effector T cells? Understanding the means by which DC and T cells communicate to initiate antigen-restricted tumor immunity and how these processes are regulated will provide a roadmap for designing novel, more potent cancer immunotherapies.



Confocal microscopy showing the take up of tumor cells (in green) coated with IgG (red) by dendritic cells and their loading on MHCII molecules (cyan). Carmi Y. et al. 2015. *Nature* 521:99-104.

Publications

Santana-Magal N., Rasoulouniriana D., Vladimirsky J., Rider P., **Carmi Y**. 2017. Isolation of monocyte-derived dendritic cells and their activation with tumor immune complexs. 2017. ***JoVE*** (in press).

Spitzer MH*, **Y. Carmi Y***, NE. Reticker-Flynn NE*, D. Madhireddy D, PF. Gherardini PF, J. Chabon J, GP. Nolan GP and EG. Engleman EG. Modeling effective cancer immunotherapy reveals the importance of systemic immunity. 2017, ***Cell*** 168, 487–502. co-equal contribution

Zhang H, Gregorio JD, Iwahori T, Zhang X, Choi O. Tolentino LL, Prestwood T, **Carmi Y**, Engleman EG. A novel subset of plasmacytoid dendritic cells induces activation and differentiation of B and T lymphocytes. 2017, ***Proc Natl Acad Sci USA***. 114:1988-1993.

Bhattacharya N, Yuan R, Prestwood TR, Hweixian Leong P, DiMaio MA, Pham TD**, Carmi Y**, Kenkel JA, Hulett R, Wang J, Winer D, Napoli JL, Engleman EG. Retinoic acid drives anti-tumor CD8+ T cell immunity in colorectal cancer. 2016. *Immunity*. 45:641-655.

Carmi Y, Prestwood TR, Spitzer MH, Linde IL, Chabon J, Reticker-Flynn NE, Bhattacharya N, Zhang H, Zhang X, Basto PA, Burt BM, Alonso MN, Engleman EG. Akt and SHP1 are dendritic cell-intrinsic checkpoints for tumor immunity. *J Clin Invest Insight.* 2016. 1: e89020.

Rider P, **Carmi Y**, Yossef R, Guttman O, Eini H, Azam T, Dinarello CA, Lewis EC. IL-1 Receptor antagonist

chimeric protein: context-specific and inflammation-restricted activation. *J Immunol*. 2015, 195:1705-12.

Segal E, Prestwood TR, van der Linden WA, **Carmi Y**, Bhattacharya N, Withana N, Verdoes M, Habtezion A, Engleman EG, Bogyo M. Detection of intestinal cancer by local, topical application of a quenched fluorescence probe for cysteine cathepsins. *Chem Biol*. 2015, 22:148-158.

Spitzer MH, Gherardini PF, Fragiadakis GK, Bhattacharya N, Yuan RT, Hotson AN, Finck R, **Carmi Y**, Zunder ER, Fantl WJ, Bendall SC, Engleman EG, Nolan GP. An interactive reference framework for modeling a dynamic immune system. *Science.* 2015, 349:1259425.

Carmi Y, Spitzer MH, Linde IL, Burt BM, Prestwood TR, Perlman N, Davidson MG, Kenkel JA, Segal E, Pusapati GV, et al. Allogeneic IgG combined with dendritic cell stimuli induce antitumour T-cell immunity. *Nature*. 2015, 521:99-104.

Carmi Y, Dotan S, Rider P, Kaplanov I, White MR, Baron R, Abutbul S, Huszar M, Dinarello CA, Apte RN, et al. The role of IL-1b in the early tumor cell induced angiogenic response. *J Immunol*. 2013, 190:3500-3509.

Carmi Y, Rinott G, Dotan S, Elkabets M, Rider P, Voronov E, Apte, RN. Microenvironment-derived IL-1 and IL-17 interact in the control of lung metastasis. *J Immunol*. 2013, 186:3462-3471.

Patents

Engleman EG and **Carmi Y**. Methods and Compositions for Antibody and Antibody-Loaded Dendritic Cell Mediated Therapy. US2015012511

Engleman EG, Spitzer M. and Carmi Y. Methods and Compositions for Treating Individuals That Have Cander and for Identifying Individuals Responsive to Immunotherapy. 62/447,959

Grants

2017	Alon Award for Outstanding Young Scientists
2017	Swiss Bridge Award: *Elucidating the Mechanisms by Which Tumor-Binding Antibodies Enable T Cells Infiltration into the Tumor Microenvironment*

Prof. Neta Erez, Ph.D.

Department of Pathology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: netaerez@post.tau.ac.il

Cancer Related Inflammation in Tumor Progression and Metastasis

Position

Associate Professor, Sackler Faculty of Medicine

Chair, Department of Pathology

Research

The main goal of our laboratory is to uncover stromal pathways that contribute to tumorigenesis and metastasis. In particular, we combine transgenic mouse models of cancer as well as clinical data to study the role of inflammation and cancer-associated fibroblasts in facilitating lung metastasis of breast cancer, and to uncover the role of neuroinflammation mediated by astrocytes in melanoma brain metastasis.

Extensive research has led to the understanding that **tumors are more than just cancer cells**: stromal cells in the tumor microenvironment play a crucial role in all stages of tumor initiation and progression, and cancer research is no longer focused only on the pathways inside tumor cells, but rather on tumors as multi-cellular organs.

The major cause of cancer mortality is metastasis to distant organs. Currently, metastatic cancers are incurable and available therapies can only prolong life to a limited extent. Therefore, uncovering the mechanisms that facilitate metastasis is an urgent and unmet clinical need. Nevertheless, changes in the metastatic microenvironment that enable the growth of disseminated tumor cells are poorly characterized, and are the major focus of our research.

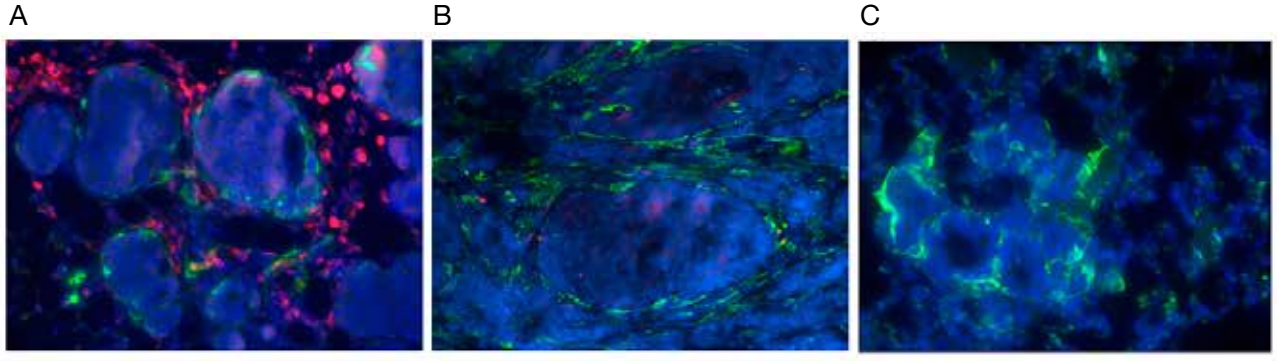
Expanding our understanding of the early stages of metastatic growth is an essential prerequisite for the discovery of novel target molecules for the development of targeted therapeutics that may prevent, rather than try to cure, metastatic disease

Publications

Erez N., Glanz S., Raz Y., Avivi C., and Barshack I. Cancer associated fibroblasts express pro-inflammatory factors in human breast and ovarian tumors. *Biochem Biophys Res Commun*. 2013 437:397-402.

Raz, Y. and **Erez N.** An inflammatory vicious cycle: fibroblasts and immune cell recruitment in cancer. *Exp Cell Res*. 2013 pii: S0014-4827:00130-4.

Rietkötter, E., Bleckmann, A., Bayerlowa, M., Menck, K., Chuang, H-N., Wenske, B., Schwartz, H. **Erez, N.**, Binder, C., Hanisch, U-K., and Pukrop T. Anti-CSF-1 treatment is effective to prevent carcinoma invasion induced by monocyte-derived cells (MCs)



A, B: Cancer Associated Fibroblast (CAFs) accumulate around mammary tumors in tissue Sections from the MMTV-PyMT transgenic mouse model. Green-aSMA, Blue-DAPI, Red-FSP-1. **C**: Immunofluorescent staining showing activated fibroblasts in lung metastases in MMTV-PyMT mice. Blue- DAPI. Green –aSMA.

but scarcely by microglia. Oncotarget. 2015, 6:15482-93.

Sharon Y., Raz Y., Cohen N., Ben-Shmuel A., Schwartz H., Geiger T., and **Erez N.** Tumor-derived Osteopontin reprograms normal mammary fibroblasts to become pro-inflammatory and tumor promoting in breast cancer. Cancer Res. 2015, 75:963-73.

Klein A, Schwartz H, Sagi-Assif O, Meshel T, Izraely S, Ben Menachem S, Ben-Shmuel A, Nahmias C, Couraud P, Witz IP and **Erez N.** Astrocytes facilitate melanoma brain metastasis via secretion of IL-23. J Pathol. 2015 236:116-127.

Schwartz H., Blacher E., Amer M., Livneh N., Abramovitz, L. Klein A., Ben-Shushan D., Soffer S., Blazquez R., Barrantes-Freer A., Müller M., Müller-Decker K., Stein R., Tsarfaty G., Satchi-Fainaro R., Umansky V., Pukrop T and **Erez N.** Incipient melanoma brain metastases instigate astrogliosis and neuroinflammation. Cancer Res. 2016. 76(15):4359-71.

Cohen N, Shani O, Raz Y, Sharon Y, Hoffman D, Abramovitz L and **Erez N**. Fibroblasts drive an immunosuppressive and growth-promoting microenvironment in breast cancer via secretion of Chitinase 3-like 1. Oncogene 2017. 36:4457-4468.

Herkel J, Schrader J, **Erez N**, Lohse A, and Cohen IR. Activation of the Akt-CREB signaling axis by a proline-rich heptapeptide confers resistance to stress-induced cell-death and inflammation. Immunology. 2017, 151:474-480.

Dror S., Sander L., Schwartz H., Sheinboim D., Barzilai A., Dishon Y., Apcher S., Golan, T., Greenberger, S., Barshack, I., Malcov, H., Zilberberg, A., Levin, L., Nessling, M., Friedmann, Y., Igras, V., Barzilay, O., Vaknine, H., Brener, R., Zinger, A., Schroeder, A., Gonen, P., Khaled, M., **Erez, N**., Hoheisel, J.D. and Levy, C. Melanoma miRNA trafficking triggers the tumor primary niche formation. Nat Cell Biol 2016 Sep;18(9):1006-17. *Selected for the Nature Cell Biology cover, Featured in Nature, Featured in Nature Cell Biology*.

Klein A, Sagi-Assif O, Meshel T, Telerman A, Izraely S, Ben-Menachem S, Bayry J, Marzese D, Ohe S, Hoon D, **Erez N**, and Witz I. CCR4 is a determinant of melanoma brain metastasis. Oncotarget 2017, 8:31079-31091.

Reviews

Servais C. and **Erez N.** From sentinel cells to inflammatory culprits: cancer-associated fibroblasts in tumor-related inflammation. *J Pathol***.** 2013; 229:198-207.

Erez N. Cancer: Angiogenic Awakening. *Nature*. 2013; 500:37-8.

Erez N. Cancer: Opening LOX to metastasis. Nature. 2015.

Erez N. Fibroblasts form a hospitable metastatic niche in the liver. Nat Cell Biol. 2016, 18:465-6.

Grants

2014–2017	Association for International Cancer Research (AICR)
2014 – 2017	Melanoma Research Alliance SABAN FAMILY FOUNDATION-TEAM SCIENCE AWARD
2014 – 2017	Israel Cancer Research Foundation (ICRF). Research Career Development Award
2015–2019	European Research Council (ERC) Starting Grant

Prof. Zvi Fishelson, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: lifish@post.tau.ac.il
URL: http://www2.tau.ac.il/Person/medicine/researcher.asp?id=agcdifeik

Molecular Analysis of Cancer Immunoresistance

Positions

Professor, Sackler Faculty of Medicine

President, International Complement Society

President, European Complement Network

Advisory Editor, *Molecular Immunology*

Associate Editor, *Frontiers in Molecular Innate Immunity*

Research

The long-term goal of our research is to develop a novel treatment for immune resistant cancers. Our research includes characterization of the mechanism of complement-dependent cytotoxicity and of the basis for elevated resistance of cancer cells to cell death, and design of novel reagents that sensitize cancer cells to cell death. Research methods used include analyses of cell growth and death and mitochondrial activity, western blotting, enzyme-linked immunosorbent assay (ELISA), immunoprecipitation, confocal fluorescence microscopy, Fluorescence-activated Cell Sorting (FACS), peptide analysis by mass spectrometry, electron microscopy, and analysis of cancer growth in animal models.

Publications

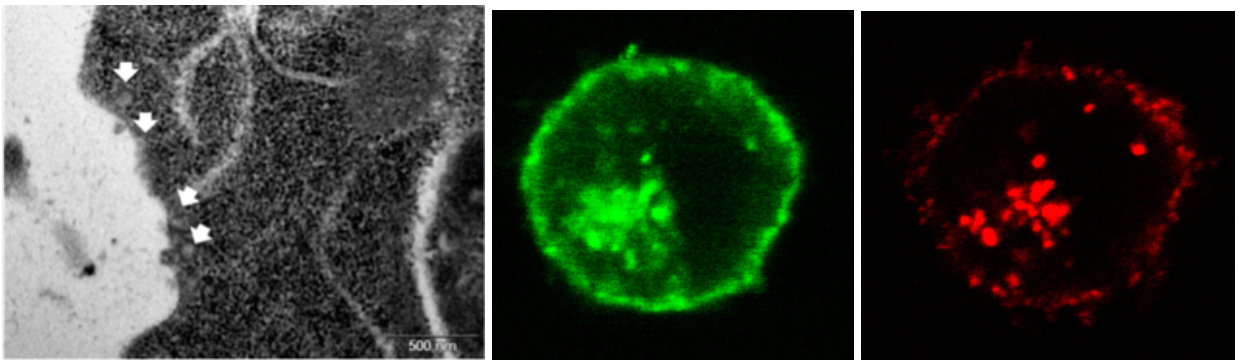
Rozenberg P, Kocsis J, Saar M, Prohászka Z, FÜst G and **Fishelson Z**. Elevated levels of mitochondrial mortalin and cytosolic HSP70 in blood as risk factors in colorectal cancer patients. *Int. J. Cancer*. 133: 514-519, 2013.

Gurevich M and **Fishelson Z**. Construction and characterization of recombinant human C9 or C7 linked to single Chain Fv directed to CD25. *Mol. Immunol*. 55: 400-408, 2013.

Saar Ray M., Moskovich O. Iosefson O. and **Fishelson Z.** Mortalin/Grp75 binds to complement c9 and plays a role in resistance to complement-dependent cytotoxicity, *J. Biol. Chem*. 2014, 289:15014-22.

Hillman Y., Mazkereth N., Farberov L., Shomron N. and **Fishelson Z.**, Regulation of complement-dependent cytotoxicity by microRNAs miR-200b, miR-200c and miR-217, *J. Immuno*l. 196: 5156-5165, 2016.

Mazkereth N., Rocca F., Schubert J.-R., Geisler C., Hillman Y., Egner A. and **Fishelson Z**., Complement triggers relocation of mortalin/GRP75 from mitochondria to the plasma membrane, *Immunobiology* 2016 221: 1395-1406.



EM analysis demonstrates elevated formation of endosomes in K562 cells responding to an ongoing immune attack (left). Caveolin-1 (green) and complement C9 (red) co-localize in early and late endocytic vesicles of K562 cancer cells following complement attack on the cells (right 2 panels).

Jubran R, Kocsis J, Garam N, Maláti É, Gombos T, Barabás L, Gráf L, Prohászka Z, Fishelson Z. Circulating mitochondrial Stress-70 protein/mortalin and cytosolic Hsp70 in blood: Risk indicators in colorectal cancer. Int J Cancer. 2017, 141:2329-2335.

Reviews

Moskovich O. and **Fishelson Z.,** Quantification of complement C5b-9 binding to cells by Flow Cytometry, in 'Methods in Molecular Biology; Complement System: Methods and Protocols' Gadjeva M. ed., Springer Science+Business Media New York, 2014, pp103-108.

Kemper C., Pangburn M. K. and **Fishelson Z.** Complement Nomenclature 2014. *Molec. Immunol.* 61: 56-58, 2014.

Grants

2015-2020 Complement-dependent cytotoxicity of cancer cells: toxic and evasion mechanisms (ISF)

2016-2018 The mitochondrion-plasma membrane interaction at super-resolution microscopy (VW Lower Saxony grant, binational with Germany (Dr. Alex Egner, Goettingen))

Prof. Tamar Geiger, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: geiger@post.tau.ac.il
http://geiger.tau.ac.il/

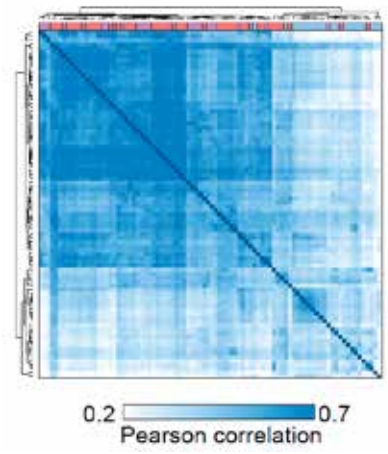
Cancer Proteomics

Position

Associate Professor, Sackler Faculty of Medicine

Research

Our main interest is to understand the mechanisms of cancer progression and drug resistance. We use state-of-the-art **mass spectrometry-based proteomics** to obtain a system-wide view of the proteomes of cancer clinical samples of tumors and body fluids. Analysis of the changes in protein levels and the modifications that occur during tumor development is aimed to discover novel regulators of transformation. Identification of cancer biomarkers in body fluids such as serum and plasma, opens new possibilities to translate these results to diagnostic tests in clinical use. Among the many identified regulators, we focus on **metabolic remodeling in cancer**. Combining proteomic and metabolomic techniques, we investigate the involvement of metabolism in cancer transformation, regulation of cell proliferation and invasion. Combination of these technologies with biochemical and genetic methods shows the significance of these candidates to cancer development and may suggest novel markers and drug targets.



Correlation matrix of proteomes of breast cancer and healthy tissue

Publications

Harel M, **Geiger T**. Plasma biomarker identification and quantification by microparticle proteomics. Methods Mol Biol. 1619:477-486 (2017).

Aviner R, Hofmann S, Elman T, Shenoy A, **Geiger T**, Elkon R, Ehrlich M, Elroy-Stein O. Proteomic analysis of polyribosomes identifies splicing factors as potential regulators of translation during mitosis. Nucleic Acids Res. 45:5945-5957 (2017).

Perl K, Ushakov K, Pozniak Y, Yizhar-Barnea O, Bhonker Y, Shivatzki S, **Geiger T**, Avraham KB, Shamir R. Reduced changes in protein compared to mRNA levels across non-proliferating tissues. BMC Genomics. 18:305 (2017).

Raini G, Sharet R, Herrero M, Atzmon A, Shenoy A, **Geiger T**, Elroy-Stein O. Mutant eIF2B leads to impaired mitochondrial oxidative phosphorylation in vanishing white matter disease. J Neurochem. 141:694-707 (2017).

Pozniak, Y., Lahat, N., Rudolph, J.D., Katzir, R., Avivi, C., Ruppin, E., Barchack, I. & **Geiger, T***. System-wide clinical proteomics of breast cancer reveals global remodeling of cellular homeostasis. Cell Systems, 2:172-84 (2016). *Corresponding author.

Tyanova, S., Albrechsten, R., Kronqvist, P., Cox, J.*, Mann, M.* & **Geiger, T.*** Quantitative clinical proteomics reveals functional maps of breast cancer subtypes. Nat Communications 7:10259 (2016). *Corresponding author

Iglesias-Gato, D., Wikstrom, P., Tyanova, S., Svensson, C., Thysell, E., Carlsson, J., Hägglöf, C., Cox, J, Andren, O., Stattin, P., Egevad, L., Widmark, A., Jartell, A., Collins, C., Bergh, A., **Geiger, T.**, Mann, M. & Flores-Morales, A. The proteome of prostate cancer. European Urology pii: S0302-2838(15)01087-8 (2015).

Furth, N., Bossel Ben-Moshe, N., Pozniak, Y., Porat, Z., **Geiger, T.**, Domany, E., Aylon, Y. & Oren, M. Downregulation of LATS kinases alters p53 to

promote cell migration. Genes Dev 29 (22): 2325-2330 (2015).

Aviner, R., Shenoy, A., Elroy-Stein, O.* & **Geiger, T.*** (2015). Uncovering hidden layers of cell cycle regulation through integrative multi-omic analysis. PLoS Genetics 11, e1005554. *Corresponding author.

Darr, J. **Geiger, T.**, Gordon, J., Isacc, S. & Eden, A. Phosphoprotemic Analysis of Snf5 Deficient Tumor Cells Reveals Activation of EGFr Signaling Which Is Dependent Upon Snf5 Expression. Cancer Genetics 207, 446 (2015).

Elbaz-Alon, Y., Eisenberg-Bord, M., Shinder, V., Stiller, S. B., Shimoni, E., Wiedemann, N., **Geiger, T.** & Schuldiner, M. Lam6 regulates the extent of contacts between organelles. Cell reports 12, 7-14 (2015).

Gat-Viks, I., **Geiger, T.**, Barbi, M., Raini, G., & Elroy-Stein, O. Proteomics-level analysis of myelin formation and regeneration in a mouse model for Vanishing White Matter disease. J Neurochemistry 134, 513-526 (2015).

Shkedy, D., Singh, N., Shemesh, K., Amir, A., **Geiger, T.**, Liefshitz, B., Harari, Y. & Kupiec, M. Regulation of Elg1 activity by phosphorylation. Cell Cycle 15 (2015).

Nathan, G., Kredo-Russo, S., **Geiger, T.**, Lenz, A., Kaspi, H., Hornstein, E., & Efrat, S. MiR-375 Promotes Redifferentiation of Adult Human β Cells Expanded In Vitro. PloS One 10, e0122108 (2015).

Shenoy, A. & **Geiger, T***. Super-SILAC: Current trends and future perspectives. Expert Reviews of Proteomics 12, 13-19 (2015). *Corresponding author.

Lossos, A., Elazar, N., Lerer, I., Schueler-Furman, O., Fellig, Y., Glick, B., Zimmerman, B.E. Azulay, H., Dotan, S., Goldberg, S., Gomori, J.M., Ponger, P., Newman, J.P., Marreed, H., Steck, A.J., Schaeren-Wiemers, N., Mor, N., Harel, M., **Geiger, T.**, Eshed-Eisenbach, Y., Meiner, V., & Peles, E. Myelin-associated glycoprotein gene mutation causes Pelizaeus-Merzbacher disease-like disorder. Brain 138, 2521-2536 (2015).

Harel, M., Oren-Giladi, P., Kaidar-Person, O., Shaked, Y., & **Geiger, T.*** Proteomics of Microparticles with SILAC Quantification (PROMIS-Quan): A Novel Proteomic Method for Plasma Biomarker Quantification. Mol Cell Proteomics 14, 1127-1136 (2015). *Corresponding author.

Salpeter, S. J., Pozniak, Y., Merquiol, E., Ben-Nun, Y., **Geiger, T.**, & Blum, G. A novel cysteine cathepsin inhibitor yields macrophage cell death and mammary tumor regression. Oncogene, Mar 23 (2015).

Sharon, Y., Raz, Y., Cohen, N., Ben-Shmuel, A., Schwartz, H., **Geiger, T.**, & Erez, N. Tumor-derived Osteopontin reprograms normal mammary fibroblasts to promote inflammation and tumor growth in breast cancer. Cancer research 75, 963-973 (2015).

Biran, A., Perelmutter, M., Gal, H., Burton, D. G., Ovadya, Y., Vadai, E., **Geiger, T.** & Krizhanovsky, V. Senescent cells communicate via intercellular protein transfer. Genes Dev 29, 791-802 (2015).

Karaköse, E., **Geiger, T.**, Flynn, K., Lorenz-Baath, K., Zent, R., Mann, M., & Fässler, R. The focal adhesion protein PINCH-1 associates with EPLIN at integrin adhesion sites. J Cell Science 128, 1023-1033 (2015).

Rivlin, N., Katz, S., Doody, M., Sheffer, M., Horesh, S., Molchadsky, A., Koifman, G., Shetzer, Y., Goldfinger, N., Rotter, V. and **Geiger, T.** Rescue of ESCs from cellular transformation by proteomic stabilization of mutant p53 and conversion into WT conformation. *Proc Natl Acad Sci USA*. 111, 7006-11 (2014).

Oren, Y.S., McClure, M.L., Rowe, S.M., Sorscher, E.J., Bester, A.C., Manor, M., Kerem, E., Rivlin, J., Mann, M., **Geiger, T.** and Kerem, B. The Unfolded Protein Response affects readthrough of Premature Termination Codons. *EMBO Molec Med*. 6, 685-701 (2014).

Pozniak, Y. and **Geiger, T**. Design and application of super-SILAC for proteome quantification. *Meth Molec Biol.* 1188, 281-91 (2014).

Aviner, R., **Geiger, T.*** and Elroy-Stein, O. Genome-wide identification and quantification of protein synthesis in cultured cells and whole tissues by puromycin-associated nascent chain proteomics (PUNCH-P). *Nat Protocols* 9, 751-760 (2014). * Single corresponding author.

Aviner, R., **Geiger, T.** and Elroy-Stein, O. PUNCH-P for global translatome profiling; Methodology, insights and comparison to other techniques. *Translation* 1, e27516 (2014).

Waldman, Y.Y., **Geiger, T.** and Ruppin, E. A genome-wide systematic analysis reveals different and predictive proliferation expression signatures of cancerous vs. non-cancerous cells. *PLoS Gen.* 9, e1003806 (2013).

Aviner, R., **Geiger, T*.** and Elroy-Stein, O*. Novel proteomic approach (PUNCH-P) reveals cell cycle-specific fluctuations in mRNA translation. *Genes and Dev* 27:1834-44 (2013). * Equal contribution corresponding authors.

Radovanac, K., Morgner, J., Schulz, J.N., Blumbach, K., Patterson, C., **Geiger, T.,** Mann, M., Krieg, T., Eckes, B., Fässler, R. and Wickström, S.A. Stabilization

of integrin-linked kinase by the Hsp90-CHIP axis impacts cellular force generation, migration and the fibrotic response. *EMBO J*. 32(10):1409-24 (2013)

Geiger, T., Velic, A., Macek, B., Lundberg, E., Kampf, C., Nagaraj, N., Uhlen, M., Cox, J. and Mann, M. Initial quantitative proteomic map of 28 mouse tissues using the SILAC mouse. *Mol Cell Proteomics* 12:1709-22 (2013)

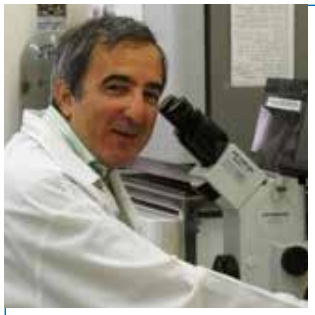
Boersema, P.J., **Geiger, T.,** Wisniewski, J.R. and Mann, M. Quantification of the N-glycosylated secretome by super-SILAC during breast cancer progression and in human blood samples. *Mol Cell Proteomics* 12:158-71 (2013)

Reviews

Shenoy, A. & **Geiger, T***. Super-SILAC: Current trends and future perspectives. Expert Reviews of Proteomics 12, 13-19 (2015). *Corresponding author.

Grants

2012-2017	Israeli Center for Research Excellence (I-CORE): Gene Regulation in Complex Human Disease
2012-2017	Israel Science Foundation (ISF) Grant: The role of metabolic pathways in the regulation of breast cancer progression.
2015-2020	European Research Council- ERC starting grant: Topoproteomic profiling of breast cancer heterogeneity
2014-2017	Israel Ministry of Science and Technology: Proteogenomic analysis of breast cancer



Prof. Shai Izraeli, M.D

Functional Genomics and Childhood Leukemia Research, Cancer Research Center, Sheba Medical Center; Department of Human Molecular Genetics & Biochemistry, Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: shai.izraeli@sheba.health.gov.il
http://eng.sheba.co.il/Research_and_Development/Research_Center_of_Leukemia/

Basic and Translational and Research of Childhood Malignancies and Leukemia

Positions

Professor, Sackler Faculty of Medicine

Chair, MD-PhD program

Dora and Gregorio Shapiro Chair of Hematological Malignancies

Research

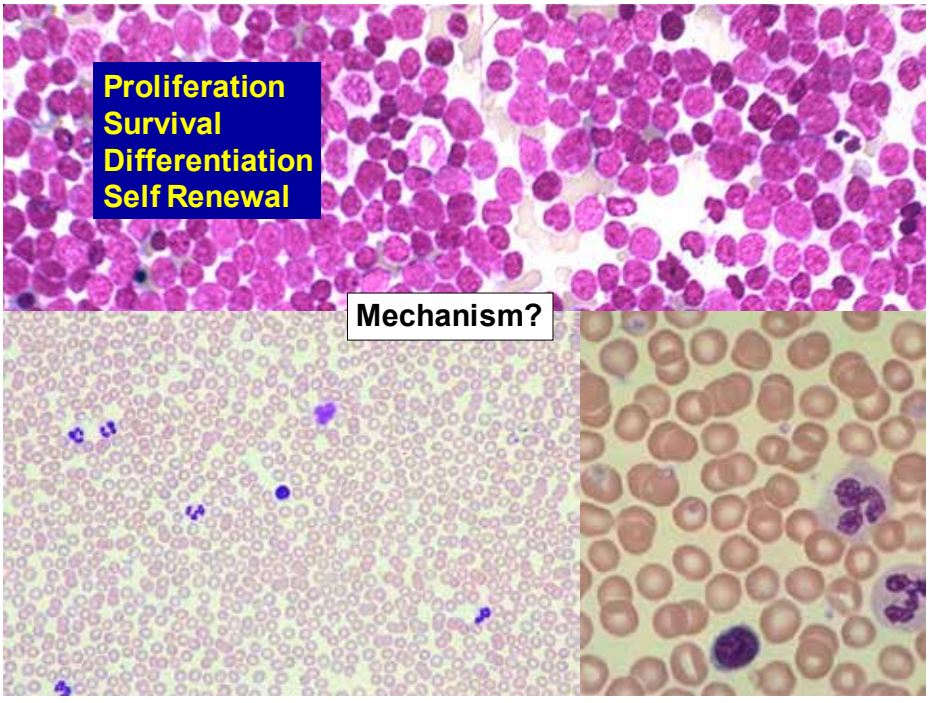
We focus on patient-driven basic research into the pathogenesis of childhood leukemia and cancer. We harness advanced molecular and cellular biology technologies utilizing in-vitro and in-vivo models with the ultimate goal of improving the care of children with cancer.

Our research is divided into two major topics:

1. Basic, translational and clinical research of leukemia.

2. The role of SIL (STIL) protein in mitosis, centrosomal biology and cancer.

Cancer is the deadliest disease of children and leukemia is the most common childhood cancer. We are interested in the fundamental question how normal blood development is diverted into leukemia. What are the genetic and biochemical abnormalities that block cell differentiation, enhance proliferation and survival and confer the unique stem cell properties of self renewal to leukemia stem cells? We focus on chromosome 21 because of the mysterious association of leukemia with Down Syndrome. We utilize advanced genomic technologies, cell based assays of transformation of primary human and mouse stem cells, mouse models including transgenic, transplantation and explants of human leukemia. Our recent discoveries of the major involvement of the TSLP-IL7R-JAK2 pathway in leukemogenesis have lead to clinical trials with novel



Carboxypeptidase E (CPE), a novel Wnt inhibitor, is excluded from the colonic crypt bottom.

inhibitors of this pathway for high-risk leukemias in children and adults. The spread of leukemia to the brain is a major clinical problem as preventive therapy to the brain consistingof chemotherapy or irradiation causes long term side effects. We are therefore studying how leukemia cells spread to the central nervous system and developing mouse models to study this challenging problem.

We have discovered that SIL, a gene cloned from childhood leukemia, is required for centrosomal biogenesis and for survival of cancer cells. Targeting SIL by siRNA cause cancer cell death at mitotic entry in-vitro and in-vivo. Current research focuses on the fundamental role of the SIL protein in centrosome generation in normal and malignant cells and on developing approaches for its targeting for cancer therapy.

Publications

Rivkin N, Chapnik E, Birger Y, Yanowski E, Curato C, Mildner A, Porat Z, Amir G, **Izraeli S**, Jung S, Hornstein E. Rac1 functions downstream of miR-142 in regulation of erythropoiesis. Haematologica, 2017. pii: haematol.2017.171736.

Meyer C, Burmeister T, Gröger D, Tsaur G, Fechina L, Renneville A, Sutton R,….., **Izraeli S**, Trakhtenbrot L, Archer P, Hancock J, Möricke A, Alten J, Schrappe M, Stanulla M, Strehl S, Attarbaschi A, Dworzak M, Haas OA, Panzer-Grümayer R, Sedék L, Szczepaßski T, Caye A, Suarez L, Cavé H, Marschalek R. The MLL recombinome of acute leukemias in 2017. Leukemia. 2017. doi: 10.1038/leu.2017.213.

Schwartzman O, Savino AM, Gombert M, Palmi C, Cario G, Schrappe M, Eckert C, von Stackelberg A, Huang JY, Hameiri-Grossman M, Avigad S, Te Kronnie G, Geron I, Birger Y, Rein A, Zarfati G, Fischer U, Mukamel Z, Stanulla M, Biondi A, Cazzaniga G, Vetere A, Wagner BK, Chen Z, Chen SJ, Tanay A, Borkhardt A, **Izraeli S**. Suppressors and activators of JAK-STAT signaling at diagnosis and relapse of acute lymphoblastic leukemia in Down syndrome. Proc Natl Acad Sci USA. 2017. 114(20):E4030-E4039.

Rabinowicz N, Mangala LS, Brown KR, Checa-Rodriguez C, Castiel A, Moskovich O, Zarfati G, Trakhtenbrot L, Levy-Barda A, Jiang D, Rodriguez-Aguayo C, Pradeep S, van Praag Y, Lopez-Berestein G, David A, Novikov I, Huertas P, Rottapel R, Sood AK, **Izraeli S**. Targeting the centriolar replication factor STIL synergizes with DNA damaging agents for treatment of ovarian cancer. Oncotarget. 2017. 8:27380-27392.

Vendramini E, Giordan M, Giarin E, Michielotto B, Fazio G, Cazzaniga G, Biondi A, Silvestri D, Valsecchi MG, Muckenthaler MU, Kulozik AE, Gattei V, **Izraeli S**, Basso G, Te Kronnie G. High expression of miR-125b-2 and SNORD116 noncoding RNA clusters characterize ERG-related B cell precursor acute lymphoblastic leukemia. Oncotarget. 2017. 8:42398-42413.

Savino AM, Sarno J, Trentin L, Vieri M, Fazio G, Bardini M, Bugarin C, Fossati G, Davis KL, Gaipa G, **Izraeli S**, Meyer LH, Nolan GP, Biondi A, Te Kronnie G, Palmi C, Cazzaniga G. The histone deacetylase inhibitor givinostat (ITF2357) exhibits potent anti-tumor activity against CRLF2-rearranged BCP-ALL. Leukemia. 2017. 31:2365-2375.

Visochek L, Castiel A, Mittelman L, Elkin M, Atias D, Golan T, **Izraeli S**, Peretz T, Cohen-Armon M. Exclusive destruction of mitotic spindles in human cancer cells. Oncotarget. 2017. 8:20813-20824.

Amar D, **Izraeli S**, Shamir R. Utilizing somatic mutation data from numerous studies for cancer research: proof of concept and applications. Oncogene. 2017. 36:3375-3383.

David, A., H. Amartely, N. Rabinowicz, M. Shamir, A. Friedler, and **S. Izraeli**. Molecular basis of the STIL coiled coil oligomerization explains its requirement for de-novo formation of centrosomes in mammalian cells. *Sci Rep*, 2016. **6**: 24296.

Townsend, E.C., M.A. Murakami, A. Christodoulou, **S. Izraeli**, …J.C. Aster, M.A. Shipp, J.D. Griffin, and D.M. Weinstock. The public repository of xenografts enables discovery and randomized phase ii-like trials in mice. *Cancer Cell*, 2016. 29: 574-86.

Williams, M.T., Y.M. Yousafzai, A. Elder, K. Rehe, S. Bomken, L. Frishman-Levy, S. Tavor, P. Sinclair, K. Dormon, D. Masic, T. Perry, V.J. Weston, P. Kearns, H. Blair, L.J. Russell, O. Heidenreich, J.A. Irving, **S. Izraeli**, J. Vormoor, G.J. Graham, and C. Halsey. The ability to cross the blood-cerebrospinal fluid barrier is a generic property of acute lymphoblastic leukemia blasts. *Blood*, 2016. 127: 1998-2006.

Amar, D., T. Hait, **S. Izraeli**, and R. Shamir. Integrated analysis of numerous heterogeneous gene expression profiles for detecting robust disease-specific biomarkers and proposing drug targets. *Nucleic Acids Res*, 2015. 43: 7779-89.

Bugarin, C., J. Sarno, C. Palmi, A.M. Savino, G. te Kronnie, M. Dworzak, A. Shumich, B. Buldini, O. Maglia, S. Sala, I. Bronzini, J.P. Bourquin, E. Mejstrikova, O. Hrusak, D. Luria, G. Basso, **S. Izraeli,** A. Biondi, G. Cazzaniga, G. Gaipa, and I.B.s.

group. Fine tuning of surface CRLF2 expression and its associated signaling profile in childhood B-cell precursor acute lymphoblastic leukemia. *Haematologica*, 2015. 100: e229-32.

Frishman-Levy, L., A. Shemesh, A. Bar-Sinai, C. Ma, Z. Ni, S. Frenkel, V. Muench, H. Bruckmueller, C. Vokuhl, K.M. Debatin, C. Eckert, M. Stanulla, M. Schrappe, K.S. Campbell, R. Loewenthal, D.M. Schewe, J. Hochman, L.H. Meyer, D. Kaufman, G. Cario, A. Porgador, and **S. Izraeli.** Central nervous system acute lymphoblastic leukemia: role of natural killer cells. *Blood*, 2015. 125: 3420-31.

Lellouche, E., L.L. Israel, M. Bechor, S. Attal, E. Kurlander, V.A. Asher, A. Dolitzky, L. Shaham, **S. Izraeli**, J.P. Lellouche, and S. Michaeli. MagRET nanoparticles: An iron oxide nanocomposite platform for gene silencing from micrornas to long noncoding RNAs. *Bioconjug Chem*, 2015. 26: 1692-701.

Mansour, M.R., C. Reed, A.R. Eisenberg, J.C. Tseng, J.C. Twizere, S. Daakour, A. Yoda, S.J. Rodig, N. Tal, C. Shochat, A. Berezovskaya, D.J. DeAngelo, S.E. Sallan, D.M. Weinstock, S. **Izraeli**, A.L. Kung, A. Kentsis, and A.T. Look. Targeting oncogenic interleukin-7 receptor signalling with N-acetylcysteine in T cell acute lymphoblastic leukaemia. *Br J Haematol*, 2015. 168: 230-8.

Shaham, L., E. Vendramini, Y. Ge, Y. Goren, Y. Birger, M.R. Tijssen, M. McNulty, I. Geron, O. Schwartzman, L. Goldberg, S.T. Chou, H. Pitman, M.J. Weiss, S. Michaeli, B. Sredni, B. Gottgens, J.D. Crispino, J.W. Taub, and **S. Izraeli**. MicroRNA-486-5p is an erythroid oncomiR of the myeloid leukemias of Down syndrome. *Blood*, 2015. 125: 1292-301.

Tursky, M.L., D. Beck, J.A. Thoms, Y. Huang, A. Kumari, A. Unnikrishnan, K. Knezevic, K. Evans, L.A. Richards, E. Lee, J. Morris, L. Goldberg, **S. Izraeli**, J.W. Wong, J. Olivier, R.B. Lock, K.L. MacKenzie, and J.E. Pimanda. Overexpression of ERG in cord blood progenitors promotes expansion and recapitulates molecular signatures of high ERG leukemias. *Leukemia*, 2015. 29: 819-27.

Tal, N., C. Shochat, I. Geron, D. Bercovich, and **S. Izraeli**. Interleukin 7 and thymic stromal lymphopoietin: from immunity to leukemia. *Cell Mol Life Sci*, 2014. 71:365-78.

Stary, J., M. Zimmermann, M. Campbell, L. Castillo, E. Dibar, S. Donska, A. Gonzalez, **S. Izraeli**, D. Janic, J. Jazbec, J. Konja, E. Kaiserova, J. Kowalczyk, G. Kovacs, C.K. Li, E. Magyarosy, A. Popa, B. Stark, Y. Jabali, J. Trka, O. Hrusak, H. Riehm, G. Masera, and M. Schrappe. Intensive chemotherapy for childhood acute lymphoblastic leukemia: results of the randomized intercontinental trial ALL IC-BFM 2002. *J Clin Oncol*, 2014. 32:174-84.

Meissner, B., T. Bartram, C. Eckert, J. Trka, R. Panzer-Grumayer, I. Hermanova, E. Ellinghaus, A. Franke, A. Moricke, A. Schrauder, A. Teigler-Schlegel, P. Dorge, A. von Stackelberg, G. Basso, C.R. Bartram, R. Kirschner-Schwabe, B. Bornhauser, J.P. Bourquin, G. Cazzaniga, J. Hauer, A. Attarbaschi, **S. Izraeli**, M. Zaliova, G. Cario, M. Zimmermann, S. Avigad, M. Sokalska-Duhme, M. Metzler, M. Schrappe, R. Koehler, G. Te Kronnie, and M. Stanulla, Frequent and sex-biased deletion of SLX4IP by illegitimate V(D)J-mediated recombination in childhood acute lymphoblastic leukemia. *Hum Mol Genet*, 2014. 23:590-601.

Izraeli, **S.,** A. Vora, C.M. Zwaan, and J. Whitlock. How I treat ALL in Down's syndrome: pathobiology and management. *Blood*, 2014. 123:35-40.

Izraeli, **S**., C. Shochat, N. Tal, and I. Geron. Towards precision medicine in childhood leukemia – Insights from mutationally activated cytokine receptor pathways in acute lymphoblastic leukemia. *Cancer Lett*, 2014. 352:15-20.

Buitenkamp, T.D., **S. Izraeli***, M. Zimmermann, E. Forestier, N.A. Heerema, M.M. van den Heuvel-Eibrink, R. Pieters, C.M. Korbijn, L.B. Silverman, K. Schmiegelow, D.C. Liang, K. Horibe, M. Arico, A. Biondi, G. Basso, K.R. Rabin, M. Schrappe, G. Cario, G. Mann, M. Morak, R. Panzer-Grumayer, V. Mondelaers, T. Lammens, H. Cave, B. Stark, I. Ganmore, A.V. Moorman, A. Vora, S.P. Hunger, C.H. Pui, C.G. Mullighan, A. Manabe, G. Escherich, J.R. Kowalczyk, J.A. Whitlock, and C.M. Zwaan*. Acute lymphoblastic leukemia in children with Down syndrome: a retrospective analysis from the Ponte di Legno study group. *Blood*, 2014. 123:70-7.

Amartely, H., A. David, M. Lebendiker, H. Benyamini, **S. Izraeli**, and A. Friedler. The STIL protein contains intrinsically disordered regions that mediate its protein-protein interactions. *Chem Commun (Camb)*, 2014. 50:5245-7.

Yoshida, K., T. Toki, Y. Okuno, R. Kanezaki, Y. Shiraishi, A. Sato-Otsubo, M. Sanada, M.J. Park, K. Terui, H. Suzuki, A. Kon, Y. Nagata, Y. Sato, R. Wang, N. Shiba, K. Chiba, H. Tanaka, A. Hama, H. Muramatsu, D. Hasegawa, K. Nakamura, H. Kanegane, K. Tsukamoto, S. Adachi, K. Kawakami, K. Kato, R. Nishimura, **S. Izraeli**, Y. Hayashi, S. Miyano, S. Kojima, E. Ito, and S. Ogawa. The landscape of somatic mutations in Down syndrome-related myeloid disorders. *Nat Genet*, 2013. 45:1293-9.

Meyer, C., et al. **Izraeli, S**. et al and R. Marschalek. The MLL recombinome of acute leukemias in 2013. *Leukemia*, 2013. 27:2165-76.

Goldberg, L., M.R. Tijssen, Y. Birger, R.L. Hannah, S.J. Kinston, J. Schutte, D. Beck, K. Knezevic, G. Schiby, J. Jacob-Hirsch, A. Biran, Y. Kloog, G. Marcucci, C.D. Bloomfield, P.D. Aplan, J.E. Pimanda, B. Gottgens, and **S. Izraeli**, Genome-scale expression and transcription factor binding profiles reveal therapeutic targets in transgenic ERG myeloid leukemia. *Blood*, 2013. 122:2694-703.

Castiel, A., L. Visochek, L. Mittelman, Y. Zilberstein, F. Dantzer, **S. Izraeli**, and M. Cohen-Armon. Cell death associated with abnormal mitosis observed by confocal imaging in live cancer cells. *J Vis Exp*, 2013. 78:e50568.

Birger, Y., L. Goldberg, T.M. Chlon, B. Goldenson, I. Muler, G. Schiby, J. Jacob-Hirsch, G. Rechavi, J.D. Crispino, and **S. Izraeli**. Perturbation of fetal hematopoiesis in a mouse model of Down syndrome's transient myeloproliferative disorder. *Blood*, 2013. 122:988-98.

Auer, F., F. Ruschendorf, M. Gombert, P. Husemann, S. Ginzel, **S. Izraeli**, M. Harit, M. Weintraub, O.Y. Weinstein, I. Lerer, P. Stepensky, A. Borkhardt, and J. Hauer. Inherited susceptibility to pre B-ALL caused by germline transmission of PAX5 c.547G>A. *Leukemia*, 2013. 28:1136-8.

Birger, Y., L. Goldberg, T.M. Chlon, B. Goldenson, I. Muler, G. Schiby, J. Jacob-Hirsch, G. Rechavi, J.D. Crispino, and **S. Izraeli**. Perturbation of fetal hematopoiesis in a mouse model of Down syndrome's transient myeloproliferative disorder. *Blood*, 2013. 122:988-98.

Reviews

Izraeli S, Eckert C. Targeted therapy of CNS leukemia? Blood. 2017. 130:562-563.

Kratz CP, **Izraeli S**. Down syndrome, RASopathies, and other rare syndromes. Semin Hematol. 2017. 54:123-128.

Savino AM, **Izraeli S**. Interleukin-7 signaling as a therapeutic target in acute lymphoblastic leukemia. Expert Rev Hematol. 2017. 10:183-185.

Izraeli, S., The acute lymphoblastic leukemia of Down Syndrome - Genetics and pathogenesis. *Eur J Med Genet*, 2016. 59:158-61.

Savino, A.M. and **S. Izraeli**, On mice and humans: the role of thymic stromal lymphopoietin in human B-cell development and leukemia. *Haematologica*, 2016. 101: 391-3.

Pui, C.H., J.J. Yang, S.P. Hunger, R. Pieters, M. Schrappe, A. Biondi, A. Vora, A. Baruchel, L.B. Silverman, K. Schmiegelow, G. Escherich, K. Horibe, Y.C. Benoit, **S. Izraeli**, A.E. Yeoh, D.C. Liang, J.R. Downing, W.E. Evans, M.V. Relling, and C.G. Mullighan. Childhood Acute Lymphoblastic Leukemia: Progress through collaboration. *J Clin Oncol*, 2015. 33: 2938-48.

Tal, N., C. Shochat, I. Geron, D. Bercovich, and **S. Izraeli**. Interleukin 7 and thymic stromal lymphopoietin: from immunity to leukemia. *Cell Mol Life Sci*, 2014. 71:365-78.

Grants

2014-2017	EU ERA-NET TRANSCANCER "TRANSALL" Validation of biomarkers for the diagnosis and risk stratification of childhood ALL
2014-2018	BSF Functional analysis of ERG GATA1
2014-2018	ISF Modelling T-lympho-myeloid leukemia
2014-2017	ISF-NSFC Hematopoietic transcription factors in leukemia – mouse models and human leukemias
2014-2017	The Israel Science Foundation (ISF) and the National Natural Science Foundation of China (NSFC), PIs Izraeli, Shai (Israel) Chen, Sai-Juan (China)
2014-2017	Israel Ministry of Health ERA-NET EU programs, PIs Izraeli, Shai (Israel), multiple Europeans PIs
2014-2018	Israel Science Foundation
2014-2018	USA-Israel Bi-National Scientific Foundation, PIs Izraeli, Shai (Israel); Crispino, John (USA)
2015-2018	DOD USAMRMC
2016-2018	Children With Cancer UK, PI Enver, Tariq (UCL), co-PI Izraeli, Shai
2016-2019	German Israel Foundation

Prof. Yona Keisari, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

URL: http://med.tau.ac.il/Professor_Yona_Keisari

Development of Cancer Treatments Integrating Radiotherapy or Electrochemical Ablation and Immunotherapy

Positions

Professor Emeritus, Sackler Faculty of Medicine

Roberts-Guthman Chair in Immunopharmacology

President, Israeli Society for Cancer Research

Associate Editor, *Mediators of Inflammation*

Research

Cancer is currently the most devastating chronic disease affecting humankind. Today solid malignant tumors are mainly treated by surgery and/or radiotherapy to eradicate the local primary lesion, and chemotherapy, that is administered mainly to destroy remaining local or distant malignant cells. In spite of the advancement in preventing and treating cancer, morbidity and mortality remain high, especially in cases when tumors are highly metastatic, or cannot be completely removed. The main goal of our research projects is to develop *in situ* tumor ablation treatments of primary tumors and incorporate them with systemic chemotherapy and immuno-stimulatory agents, into combined treatment protocols.

In order to achieve efficient primary tumor ablation we developed two novel and powerful treatment modalities for solid cancer, which can be used instead or in combination with surgery. The first treatment, developed with Prof. Rafi Korenstein (Dept. Physiology & Pharmacology), is base on the use of intratumoral unipolar pulsed electric currents for the ablation (ECTA) of solid primary tumors. ECTA can be enforced by the concomitant use of chemotherapeutic agents in the treatment of tumors. The second cancer treatment, developed with Prof. Itzhak Kelson (School of Physics & Astronomy), is based on insertion into the tumor of radioactive wires that spread in the tumor alpha emitting atoms and can also be augmented by chemotherapy.

Our teams proved that these treatment modalities effectively destroy primary tumors, and reduce the metastatic load in experimental animal and human cancer models of melanoma, breast, colon, prostate, pancreas, lung, and squamous cell carcinomas. We found that *in situ* ablation of primary antigenic tumors led to the activation of immunological reactions, destroying remaining malignant cells in the primary tumor as well as in distant metastases.

Immunopharmacological methods aimed to stimulate the patient's immune response against the cancer after local tumor ablation can make use of several approaches and we currently study the following: (1) Immunostimulation by adjuvants such as the oligonucleotides, CpG, which enforce weak immune reactions. (2) Inhibition of immunosuppressive mechanisms such as T-regulatory and Myeloid Derived Suppressor cells (MDSC). (3) Combination with inhibitors of immunological checkpoints such as anti CTLA-4 or anti PDL1/PD1.

Publications

Milrot, E., Jackman, A., Flescher, E., Gonen, P., Kelson, I., **Keisari, Y.**, Sherman, L. Enhanced killing of cervical cancer cells by combinations of methyl jasmonate with cisplatin, X or alpha radiation. Invest. *New Drugs*. 31:333-44, 2013.

Tepper, M., Shoval, A., Hoffer, O., Confino, H., Kelson, I., **Keisari, Y.**, Gannot, I. Thermographic investigation of tumor size, and its correlation to tumor relative temperature, in mice with transplantable solid breast carcinoma. *J Biomed Optics*. 18:111410, 2013.

Keisari, Y., Hochman, I., Confino, H., Korenstein, R., Kelson, I. Activation of local and systemic anti-tumor immune responses by ablation of solid tumors with intra-tumoral electrochemical or alpha radiation

treatments. *Cancer Immunol Immunother*. 63:1-9, 2014.

Reitkopf-Brodutch, S., Confino, H., Schmidt, M., Cooks, T., Efrati, M., Arazi, L., Rath-Wolfson, L., Marshak, G., Kelson, I., **Keisari Y**. Ablation of experimental colon cancer by intratumoral ^{224}Radium Loaded wires is mediated by alpha particles released from atoms which spread in the tumor and can be augmented by chemotherapy. *Int J Radiation Biol*. 2014 2:1-15.

Confino, H., Hochman, I., Efrati, M., Schmidt, M., Umansky, V., Kelson, I., **Keisari, Y**. Tumor ablation by intratumoral Ra-224 loaded wires induces anti-tumor immunity against experimental metastatic tumors. *Cancer Immunol Immunother*. 2014 64:191-199.

Confino H, Schmidt M, Efrati M, Hochman I, Umansky V, Kelson I, **Keisari Y**. Inhibition of mouse breast adenocarcinoma growth by ablation with intratumoral alpha-irradiation combined with inhibitors of immunosuppression and CpG. First online: 06 August 2016.

Shoval A, Tepper M, Tikochkiy J, Ben Gur L, Markovich G, **Keisari Y**, Gannot I. Magnetic Nanoparticles Based Acoustical Detection and Hyperthermic Treatment of Cancer, in vitro and in vivo Studies. *J. Nanophotonics.* 10:036007, 2016.

Maman S, Sagi-Assif O, Yuan W, Ginat R, Meshel T, Zubrilov I, **Keisari Y**, Lu W, Lu W, Witz IP. The beta subunit of hemoglobin (HBB2/HBB) suppresses neuroblastoma growth and metastasis. *Cancer Res.* 77:14-26, 2017.

Chapters and Reviews

Keisari Y., Korenstein R. In-situ ablation of solid tumors by electric forces and its effect on the tumor microenvironment and anti-tumor immunity. In: Tumor Ablation: effects on systemic and local anti-tumor immunity and on other tumor-microenvironment interactions. Y. Keisari, Ed. Springer, 2013, Ch. 8, pp. 133-153.

Keisari Y. Tumor abolition and antitumor immunostimulation by physico-chemical tumor ablation. *Frontiers Biosc. Landmark*, 22: 310-347, 2017.

Books

Keisari Y. Tumor Ablation: effects on systemic and local anti-tumor immunity and on other tumor-microenvironment interactions. Springer, 2013.

Grants

2016-2018 Ramot- Alpha Tau Medical Research Contract

Prof. Rafi Korenstein, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: korens@post.tau.ac.il

Interaction of Nanomaterials and Electromagnetic Fields with Cells

Positions

Professor Emeritus, Sackler Faculty of Medicine

Chair, Commission K of the Israel National Committee for Radio Science of Israel Academy of Sciences and Humanities on Electromagnetics in Biology and Medicine

Editorial Board, *Bioelectromagnetics*

Research

The research activity addresses the following lines of research:

Adsorption and uptake of nanoparticles by cells in relation to drug delivery and toxicity; Enhancement of uptake by electrical and chemical means. Treatment of cancer by electrochemical based approach; assessment of genetic and epigenetic risks following in-vitro exposure to electromagnetic fields associated with cell phone communication. Physiological regulation and underlying mechanism of cell membrane-cortical skeleton nanoscale mechanical fluctuations. Research methods used include routine cell biology and biochemical methodologies with emphasis on special cutting edge light microscopies possessing nanometric resolution such as Digital Holographic Microscopy (see below).

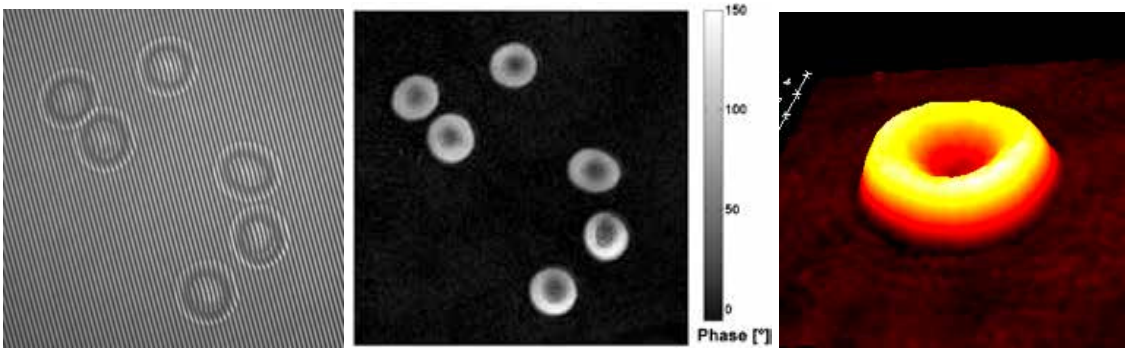
Publications

Bañares M.A., Haase A., Tran L., Lobaskin V., Oberdörster G., Rallo R., Leszczynski J., Hoet P., **Korenstein R.**, Hardy B., and Puzyn T. (2017) CompNanoTox2015: novel perspectives from a European conference on computational nanotoxicology on predictive nanotoxicology. *Nanotoxicology*, DOI: 10.1080/17435390.2017.1371351.

Maguire C.M., Sillence K., Roesslein M., (….) **Korenstein R.,** Reidiker M., Wick P., Hole P., Prina-Mello A. (2017) Benchmark of nanoparticle tracking analysis on measuring nanoparticle sizing and concentration. *Journal of Micro- and Nano-Manufacturing* 5 / 041002-1.

Oziel M., **Korenstein R**., and Rubinsky B. (2017) Radar based technology for non-contact monitoring of accumulation of blood in the head: A numerical study. *PLoS ONE* 12(10): e0186381.

Habaza, M., Kirschbaum, M., Guernth-Marschner, C., Dardikman, G., Barnea, I., **Korenstein, R.,** Duschl,



Hologram image of red blood cells (left), reconstructed phase image (middle) and 3D reconstruction of a single red blood cell (right)

C., Shaked, N.T. (2016) Rapid 3D refractive-index imaging of live cells in suspension without labeling using dielectrophoretic cell rotation. *Advanced Science* 4(2),1600205.

Ophir N., Bar Shai A., Alkalay Y., Israeli S., **Korenstein R.**, Kramer M.R., Fireman E. (2016) Artificial stone dust-induced functional and inflammatory abnormalities in exposed workers monitored quantitatively by biometrics. *European Respiratory Journal Open Research,* 2(1), 00086-2015

Toropova, A.P., Toropov, A.A., Benfenati, E., **Korenstein, R.**, Leszczynska, D., Leszczynski, J. (2015) Optimal nano-descriptors as translators of eclectic data into prediction of the cell membrane damage by means of nano metal-oxides. *Environ Sci Pollut Res Int* 22, 745-757.

Turko, N.A., Barnea, I., Blum, O., **Korenstein, R.,** Shaked, N.T. (2015) Detection and controlled depletion of cancer cells using photothermal phase microscopy. *J Biophotonics* 8, 755-763.

Ben-Dov, N. and **Korenstein R.** (2015) The uptake of HIV Tat peptide proceeds via two pathways which differ from macropinocytosis. *Biochim Biophys Acta* 1848, 869-877.

Toropova, A.A., Toropov, A.A., Benfenati, E., **Korenstein R.** (2014) QSAR model for cytotoxicity of SiO2 nanoparticles on human lung fibroblasts. *J Nanoparticle Res* 16 (2) 2282

Keisari, Y., Hochman, I., Confino, H., **Korenstein, R**., Kelson, I. (2014) Activation of local and systemic anti-tumor immune responses by ablation of solid tumors with intratumoral electrochemical or alpha radiation treatments. *Cancer Immunol Immunother* 63,1-9

Madi L., Rosenberg-Haggen, B., Nyska, A., and **Korenstein, R**. (2013) Enhancing pigmentation via activation of A3 adenosine receptors in B16 melanoma cells and in human skin explants. *Exp Dermatol* 22, 74-77.

Hole P., Sillence K., Hannell C., Maguire CM Roesslein M, Suarez G, Capracotta S, Magdolenova Z, Horev-Azaria L, Dybowska A, Cooke L, Haase A, Contal S, Manø S, Vennemann A, Sauvain J-J, Staunton KC, Anguissola S, Luch A, Dusinska M, **Korenstein R**, Gutleb AC, Wiemann M, Prina-Mello A, Riediker M, Wick P., (2013) Interlaboratory comparison of size measurements on nanopartcles using Nanoparticle Tracking Analysis (NTA). *J Nanopart Res* 15, 2101.

Wolf-Goldberg T., Barbul, A., Ben-Dov N**., Korenstein R**. (2013) Low electric fields induce ligand-independent activation of EGF receptor and ERK via electrochemical elevation of H^+ and ROS concentrations. *Biochim Biophys Acta* 1833, 1396–1408

Ben-Dov N. and **Korenstein R**. (2013) Proton-induced endocytosis is dependent on cell membrane fluidity, lipid-phase order and the membrane resting potential. *Biochim Biophys Acta* 1828, 2672-2681

Ben-Dov N., and **Korenstein R**. (2013) Actin-cytoskeleton rearrangement modulates proton-induced uptake. *Exp Cell Res*. 319, 946-954.

Horev-Azaria L., Baldi G., Beno D., Bonacchi D, Golla-Schindler U, Kirkpatrick JC, Kolle S, Landsiedel R, Maimon O, Marche PN, Ponti J, Romano R, Rossi F, Sommer D, Uboldi C, Unger RE, Villiers C, **Korenstein R.** (2013) Predictive Toxicology of cobalt ferrite nanoparticles: comparative in-vitro study of different cellular models using methods of knowledge discovery from data*. Part Fibre Toxicol* 10:32.

Goñi-de-Cerio F., Mariani V., Cohen D., **Korenstein R.** et al., (2013) Biocompatibility study of two di-block co-polymeric NPs for biomedical applications by *in vitro* toxicity testing. *J Nanopart Res* 15:2036

Chapter

Keisari Y. and **Korenstein R**. (2013) *In-situ* ablation of solid tumors by electric forces and its effect on the tumor microenvironment and anti-tumor immunity. In: Tumor Ablation: effects on systemic and local anti-tumor immunity and on other tumor-microenvironment interactions. Y. Keisari, Ed. Springer, Dordrecht, 2013, Ch. 8, pp. 133-153.

Grants

2015-2018	European Commission – Horizon 2020 ERA-NET funded consortium on "Establishing nanomaterial grouping/ classification strategies according to toxicity and biological effects for supporting risk assessment" (achronym "NanoToxClass").
2016-2019	European Commission – Horizon 2020 EC funded consortium on "High level Integrated Sensor for Nanotoxicity Screening (achronym "HISENTS").

Prof. Rina Rosin-Arbesfeld, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: arina@post.tau.ac.il

The Wnt Signaling Pathway and Colorectal Cancer

Position

Associate Professor, Sackler Faculty of Medicine

Chair, Search Committee

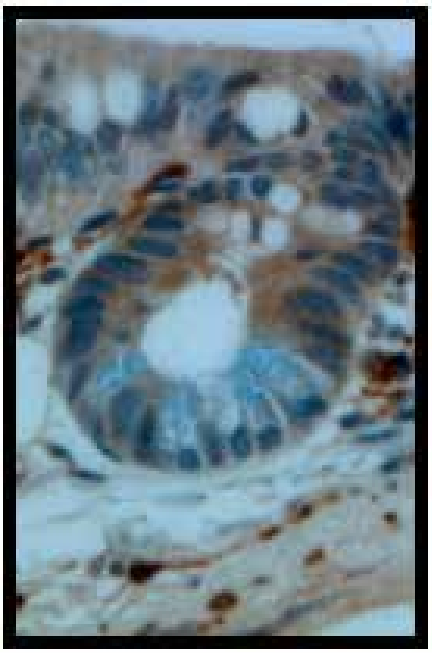
Research

The Wnt signaling pathway is involved in virtually every aspect of human development, as well as in adult homeostasis. Hyperactivation of this pathway has been linked to a wide range of cancers and especially colorectal cancer. Our aim is to understand the molecular events underlying Wnt signal transduction, as well as develop novel therapeutic strategies to fight colorectal cancer.

Current projects in the lab include:

1. Identifying and characterizing new Wnt signaling components.

2. Developing new anti-colorectal cancer treatment strategies.



Carboxypeptidase E (CPE), a novel Wnt inhibitor, is excluded from the colonic crypt bottom.

Publications

Shalev M, Kandasamy J, Skalka N, Belakhov V, **Rosin-Arbesfeld R**, Baasov T. Development of generic immunoassay for the detection of a series of aminoglycosides with 6'-OH group for the treatment of genetic diseases in biological samples. *J Pharm Biomed Anal*. 75:33-40, 2013

Skalka N, Caspi M, Caspi E, Loh YP, **Rosin-Arbesfeld R**. Carboxypeptidase E: a negative regulator of the canonical Wnt signaling pathway. *Oncogene*. 32:2836-47, 2013

Dovrat S, Caspi M, Zilberberg A, Lahav L, Firsow A, Gur H, **Rosin-Arbesfeld R**. 14-3-3 and β-catenin are secreted on extracellular vesicles to activate the oncogenic Wnt pathway. *Mol Oncol*. pii: S1574-7891(14)00059-3, 2014.

Naumov I, Zilberberg A, Shapira1 S, Avivi1 D, Kazanov1 D, **Rosin-Arbesfeld R**, Arber N, Kraus S. CD24 knockout prevents colorectal cancer in chemically induced colon carcinogenesis and in APC_{Min} /CD24 double knockout transgenic mice. *Int J Cancer*. 2014 Feb 5. doi: 10.1002/ijc.28762.

Raviv S, Bharti K, Rencus-Lazar S, Cohen-Tayar Y, Schyr R, Evantal N, Meshorer E, Zilberberg A, Idelson M, Reubinoff B, Grebe R, **Rosin-Arbesfeld R**, Lauderdale J, Lutty G, Arnheiter H, Ashery-Padan R. (2014) PAX6 regulates melanogenesis in the retinal pigmented epithelium through feed-forward regulatory interactions with MITF. *PLoS Genet*. 10(5):e1004360.

Domke LM, Rickelt S, Dörflinger Y, Kuhn C, Winter-Simanowski S, Zimbelmann R, **Rosin-Arbesfeld R,** Heid H, Franke WW. (2014) The cell-cell junctions of mammalian testes: I. The adhering junctions of the seminiferous epithelium represent special differentiation structures. *Cell Tissue Res*. 8(5):894-911.

Caspi M, Peri G, Skalka N, Meysel S, Firsow A Amit M, **Rosin-Arbesfeld R.** (2014) Aldolase positively

regulates of the canonical Wnt signaling pathway. *Molecr Cancer*. 13(1):164.

Oz S, Kapitansky O, Ivashco-Pachima Y, Malishkevich A, Giladi E, Skalka N, **Rosin-Arbesfeld R**, Mittelman L, Segev O, Hirsch JA, Gozes I. (2014) The NAP-motif of activity-dependent neuroprotective protein (ADNP) regulates dendritic spines through microtubule end binding proteins. *Mol Psyc*h 19(10):1115-24.

Sominsky S, Kuslansky Y, Shapiro B, Jackman A, Haupt Y, **Rosin-Arbesfeld R**, Sherman L. (2014) HPV16 E6 and E6AP differentially cooperate to stimulate or augment Wnt signaling. *Virology*, 468-470:510-23. 28.

Franke WW, Zimbelmann R, Dörflinger , Kuhn C, Frey N, Heid H, **Rosin-Arbesfeld R.** (2015) Striatin family proteins, near-ubiquitous in mammalian cells, as constitutive components of the cytoplasmic plaques of the zonulae adhaerentes of simple epithelia, specific domains in the tessellate junctions of stratified epithelia and the myocardiac composite junctions. *Cell Tissue Res* 359(3):779-97.

Selvaraja P, Huanga JSW, Chena A, Skalka N, **Rosin-Arbesfeld R**, Loh YP. (2015) Neurotrophic factor-α1 modulates NGF-induced neurite outgrowth through interaction with Wnt-3a and Wnt-5a in PC12 cells and cortical neurons. *Mol. Cell. Neuro.* 68:222-233.

Caspi M, Firsow A, Rajkumar R, Skalka N, Moshkovitz I, Munitz A, Pasmanik-Chor M, Greif H, Megido D, Kariv R, Rosenberg DW, **Rosin-Arbesfeld R**. (2016). A flow cytometry-based reporter assay identifies macrolide antibiotics as nonsense mutation read-through agents. *J Mol Med (Berl)*. 94:469-482.

Feldman M, Hershkovitz, Sklan EH, Kahila Bar-Gal G, Pap I, Szikossy I, **Rosin-Arbesfeld R.** (2016). Detection of a tumor suppressor gene variant predisposing to colorectal cancer in an 18th century Hungarian mummy. *PLoS One*. 11:e0147217.

Skalka N, Caspi M, Lahav-Ariel L, Loh YP, Hirschberg K and **Rosin-Arbesfeld R.** (2016) Carboxypeptidase E (CPE) inhibits the secretion and activity of Wnt3a. Oncogene. Jul 4. doi: 10.1038/onc.2016.173.

Yedid N, Kalma Y, Malcov M, Amit A, Kariv R; Caspi M **Rosin-Arbesfeld R***, Ben-Yosef D (2016) The effect of a germline mutation in the APC gene on ß-catenin in human embryonic stem cells. BMC Cancer. *Equally corresponding authors.

Palevski D, Levin-Kotler LP, Kain D, Naftali-Shani N, Landa N, Ben-Mordechai T, Konfino T, Holbova R, Molotski N, **Rosin-Arbesfeld R**, Lang RA, Leor J. (2017) Loss of macrophage Wnt secretion improves remodeling and function after myocardial infarction in mice. *J Am Heart Assoc*. 6(1).

Grants

2014-2017	ISF
2015-2017	Rising Tide Foundation
2015-2018	Gateway for Cancer Research
2016-2018	Kamin
2016-2018	Sponsored research – Cempra

Prof. Ronit Satchi-Fainaro, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: ronitsf@post.tau.ac.il
URL: http://medicine.mytau.org/satchi-fainaro/

Angiogenic Switch Using Rationally-Designed Theranostic Nanomedicines

Positions

Chair, Department of Physiology and Pharmacology

Professor, Sackler Faculty of Medicine

President, Israeli Chapter of the Controlled Release Society (ICRS)

Chair, Tel Aviv University Institutional Animal Care and Use Committee (IAUCUC)

Faculty Coordinator, Postgraduate Program in Nanotechnology

Associate Editor, *Advanced Drug Delivery Reviews*

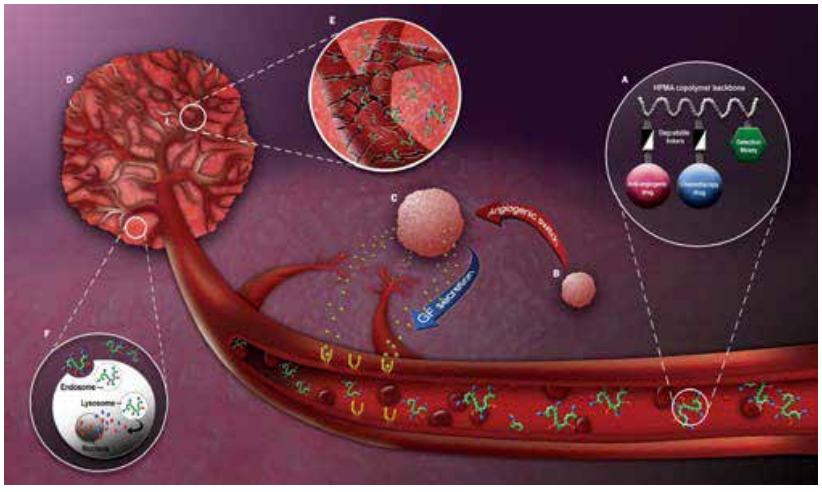
Associate Editor, *Nanomedicine: Nanotechnology, Biology and Medicine*

Co-Editor-in-Chief, *Clinical Cancer Drugs*

Research

Our research interests include investigations relating to tumor biology, tumor dormancy, mechanism of action of angiogenesis inhibitors, self-assembly of polymeric architectures and novel approaches to target cancer. Throughout, we have maintained an interest in understanding the biological rationale for the design of polymer therapeutics suitable for transfer into clinical testing. Our primary interests are the molecular basis of tumor angiogenesis and the rational design of polymer therapeutics. Our research includes identification and characterization of genes and microRNAs associated with the switch from a dormant avascular tumor phenotype to a fast-growing angiogenic tumor in human cancers and their corresponding mouse models.

We focus on the design and characterization of novel drug delivery platforms, including dendrimers and hyperbranched polymer–based nanoparticles, and the design of highly-selective targeting molecules integrating biology, chemistry, protein engineering, computational approaches, material sciences and nanotechnology to selectively guide drugs into pathological sites. Our vision is that novel approaches to target anticancer, anti-angiogenic drugs, miRNA and siRNAs to endothelial and tumor cells to potentially treat angiogenesis-dependent diseases could transform cancer into a chronically-manageable disease. Research methods used include sequencing, gene cloning, quantitative RT-PCR, immunofluorescence, cell culture, scanning electron microscopy, mass spectrometry, MALS, AFM, NMR, HPLC, in situ hybridization, bioinformatics, polymer chemistry, molecular imaging, angiogenesis



The angiogenic switch and the use of nanomedicines such as Polymer Therapeutics to treat angiogenic tumors. The enhanced permeability and retention (EPR) effect allows nanoconjugates to extravasate through the tumor leaky vessels, accumulate in the tumor bed selectively and internalize into the tumor epithelial and tumor endothelial cells via endocytosis.

assays, animal models of cancer (human xenografts in mice, syngeneic and transgenic mice models), pharmacokinetics and pharmacodynamics and 3D printing.

Publications

Miller K, Clementi C, Polyak D, Eldar-Boock A, Benayoun L, Barshack I, Shaked Y, Pasut G and **Satchi-Fainaro R**, Anti-angiogenic activity of polyethyleneglycol-based paclitaxel and alendronate for the treatment of breast cancer bone metastases, *Biomaterials*, 34: 3795–3806 (2013).

Chuderland D, Ben-Ami I, Kaplan-Kraicer R, Grossman H, Komsky A, **Satchi-Fainaro R**, Eldar-Boock A, Ron-El R, Shalgi R, Hormonal regulation of pigment epithelium derived factor (PEDF) in granulosa cells, *Molecular Human Reproduction*, 19, 72-81 (2013).

Ferber S, Tiram G and **Satchi-Fainaro R**, Evaluation of microvessels density, morphology and functionality in matrigel plugs by non-invasive intravital microscopy, *The Journal of Visualized Experiments (JoVE)*, in press (2014).

Redy O, Kisin-Finfer E, Shiran Ferber, **Satchi-Fainaro R*,** and Shabat D*, Synthesis and use of qcy7-derived modular probes for detection and imaging of biologically relevant analytes, *Nature Protocols*, 9:27-36 (2014). *Corresponding authors

Kisin-Finfer E, Ferber S, Blau R, **Satchi-Fainaro R**, Shabat D, Synthesis and evaluation of new NIR-fluorescent probes for cathepsin B: ICT versus FRET as a turn-ON mode-of-action, *Bioorganic and Medicinal Chemistry Letters*, 24:2453-8 (2014).

Ferber S, Baabur-Cohen H, Blau R, Epshtein Y and **Satchi-Fainaro R**, Nanomedicines for personalized theranostics of angiogenesis-dependent diseases, *Cancer Letters*, 352:81-89 (2014).

Markovsky E, Baabur-Cohen H, **Satchi-Fainaro R,** Anticancer polymeric nanomedicine bearing synergistic drug combination is superior to a mixture of individually-conjugated drugs**,** *Journal of Controlled Release*, 187: 145–157 (2014). **(Cover feature)**.

Redy-Keisar O, Ferber S, **Satchi-Fainaro R*** and Shabat D*, NIR Fluorogenic Dye as a Modular Platform for Prodrug Assembly: Real-Time in vivo Monitoring of Drug Release, *ChemMedChem,* 10(6): 999-1007 (2015). *Corresponding authors.

Scomparin A, Salmaso S, Eldar-Boock A, Ben-Shushan D, Ferber S, Tiram G, Shmeeda H, Landa-Rouben N, Leor J, Caliceti P, Gabizon A, **Satchi-Fainaro R**, A comparative study of folate receptor-targeted doxorubicin delivery systems: dosing regimens and therapeutic index, *Journal of Controlled Release*, 208 106-120 (2015).

Bonzi G, Salmaso S, Scomparin A, Eldar-Boock A, **Satchi-Fainaro R**, Caliceti P, A novel pullulan bioconjugate for selective breast cancer bone metastases treatment, *Bioconjugate Chemistry* 26(3):489-501 (2015).

Tiram G, Segal E, Krivitsky A, Shreberk-Hassidim R, Ferber S, Ofek P, Udagawa T, Edry L, Shomron N, Roniger M, Kerem B, Shaked Y, Aviel-Ronen S, Barshack I, Calderón M, Haag R and **Satchi-Fainaro R**, Identification of Dormancy-Associated MicroRNAs for the Design of Osteosarcoma-Targeted Dendritic Polyglycerol Nanopolyplexes, *ACS Nano* 10(2): 2028-2045 (2016).

Fisusi FA, Siew A, Chooi KW, Okubanjo O, Garrett N, Lalatsa K, Serrano D, Summers I, Moger J, Stapleton P, **Satchi-Fainaro R**, Schätzlein AG, Uchegbu IF, Lomustine Nanoparticles Enable Both Bone Marrow Sparing and High Brain Drug Levels – A Strategy for Brain Cancer Treatments, *Pharmaceutical Research* 33 (5), 1289-1303 (2016).

Schwartz H, Blacher E, Amer M, Livneh N, Abramovitz L, Klein A, Ben-Shushan D, Soffer S, Blazquez R, Barrantes-Freer A, Müller M, Müller-Decker K, Stein R, Tsarfaty G, **Satchi-Fainaro R**, Umansky V, Pukrop T, Erez N, Incipient melanoma brain metastases instigate astrogliosis and neuroinflammation, *Cancer Research*, DOI: 10.1158/0008-5472.CAN-16-0485 (2016).

Golan M, Feinshtein V, Polyak D, Scomparin A, **Satchi-Fainaro R**, David A, Inhibition of gene expression and cancer cell migration by CD44v3/6-targeted polyion complexes, *Bioconjugate chemistry* 27 (4), 947-960 (2016).

Ofek P, Calderón M, Sheikhi Mehrabadi F, Krivitsky A, Ferber S, Tiram G, Yerushalmi N, Kredo-Russo S, Grossman R, Ram Z, Haag R, **Satchi-Fainaro R**, Restoring the oncosuppressor activity of microRNA-34a in glioblastoma using a polyglycerol-based polyplex, *Nanomedicine: Nanotechnology, Biology and Medicine*, pii: S1549-9634(16)30063-6. doi: 10.1016 (2016).

Polyak D, Krivitsky A, Scomparin A, Eliyahu S, Kalinski H, Avkin-Nachum S, **Satchi-Fainaro R**, Systemic delivery of siRNA by aminated poly(α) glutamate for the treatment of solid tumors, *Journal of Controlled Release*, 257:132-142 (2017).

Baabur-Cohen H, Vossen L, Rune Krüger H, Eldar-boock A, Yeini E, Landa-Rouben N, Tiram G, Wedepohl S, Markovsky E, Leor J, Calderón M and **Satchi-Fainaro R**, In vivo comparative study of distinct polymeric architectures bearing a combination of paclitaxel and doxorubicin at a synergistic ratio, *Journal of Controlled Release*, 257:118-131 (2017).

Krivitsky A, Polyak D, Scomparin A, Eliyahu S, Ori A, Avkin Nachum S, Krivitsky V, **Satchi-Fainaro R.** Structure-function correlation of aminated poly(α) glutamate as siRNA nanocarriers. *Biomacromolecules*. 17:2787-2800 (2016).

Shatsberg Z, Zhang X, Ofek P, Malhotra S, Krivitsky A, Scomparin A, Tiram G, Calderón M, Haag R, **Satchi-Fainaro R.** Functionalized nanogels carrying an anticancer microRNA for glioblastoma therapy, Journal of Controlled Release, 239:159-68 (2016).

Gnaim S, Scomparin A, Li X, Baran PS, Rader C, **Satchi-Fainaro R**, Shabat D. Tagging the Untaggable: A Difluoroalkyl-Sulfinate Ketone-Based Reagent for Direct C-H Functionalization of Bioactive Heteroarenes, Bioconjugate Chemistry, 27:1965-71 (2016).

Hananya N, Eldar-Boock A, Bauer CR, **Satchi-Fainaro R**, Shabat D, Remarkable Enhancement of Chemiluminescent Signal by Dioxetane-Fluorophore Conjugates: Turn-ON Chemiluminescence Probes with Color Modulation for Sensing and Imaging, Journal of the American Chemical Society (JACS). 138):13438-13446 (2016).

Alishekevitz D, Gingis-Velitski S, Kaidar-Person O, Gutter-Kapon L, Scherer SD, Raviv Z, Merquiol E, Ben-Nun Y, Miller V, Rachman-Tzemah C, Timaner M, Mumblat Y, Ilan N, Loven D, Hershkovitz D, **Satchi-Fainaro R**, Blum G, P Sleeman J, Vlodavsky I, Shaked Y, Macrophage-Induced Lymphangiogenesis and Metastasis following Paclitaxel Chemotherapy Is Regulated by VEGFR3, Cell Reports 17:1344-1356 (2016).

Markovsky E, Eldar-Boock A, Ben-Shushan D, Baabur-Cohen H, Yeini E, Many A, Pisarevsky E, Aviel-Ronen S, Barshack I, **Satchi-Fainaro R**, Targeting NCAM-expressing neuroblastoma with polymeric precision nanomedicine, Journal of Controlled Release, 249:162-172 (2017).

Zupančič E, Curato C, Paisana M, Rodrigues C, Porat Z, Viana AS, Afonso CAM, Pinto J, Gaspar R, Moreira JN, **Satchi-Fainaro R**, Jung S, Florindo HF, Rational design of nanoparticles towards targeting antigen-presenting cells and improved T cell priming. Journal of Controlled Release, 258:182-195 (2017).

Ferguson EL, Scomparin A, Hailu H, **Satchi-Fainaro R**. HPMA Copolymer-phospholipase C and Dextrin-Phospholipase A2 as Model Triggers for Polymer Enzyme Liposome Therapy (PELT). Journal of Drug Targeting, 21:1-33. (2017).

Markovsky E*, Vax E*, Ben-Shushan D, Eldar-Boock A, Shukrun R, Yeini E, Barshack I, Caspi R, Harari-Steinberg O, Pode-Shakked N, Dekel B, **Satchi-Fainaro R**, Wilms' tumor NCAM-expressing cancer stem cells as potential therapeutic target for polymeric nanomedicine, Molecular Cancer Therapeutics, 16, 2462-72 (2017).

Eldar-Boock A, Blau R, Ryppa C, Baabur-Cohen H, Many A, Vicent MJ, Kratz F, Sanchis J, **Satchi-Fainaro R.** Integrin-Targeted Nano-Sized Polymeric Systems for Paclitaxel Conjugation: A Comparative Study. Journal of Drug Targeting. 8:1-16 (2017).

Hananya N, Green O, Blau R, Satchi-Fainaro R*, Shabat D*, Highly-Efficient Chemiluminescence Probe for Detection of Singlet Oxygen in Living Cells. Angewandte Chemie Int Ed Engl., doi: 10.1002/anie.201705803 (2017). Co-Corresponding authors.

Green O, Gnaim, S, Blau R, Eldar-Boock A, **Satchi-Fainaro R,** Shabat D, Near-infrared dioxetane luminophores with direct chemiluminescence emission mode. *Journal of the American Chemical Society (JACS)* 139:13243-13248 (2017).

Ferber S*, Tiram G*, Sousa-Herves A*, Eldar-Boock A, Krivitsky A, Ofek P, Scomparin A, Yeini E, Vossen LI, Licha K, Grossman R, Ram Z, Henkin J, Ruppin E, Auslander N, Haag R, Calderón M and **Satchi-Fainaro R**. Co-targeting the tumor endothelium and P-selectin-expressing glioblastoma cells leads to a remarkable therapeutic outcome. *eLife,* pii: e25281(2017).

Krivitsky A*, Polyak D*, Scomparin A*, Eliyahu S, Ofek P, Tiram G, Kalinski H, Avkin-Nachum S, Feiner Gracia N, Albertazzi L, **Satchi-Fainaro R**. Amphiphilic poly(α)glutamate polymeric micelles for systemic administration of siRNA to tumors. *Nanomedicine, in press* 2017 *equal contribution.

Gibori H, Eliyahu S, Krivitsky A, Ben-Shushan D, Epshtein Y, Ofek P, Lee JS, Ruppin E, Merquiol E, Blum G, and **Satchi-Fainaro R**. An amphiphilic polymeric nanocarrier bearing a synergistic combination of miR-34a-PLK1 siRNA for pancreatic cancer therapy, *Nature Communications,* in press (2017).

Reviews

Ferber S, Tiram G and Satchi-Fainaro R, Targeting Drugs to Cancer: A Tough Journey to the Tumor

Cell, In Cancer Targeted Drug Delivery: An Elusive Dream, Eds. Han Bae Y, Mrsny R and Park K, Springer Science and Business Media, New York, Part V, pp 509-542 (2013).

Scomparin A*, Tiram G*, Satchi-Fainaro R, Nanoscale-Based Delivery of RNAi for Cancer Therapy, Erdmann VA and Barciszewski J (Eds.), In: DNA and RNA Nanobiotechnologies in Medicine: Diagnosis and Treatment of Diseases, RNA Technologies, Springer-Verlag Berlin Heidelberg, 349-372 (2013)

Eldar-Boock A*, Polyak D*, Scomparin A, **Satchi-Fainaro R**, Nano-sized polymers and liposomes designed to deliver combination therapy for cancer, *Current Opinion in Biotechnology*, 24: 682–689 (2013).

Ofek P, Tiram G, **Satchi-Fainaro R**, RNAi Anti-angiogenic Nanomedicines, *Advanced Drug Delivery Reviews*, in press (2014).

Polyak D*, Eldar-Boock A*, Baabur-Cohen H and **Satchi-Fainaro R**, Polymer conjugates for focal and targeted delivery of drugs, *Polymers for Advanced Technologies*, 24, 777–790 (2013).

Tiram G, Scomparin A, Ofek P and **Satchi-Fainaro R,** Interfering cancer with polymeric siRNA nanocarriers, *Journal of Biomedical Nanotechnology*, 10, 50-66 (2014).

Ben-Shushan D*, Markovsky E*, Gibori H*, Tiram G, Scomparin A, **Satchi-Fainaro R**, Overcoming obstacles in microRNA delivery towards improved cancer therapy, *Drug Delivery and Translational Research*, 4, 38-49 (2014).

Tiram G, Scomparin A, Ofek P and **Satchi-Fainaro R,** Interfering cancer with polymeric siRNA nanocarriers*, Journal of Biomedical Nanotechnology*, 10, 50-66 (2014).

Scomparin A, Polyak D, Krivitsky A, **Satchi Fainaro R**, Achieving successful delivery of oligonucleotides - From physico-chemical characterization to in vivo evaluation, *Biotechnology Advances*, 33 (6pt3) 1294-1309 (2015).

Blau R, Krivitsky A, Epshtein Y, Satchi-Fainaro R, Are nanotheranostics and nanodiagnostics-guided drug delivery stepping stones toward precision medicine? Drug Resistance Updates, in press (2016).

Ofek P, Tiram G, Satchi-Fainaro R, RNAi Anti-angiogenic Nanomedicines, Advanced Drug Delivery Reviews, in press (2016).

Blau R, Krivitsky A, Epshtein Y, Satchi-Fainaro R. Are nanotheranostics and nanodiagnostics-guided drug delivery stepping stones towards precision medicine? Drug Resistance Updates, 27:39-58 (2016).

Ofek P, Tiram G, Satchi-Fainaro R. Angiogenesis regulation by nanocarriers bearing RNA interference. Advanced Drug Delivery Reviews, in press (2017).

Blau R, Neeman M, Satchi-Fainaro R, Emerging nanomedical solutions for angiogenesis regulation, Advanced Drug Delivery Reviews, in press (2017).

Scomparin A, Florindo HF, Tiram G, Satchi-Fainaro R, Two-step polymer- and liposome- enzyme prodrug therapies for cancer: PDEPT and PELT concepts and future perspectives, Advanced Drug Delivery Reviews, in press (2017).

Satchi-Fainaro R, Vicent MJ, Richardson S, Editorial-Professor Ruth Duncan Coined the Term Polymer Therapeutics, Journal of Drug Targeting, in press (2017).

Grants

2012-2017	Israel National Nanotechnology Initiative (INNI), Focal Technology Area in nanotechnology, "Theranostic Nanomedicines for Personalized Medicine"
2014-2019	European Research Council (ERC) Consolidator Award. PolyDorm: "Uncovering the molecular and cellular mechanism of tumor dormancy for the rational design of theranostic nanomedicines"
2014–2018	Israel Science Foundation (ISF) Grant
2014 – 2017	Melanoma Research Alliance SABAN Family Foundation-Team Science Award

Prof. Yosef Shiloh, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: yossih@post.tau.ac.il
Lab web site: http://www.tau.ac.il/~yossih/

The ATM-Mediated DNA Damage Response

Positions

Professor Emeritus, Sackler Faculty of Medicine

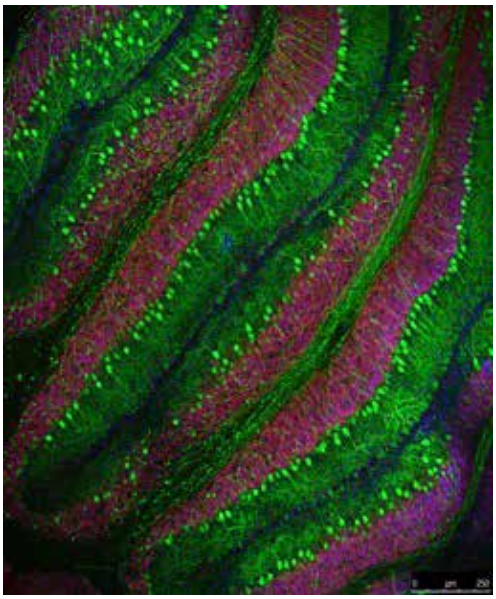
David and Inez Myers Chair in Cancer Genetics

ICRF Research Professorship

Research

Our laboratory investigates the cellular DNA damage response. This research stems from our interest in the human genetic disorder ataxia-telangiectasia (A-T), in which a central axis of the DNA damage response is missing.

Genetic defects in the DNA damage response lead to genomic instability syndromes, which usually include tissue degeneration, cancer predisposition, and sensitivity to specific DNA damaging agents. A prototype genomic instability syndrome is A-T. The disease is characterized by neuronal degeneration, immunodeficiency, chromosomal instability, sensitivity to ionizing radiation, and cancer predisposition. Our lab has been investigating A-T since its establishment in 1985. In 1995, after 8 years of intensive work, we identified the gene that is defective (mutated) in A-T patients and called it *ATM* (A-T, Mutated). We went on to study the activity of its product, the ATM protein, which turned out to be an enzyme with an activity alled “protein kinase”.



Microscopic image of a slice of mouse cerebellum in culture. The cells stained green are called Purkinje cells. These cells are the first to be damaged and lost in A-T patients. Such cultures are used to study the DNA damage response in this complex organ.

Our current research is aimed at a broader understanding of the ATM-mediated DNA damage response. Particular attention is paid to the molecular and physiological basis of A-T, which may eventually lead to new treatment modalities for the disease. We investigate this system with cell biology methods, gene targeting in mice, and systems biology strategies including high-throughput screens, advanced proteomics and bioinformatics. A study is underway aimed at understanding the DNA damage response in the part of the brain called the cerebellum, which is badly damaged in A-T patients. Another project is searching for a drug treatment for A-T patients based on our recent understanding of the disease.

Publications

Tzur-Gilat, A., Ziv, Y., Dusart, I., Mittelman, L., Barzilai, A., and **Shiloh, Y.** (2013) Studying the cerebellar DNA damage response in the tissue culture dish. *Mech. Ageing Dev*. 134:496-505.

Rasmussen LJ, **Shiloh Y**, Bergersen LH, Sander M, Bohr VA, Tønjum T. (2013) DNA damage response, bioenergetics, and neurological disease: the challenge of maintaining brain health in an aging human population. *Mech Ageing Dev*. 134:427-33

Rashi-Elkeles S, Warnatz HJ, Elkon R, Kupershtein A, Chobod Y, Paz A, Amstislavskiy V, Sultan M, Safer H, Nietfeld W, Lehrach H, Shamir R, Yaspo ML, **Shiloh Y**. (2014) Parallel profiling of the transcriptome,

cistrome, and epigenome in the cellular response to ionizing radiation. *Sci Signal*. M7(325):rs3.

Meir, M., Galanty, Y., Kashani, L., Blank, M., Khosravi, R., Fernández-Ávila, M.J., Cruz-Garcia, A., Star, A., Shochat, L., Thomas, Y., Garrett, L.J., Chamovitz, D.A., Bodine, D.M., Kurz, T., Huertas, P., Ziv, Y., and **Shiloh, Y.** (2015) The COP9 signalosome is vital for timely repair of DNA double-strand breaks. *Nucleic Acids Res.* 43: 4517-4530.

Tal E, **Shiloh Y**. (2017) Monitoring the ATM-mediated DNA damage response in the cerebellum using organotypic cultures. *Methods Mol Biol* 1599 419-430.

Reviews

Shiloh, Y., and Ziv, Y. (2013) The ATM protein: regulating the DNA damage response, and more. *Nature Rev. Mol. Cell Biol*. 14:197-210.

Shiloh, Y. (2014) ATM: expanding roles as a chief guardian of genome stability. Exp. Cell Res. 329:154-161. Ribezzo, F., Shiloh, Y., and Schumacher, B. (2016) Systemic DNA damage responses in aging and diseases. *Seminars in Cancer Biology* 38:26-35.

Tal, E. and **Shiloh, Y.** (2016) Monitoring the ATM-mediated DNA damage response in the cerebellum using organotypic cultures. *Methods in Molecular Biology* 1599:419-430.

Barzilai, A., Schumacher, B., and **Shiloh, Y.** (2017) Genome instability: linking ageing and brain degeneration. *Mechanisms of Ageing and Development* 161 (PtA):4-18.

Shiloh, Y., and Lederman, H. (2017) Ataxia-telangiectasia (A-T): an emerging dimension of premature ageing. *Ageing Research Reviews* 33:76-88.

Grants

2014 – 2021	Israel Cancer Research Fund (ICRF Professorship)
2014 – 2017	Israel Science Foundation (Joint ISF-NSFC Program with the National Natural Science Foundation of China)
2015 – 2020	The A-T Children's Project
2016 – 2017	The A-T Ease Foundation
2016- 2020	US-Israel Binational Science Foundation
2015 – 2017	Dr. Miriam and Sheldon G. Adelson Medical Research Foundation

Prof. Ilan Tsarfaty, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: ilants@post.tau.ac.il

Met Proto-Oncogene and its Ligand, HGF/SF and Breast Cancer

Position

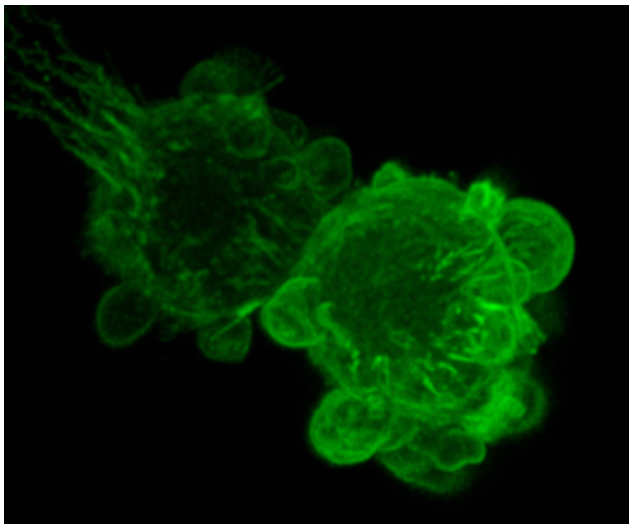
Associate Professor, Sackler Faculty of Medicine

Director, Sackler Cellular and Molecular Imaging Center (SCMIC)

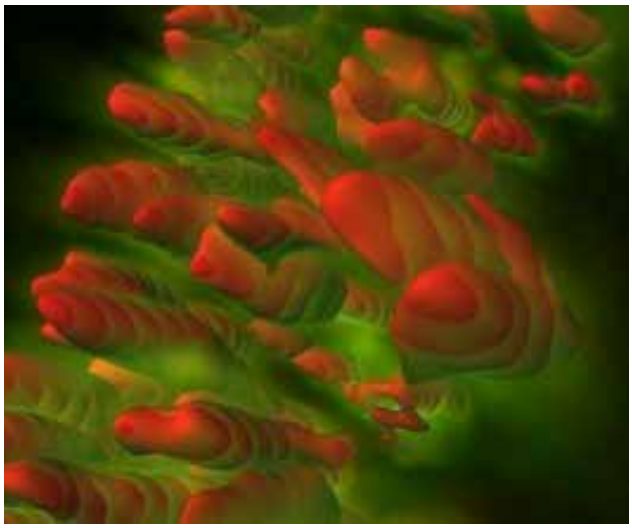
Research

Breast cancer is the most common malignant disease in western women. In the majority of cases the cause of death in cancer patients is not the primary tumors, but complications derived from metastases at distant sites. The *met* proto-oncogene product (Met – a receptor tyrosine kinase) and its ligand, hepatocyte growth factor/scatter factor (HGF/SF), mediate cell motility and proliferation *in* vitro and tumorigenicity, angiogenesis and metastasis *in vivo*. Mimp/Mtch2, a mitochondrial carrier homologue cloned in our lab, is induced by Met-HGF/SF signaling and is involved in metabolic and bioenergetic processes. We have previously shown that activation of Met by HGF/SF induces an increase in tumor blood volume in a dose-dependent manner. Mimp/Mtch2 reduces cells proliferation *in vitro* and tumor growth *in vivo*. Several anti-Met targeted therapies are in development and some have entered phase III clinical trials.

The goal of our studies is to further understand the role of Met-Mimp/Mtch2 in cancer progression and metastasis, and to develop modalities for personalizing targeted Met therapy. Fluorescent tagged–Met proteins were used to study Met mitogenic effect on cells. Met induced cell motility is mediated by the formation of membrane structures such as ruffles, pseudopodia and blebs. Over expression of GFP-Met WT results in its constitutive activation, cell rounding and detachment, and dynamic non-apoptotic membrane blebbing. Bleb retraction results in numerous membrane microspikes where CFP-Met WT, YFP-actin and membrane markers accumulate. Expression of Dominant-Negative (DN) YFP-Met alone did not induce any membrane blebbing, and co-expression of CFP-Met WT and YFP-Met DN significantly reduces membrane blebbing. Using confocal based molecular imaging we also show that Mimp/Mtch2 reduces the levels of reactive oxygen



Met localization in blebbing cells



Mimp localization in mitochondrial cells (Red inner mitochondria marker, Green Mimp-GFP)

species ROS and prevents the HGF/SF induced increase in ROS. Mimp/Mtch2 also reduces the polarization of the mitochondrial membrane potential.

To study Met activation by HGF/SF *in vivo*, we used a xenograft mouse model in which DA3 cells expressing the fluorescent protein mCherry (DA3-mCherry) are injected orthotropicly into mice mammary glands. Contrast media ultrasound-based Met functional molecular imaging (FMI) demonstrated that HGF/SF-induced increased hemodynamics is dependent on Met concentration and can be dramatically reduce upon inhibition of the receptor and it's signaling pathway; Whole animal spectral imaging enabled detection of sub-millimeter metastases demonstrating fast developing micrometastatic spread of the tumor; Macro to Micro and two photon confocal imaging demonstrated HGF/SF-induced changes in blood flow at single vessel resolution, localization of metalloprotease and catapsine activity at the tumor edge and increase in single cell motility.

Met molecular imaging demonstrated that Met signaling modulation plays a major role in breast cancer tumor growth and development. These emerging MI modalities may help tailor Met-targeted therapy.

Publications

Shaul, P. Frenkel, M. Goldstein, Mittelman, L., Grunwald, A., Ebenstein, Y. **Tsarfaty, I**. Fridman, M. The structure of anthracycline derivatives determines their subcellular localization and cytotoxic activity. *ACS Medicinal Chemistry Letters* 2013. 4, 323-328.

Rivlin, M. Horev, J. **Tsarfaty, I.** Navon G. Molecular imaging of tumors and metastases using chemical exchange saturation transfer (CEST) MRI. *Sci Rep*.2013. 25;3:3045.

Zaritsky, A., Manor, N., Wolf, L., Ben-Jacob, E. & **Tsarfaty, I**. Benchmark for multi-cellular segmentation of bright field microscopy images. *BMC Bioinformatics* 2013, 14**:**319.

Laser-Azogui, A., Diamant-Levi, T., Israeli, S., Roytman, Y. & **Tsarfaty**, I. Met-induced membrane blebbing leads to amoeboid cell motility and invasion. *Oncogene* 2014. 33:1788-98.

Natan, S*. Tsarfaty, G*. Horev, J. Haklai, R. Kloog, Y. **Tsarfaty, I.** Interplay between HGF/Sf–Met-Ras signaling, tumor metabolism and blood flow as a potential target for breast cancer therapy. *Oncoscience* 2014.1:30.

Ninio-Many, L. Grossman, H. Levi, M. Zilber S., **Tsarfaty I.** Shomron, N. Tuvar, A. Chuderland, M Stemmer, D. S. Ben-Aharon, I. Shalgi, R. MicroRNA miR-125a-3p modulates molecular pathway of motility and migration in prostate cancer cells. *Oncoscience* 2014. 1:250.

Huang B, Jolly MK, Lu M, **Tsarfaty I**, Ben-Jacob E, Onuchic JN. Modeling the transitions between collective and solitary migration phenotypes in cancer metastasis. *Sci Rep*. 2015. 5:17379.

Hecht I, Natan S, Zaritsky A, Levine H, **Tsarfaty I**, Ben-Jacob E. The motility-proliferation-metabolism interplay during metastatic invasion. *Sci Rep.* 2015. 4;5:13538.

Hecht I, Bar-El Y, Balmer F, Natan S, **Tsarfaty I**, Schweitzer F, Ben-Jacob E. Tumor invasion optimization by mesenchymal-amoeboid heterogeneity.*Sci Rep*. 2015. 5:10622. Erratum in: *Sci Rep*. 2015;5:12121.

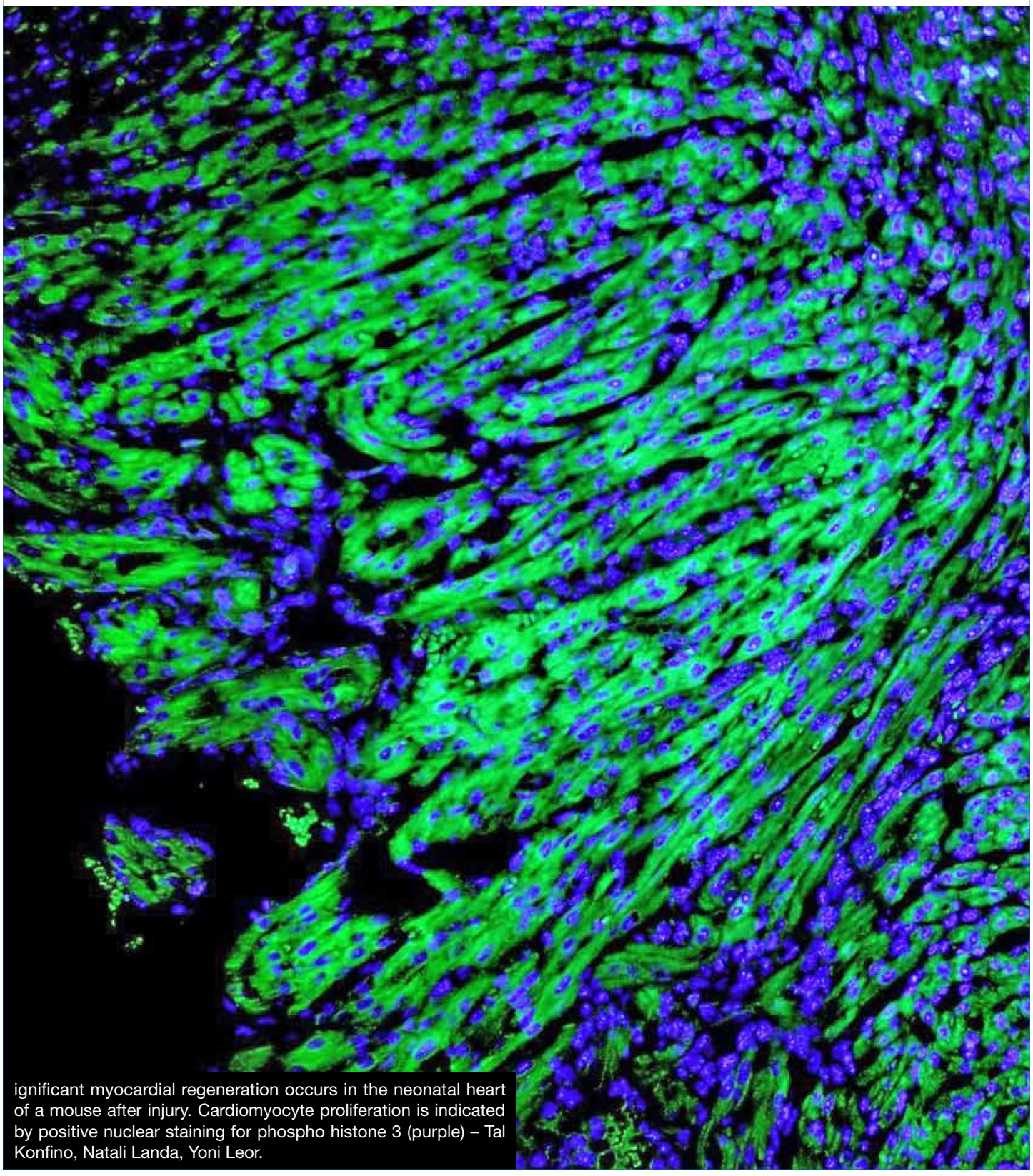
Zaritsky A, Natan S, Kaplan D, Ben-Jacob E, **Tsarfaty I**. Live time-lapse dataset of in vitro wound healing experiments. *Gigascience.* 2015. ;4:8.

Bar-Lev Y, Moshitch-Moshkovitz S, Tsarfaty G, Kaufman D, Horev J, Resau JH, **Tsarfaty I**. Mimp/Mtch2, an obesity susceptibility gene, induces alteration of fatty acid metabolism in transgenic mice. *PLoS One*. 2016;11.

Grants

2017-2019 Israel Science Foundation

Cardiovascular Research and Diseases



ignificant myocardial regeneration occurs in the neonatal heart of a mouse after injury. Cardiomyocyte proliferation is indicated by positive nuclear staining for phospho histone 3 (purple) – Tal Konfino, Natali Landa, Yoni Leor.

Prof. Bernard Attali, Ph.D.

Department of Physiology & Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: battali@post.tau.ac.il
http://www2.tau.ac.il/Person/medicine/researcher.asp?id=achigijid

Normal and Diseased Potassium Channels in Human Brain and Heart

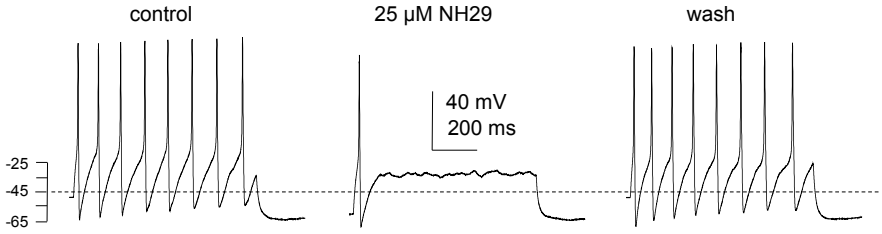
Position

Professor, Sackler Faculty of Medicine

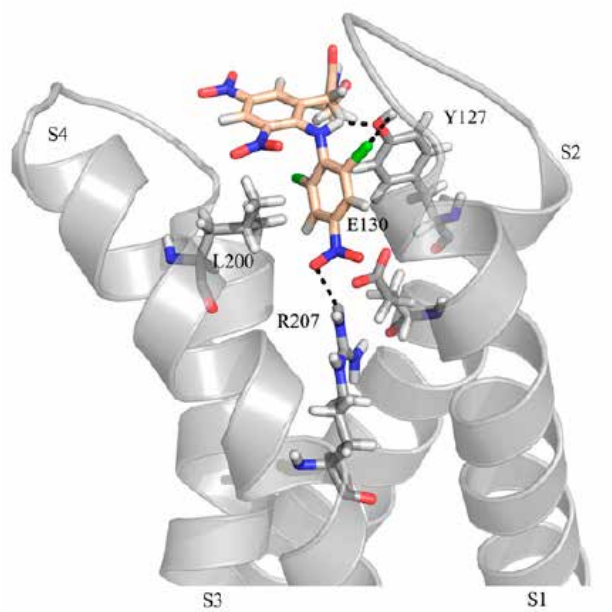
Andy Libach Professorial Chair in Clinical Pharmacology and Toxicology

Research

Reaching an understanding in molecular terms of the mechanisms by which changes in membrane potential regulate cellular events is the main concern of our research. We focus our interest on potassium channels because they play crucial roles in many cellular functions such as shaping cardiac and neuronal action potentials, tuning neuronal firing patterns, synaptic integration or modulating neurotransmitter release. Using the powerful combination of molecular biology, biophysics, biochemistry and electrophysiology, our research aims at elucidating the structural, biophysical and physiological attributes of potassium channels in human brain and heart and whose mutations lead to



Activation of M-type potassium channels by our homemade NH29 opener inhibits evoked spike discharge in dorsal root ganglion sensory neurons.



Docking of the NH29 gating-modifier molecule onto the voltage sensor domain of the Kv7.2 potassium channel.

major neurological and cardiovascular disorders like epilepsy, myokymia, atrial or ventricular fibrillation.

Publications

Manuscripts

Weisbrod D, Peretz A, Ziskind A, Menaker N, Oz S, Barad L, Eliyahu S, Itskovitz-Eldor J, Dascal N, Khananshvili D, Binah O, **Attali B**. (2013) SK4 Ca2+ activated K+ channel is a critical player in cardiac pacemaker derived from human embryonic stem cells. *Proc Natl Acad Sci USA*. 110:E1685-94.

Kornilov P, Peretz A, Lee Y, Son K, Lee JH, Refaeli B, Roz N, Rehavi M, Choi S, **Attali B**. (2014) Promiscuous gating modifiers target the voltage sensor of Kv7.2, TRPV1, and Hv1 cation channels. *FASEB J*. 28:2591-602.

Gourgy-Hacohen O, Kornilov P, Pittel I, Peretz A, **Attali B***, Paas Y* (2014). Capturing distinct KCNQ2 channel resting states by metal ion bridges in the voltage-sensor domain. *J Gen Physiol*. 144:513-27.

Sachyani D, Dvir M, Strulovich R, Tria G, Tobelaim W, Peretz A, Pongs O, Svergun D, **Attali B**, Hirsch JA. (2014) Structural basis of a Kv7.1 potassium channel gating module: studies of the intracellular c-terminal domain in complex with calmodulin. Structure. 22:1582-94.

Patrich E, Piontkewitz Y, Peretz A, Weiner I, **Attali B**. (2016). Maturation- and sex-sensitive depression of hippocampal excitatory transmission in a rat schizophrenia model. *Brain Behav Immun*. 51:240-51.

Patrich E, Piontkewitz Y, Peretz A, Weiner I, **Attali B**. (2016). Maternal immune activation produces neonatal excitability defects in offspring hippocampal neurons from pregnant rats treated with poly I:C. *Sci Rep*. 8;6:19106.

Strulovich R, Tobelaim WS, **Attali B**, Hirsch JA. (2016) Structural insights into the M-Channel proximal C-terminus/calmodulin complex. Biochemistry. 55:5353-65.

Ding Q, Fang S, Chen X, Wang Y, Li J, Tian F, Xu X, **Attali B**, Xie X, Gao Z. (2017) TRPA1 channel mediates organophosphate-induced delayed neuropathy. *Cell Discov.* 3:17024.

Haron-Khun S, Weisbrod D, Bueno H, Yadin D, Behar J, Peretz A, Binah O, Hochhauser E, Eldar M, Yaniv Y, Arad M, **Attali B**. (2017) SK4 K+ channels are therapeutic targets for the treatment of cardiac arrhythmias. *EMBO Mol Med*. 9:415-429.

Tobelaim WS, Dvir M, Lebel G, Cui M, Buki T, Peretz A, Marom M, Haitin Y, Logothetis DE, Hirsch JA, **Attali B**. (2017) Competition of calcified calmodulin N lobe and PIP2 to an LQT mutation site in Kv7.1 channel. *Proc Natl Acad Sci USA*. 114:E869-E878.

Lezmy J, Lipinsky M, Khrapunsky Y, Patrich E, Shalom L, Peretz A, Fleidervish IA, **Attali B**. (2017) M-current inhibition rapidly induces a unique CK2-dependent plasticity of the axon initial segment. *Proc Natl Acad Sci USA*. 2017 pii: 201708700.

Tobelaim WS, Dvir M, Lebel G, Cui M, Buki T, Peretz A, Marom M, Haitin Y, Logothetis DE, Hirsch JA, **Attali B**. (2017) Ca2+-Calmodulin and PIP2 interactions at the proximal C-terminus of Kv7 channels. Channels (Austin). doi: 10.1080/19336950.2017.1388478.

Reviews

Kornilov P, Peretz A, **Attali B.** (2013) Channel gating pore: a new therapeutic target. *Cell Res.* 23:1067-8.

Dvir M, Peretz A, Haitin Y, **Attali B**. (2014) Recent molecular insights from mutated I_{KS} channels in cardiac arrhythmia. *Curr Opin Pharmacol*. 15:74-82.

Alexander SP, Kelly E, Marrion N, Peters JA, Benson HE….**Attali, B**..et CGTP Collaborators. (2015) The Concise Guide to PHARMACOLOGY 2015/16: Overview. *Br J Pharmacol*. 172:5729-43.

Attali B, Gao ZB. (2016). Ion channels research in the post-genomic era. *Acta Pharmacol Sin*. 37:1-3.

Weisbrod D, Khun SH, Bueno H, Peretz A, **Attali B**. (2016). Mechanisms underlying the cardiac pacemaker: the role of SK4 calcium-activated potassium channels. *Acta Pharmacol Sin*. 37:82-97.

Grants

2013-2017	Israel Academy of Science, (ISF:1215/13). Role of SK4 Ca2+-activated K+ channels in the developing human cardiac pacemaker using embryonic stem cell-derived cardiomyocytes as a model. (PI).
2013-2017	Fields Fund for Cardiovascular Research (Co-PI).
2014-2017	Israel Science Foundation-China (The ISF-NSFC joint program, 2092/14)

Prof. Nathan Dascal, Ph.D.

Dept. of Physiology and Pharmacology
Sackler School of Medicine

TEL AVIV UNIVERSITY

Email: dascaln@post.tau.ac.il
URL: http://medicine.mytau.org/dascal/

Signal Transduction by Neurotransmitters in Brain and Heart in Health and Disease

Position

Professor of Physiology, Sackler Faculty of Medicine

Morris and Helen Mauerberger Chair for Neuropharmacology

Research

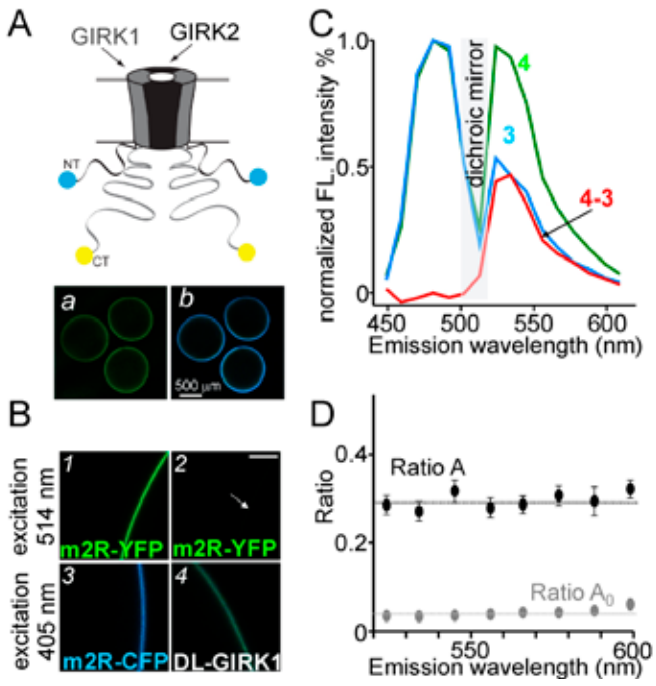
Electrical activity of excitable cells is their most important feature, which allows the performance of fundamental functions of brain, heart and muscle. We are addressing a key issue in modern cardiology and neurobiology: how neurotransmitters regulate cardiac cells and neurons by acting on ion channels – proteins that underlie the electrical activity in these cells; and how errors in these processes cause disease. Main projects in the lab:

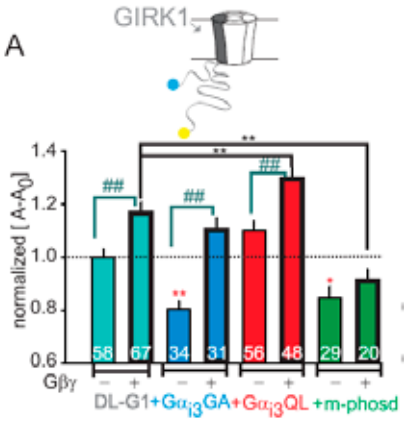
Function and regulation of receptors, G proteins, Ca^{2+} and K^{+} channels in health and disease; Ion channel-related hereditary cardiac and neurological disorders (channelopathies); Mechanisms of coupling of G protein-coupled receptors with effectors; Molecular mechanisms of bipolar disorder.

Research methods: Electrophysiology, Neurophysiology, Heterologous Expression, Protein Biochemistry, Fluorescence Resonance Energy Transfer (FRET), Molecular biology, Mathematical and Kinetic Modeling and Simulation, Immunocytochemistry

Publications

Edvardson S, Oz S, Abulhijaa FA, Taher FB, Shaag A, Zenvirt S, **Dascal N** & Elpeleg O. (2013). Early infantile epileptic encephalopathy associated with a high voltage-gated calcium channelopathy. *J Med Genet* **50**, 118-123





Studying GIRK channels expressed in a heterologous system (*Xenopus* oocytes). Intramolecular fluorescence resonance energy transfer (i-FRET) shows interactions of cytosolic N- and C-termini of the channel. **A**, GIRK channel labeled with two fluorescent proteins. **B**, Imaging the expressed fluorescent proteins with a confocal microscope. **C, D,** Example of use of FRET analysis to study conformational changes in the channel caused by neurotransmitter, G proteins or drugs. **E,** Gα and Gβγ synergistically alter the conformation of GIRK1 subunit.

Treiber F, Rosker C, Keren-Raifman T, Steinecker B, Gorischek A, **Dascal N** & Schreibmayer W. (2013) Molecular basis of the facilitation of the heterooligomeric GIRK1/GIRK4 complex by cAMP dependent protein kinase. *Biochim Biophys Acta* 1828, 1214-1221.

Oz S, Benmocha A, Sasson Y, Sachyani D, Almagor L, Lee A, Hirsch JA & **Dascal N**. (2013). Competitive and non-competitive regulation of calcium-dependent inactivation in $Ca_V1.2$ L-type Ca^{2+} channels by calmodulin and Ca^{2+}-binding protein 1. *J Biol Chem*. 288, 12680-12691.

Weisbrod, D., Peretz, A., Ziskind, A., Menaker, N., Oz, S., Barad, L., Eliyahu, S., Itskovitz-Eldor, J., **Dascal, N.**, Khananshvili, D., Binah, O., and Attali, B. (2013) SK4 Ca^{2+} activated K^+ channel is a critical player in cardiac pacemaker derived from human embryonic stem cells. *Proc Natl Acad Sci USA* 110, E1685-1694.

Farhy Tselnicker I, Tsemakhovich V, Rishal I, Kahanovitch U, Dessauer CW & **Dascal N**. (2014). Dual regulation of G proteins and the G-protein–activated K^+ channels by lithium. *Proc Natl Acad Sci USA* 111, 5018-5023.

Edelheit O, Ben-Shahar R, **Dascal N**, Hanukoglu A & Hanukoglu I. (2014). Conserved charged residues at the surface and interface of epithelial sodium channel (ENaC) subunits: roles in cell surface expression and Na^+ self-inhibition response. *FEBS J*. 281:2097-111.

Benmocha Guggenheimer A, Almagor L, Tsemakhovich V, Tripathy DR, Hirsch JA,**Dascal N**. Interactions between N and C termini of α1C subunit regulate inactivation of CaV1.2 L-type Ca(2+). *Channels* (Austin). 2016;10:55-68.

Yakubovich D, Berlin S, Kahanovitch U, Rubinstein M, Farhy-Tselnicker I, Styr B, Keren-Raifman T, Dessauer CW, **Dascal N**. A quantitative model of the GIRK1/2 channel reveals that its basal and evoked activities are controlled by unequal stoichiometry of Gα and G$\beta\gamma$. *PLoS Comput Biol*. 2015;11

Kahanovitch U, Tsemakhovich V, Berlin S, Rubinstein M, Styr B, Castel R, Peleg S, Tabak G, Dessauer CW, Ivanina T, **Dascal N**.Recruitment of G$\beta\gamma$ controls the basal activity of G-protein coupled inwardly rectifying potassium (GIRK) channels: crucial role of distal C terminus of GIRK1.*J Physiol.* 2014;592:5373-90.

Oz S, Pankonien I, Belkacemi A, Flockerzi V, Klussmann E, Haase H & **Dascal N**. (2017). Protein kinase A regulates C-terminally truncated CaV1.2 in Xenopus oocytes: roles of N- and C-termini of the α1C subunit. *J Physiol London,* 595, 3181–3202.

Kahanovitch U, Berlin S & Dascal N. (2017) Collision coupling in the GABAB receptor - G protein - GIRK signaling cascade. *FEBS Lett* 591, 2816-2825

Dascal N & Rubinstein M. (2017) Lithium reduces the span of G protein-activated K+ (GIRK) channels inhibition in hippocampal neurons. *Bipolar Disord*, in press. DOI: 10.1111/bdi.12536.

Keren Raifman T, Kumar P, Haase H, Klussmann E, Dascal N & Weiss S. (2017) Protein kinase C enhances plasma membrane expression of cardiac L-type calcium channel, CaV1.2. *Channels (Austin)*, 1-12.

Reviews

Dascal N, Kahanovitch U. The roles of G$\beta\gamma$ and Gα in gating and regulation of GIRK channels. *Int Rev Neurobiol*. 2015;123:27-85.

Weiss S, **Dascal N**. Molecular aspects of modulation of L-type calcium channels by protein kinase C. *Curr Mol Pharmacol*. 2015;8:43-53.

Weiss S, Oz S, Benmocha A, **Dascal N**. (2013) Regulation of cardiac L-type Ca^{2+} channel $Ca_V1.2$ via the β-adrenergic-cAMP-protein kinase A pathway: old dogmas, advances, and new uncertainties. *Circ Res* 2013, 113:617-31.

Grants

2014-2018 Subunit composition-determined physiology of GIRK channels (competitive continuation). US-Israel Binational Science Foundation (BSF). With C.W. Dessauer (Texas Univ.)

2014-2018 Li+ regulates neuronal ion channels: molecular mechanisms and relation to bipolar disorder. Israel Science Foundation (ISF)

2015-2018 Molecular mechanisms of disease caused by dysfunction of cardiovascular GIRK channels. Joint Israel-India grant managed by ISF (with Prof. A.K. Bera, IIT)

Dr. Michal Katz-Leurer, Ph.D.

Department of Physical Therapy
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: michalkz@post.tau.ac.il

Investigating the Cardiac Autonomic System Among Brain Damaged Patients

Position

Senior Lecturer

Chair, Department of Physical Therapy

Research

Stroke, traumatic brain injury and cerebral palsy are the most common causes of physical disability. Autonomic instability is common phenomenon post brain damage, with signs and symptoms of hyper-stimulation of the sympathetic nervous system. We study the connections between physical disability and the cardiac autonomic regulation system. We assess the cardiac autonomic response to different stimulus and its immediate and long-lasting adaptation to different physical training protocols.

Publications

Leizerowitz G, **Katz-Leurer M**. Feasibility, stability and validity of the four square step test in typically developed children and children with brain damage. Brain Inj. 2017;31:1356-1361.

Cohen-Holzer M, Sorek G, Schweizer M, **Katz-Leurer M**. The influence of a constraint and bimanual training program using a variety of modalities on endurance and on the cardiac autonomic regulation system of children with unilateral cerebral palsy: A self-control clinical trial. NeuroRehabilitation. 2017;41:119-126.

Amichai T, Eylon S, Dor-Haim H, Berger I, **Katz-Leurer M**. Cardiac autonomic system response to submaximal test in children with cerebral palsy. Pediatr Phys Ther. 201729:125-128.

Cohen-Holzer M, **Katz-Leurer M**, Meyer S, Green D, Parush S. The effect of bimanual training with or without constraint on hand functions in children with unilateral cerebral palsy: a non-randomized clinical trial. Phys Occup Ther Pediatr. 2017;37:516-527.

Cohen-Holzer M, Sorek G, Kerem J, **Katz-Leurer M.** The impact of combined constraint-induced and bimanual arm training program on the perceived hand-use experience of children with unilateral cerebral palsy. Dev Neurorehabil. 2017;20:355-360.

Steinhart S, Kornitzer E, Baron AB, Wever C, Shoshan L, **Katz-Leurer M**. Independence in self-care activities in children with myelomeningocele: exploring factors based on the International Classification of Function model. Disabil Rehabil. 2016;10:1-7.

Katz-Leurer M, Rotem H, Shofer M, Meyer S.Pediatric cardio-autonomic response to variable effort after severe traumatic brain injury. Brain Inj. 2016,15:1-4.

Raphaely Beer N, Bornstein NM, Soroker N, **Katz-Leurer M.** Autonomic cardiac response to static and dynamic muscle contractions in post-stroke and healthy subjects. Eur Neurol. 2016;75:207-12.

Cohen-Hozler M, Sorek G, Kerem J, Schless S, Freedman R, Rotem H, Schweitzer M,**Katz-Leurer M.** The influence of intense combined training on upper extremity function in children with unilateral cerebral palsy: does initial ability matter? Phys Occup Ther Pediatr. 2016 6:1-12.

Shapira-Vadler O, Treger I, **Katz-Leurer M.** Muscle strength, function and heart autonomic regulation system recovery at the sub-acute stage post stroke. Eur Neurol. 2015;74:154-7

Mori T, Lustman A, **Katz-Leurer M.**Self-measurement of upper extremity volume in women post-breast cancer: reliability and validity study. Physiother Theory Pract. 2015;31:283-7.

Cohen-Holzer M, Sorek G, Schless S, Kerem J, **Katz-Leurer M.** The influence of a constraint and bimanual training program using a variety of modalities, on upper extremity functions and gait parameters among children with hemiparetic cerebral palsy: a case series. Phys Occup Ther Pediatr. 2016;3617-27.

Bartur G, Vatine J.J, Raphaely-Beer N, Peleg S, **Katz-Leurer M.** Heart rate autonomic regulation system at rest and during paced breathing among patients with CRPS as compared to age matched healthy controls. Pain Med. 2014;15:1569-74

Carmeli E, **Katz-Laurer M**, Scena S, Kodesh E, Steindler R. Functional reach test performance in distance and velocity – A pilot study. European Journal of Physiotherapy. 2014;16:168-172

Katz-Leurer M, Zohar N, Boum A, Keren O. Monitoring changes in heart rate, as an indicator of the cardiovascular autonomic nervous function, among patients at the sub-acute phase post-brain damage during a physiotherapy session: a preliminary investigation. Brain Inj. 2014;28:127-31.

Amichai T, **Katz-Leurer M**. Heart rate variability in children with cerebral palsy: Review of the literature and meta-analysis. NeuroRehabilitation 2014;35:113-22.

Israeli-Mendlovic H, Mendlovic J, **Katz-Leurer M.** Heart rate and heart rate variability parameters at rest, during activity and passive standing among children with cerebral palsy GMFCS IV-V. Dev Neurorehabil. 2014;17:398-402.

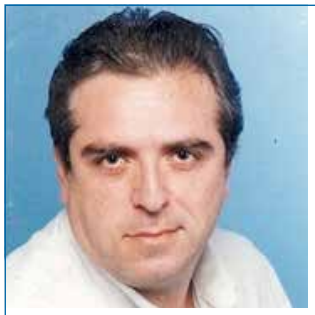
Zuk L, Tlumek H, **Katz-Leurer M,** Peretz C, Carmeli E. A new tool for identifying children with motor problems: reliability and validity study. J Child Neurol. 2014;29:592-8.

Katz-Leurer M, Rotem H, Meyer S. Effect of concurrent cognitive tasks on temporo-spatial parameters of gait among children with cerebral palsy and typically developed controls. Dev Neurorehabil. 2013;17:363-7.

Hajuj H, Jamil A, **Katz-Leurer M**. The associations between motor ability, walking activity and heart rate and heart rate variability parameters among children with cerebral palsy and typically developed controls. NeuroRehabilitation 2013;33:113-9.

Grants

2018-2020 European Research Projects on External Insults to the Nervous System



Prof. Daniel Khananshvili, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: dhanan@post.tau.ac.il

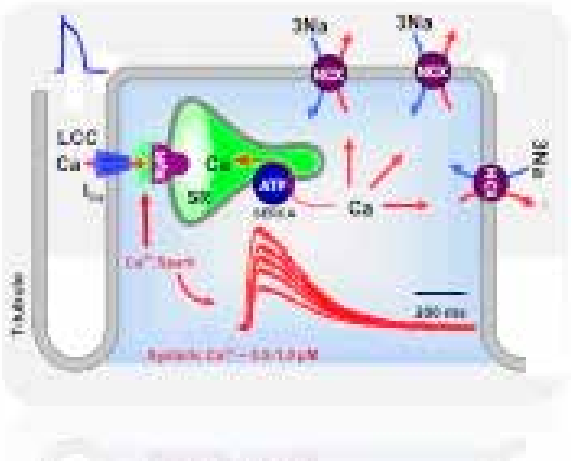
Mechanisms, Regulation and Pharmacology of Calcium Transporting NCX Proteins

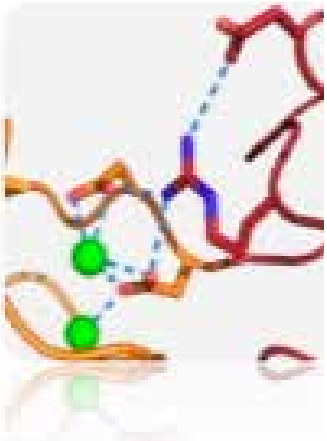
Positions

Professor, Sackler Faculty of Medicine

Research

Calcium (Ca^{2+}) is a major regulator in the living cell. In many cell-types the Na^{+}/Ca^{2+} exchanger proteins (NCX) represent a major Ca^{2+} extruding system and thus, play a key role in regulating the Ca^{2+}-dependent events in the cell. Three NCX genes form numerous splice variants, which are expressed in a tissue-specific manner to regulate excitation–contraction coupling in heart, long-term potentiation and learning in brain, blood pressure, immune responses, neurotransmitter and hormone secretion, kidney Ca^{2+} reabsorption, mitochondrial bioenergetics, etc. Altered expression and regulation of NCX proteins is a chief contributor to Ca^{2+}-driven tissue-remodeling in heart failure, cerebral ischemia, hypertension, diabetes, renal malfunction, muscle dystrophy, *etc*. For example, in cardiac disease a single isoform/splice variant (NCX1.1) is overexpressed, thereby representing a primary concern for life-threating arrhythmias and contractile malfunction. Selective pharmacological targeting of NCX variants is expected to recover Ca^{2+} homeostasis in predefined cell types and thus, may improve desired activity of altered tissues/organs. Since this breakthrough remains challenging our research efforts are focused on two principle issues: a) To resolve structure-activity relationships underlying the function and regulation of diverse NCX variants; b) To develop new experimental approaches for selective pharmacological targeting of tissue-specific NCX variants with a goal of providing new opportunities for preventing and effective treatment of harmful diseases. In this respect we investigate structure-activity relationships in the wild-type and mutated proteins by exploring a wide spectrum of techniques (stopped-flow and ion-flux assays, FRET, SAXS, ITC, X-ray crystallography, confocal microscopy, patch-clamp, etc). In searching the regulatory mechanisms of CBD1 and CBD2 domains we found that the tissue-specific splice segment, located on CBD2, shapes the regulatory specificity of the primary Ca^{2+} sensor located on CBD1. These findings may allow the identification of drug candidates targeting the disease-related NCX variants.





Publications

Edri I, Goldenberg M, Lisnyansky M, Strulovich R, Newman H, Loewenstein A, **Khananshvili D**, Giladi M, Haitin Y. Overexpression and purification of human Cis-prenyltransferase in *Escherichia coli.* J Vis Exp. 2017 Aug 3;(126).

Giladi M, van Dijk L, Refaeli B, Almagor L, Hiller R, Man P, Forest E, **Khananshvili D**. Dynamic distinctions in the Na+/Ca2+ exchanger adopting the inward- and outward-facing conformational states. *J Biol Chem.* 2017, 292:12311-12323.

Giladi M, Lee SY, Ariely Y, Teldan Y, Granit R, Strulovich R, Haitin Y, Chung KY, **Khananshvili D**. Structure-based dynamic arrays in regulatory domains of sodium-calcium exchanger (NCX) isoforms. *Sci Rep*. 2017, 7:993.

Giladi M, Edri I, Goldenberg M, Newman H, Strulovich R, **Khananshvili D**, Haitin Y, Loewenstein A. Purification and characterization of human dehydrodolychil diphosphate synthase (DHDDS) overexpressed in E. *coli. Protein Expr Purif*. 2017, 132:138-142.

Lee SY, Giladi M, Bohbot H, Hiller R, Chung KY and **Khananshvili D** (2016) Structure-dynamic basis of splicing dependent regulation in tissue-specific variants of the sodium-calcium exchanger (NCX1), *FASEB J* 30:1356-1366.

Tal I, Kozlovsky T, Brisker D, Giladi M and **Khananshvili D** (2016) Kinetic and equilibrium properties of regulatory Ca2+-binding domains in sodium-calcium exchangers 2 and 3. *Cell Calcium* 59:181-188.

Refaeli B, Giladi M, Hiller R and **Khananshvili D** (2016) Structure-based engineering of lithium transporting capacity in the archaeal sodium-calcium exchanger (NCX_Mj) *Biochemistry* 55:1673-1676.

Giladi M, Almagor L, van Dijk L, Hiller R, Man P, Forest E and **Khananshvili D** (2016) Asymmetric preorganisation of inverted pair residues in the sodium-calcium exchanger. *Scientific Reports*, 16:(20753)1-13.

Giladi M, Lee SY, Hiller R, Chung KY, and **Khananshvili D** (2015) Structure-dynamic determinants governing a mode of regulatory response and propagation of allosteric signal in splice variants of Na+/Ca2+ exchange (NCX) Proteins, *Biochem J* 465:489–501.

Marinelli F, Almagor L, Hiller R, Giladi M, **Khananshvili D***, and Faraldo-Gómez JD. Sodium recognition by the Na^+/Ca^{2+} exchanger in the outward-facing conformation. (*Corresponding Author). *Proc Natl Acad Sci USA*, 2014, doi:10.1073/pnas.111:E5354-62.

Giladi M, Lee S-Y, Hiller R, Chung K-Y, and **Khananshvili, D**. Structure-dynamic determinants governing a mode of regulatory response and propagation of allosteric signal in splice variants of Na^+/Ca^{2+} exchange (NCX) proteins. *Biochem J*, doi:10.1042/BJ20141036

Almagor L, Giladi M, van Dijk L, Buki T, Hiller R, and **Khananshvili D.** Functional asymmetry of bidirectional ca^{2+}-movements in an archaeal sodium-calcium exchanger (NCX_Mj). *Cell Calcium* 2014, 56:276-284.

Giladi M, Michaely L, Almagor A, Bar-On D, Buki T, Ashery U**, Khananshvili**, Hirsch JA. The C2B domain is the primary Ca^{2+} sensor in DOC2B: A structural and functional analysis. *J Mol Biol,* 2013, 425:4629–4641.

Giladi M, Hiller R, Hirsch JA, **Khananshvili D**. Population shift underlies Ca^{2+}-induced regulatory transitions in the sodium-calcium exchanger (NCX). *J Biol Chem*, 2013, 288:23141-23149.

Giladi, M. and **Khananshvili, D**. Molecular determinants of allosteric regulation in NCX proteins. *Adv Exp Med and Biol*, 2013, 961:35-48**.**

Khananshvili D, Binah O, Attali B. The Ca^{2+}-activated K^+ channel IKCa/SK4: a critical new player in human embryonic cardiac pacemaker. *Proc Natl Acad Sci USA,* 2013, 110:1685-1694.

Reviews

Khananshvili D. How a helix imposes palmitoylation of a membrane protein: What one can learn from NCX. *J Biol Chem*. 2017, 292:10753-10754.

Giladi M, Shor R, Lisnyansky M, **Khananshvili D.** Structure-functional basis of ion transport in Sodium-Calcium Exchanger (NCX) proteins. *Int J Mol Sci*. 2016, 17(11).

Giladi M, Tal I, and **Khananshvili D** (2016) Structural Features of Ion Transport and Allosteric Regulation in Sodium-Calcium Exchanger (NCX) Proteins. *Frontiers of Physiology*, 7:(30)1-13.

Khananshvili D (2016) Long-range allosteric regulation of pumps and transporters: What can we learn from mammalian NCX antiporters, *Advances in Biochemistry in Health and Disease*, 14:93-115.

Khananshvili D (2014) Sodium-Calcium Exchangers (NCX): Molecular Hallmarks Underlying the Tissue-specific and Systemic Functions, *Plügers Arch* 466:43–60

Khananshvili, D. Sodium-Calcium Exchangers (NCX): Molecular Hallmarks Underlying Tissue-

Specific and Systemic Functions, *Pflügers Arch* (in press)

Khananshvili, D. SLC8 gene family of sodium-calcium exchangers (NCX): Structure, function and regulation in health and disease**.** *Mol Asp Med* 34:220-35, 2013.

Giladi, M. and **Khananshvili, D**. (2013) Molecular determinants of allosteric regulation in NCX proteins. *Adv Exp Med Biol* 961:35-48.

Boyman L, GSB Williams, **Khananshvili D**, Sekler I, WJ Lederer. NCLX: The mitochondrial sodium calcium exchanger. *J Mol Cell Cardiology* 2013, 59:205-213.

Grants

2013-2017 Fields Center of Molecular Cardiology

2014-2018 Israeli Science Foundation

Prof. Jonathan Leor, M.D.

Neufeld Cardiac Research Institute, Tel Aviv University; Tamman Cardiovascular Institute, Sheba Medical Center; Sheba Center of Regenerative Medicine, Stem Cells and Tissue Engineering

TEL AVIV UNIVERSITY

Email: leorj@post.tau.ac.il

Cardiovascular Regenerative Medicine and Targeting of Inflammation and Fibrosis

Positions

Professor of Cardiology, Sackler Faculty of Medicine

Director, Neufeld Cardiac Research Institute, Tel Aviv University

Director, Tamman Cardiovascular Research Institute, Sheba Medical Center

Director, Sheba Center of Regenerative Medicine, Stem Cells and Tissue Engineering

David Halpern Professor of Cellular and Molecular Cardiology

Research

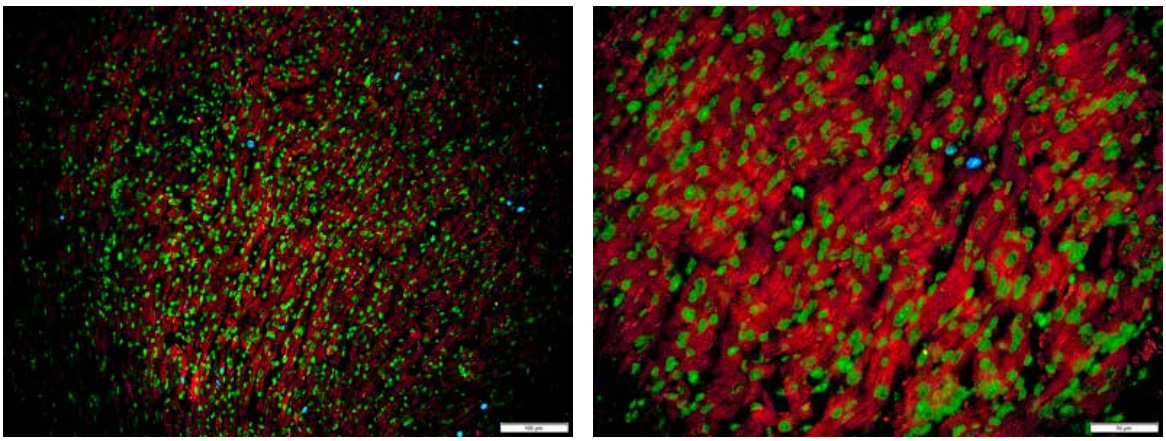
Our lab is focused on translational research. Specifically, we study cardiovascular regenerative medicine, stem cells and tissue engineering. In addition, we aim to target cardiovascular inflammation and fibrosis using novel nano-medicine and a theranostic (therapy + diagnosis) approach. We use a combination of gene profiling, new biomaterials, liposomes, tissue engineering, physiological testing, and molecular imaging technologies, to understand heart cell biology in vitro and in vivo. Particularly, we work on the development of novel nano-therapies for cardiovascular disease.

Publications

Palevski D, Levin-Kotler LP, Kain D, Naftali-Shani N, Landa N, Ben-Mordechai T, Konfino T, Holbova R, Molotski N, Rosin-Arbesfeld R, Lang RA and **Leor J**. Loss of Macrophage Wnt Secretion Improves Remodeling and Function After Myocardial Infarction in Mice. *J Am Heart Assoc*. 2017;6.

Ben-Mordechai T, Kain D, Holbova R, Landa N, Levin LP, Elron-Gross I, Glucksam-Galnoy Y, Feinberg MS, Margalit R and Leor J. Targeting and modulating infarct macrophages with hemin formulated in designed lipid-based particles improves cardiac remodeling and function. *J Control Release*. 2017, 257:21-31..

Zager Y, Kain D, Landa N, **Leor J** and Maor E. Optimization of Irreversible Electroporation Protocols for In-vivo Myocardial Decellularization. *PLoS One*. 2016;11:e0165475.



Myocardial regeneration in a neonatal heart of a mouse, 3 days after apical resection. We used the heart of a newborn mouse to study the mechanism of myocardial regeneration and repair. The regenerating myocardium is characterized by cardiomyocyte (cardiac actin, red) dedifferentiation, and proliferation. Phospho-histone 3 immunostaining detects dividing nuclei (blue) and mitotic activity. Nuclei are stained green with DAPI

Roichman A, Kanfi Y, Glazz R, Naiman S, Amit U, Landa N, Tinman S, Stein I, Pikarsky E, **Leor J** and Cohen HY. SIRT6 Overexpression Improves Various Aspects of Mouse Healthspan. *J Gerontol A Biol Sci Med Sci*. 2016.

Madonna R, Van Laake LW, Davidson SM, Engel FB, Hausenloy DJ, Lecour S, **Leor J**, Perrino C, Schulz R, Ytrehus K, Landmesser U, Mummery CL, Janssens S, Willerson J, Eschenhagen T, Ferdinandy P and Sluijter JP. Position Paper of the European Society of Cardiology Working Group Cellular Biology of the Heart: cell-based therapies for myocardial repair and regeneration in ischemic heart disease and heart failure. *Eur Heart J*. 2016;37:1789-98.

Leor J, Palevski D, Amit U and Konfino T. Macrophages and regeneration: Lessons from the heart. *Semin Cell Dev Biol*. 2016;58:26-33.

Katz A, Maor E, **Leor J** and Klempfner R. Addition of beta-blockers to digoxin is associated with improved 1- and 10-year survival of patients hospitalized due to decompensated heart failure. *Int J Cardiol*. 2016;221:198-204.

Baabur-Cohen H, Vossen LI, Kruger HR, Eldar-Boock A, Yeini E, Landa-Rouben N, Tiram G, Wedepohl S, Markovsky E, **Leor J**, Calderon M and Satchi-Fainaro R. In vivo comparative study of distinct polymeric architectures bearing a combination of paclitaxel and doxorubicin at a synergistic ratio. *J Control Release*. 2016.

Roichman A, Kanfi Y, Glazz R, Naiman S, Amit U, Landa N, Tinman S, Stein I, Pikarsky E, **Leor J** and Cohen HY. SIRT6 Overexpression Improves Various Aspects of Mouse Healthspan. *J Gerontol A Biol Sci Med Sci*. 2016.

Madonna R, Van Laake LW, Davidson SM, Engel FB, Hausenloy DJ, Lecour S, **Leor J**, Perrino C, Schulz R, Ytrehus K, Landmesser U, Mummery CL, Janssens S, Willerson J, Eschenhagen T, Ferdinandy P and Sluijter JP. Position Paper of the European Society of Cardiology Working Group Cellular Biology of the Heart: cell-based therapies for myocardial repair and regeneration in ischemic heart disease and heart failure. *Eur Heart J*. 2016;37:1789-98.

Leor J, Palevski D, Amit U and Konfino T. Macrophages and regeneration: Lessons from the heart. *Semin Cell Dev Biol*. 2016.

Katz A, Maor E, **Leor J** and Klempfner R. Addition of beta-blockers to digoxin is associated with improved 1- and 10-year survival of patients hospitalized due to decompensated heart failure. *Int J Cardiol*. 2016;221:198-204.

Kain D, Amit U, Yagil C, Landa N, Naftali-Shani N, Molotski N, Aviv V, Feinberg MS, Goitein O, Kushnir T, Konen E, Epstein FH, Yagil Y and **Leor J**. Macrophages dictate the progression and manifestation of hypertensive heart disease. *Int J Cardiol*. 2016;203:381-95.

Baabur-Cohen H, Vossen LI, Kruger HR, Eldar-Boock A, Yeini E, Landa-Rouben N, Tiram G, Wedepohl S, Markovsky E, **Leor J**, Calderon M and Satchi-Fainaro R. In vivo comparative study of distinct polymeric architectures bearing a combination of paclitaxel and doxorubicin at a synergistic ratio. *J Control Release*. 2016.

Scomparin A, Salmaso S, Eldar-Boock A, Ben-Shushan D, Ferber S, Tiram G, Shmeeda H, Landa-Rouben N, **Leor J,** Caliceti P, Gabizon A and Satchi-Fainaro R. A comparative study of folate receptor-targeted doxorubicin delivery systems: dosing regimens and therapeutic index. *J Control Release*. 2015;208:106-20.

Konfino T, Landa N, Ben-Mordechai T and **Leor J**. The type of injury dictates the mode of repair in neonatal and adult heart. *J Am Heart Assoc*. 2015;4:e001320.

D'Uva G, Aharonov A, Lauriola M, Kain D, Yahalom-Ronen Y, Carvalho S, Weisinger K, Bassat E, Rajchman D, Yifa O, Lysenko M, Konfino T, Hegesh J, Brenner O, Neeman M, Yarden Y, **Leor J,** Sarig R, Harvey RP and Tzahor E. ERBB2 triggers mammalian heart regeneration by promoting cardiomyocyte dedifferentiation and proliferation. *Nat Cell Biol*. 2015;17:627-38.

Ben-Mordechai T, Palevski D, Glucksam-Galnoy Y, Elron-Gross I, Margalit R and **Leor J.** Targeting macrophage subsets for infarct repair. *J Cardiovasc Pharmacol Ther*. 2015;20:36-51.

Sadek HA, Martin JF, Takeuchi JK, **Leor J**, Nie Y, Giacca M and Lee RT. Multi-investigator letter on reproducibility of neonatal heart regeneration following apical resection. *Stem Cell Reports*. 2014;3:1.

Perricone C, Rinkevich S, Blank M, Landa-Rouben N, Alessandri C, Conti F, **Leor J,** Shoenfeld Y and Vatesini G. The autoimmune side of rheumatic fever. *Isr Med Assoc J*. 2014;16:654-5.

Frey N, Linke A, Suselbeck T, Muller-Ehmsen J, Vermeersch P, Schoors D, Rosenberg M, Bea F, Tuvia S and **Leor J**. Intracoronary delivery of injectable bioabsorbable scaffold (IK-5001) to treat left ventricular remodeling after ST-elevation myocardial infarction: a first-in-man study. *Circ Cardiovasc Interv*. 2014;7:806-12.

Rinkevich-Shop S, Landa-Rouben N, Epstein FH, Holbova R, Feinberg MS, Goitein O, Kushnir T, Konen E and **Leor J**. Injectable collagen implant improves survival, cardiac remodeling, and function in the early period after myocarditis in rats. *J Cardiovasc Pharmacol Ther*. 2014;19:470-80.

Rinkevich-Shop S, Konen E, Kushnir T, Epstein FH, Landa-Rouben N, Goitein O, Ben Mordechai T, Feinberg MS, Afek A and **Leor J**. Non-invasive assessment of experimental autoimmune myocarditis in rats using a 3 T clinical MRI scanner. *Eur Heart J Cardiovasc Imaging*. 2013;14:1069-79.

Overgaard CB, Dzavik V, Buller CE, Liu L, Banasiak W, Devlin G, Maggioni AP, **Leor J**, Burton JR, Reis G, Ruzyllo W, Forman SA, Lamas GA, Hochman JS and Investigators OAT. Percutaneous revascularization and long term clinical outcomes of diabetic patients randomized in the Occluded Artery Trial (OAT). *Int J Cardiol*. 2013;168:2416-22.

Naftali-Shani N, Itzhaki-Alfia A, Landa-Rouben N, Kain D, Holbova R, Adutler-Lieber S, Molotski N, Asher E, Grupper A, Millet E, Tessone A, Winkler E, Kastrup J, Feinberg MS, Zipori D, Pevsner-Fischer M, Raanani E and **Leor J**. The origin of human mesenchymal stromal cells dictates their reparative properties. *J Am Heart Assoc*. 2013;2:e000253.

Mina Y, Rinkevich-Shop S, Konen E, Goitein O, Kushnir T, Epstein FH, Feinberg MS, **Leor J** and Landa-Rouben N. Mast cell inhibition attenuates myocardial damage, adverse remodeling, and dysfunction during fulminant myocarditis in the rat. *J Cardiovasc Pharmacol Ther*. 2013;18:152-61.

Ben-Mordechai T, Holbova R, Landa-Rouben N, Harel-Adar T, Feinberg MS, Abd Elrahman I, Blum G, Epstein FH, Silman Z, Cohen S and **Leor J**. Macrophage subpopulations are essential for infarct repair with and without stem cell therapy. *J Amer Coll Cardiol*. 2013;62:1890-901.

Adutler-Lieber S, Ben-Mordechai T, Naftali-Shani N, Asher E, Loberman D, Raanani E and **Leor J**. Human macrophage regulation via interaction with cardiac adipose tissue-derived mesenchymal stromal cells. *J Cardiovasc Pharmacol Ther*. 2013;18:78-86.

Grants

2014-2019 Israel Science Foundation, Role of macrophages in myocardial regeneration

Dental Health and Medicine

Dr. Lihi Adler-Abramovich, Ph.D.

Department of Oral Biology
The Goldschleger School of Dental Medicine
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: lihiA@tauex.tau.ac.il
URL: https://en-med.tau.ac.il/profile/lihia

Bioinspired Materials for Nanotechnological Application

Positions

Senior Lecturer, Sackler Faculty of Medicine

Affiliated, TAU Center for Nanoscience and Nanotechnology

Research

Work in our Laboratory of Bioinspired Materials is focused on mimicking self-assembly processes that occur in nature, including biomineralization and the organization of short peptides and amino acids into ordered nanostructures. We are a material science laboratory with an emphasis on organic chemistry and medical-biological applications. The group is developing new organic materials that are used for various applications, such as 3D hydrogels for bone tissue regeneration, which exhibit extraordinary mechanical properties and durability, along with biocompatibility and controlled drugs release. A central technique is the formation of hybrid hydrogels, using two or more different building blocks, resulting in a 3D hydrogel with novel and diverse properties that can be easily fine-tuned. In addition, the laboratory is interested in antimicrobial activity of nanostructures for coatings and incorporation into composite materials for dental medicine application.

Publications

Ghosh, S., **Adler-Abramovich, L.**, Gazit, E., Verma, S. Spacer driven morphological twist in Phe-Phe dipeptide conjugates. *Tetrahedron*; 2013: 69, 2004-2009.

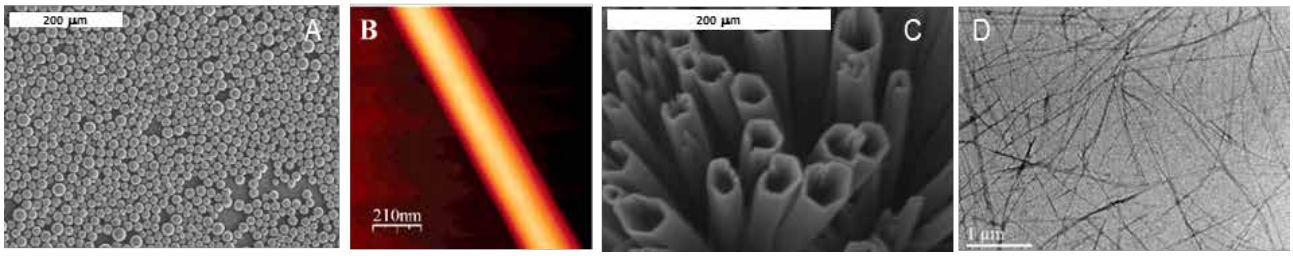
Ischakov, R., **Adler-Abramovich, L.**, Buzhansky, L., Shekhter, T., Gazit, E. Peptide-based hydrogel nanoparticles as effective drug delivery agents. *Bioorg. Med. Chem*.; 2013: 21, 3517-3522.

Kaur, G., **Adler-Abramovich, L.**, Gazit, E., Verma, S. Ultrastructure of metallopeptide-based soft spherical morphologies. *R. Soc. Chem. Adv.*; 2014: 4, 64457-64465.

Azuri, I., **Adler-Abramovich, L.**, Gazit, E., Hod, O., Kronik, L. Why are diphenylalanine-based peptide nanostructures so rigid? Insights from first principles calculations. *J. Am. Chem. Soc.*; 2014: 136, 963-969.

Mason, T.O., Chirgadze, D.Y., Levin, A., **Adler-Abramovich, L.**, Gazit, E., Knowles, T.P.J., Buell, A.K. Expanding the solvent chemical space for self-assembly of dipeptide nanostructures. *ACS Nano.*; 2014: 8, 1243-1253.

Mossou, E., Teixeira, S.C.M., Mitchell, E.P., Mason, S.A., **Adler-Abramovich, L.**, Gazit, E., Forsyth, V.T. The self-assembling zwitterionic form of



Self-Assembled Nano-Structures: (A) Scanning electron microscopy micrograph of peptide nanospheres. **(B)** Atomic force microscopy image of a peptide nanotube. **(C)** Array of ordered vertically aligned peptide nanotubes. **(D)** Transmittance electron microscopy micrograph of 3D hydrogel demonstrating the presence of elongated fibrils.

L-phenylalanine at neutral pH. *Acta Crystallogr., Sect. C.*; 2014: 70, 326-331.

Fichman, G., **Adler-Abramovich, L.**, Manohar, S., Mironi-Harpaz, I., Guterman, T. Seliktar, D., Messersmith, P.B., Gazit, E. Seamless metallic coating and surface adhesion of self-assembled bio-inspired nanostructures based on di-(3, 4-dihydroxy-L-phenylalanine) peptide motif. *ACS Nano*; 2014: 22, 7220-7228.

Fichman, G., Guterman, T., **Adler-Abramovich, L.**, Gazit, E. The use of the calcitonin minimal recognition module for the design of DOPA-containing fibrillar assemblies. *Nanomaterials*; 2014: 4, 726-740.

Levin, A., Mason, T.O. **Adler-Abramovich, L.**, Buell, A.K. Meisl, G., Galvagnion, C.Ostwald's rule of stages governs structural transitions and morphology of dipeptide supramolecular polymers. Nature Commun. 2014; 5, 5219.

Ostrov, N., Fichman, G., **Adler-Abramovich, L.**, Gazit. E. FtsZ Cytoskeletal filaments as a template for metallic nanowire fabrication. *J. Nanosci. Nanotechnol.* 2015; 15, 556-561.

Tao, K., Yoskovitz, E., **Adler-Abramovich, L.**, Gazit, E. Optical property modulation of Fmoc group by pH-dependent self-assembly. *RSC Advances*; 2015: 5, 73914-73918.

Fichman, G., Guterman, T., **Adler-Abramovich, L.**, Gazit, E. Synergetic functional properties of two-component single amino acid-based hydrogels. *CrystEngComm.*; 2015: 17, 8105-8112.

Shaham-Niv, S., **Adler-Abramovich, L.**, Schnaider, L., Gazit E. Extension of the generic amyloid hypothesis to nonproteinaceous metabolite assemblies. *Sci. Adv.*; 2015: 1, e1500137.

Arnon, Z., **Adler-Abramovich, L.**, Levin, A., Gazit E. Solvent-induced self-assembly of highly hydrophobic tetra-and pentaphenylalanine peptides. *Isr. J. Chem.*; 2015: 5, 756-762. 5. Featured in the cover of the issue.

De Luigi, A., Mariani, A., De Paola, M., Re Depaolini, A., Colombo, L., Russo, L., Rondelli, V., Brocca, P., **Adler-Abramovich, L.**, Gazit, E., Del Favero, E., Cantù, L., Salmona. M. Doxycycline hinders phenylalanine fibril assemblies revealing a potential novel therapeutic approach in phenylketonuria. *Sci. Rep.*; 2015: 5

Tao, K., **Adler-Abramovich, L.**, Gazit, E. Controllable Phase Separation by Boc-modified lipophilic acid as a multifunctional extractant. *Sci. Rep.*; 2015: 5, 17509

Pellach M., Atsmon-Raz Y., Simonovsky E., Gottlieb H., Jacoby G., Beck R., **Adler-Abramovich L.**, Miller Y., Gazit E. Spontaneous structural transition in phospholipid-inspired aromatic phosphopeptide nanostructures. *ACS Nano.* 2015; 9: 4085-4095.

Berger, O., **Adler-Abramovich, L.**, Levy-Sakin, M., Grunwald, A. Bachar, M., Buzhansky, L., Mossou, E., Forsyth, T., Ebenstein, Y., Frolow, F., Shimon, L.J.W., Patolsky, F., Gazit, E. Light emitting self-Assembled peptide nucleic acids exhibit both stacking and watson-crick base-pairing. *Nature Nanotechnol.* 2015; 10: 353-360. Selected for the cover of the journal.

Mondal, S.*, **Adler-Abramovich, L.***, Lampel, A., Bram, Y., Lipstman, S., Gazit, E. Formation of functional super-helical assemblies by constrained single heptad repeat. *Nature Commun.*; 2015: 6, 8615. *Both authors contributed equally to the work.

Pellach, M., Mondal, S., Shimon, L., **Adler-Abramovich, L.**, Buzhansky, L., Gazit, E. Molecular Engineering of Self-Assembling Diphenylalanine Analogues Results in the Formation of Distinctive Microstructures. *Chem. Mater.* 2016; 28: 4341–4348.

Fichman, G., Guterman, T., Damron, J., **Adler-Abramovich, L.**, Schmidt, J., Kesselman, E., Shimon, L. J.W., Ramamoorthy, A., Talmon, Y., Gazit, E. Spontaneous structural transition and crystal formation in minimal supramolecular polymer model. Sci. Adv.; 2016: 2, e1500827.

Berger, O., Yoskovitz, E., **Adler-Abramovich, L.**, Gazit, E. Spectral transition in bio-inspired self-assembled peptide nucleic acid photonic crystals. *Adv. Mater*.; 2016: 28, 2195 Selected for the cover of the journal.

Levin, A., Michaels, T.C.T., **Adler-Abramovich, L.**, Mason, T.O., Müller, T., Zhang, B., Mahadevan, L., Gazit, E., Knowles, T. P. J. Elastic instability-mediated actuation by a supra-molecular polymer. *Nat. Phys.*; 2016: 12, 926–930.

Guo, C., Arnon, Z.A., Qi, R., Zhang, Q., **Adler-Abramovich, L.**, Gazit, E., Wei, G. Expanding the Nanoarchitectural Diversity Through Aromatic Di- and Tri-Peptide Coassembly: Nanostructures and Molecular Mechanisms. *ACS nano;* 2016: 10, 8316-8324.

Adler-Abramovich, L., Marco, P., Arnon, Z.A., Creasey, Michaels, T.C.T., Levin, A., Scurr, D.J., Roberts C.J., Knowles, T. P. J., Tendler, S.J.B. Gazit, E. Controlling the Physical Dimensions of Peptide Nanotube by Supramolecular Polymer Co-assembly. *ACS Nano.*; 2016: 10, 7436-7442.

Arnon, Z.A., Vitalis, A., Levin, A., Michaels, T.C.T., Caflisch, A., Knowles, T.P.J., **Adler-Abramovich, L.***, Gazit, E.*. Dynamic microfluidic control of supramolecular peptide self-assembly. *Nat. Commun.*; 2016: 7, 13190. *Both Corresponding authors.

Shekhter-Zahavi, T., Oron-Herman, M., Kostenich, G., Rub, E., Salitra, Y., Buzhansky, L., Orenstein, L., Gazit, E.*, **Adler-Abramovich, L.***. Molecular Engineering of Somatostatin Analogue with Minimal Dipeptide Motif Induces the Formation of Functional Nanoparticles. *ChemNanoMat*; 2016: *Both Corresponding authors.

Schnaider L, Brahmachari S, Schmidt NW, Mensa B, Shaham-Niv S, Bychenko D, **Adler-Abramovich L**, Shimon LJW, Kolusheva S, DeGrado WF, Gazit E. Self-assembling dipeptide antibacterial nanostructures with membrane disrupting activity. *Nat Commun.* 2017;8:1365.

Ghosh M, Halperin-Sternfeld M, Grigoriants I, Lee J, Nam KT, **Adler-Abramovich L**. Arginine-presenting peptide hydrogels decorated with hydroxyapatite as biomimetic scaffolds for bone regeneration. *Biomacromolecules*. 2017, doi: 10.1021/acs.biomac.7b00876.

Halperin-Sternfeld M, Ghosh M, Sevostianov R, Grigoriants I, **Adler-Abramovich L**. Molecular co-assembly as a strategy for synergistic improvement of the mechanical properties of hydrogels. *Chem Commun (Camb)*. 2017;53:9586-9589.

Brahmachari S, Arnon ZA, Frydman-Marom A, Gazit E, **Adler-Abramovich L**. Diphenylalanine as a reductionist model for the mechanistic characterization of β-amyloid modulators. *ACS Nano.* 2017;11:5960-5969.

Mondal S, Varenik M, Bloch DN, Atsmon-Raz Y, Jacoby G, **Adler-Abramovich L**, Shimon LJ, Beck R, Miller Y, Regev O, Gazit E. A minimal length rigid helical peptide motif allows rational design of modular surfactants. *Nat Commun*. 2017;8:14018.

Ben-Nun Y, Fichman G, **Adler-Abramovich L**, Turk B, Gazit E, Blum G. Cathepsin nanofiber substrates as potential agents for targeted drug delivery. *J Control Release*. 2017;257:60-67.

Halperin-Sternfeld M., Ghosh M., Sevostianov R., Grigoriants I. and **Adler-Abramovich L**. Molecular co-assembly as a strategy for synergistic improvement of the mechanical properties of hydrogels. *Chem. Commun.*; 2017, 53, 9586-9589

Ghosh M., Halperin-Sternfeld M., Grigoriants I., Lee J., Tae Nam K. and **Adler-Abramovich L.** Arginine-presenting peptide hydrogels decorated with hydroxyapatite as biomimetic scaffolds for bone regeneration. *Biomacromolecules*; 2017, 18, 3541-3550.

Reviews

Adler-Abramovich, L., Gazit, E. The physical properties of supramolecular peptide assemblies: from building block association to technological applications. *Chem. Soc. Rev.*; 2014: 43, 6881-6893. Selected for the cover of the journal.

Tao, K., Levin, A., **Adler-Abramovich, L.**, Gazit, E. Fmoc-modified amino acids and short peptides: simple bio-inspired building blocks for the fabrication of functional materials. *Chem. Soc. Rev.*; 2016: 45, 3935-3953.

Grants

2016 – 2019	Model system for biomineralization and bone formation in microgravity, Space Program, Ministry of Science, Technology and Space.
2017-2020	Synthesis and characterization of 3D nanostructure for bone tissue regeneration, Israel Science Foundation (ISF) - New-Faculty Equipment Grants.
2017-2021	Biomineralized self-assembled peptide hydrogel scaffolds for bone tissue regeneration, Israel science foundation (ISF) - Individual Research Grants.
2017-2021	Smart bionanomaterials for solar-driven hydrogen production, Israel Science Foundation (ISF) - Research Centers
2017-2022	SNOW-Non woven smart materials, Maagad-Israeli Innovation Authority
2018-2020	Development of dental materials with anti-biofilm properties, Kamin-Israeli Innovation Authority
2018-2021	Developing a platform of peptides nano-structures containing enzymes capable of degrading signal molecules involved in cell to cell communication, Ministry of Agriculture

Prof. Tamar Brosh, Ph.D.

Department of Oral Biology
Goldschleger School of Dental Medicine
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: tbrosh@post.tau.ac.il

Biochemical Aspects of Dental Restorations and Orthodontic Tooth Movement

Positions

Professor, Sackler Faculty of Medicine

Head, Department of Oral Biology

Research

Biomechanical behavior and response to dental treatments are studied in our laboratory and our *in vivo* studies.

Restorative materials, including bonding materials, are tested for performance (e.g., durability and strength). We work on improving their properties by combining nano-tubes with the materials (in cooperation with the Molecular Microbiology and Biotechnology Department). For this, we study their shear strength (Fig. a), diametral-tensile strength and shear bond strength.

Aiming to understand the phenomenon of vertical root fractures, we work on evaluating the influence of various posts materials (used in endodontic treatment) on root-surface strain development by measuring the surface strains with strain gauges.

Regarding orthodontics, we try to understand the behavior and influence of transparent aligners on the movement of teeth *in vivo* (Fig. b).

Publications

Levartovsky S, Levy G, **Brosh T,** Harel N, Ganor Y, Pilo R. Dimensional stability of polyvinyl siloxane impression material reproducing the sulcular area. *Dent Mater J*. 2013; 32:25-31.

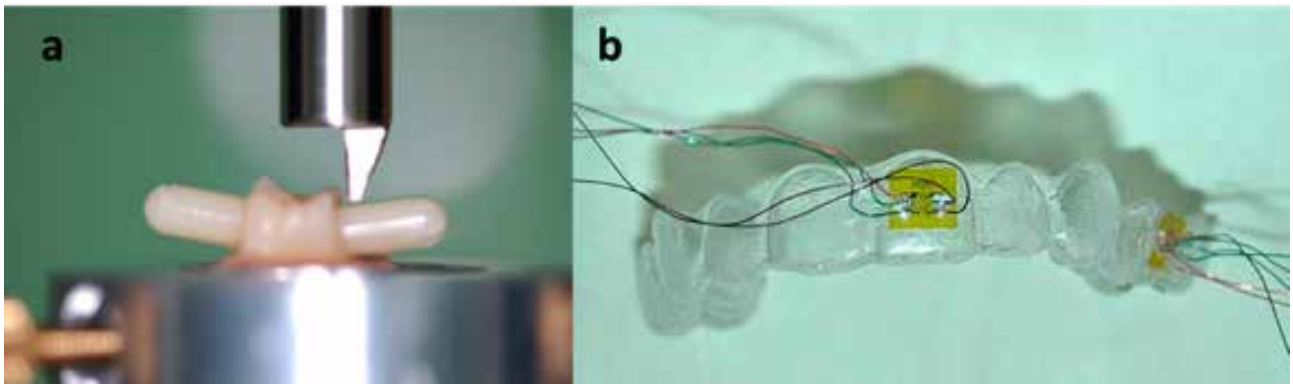
Heller S, **Brosh** T, Kosashvili Y, Velkes S, Burg A, Dudkiewicz I. Locking versus standard screw fixation for acetabular cups: is there a difference? *Arch Orthop Trauma Surg*. 2013; 133:701-5.

Herman A, Avivi E, **Brosh T,** Schwartz I, Liberman B. Biomechanical properties of bone treated by magnetic resonance-guided focused ultrasound — an in vivo porcine model study. *Bone*. 2013; 92-97.

Levartovsky S, Levy G, **Brosh T,** Harel N, Ganor Y, Pilo R. The effect of one-step vs. two-step impression techniques on long-term accuracy and dimensional stability when the finish line is within the gingival sulcular area. *J Prosthodont*. 2014; 23:124-33.

Brosh T, Yekaterina BE, Pilo R, Shpack N, Geron S. Can cone beam CT predict the hardness of interradicular cortical bone? *Head & Face Medicine,* 2014, 15;10:12.

Brosh T, Rozitsky D, Geron S, Pilo R.Tensile mechanical properties of swine cortical mandibular bone. *PLoS One*. 2014;9.



a. Shear bond test experiment. b. Transparent aligner equipped with strain gauges

Shpack N, **Brosh T**, Mazor Y, Shapinko Y, Davidovitch M, Sarig R, Reimann S, Bourauel C, Vardimon AD.Long- and short-term effects of headgear traction with and without the maxillary second molars. *Am J Orthod Dentofacial Orthop*. 2014;146:467-76.

Dolkart O, Liron T, Chechik O, Somjen D, **Brosh T**, Maman E, Gabet Y.Statins enhance rotator cuff healing by stimulating the COX2/PGE2/EP4 pathway: an in vivo and in vitro study. *Am J Sports Med*. 2014 ;42:2869-76.

Dolkart O, Chechik O, Zarfati Y, **Brosh T**, Alhajajra F, Maman E. A single dose of platelet-rich plasma improves the organization and strength of a surgically repaired rotator cuff tendon in rats. *Arch Orthop Trauma Surg*. 2014;134:1271-7.

Amar E, Snir N, Sher O, **Brosh T**, Khashan M, Salai M, Dolkart O.Platelet-rich plasma did not improve early healing of medial collateral ligament in rats. *Arch Orthop Trauma Surg*. 2015 135:1571-7.

Pilo R, Metzger Z, **Brosh T**. Strain distribution in root surface dentin of maxillary central incisors during lateral compaction. *PLoS One*. 2016;11.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Hershkovitz I, **Brosh T**.The impact velocity and bone fracture pattern: Forensic erspective. *Forensic Sci Int*. 2016, 7;266:54-62.

Masarwi M, Gabet Y, Dolkart O, **Brosh T**, Shamir R, Phillip M, Gat-Yablonski G. Skeletal effect of casein and whey protein intake during catch-up growth in young male Sprague-Dawley rats. *Br J Nutr.* 2016;116:59-69.

Pilo R, **Brosh T**, Geron V, Levartovsky S, Eliades G . Effect of silane reaction time on the repair of a nanofilled composite using tribochemical treatment. *J Adhes Dent*. 2016;18:125-34.

Maman E, Yehuda C, Pritsch T, Morag G, **Brosh T**, Sharfman Z, Dolkart O. Detrimental effect of repeated and single subacromial corticosteroid injections on the intact and injured rotator cuff: a biomechanical and imaging study in rats. *Am J Sports Med*. 2016 44:177-82.

Dolkart O, Chechik O, Bivas A, Brosh T, Drexler M, Weinerman Z, Maman E. Subacromial corticosteroid injections transiently decrease suture anchor pullout strength: biomechanical studies in rats. *J Shoulder Elbow Surg* 2017.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, Hershkovitz I. The influence of impact direction and axial loading on the bone fracture pattern. *Forensic Sci Int* 2017; 277:197-206.

Alon D, Stein GY, Hadas-Golan V, Tau L, Brosh T, Turner D. Immunogenicity of Sci-B-Vac (a Third-Generation Hepatitis B Vaccine) in HIV-Positive Adults. *Isr Med Assoc J* 2017; 19:143-146.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, Hershkovitz I. The effect of impact tool geometry and soft material covering on long bone fracture patterns in children. *Int J Legal Med* 2017; 131:1011-1021.

Pilo R, Metzger Z, Brosh T. Effect of root morphology on the susceptibility of endodontically treated teeth to vertical root fracture: An ex-vivo model. *J Mech Behav Biomed Mater* 2017; 69:267-274.

Gigi R, Dolkart O, Sharfman ZT, Goldstein Y, Brosh T, Rath E, Maman E, Chechik O. Biomechanical evaluation of two arthroscopic techniques for biceps tenodesis: triple loop suture versus simple suture. *J Shoulder Elbow Surg* 2017; 26:165-169.

Prof. Ilana Eli, D.M.D.

Department of Oral Biology
Goldschleger School of Dental Medicine
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: elilana@post.tau.ac.il

Behavioral Sciences in Dentistry

Positions

Professor, Sackler Faculty of Medicine

Research

Our group specializes particularly in the field of behavioral sciences in dentistry including clinical hypnosis, oro-related behavioral dysfunctions, psycho physiological aspects of acute and chronic pain, and stress in clinical and other settings.

Research topics:

1. Stress, pain and behavior in dental care
2. Oro-related behavioral dysfunctions (dental fear, anxiety and phobia, excessive gagging reflex)
3. Chronic orofacial pain and TMD
4. Psychosocial factors in pain
5. Sexual and oral functioning

Publications

E. Elran, G. Bronner , N. Uziel, **I. Eli**, ND Kitrey, G. Raviv. Impact of vaginal penetration difficulties on sexual function of women and their male partners. *The European Journal of Contraception and Reproductive Health Care,* 19:352-358*,* 2014

I. Eli. Stress and patients' ability to comply with or adhere to treatment regimens. *J Oral Facial Pain Headache*, 28, 297, 2014.

G. Bronner, N. Kitrey, N. Uziel, **I. Eli**, G. Raviv, J. Ramon, E. Elran. Correlation between premature ejaculation and female vaginal penetration difficulties. *Int J Impot Res,* 7:152-156, 2015.

I. Eli. Hypnosis as a treatment modality for chronic pain management: Level of evidence. *J Oral Facial Pain Headache*, 30, 85-86, 2016.

A. Emodi-Perlman, I**. Eli**, P. Friedman-Rubin, T. Greenberg, S. Heiliczer, E. Winocur. Occupation as potential factor for temporomandibular disorders, bruxism and cervical pain- a controlled comparative study. *Eur J Oral Sci*, 2016 (in press).

Reiter S, **Eli I**, Friedman-Rubin P, Emodi-Perlman A, Ziv-Baran T, Winocur E. Comparing Axis II scores according to the RDC/TMD and DC/TMD in Israeli patients. *J Oral Facial Pain Headache*. 2017;31:323–330.

Friedman Rubin P, **Eli I**, Greenbaum T, Shapira K, Emodi-Perelman A, Winocur E. Potential orofacial hazards of resistance training: A controlled comparative study*. Cranio*. 2017, 1-8.

Chapters

I. Eli and R. Gatchel. Psychosocial and Behavioral Modes of Orofacial Pain. In: *Orofacial Pain*, B. Sessle (Ed.), IASP Press, Seattle, USA 251-268

Dr. Rachel Sarig, Ph.D., D.M.D.

Department of Orthodontic & Department of Oral Biology, Maurice and Gabriela Goldschleger School of Dental Medicine, Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: sarigrac@post.tau.ac.il

Facial and Dental Anthropology: Evolutionary Aspects in Physiological and Pathological Processes in Human Dentition

Position

Lecturer, Maurice and Gabriela Goldschleger School of Dental Medicine, Sackler Faculty of Medicine

Research

Many of the current oral diseases and malformations have their roots in our evolutionary history. Knowing the evolutionary processes that led to the current shape and size of our skull and mandible may greatly bear on our understanding of phenomena such as malocclusions (i.e., crowding, rotation, overbite), dental malformations (i.e. impaction, missing and supernumerary teeth) and oral diseases (caries, attrition, periodontal diseases). Treatment strategy should take into consideration evolutionary reasoning involved in shaping our face and jaws, ignoring them may end, in the long run, in treatments' failure.

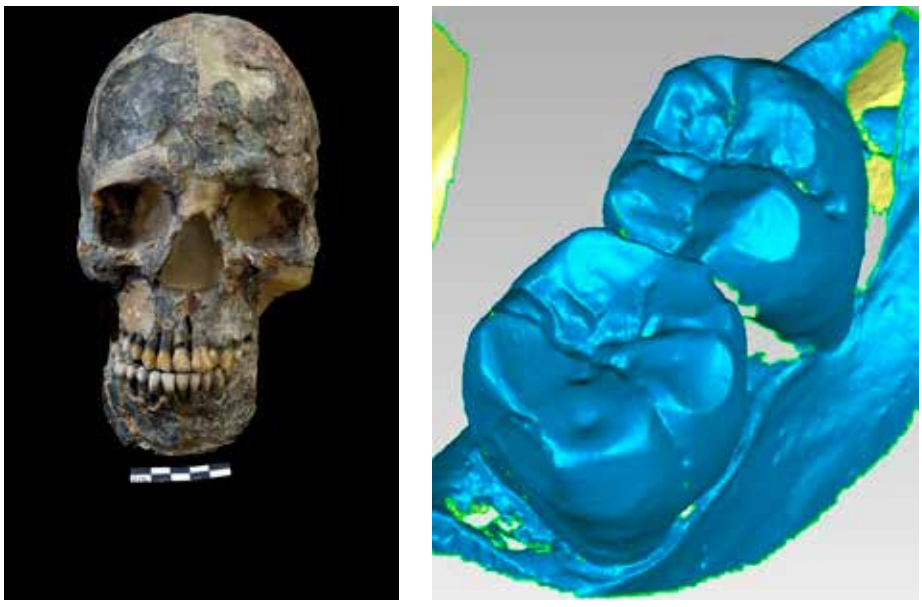
Understanding the evolutionary constrains that have acted through time on our masticatory system may help us planning and establishing better treatment strategies. Long-term evolutionary processes such as decrease in jaws and teeth size, higher prevalence of impacted teeth and the loss of teeth in the arch, are all important factors that should be considered.

Publications

R. Sarig, N. Lianopoulos, I. Hershkovitz, AD. Vardimon. The arrangement of the interproximal interface in the human permanent dentition. Clinical Oral Investigation, 17, 731–738, 2013.

J. Abbas, K. Hamoud, H. May, N. Peled, **R. Sarig**, D. Stein, D. Alperovitch-Najenson, I. Hershkovitz. Socioeconomic and physical characteristics of degenerative lumbar spinal stenosis individuals. Spine, 38, 554-556, 2013.

N. Shpack, RG. Bar-Ness, D. Gazit, **R. Sarig**, AD. Vardimon. Efficacy of three hygienic protocols in reducing biofilm adherence to removable



Malocclusion of developmental origin already present in early anatomically modern humans (AMH) (the present case being the oldest known case, dated to ca. 100,000 years) (A). Morphological evaluation of molar teeth using 3D scanning and geometric morphometric analysis (B).

thermoplastic appliance. Angle Orthodontics, 84, 161-170, 2013.

R. Sarig, V. Slon, J. Abbas, H. May, N. Shpack, AD. Vardimon, I. Hershkovitz. Malocclusion in early anatomically modern human: a reflection on the etiology of modern dental misalignment. PloS One, 8, e80771, 2013.

V. Slon, **R. Sarig**, I. Hershkovitz, H. Khalaily, I. Milevski. The plastered skulls from the Pre-Pottery Neolithic B site of Yiftahel (Israel) – A computed tomography-based analysis. PloS One, 9, e89242, 2014.

R. Sarig, AM. Tillier. Reconstructing cultural behavior from dental wear studies: Is para-facets analysis approach scientifically valid? HOMO-Journal of Comparative Human Biology, 65, 181-186. 2014.

R. Sarig, I. Hershkovitz ,N. Shvalb, T. Sella-Tunis, H. May, AD. Vardimon. Proximal Attrition Facet: morphometric, demographic and aging characteristic. European Journal of Oral Sciences. 122, 271-278, 2014

Hershkovitz, I., Spigelman, M., **Sarig, R**., Lim, D. S., Lee, I. S., Oh, C. S., May, H., Boaretto, E., Kim, Y.S., Lee, S.D., Peled, N., Kim, M.J., Toledano, T., Bar-Gal G.K., Shin, D. H. A possible case of cherubism in a 17th-Century Korean mummy. PloS One, 9, e102441, 2014

Shpack, N., Brosh, T., Mazor, Y., Shapinko, Y., Davidovitch, M., **Sarig, R**., Reimann, S., Bourauel, C., Vardimon, A. D. Long-and short-term effects of headgear traction with and without the maxillary second molars. American Journal of Orthodontics and Dentofacial Orthopedics, 146, 467-476,2014

Levartovsky, S., Matalon, S., **Sarig, R**., Baruch, O., & Winocur, E. The association between dental wear and reduced vertical dimension of the face: a morphologic study on human skulls. Archives of Oral Biology, 2014.

Sarig, R., Vardimon, A.D., Sussan, S., hhhBenny, L., Sarne, O., Hershkovitz I., Nir, S. Pattern of maxillary and mandibular proximal enamel thickness at the contact area of the permanent dentition from first molar to first molar. American Journal of Orthodontics and Dentofacial Orthopedics 147, 435-444. 2014.

Sarig, R., Hershkovitz I., Nir, S., May H., Vardimon, A.D. Rate and pattern of Inter-Proximal Dental Attrition. European Journal of Oral Sciences 123, 276-281. 2015.

Hardy K., Radini A., Buckley., **Sarig R.,** Copeland L., Gopher A., Barkai R. Dental calculus reveals potential respiratory irritants and ingestion of essential plant-based nutrients at Lower Palaeolithic Qesem Cave Israel. Quaternary International, 398, 129-135. 2015.

Hershkovitz, I., Weber, G.W., Fornai, C., Gopher, A., Barkai, R., Slon, V., Quam, R., Gabet, Y., **Sarig R.** New Middle Pleistocene dental remains from Qesem Cave (Israel) Quaternary International, 398, 148-158. 2016.

Sarig, R., Gopher, A., Barkai, R., Rosell, J., Blasco, R., Weber, G.W., Fornai, C., Sella-Tunis, T., Hershkovitz, I. How did the qesem cave people use their teeth? Analysis of dental wear patterns. Quaternary International, 398, 136-14. 2016.

Weber, G.W. Fornai, C., Gopher, A., Barkai, R., **Sarig, R.**, Hershkovitz, I. The Qesem cave hominin material (Part 1): A morphometric analysis of the mandibular premolars and molar. Quaternary International, 398, 159-174. 2016.

Fornai, C., Benazzi, S., Gopher, A., Barkai, R., **Sarig, R.,** Bookstein, F. L., Hershkovitz, I., Weber, G. W. The Qesem Cave hominin material (part 2): A morphometric analysis of dm 2-QC2 deciduous lower second molar. Quaternary International, 398, 175-189.2016 .

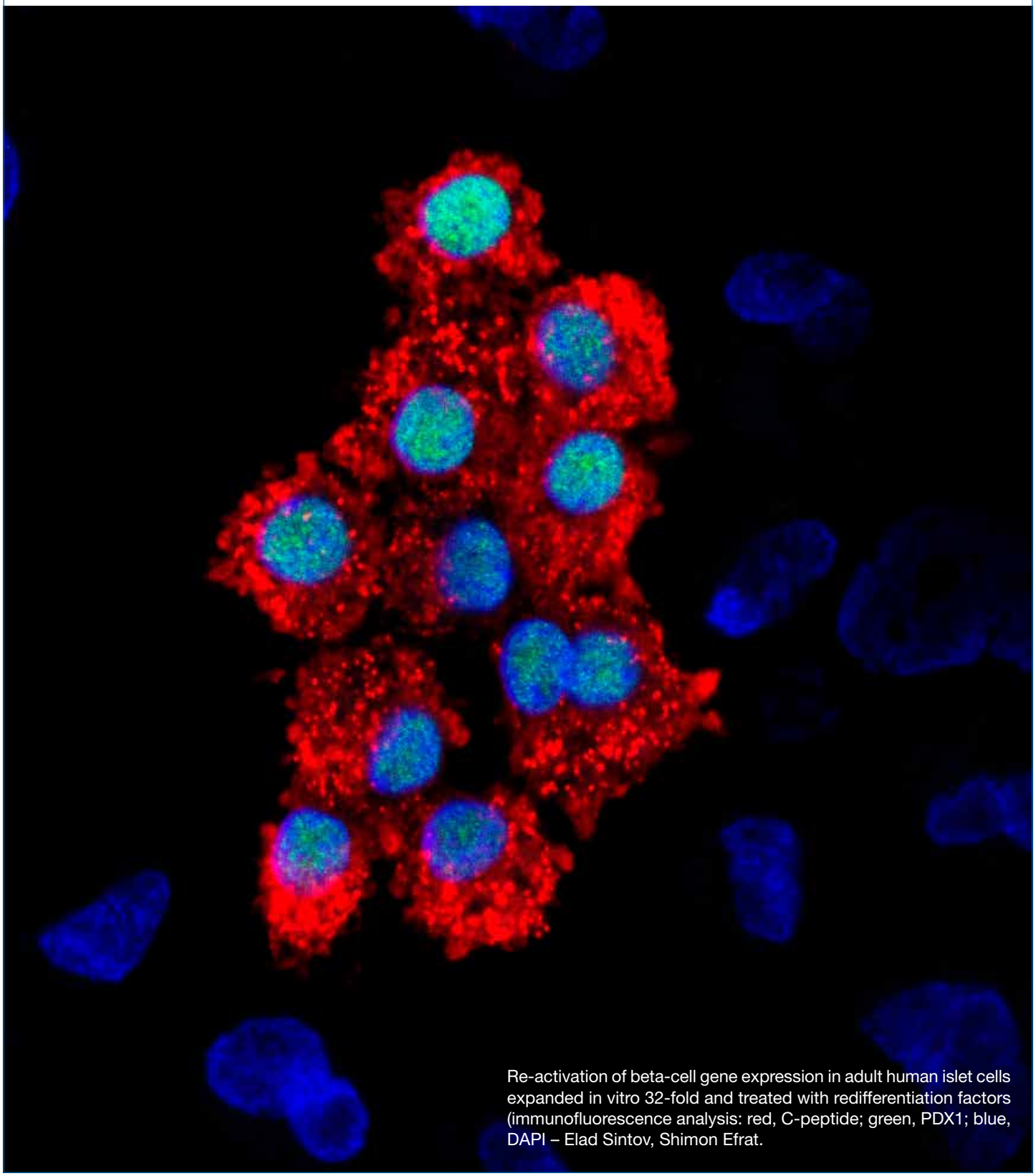
Sarig, R., Tillier, A. M. Dental wear patterns in early modern humans from Skhul and Qafzeh: A response to Luca Fiorenza and Ottmar Kullmer. HOMO-Journal of Comparative Human Biology, 67, 85-87. 2016.

Tunis TS, **Sarig R**, Cohen H, Medlej B, Peled N, May H. Sex estimation using computed tomography of the mandible. Int J Legal Med. 2017, doi: 10.1007/s00414-017-1554-1

Grants

2016-2019 Israel Science Foundation

Diabetes, Metabolic and Endocrine Diseases



Re-activation of beta-cell gene expression in adult human islet cells expanded in vitro 32-fold and treated with redifferentiation factors (immunofluorescence analysis: red, C-peptide; green, PDX1; blue, DAPI – Elad Sintov, Shimon Efrat.

Prof. Shimon Efrat, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: sefrat@post.tau.ac.il

Cell Replacement Therapy for Diabetes

Position

Professor, Sackler Faculty of Medicine

Chair, Department of Human Molecular Genetics and Biochemistry

Nancy Gluck Regan Chair in Juvenile Diabetes

Research

Our research focuses on the development of a cell replacement therapy for diabetes, in which the insulin-producing pancreatic beta cells are destroyed or malfunction.

Our approaches for generation of an abundant source of cells for transplantation include expansion and differentiation in tissue culture of beta cells from human organ donors, as well as differentiation of human stem cells into insulin-producing cells.

Publications

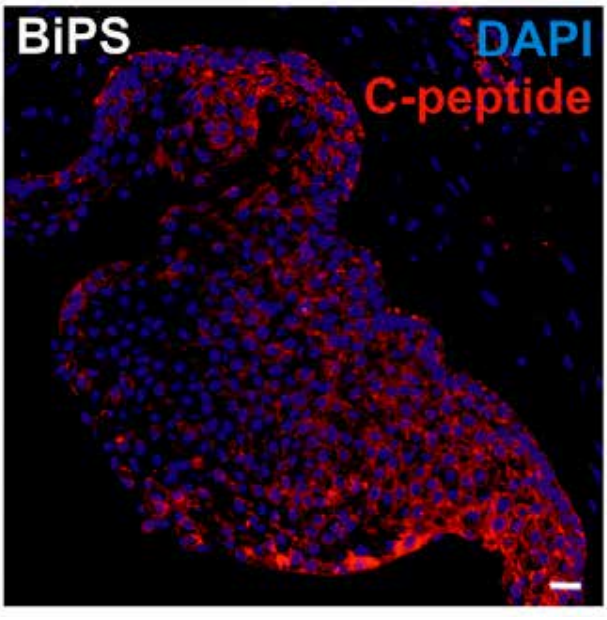
Lenz A, Toren-Haritan G, **Efrat S**. (2014) Redifferentiation of Adult Human β Cells Expanded In Vitro by Inhibition of the WNT Pathway. *PLoS One*. 9:e112914.

Nathan G, Kredo-Russo S, Geiger T, Lenz A, Kaspi H, Hornstein E, **Efrat S** (2015) miR-375 promotes redifferentiation of adult human β cells expanded in vitro. *PLoS One* 10: e0122108.

Sintov E, Nathan G, Knoller S, Pasmanik-Chor M, Russ HA, **Efrat S** (2015) Inhibition of ZEB1 expression induces redifferentiation of adult human β cells expanded in vitro. *Sci Rep* 5:13024.

Toren-Haritan G, **Efrat S** (2015) TGFβ pathway inhibition redifferentiates human pancreatic islet β cells expanded in vitro. *PLoS One* 10: e0139168.

Friedman-Mazursky O, Elkon R, Efrat S (2016) Redifferentiation of human islet β cells expanded in vitro by inhibition of ARX. *Sci Rep* 6:20698.



Pluripotent stem cells derived from human beta cells can be greatly multiplied in tissue culture and then induced to redifferentiate into insulin-producing cells. Red, staining for insulin; blue, cell nuclei.

Thurner M, Shenhav L, Wesolowska-Andersen A, Bennett AJ, Barrett A, Gloyn AL, McCarthy MI, Beer NL, **Efrat S**. (2017) Genes associated with pancreas development and function maintain open chromatin in iPSCs generated from human pancreatic beta cells. *Stem Cell Reports*. pii: S2213-6711(17)30427-7.

Reviews

Efrat S (2013) Recent progress in generation of human surrogate beta cells. *Curr Opin Endocrinol Diab Obes* 20:259-264.

Bar Y, Efrat S (2014) The Notch pathway in beta-cell growth and differentiation. In The Pancreatic Beta Cell, Litwack G (ed.), Vitamins and Hormones vol. 95, Academic Press/Elsevier, pp. 391-405.

Efrat S (2016) Mechanisms of adult human β-cell in-vitro dedifferentiation and redifferentiation. *Diabetes Obes Metab* (in press).

Grants

2012-2017	Innovative Medicines Initiative (IMI)
2013-2017	Israel Science Foundation (ISF)
2015-2017	Kadimastem Ltd.
2015-2018	Rosetrees Trust

Prof. Koret Hirschberg, Ph.D.

Department of Pathology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: koty@post.tau.ac.il
URL: http://www2.tau.ac.il/Person/medicine/researcher.asp?id=agjjgihh
dl.dropbox.com/u/236135/Site/Home.html

Intracellular Membrane Trafficking

Position

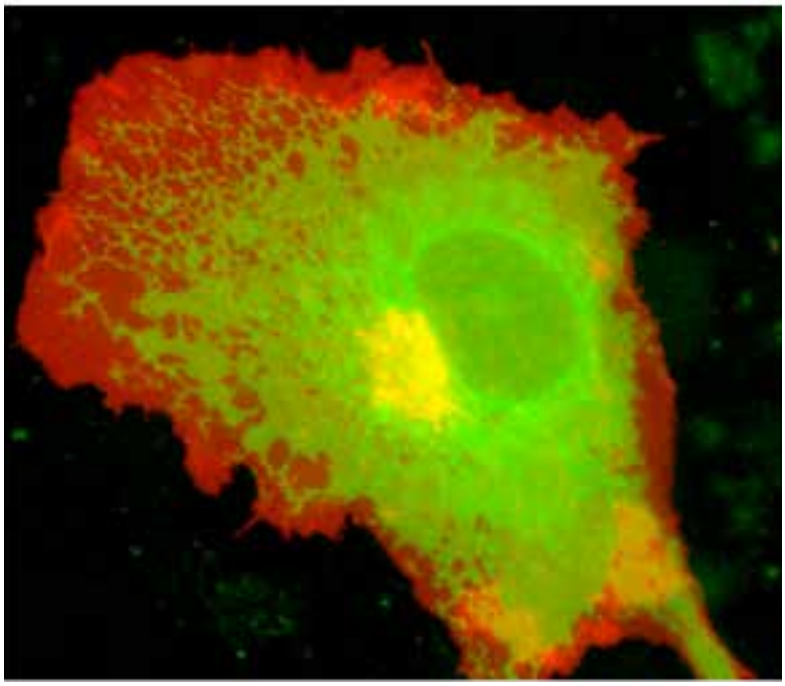
Professor, Sackler Faculty of Medicine

Research

Our laboratory focuses on investigating the protein and membrane interactions that delineate membrane transport processes. We are especially interested in the functions of cargo recognition, concentration and targeted delivery to distinct cellular membranes. All transport processes use the membrane as their final substrate for example: fusion, budding, generation of distinct domains and the establishment of curvature. Combined, these functions shape the cellular transport machinery, one of the major systems that maintain homeostasis communication and response to the external environment in health and disease.

To understand these processes in detail, one must recognize that protein–protein as well as protein-lipid interactions are involved. Studying the later, namely protein-lipid interaction is challenging since these interactions are less specific and complex experimental systems are to be used. In other words, to study the association between a protein to its proximal native lipid environment, membranes cannot be disrupted or solubilized.

In our laboratory, we combine traditional biochemical analysis with live cell imaging and quantitative kinetic modeling to gather information on the dynamic features of the cellular secretory transport machinery. Experiments are carried out using expression of fluorescent protein tagged proteins in living intact cells using laser scanning confocal microscopes. We use a range of state-of-the-art experimental setups



The secretory membrane system: PM (red), Golgi apparatus (yellow) and ER (green).

such as: Time-lapse imaging, three-dimensional reconstruction, multicolor imaging, photobleaching/photoactivation–based manipulations and Bi-Molecular fluorescent complementation (BiFC). Kinetic modeling and simulation software is often used to extract values of kinetic coefficients or to perform model testing from the wealth of information hidden in the images sequences.

Publications

David N, Yaffe Y, Hagoel L, Elazar M, Glenn JS, **Hirschberg K**, Sklan EH. The interaction between the Hepatitis C proteins NS4B and NS5A is involved in viral replication. *Virology*. 475C:139-149. 2014

Yaffe Y, Hagger I , Nevo Yassaf I, Shepshelovitch J, Sklan EH, Elkabetz Y, Yeheskel A, Pasmanik-Chor M, Benzing C, Macmillan A, Gaus K, Eshed-Eisenbach Y, Peles E, **Hirschberg K**. The myelin proteolipid Plasmolipin, forms oligomers and induces liquid ordered membranes in the Golgi apparatus. *J. Cell Science* 128, 2293-302. 2015.

Skalka N., Caspi M., Lahav-Ariel L., Loh Y.P., **Hirschberg K.**, Rosin-Arbesfeld R. Carboxypeptidase E (CPE) inhibits the secretion and activity of Wnt3a. *Oncogene* 35, 6416-28. 2016.

Yonemura Y., Li X., Muller K., Kramer A., Atigbire P., Mentrup T., Feuerhake T., Kroll T., Shomron O., Nohl R., Arndt H.D., Hoischen C., Hemmerich P., **Hirschberg K.**, Kaether C., Inhibition of cargo export at ER exit sites and the trans-Golgi network by the secretion inhibitor FLI-06, *J Cell Sci*. 129, 3868-77. 2016. *- co-corresponding author

Nevo-Yassaf I, Lovelle M., Nahmias Y., **Hirschberg K ***, Sklan E. H.*. Live cell Imaging and analysis of lipid droplets biogenesis in HCV infected cells. *Methods*. S1046-2023,16, 30491-1. 2017. *- co-corresponding author

Grants

2016-2018 Jerom Lejune Foundation

2016-2019 Israel Science Foundation (ISF)

Dr. Limor Landsman, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: limorl@post.tau.ac.il
Website: landsmanlab.tau.ac.il

Beta-Cell Function and Dysfunction: the Role of Microenvironmental Cues

Position

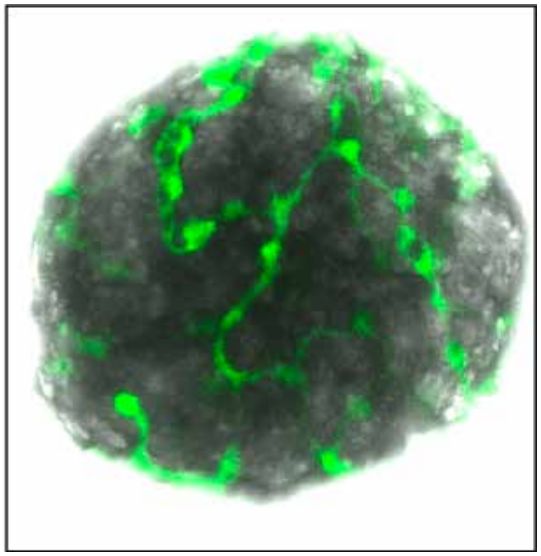
Senior Lecturer, Sackler Faculty of Medicine

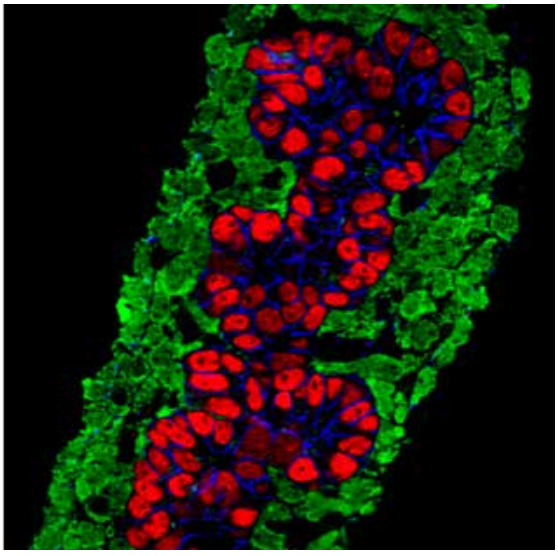
Research

Maintenance of blood glucose levels is dependent upon the tight regulation of insulin secretion from pancreatic beta-cells. Insufficient insulin secretion, whether due to reduced beta-cell numbers, or impaired beta-cell function, leads to diabetes. Our group studies how insulin-producing beta-cells maintain their functionality in health, and how it is lost in diabetes. To this end, we research the cross talk between insulin-producing cells and cells in their microenvironment. Our results indicate the pivotal role of pericytes in the regulation of insulin secretion, and blood glucose levels. Using transgenic mouse models, we study how insulin-producing cells communicate with their microenvironment, and how this communication is affected during diabetes.

In addition, we study how the pancreas develops during embryogenesis. Our findings, along with previous findings, help to consolidate that pancreas mesenchymal cells are crucial for proper pancreas and beta-cell embryonic development. Using transgenic mouse models, we investigate what signals are produced by mesenchymal cells, and how these signals may guide beta-cell development.

In summary, our goals are to uncover the different aspects of pancreas biology, namely its development in the embryo, and its function in the adult. We aim to answer these scientific questions by focusing on the interplay between beta-cells and other pancreatic cell types in both healthy and diseased mouse models.





Beta-cell microenvironment in the embryonic and adult pancreas. Left, Mesenchymal cells (green) surround the developing pancreatic bud (red and blue) and support normal organogenesis. Right, Pericytes (green) form a network around the Islet of Langerhans (gray) in the adult pancreas and support insulin secretion from beta-cells.

Publications

Avraham-Davidi I, Yona S, Grunewald M, **Landsman L**, Cochain C, Silvestre JS, Mizrahi H, Faroja M, Strauss-Ayali D, Mack M, Jung S, Keshet E. (2013) On-site education of VEGF-recruited monocytes improves their performance as angiogenic and arteriogenic accessory cells. *J Exp Med* 210, 2611-25.

Guo T., **Landsman L.,** Li N., Hebrok M. (2013) Factors expressed by murine embryonic pancreatic mesenchyme enhance generation of insulin-producing cells from hESCs. *Diabetes* 62:1581-92.

Sasson A., Rachi E., Sakhneny L, Baer D., Lisnyansky M., Epshtein A. and **Landsman L**. (2016) Islet pericytes are required for beta-cell maturity. *Diabetes*, 65:3008-3014.

Russ HA, **Landsman L**, Moss CL, Higdon R, Greer RL, Kaihara K, Salamon R, Kolker E, and Hebrok M. (2016) Dynamic proteomic analysis of pancreatic mesenchyme reveals novel factors that enhance human embryonic stem (hESC) to pancreatic cell differentiation. *Stem Cells International*. 6183562

Epshtein A, Sakhneny L and **Landsman L**. (2017) Isolating and analyzing cells of the pancreas mesenchyme by flow-cytometry. *JoVE* 119, e55344

Hibsher D, Epshtein A, Oren N and **Landsman L**. (2016) Pancreatic mesenchyme regulates islet cellular composition in a patched/hedgehog-dependent manner. *Sci Rep* 6, 38008.

Epshtein A, Rachi E, Sakhneny L, Mizrachi S, Baer D and **Landsman L**. (2017) Neonatal pancreatic pericytes support beta-cell proliferation. Mol Metab, 6, 1330-1338.

Grants

2013–2018	European Research Council (ERC) Starter Grant ß-cell dysfunction in diabetes: elucidating the role of islet-associated mesenchymal cells
2014-2017	Israel Ministry of Health Elucidating the role of pancreatic mesenchyme secreted factors in beta-cell function and diabetes progression
2016 – 2018	German-Israeli Foundation (GIF), with Dr. Francesca Spagnoli
2017 - 2019	European Foundation for the Study of Diabetes (EFSD) / Novo Nordisk Programme for Diabetes Research in Europe

Prof. Drorit Neumann, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: histo6@post.tau.ac.il
http://neumann.mytau.org/

Erythropoietin and Its Receptor in Health and Disease – Basic and Clinical Aspects

Positions

Professor, Sackler Faculty of Medicine

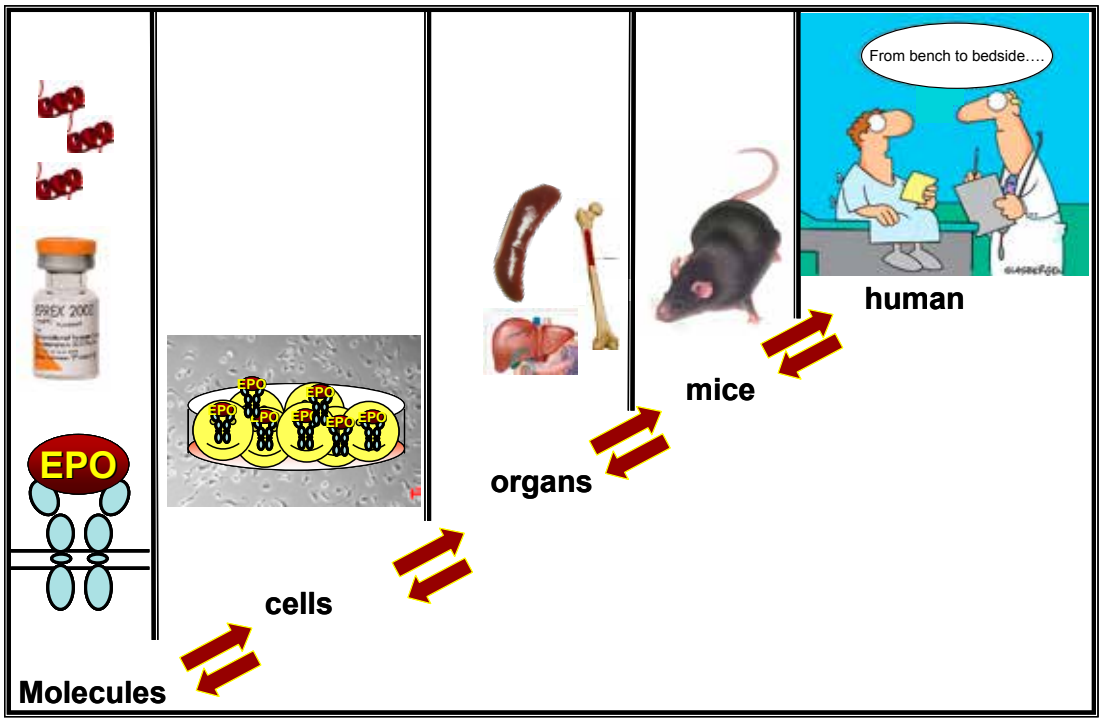
Head, Dr. Miriam and Sheldon Adelson Graduate School of Medicine, Sackler Faculty of Medicine

Research

Our research is focused on erythropoietin (EPO), the major hormone that regulates erythropoiesis, operating via activation of its cell surface receptor (EPO-R) on erythroid progenitor cells. Our choice to work on this EPO/EPO-R system was initiated to employ it as a model for understanding basic mechanisms of hormone/receptor function and regulation. Through this research, in a longstanding collaboration with Prof. Mittelman from the Sourasky Medical Center, we made a novel, original discovery, suggesting that EPO may actually act as a pleiotropic hormone with anti-neoplastic, immunomodulatory activities. Our research is thus focused on both the basic mechanisms of hormone/receptor interaction, as well as the function of this hormone as an immunomodulator, and as we have most recently shown, a regulator of bone metabolism (in collaboration with Dr. Yankel Gabet from the Department of Anatomy and Anthropology, Sackler Faculty of Medicine). The studies are based on a variety of in-vitro and murine experimental models, and also include an avenue of elucidating the relevance and possible clinical application of the results.

Publications

Oster H. S., S. Prutchi-Sagiv, O. Halutz, E. Shabtai, M. Hoffman, **D. Neumann**, M. Mittelman. Erythropoietin treatment is associated with an augmented immune response to the influenza vaccine in hematologic patients. *Exp. Hematol*. 41:167-71 (2013).



Bento C., M Percy, H. Cario*, B. Gardie, T. M. Magalhães, R. van Wijk, S. Perrotta, D. R. Fulvi, H. Almeida, C. Rossi, F. Girodon, M. Åström, **D. Neumann**, S. Schnittger, B. Landin, M. Minkov, M. L. Randi, S. Rives, L. Ribeiro, S. Hermouet, M. F. McMullin*, on behalf of ECE-Consortium§ Genetic basis of Congenital Erythrocytosis: mutation update and online databases. *Hum Mut*, 35:15–26 (2014).

Reinbothe S., A.M. Larsson, M. Vaapil, C. Wigerup, J. Sun, A. Jögi, **D. Neumann**, L. Rönnstrand, S. Påhlman EPO-independent functional EPO receptor in breast cancer enhances estrogen receptor activity and promotes cell proliferation Biochem. *Biophys. Res. Com*. 445: 163–169 (2014).

Ohana Haim Y., N. Deshet Unger, M. C. Souroujon, M. Mittelman and **D. Neumann** Resistance of LPS-activated bone marrow derived macrophages to apoptosis mediated by dexamethasone *Sci. Rep*. 4: 4323 (2014).

Gross M., N. Ben-Califa, M. F. McMullin, M. J. Percy, C. Bento, H. Cario, M. Minkov and **D. Neumann.** Polycythemia-inducing mutations in the erythropoietin receptor (EPOR): Mechanism and function as elucidated by epidermal growth factor receptor (EGFR) – EPOR chimeras. *Br. J. Haematol.* 165:519-28 (2014).

Maxwell P., F. Melendez-Rodríguez, K. B Matchet, J. Aragones, N. Ben-Califa, H. Jaekel, L. Hengst, H. Lindner, A. Bernardini, U. Brockmeier, J. Fandrey, F. Grunert, H. Oster, M. Mittelman, M. El-Tanani, M. Thiersch, E. M. Schneider Gasser, M. Gassmann, D. Dangoor, R. J. Cuthbert, A. Irvine, A. Jordan, T. Lappin, J. Thompson and **D. Neumann.** Novel antibodies directed against the human erythropoietin receptor: creating a basis for clinical implementation. *Br. J. Haematology* 168:429-42 (2015). **The work represents efforts of European consortium EpoCan, FP7 call, coordinated by Prof D. Neumann.*

Hiram-Bab S., T. Liron, N. Deshet-Unger, M. Mittelman, M. Gassmann, M. Rauner, K. Franke, B. Wielockx, **D. Neumann** and Y.I Gabet. Erythropoietin directly stimulates osteoclast precursors and induces bone loss. *FASEB J*. 29(5):1890-900, (2015) *Commentary on manuscript: Nat Rev Endocrinol. 11:2643-2644. 2015*

Rauner M, K. Franke, M. Murray RP Singh, S. Hiram-Bab, U. Platzbecker, M. Gassmann, M. Socolovsky, **D. Neumann**, Y. Gabet, T. Chavakis, LC Hofbauer, B. Wielockx. Increased EPO levels are associated with bone loss in mice lacking phd2 in epo-producing cells. *J Bone Miner Res*. 31:1877-1887 (2016).

Deshet-Unger N., S. Hiram-Bab, Y. Haim-Ohana, M. Mittelman, Y. Gabet, **D. Neumann**. Erythropoietin treatment in murine multiple myeloma: immune gain and bone loss *Sci Rep*.6:30998-31009 (2016).

Gilboa D, Haim-Ohana Y, Deshet-Unger N, Ben-Califa N, Hiram-Bab S, Reuveni D, Zigmond E, Gassmann M, Gabet Y, Varol C, **Neumann D**. Erythropoietin enhances Kupffer cell number and activity in the challenged liver. *Sci Rep*. 7:10379 (2017)

Chapters and Reviews

Ohana Y., Liron T., Prutchi-Sagiv, S., Mittelman M. Souroujon M.C. and **D. Neumann** Erythropoietin second edition Handbook of Biologically Active Peptides (Abba J. Kastin, ed.), Elsevier, San Diego, pp 1619-1626 (2013).

Hiram-Bab S, **Neumann D,** Gabet Y. Erythropoietin in bone - Controversies and consensus. *Cytokine*. 89:155-159 (2017).

Hiram-Bab S., **Neumann D.** and Gabet Y. Context-Dependent Skeletal Effects of Erythropoietin. *Vitam Horm*. 105:161-179 (2017).

Grants

2015-2017	Israel Cancer Association – Erythropoietin in multiple myeloma – improving outcome without compromising bone
2017-2021	Israel Science Foundation - A Role for Erythropoietin in Regulation of Bone Metabolism by Monocytes and B cells
2018-2020	German Israeli Foundation (Together with Y. Gabet, TAU and B. Wielockx and M. Rauner, Dresden) – Pathophysiological impact of erythropoietin on bone density and strength

Prof. Edgar Pick, M.D., Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: epick@post.tau.ac.il
URL: http://www2.tau.ac.il/Person/medicine/researcher.asp?id=ahheikije

Assembly of the Superoxide-Generating NADPH Oxidase Complex in Health and Disease

Position

Professor Emeritus, Sackler Faculty of Medicine

Julius Friedrich Cohnheim Laboratory of Phagocyte Research

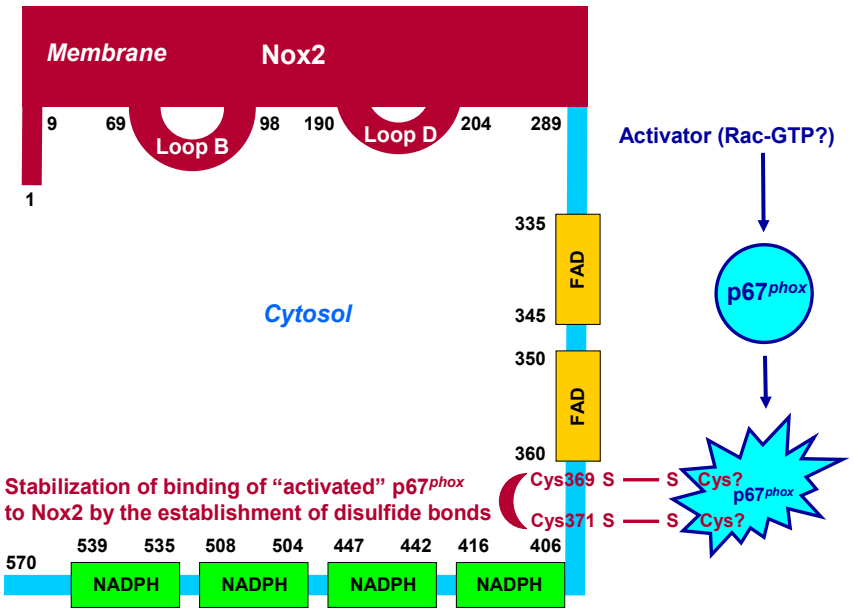
Member, Editorial Board, *The FASEB Journal*

Member, Editorial Board, *International Journal of Hematology Research*

Research

We are studying the production of reactive oxygen species (ROS) by phagocytes. ROS are generated by an enzyme complex, known as the NADPH oxidase. Our group is responsible for many of the seminal advances in the biochemistry and molecular biology of the NADPH oxidase complex, including: the standard micro-assay for the measurement of ROS (1130 citations); the design of a universally used method for measuring H2O2 production by cells in culture (1084 citations); the development of the first cell-free system of ROS production leading to the discovery of the cytosolic oxidase components (377 + 366 = 743 citations); the discovery of the role of the small GTPase Rac in oxidase activation (951 citations); the introduction of "peptide walking" to identify sites of protein-protein interaction, and the construction of chimeric cytosolic oxidase activators. The laboratory is equipped for the performance of advanced biochemical and molecular biology techniques.

The most recent interest of our group is focused on the mapping of the hotspots of interaction between the catalytic oxidase component Nox2 and the cytosolic activator p67^{phox}. We found that the dehydrogenase region of Nox2 (residues 288-570) contains a Cys-Gly-Cys (CGC) triad (residues 369-371), which serves as a binding site for p67^{phox}. This finding is based



Schematic representation of the stabilization of binding of "activated" p67^{phox} to the dehydrogenase region of Nox2, involving the establishment of disulfide bonds between cysteines 369 and 371 in Nox2 and yet unidentified cysteines in p67^{phox}

on a novel methodology, designed by us, in which we measure the binding of recombinant p67^{phox} to an array of synthetic overlapping peptides covering the sequence of the dehydrogenase region of Nox2. Two Nox2 peptides that share the CGC triad, at their C- and N-termini, respectively, were found to bind p67^{phox}. "Mutating" either C369 or C371 to R resulted in loss of p67^{phox} binding. Chemical reduction of CGC-containing peptides also led to loss of binding. Linking the two cysteines by a disulfide bond resulted in a marked increase in binding. We concluded that binding of p67^{phox} to the catalytic component of the NADPH oxidase complex is redox regulated and involves the establishment of disulfide bonds between p67^{phox} and Nox2. The CGC triad might have a dual role by acting both as a protein disulfide isomerase (PDI) and by providing the cysteines for the establishment of disulfide bonds with p67^{phox}. This novel hypothesis rests on the evidence that the CGC motif mimics functionally and structurally the CGHC catalytic site of members of the PDI family. Recently, we showed that a recombinant Nox2 construct possesses

PDI activity, exhibits limited sequence similarity with PDIA3, and reacts with an anti-PDIA3 antibody.These findings have a key *in vivo* equivalent because a C369R mutation in human Nox2 causes Chronic Granulomatous Disease (CGD), an inborn defect resulting in the inability of phagocytes to produce ROS, leading to the failure to resist infections by bacteria and fungi.

Publications

Roos, D., van Buul, J. D., Tool, A. T. J., Matute, J. D., Marchal, C. M., Hayee, B., Köker, M. Y., de Boer, M., van Leeuwen, K., Segal, A. W., **Pick, E.**, and Dinauer M. C. Two CGD families with a hypomorphic mutation in the activation domain of p67-*phox*. *J. Clin. and Cell. Immunol*. 5:3, 2014

Dahan I, Smith SM, **Pick E.** A Cys-Gly-Cys triad in the dehydrogenase region of Nox2 plays a key role in the interaction with p67phox. *J Leukoc Biol*. 98:859-74, 2015

Bechor, E., Dahan, I., Fradin, T., Berdichevsky, Y., Zahavi, A., Federman Gross, A., Rafalowski, M., and **Pick, E**. The dehydrogenase region of the NADPH oxidase component Nox2 acts as a protein disulfide isomerase (PDI) resembling PDIA3 with a role in the binding of the activator protein p67*phox*. *Front. Chem.* 3:3, 2015

Dahan, I., Smith S. M. E., and **Pick, E**. A Cys-Gly-Cys triad in the dehydrogenase region of Nox2 plays a key role in the interaction with p67*phox*. *J. Leukoc. Biol*. 98: 859-874, 2015

Pick, E. Absolute and relative activity values in assessing the effect of NADPH oxidase inhibitors. *Antiox. Redox Signal*. 23: 1250-1251, 2015

Chapters/Reviews

Pick, E., Cell-Free NADPH Oxidase Activation Assays – *"In Vitro Veritas",* In *Neutrophil Methods and Protocols*, 2nd Edition (Quinn, M. T., and DeLeo, F. R., eds), 339-403. Humana Press, 2014.

Pick, E., Role of the Rho GTPase Rac in the activation of the phagocyte NADPH oxidase: Outsourcing a key task. *Small GTPases*, 5(1), 2014.

Grants

2017-2018 Blavatnik Center for Drug Research, Synthetic peptides preventing the uncoupling of an autoinhibitory loop in the cytosolic component p67phox as models for the design of small molecular weight NADPH oxidase inhibitors

2017-2020 Israel Science Foundation (ISF), Uncoupling of an intramolecular bond in the cytosolic component p67-phox is the crucial event in the activatin of the NADPH oxidase in phagocytes

Prof. Haim Werner, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: hwerner@post.tau.ac.il
URL: www2.tau.ac.il/Person/medicine/researcher.asp?id=acemjkgjc

Molecular Biology of the Insulin-Like Growth Factor System

Positions

Professor, Sackler Faculty of Medicine

Head, Yoran Institute for Human Genome Research

Lady Davis Chair in Biochemistry

Research

The insulin-like growth factors (IGF1, IGF2) are a family of hormones with important roles in growth and development. The biological actions of the IGFs are mediated by the IGF1 receptor (IGF1R), a cell-surface receptor related to the insulin receptor. The IGF1R signaling pathway has an important role in the biochemical chain of events linking obesity, diabetes, and cancer. Our work is aimed at understanding the molecular and cellular events responsible for IGF1R expression in cancer. These studies are expected to generate information that might translate into more efficient IGF1R targeting approaches. Furthermore, a better understanding of the molecular biology of the IGF system will have important ramifications in areas such as obesity, metabolic syndrome, diabetes, and cancer research. Specific topics include:

- Interplay between the IGF signaling pathways and cancer genes (p53, BRCA).
- IGF1R targeting as a therapeutic approach in cancer.
- Epigenetic mechanisms in cancer development.
- Biological activities of insulin analogues.
- Metabolism and cancer.

Publications

Sarfstein, R., Friedman, Y., Attias-Geva, Z., Fishman, A., Bruchim, I. and **Werner, H.** (2013) Metformin down-regulates the insulin/IGF-I signaling pathway and inhibits different uterine serous carcinoma cells proliferation and migration in p53-dependent or -independent manners. *PLoS One* 8:e61537.

Bitelman, C., Sarfstein, R., Sarig, M., Attias-Geva, Z., Fishman, A., **Werner, H.** and Bruchim, I. (2013) IGF1R-directed targeted therapy enhances the cytotoxic effect of chemotherapy in endometrial cancer. *Cancer Lett.* 335:153-159.

Hermani, A., Shukla, A., Medunjanin, S., **Werner, H.** and Mayer, D. (2013) Insulin-like growth factor binding protein-4 and -5 modulate ligand-dependent estrogen receptor-a activation in breast cancer cells in an IGF-independent manner. *Cell Signal.* 25:1395-1402.

Weinstein, D., Sarfstein, R., Laron, Z. and **Werner, H.** (2014) Insulin receptor compensates for IGF1R inhibition and directly induces mitogenic activity in prostate cancer cells. *Endocrine Connect.* 3:24-35.

Canetti, L., **Werner, H.** and Leikin-Frenkel, A. (2014) Linoleic and alpha-linolenic acids ameliorate streptozotocin-induced diabetes in mice. *Arc. Physiol Biochem.* 120:34-39.

Rubinfeld, H., Kammer, A., Cohen, O., Gorshtein, A., Cohen, Z.R., Hadani, M., **Werner, H.** and Shimon, I. (2014) IGF1 induces cell proliferation in human pituitary tumors – Functional blockade of IGF1 receptor as a novel therapeutic approach in non-functioning tumors. *Mol Cell Endocrinol.* 390:93-101.

Bruchim, I., Sarfstein, R., Reiss, A., Flescher, E. and **Werner, H.** (2014) IGF1R tyrosine kinase inhibitor enhances the cytotoxic effect of methyl jasmonate in endometrial cancer. Cancer Lett. 352:214-219.

Aizen, D., Sarfstein, R., Bruchim, I., Weinstein, D., Laron, Z. and **Werner, H.** (2015) Proliferative and signaling activities of insulin analogues in endometrial cancer cells. Mol. Cell. Endocrinol. 406:27-39.

Solomon-Zemler, R., Weingarten, G., Sarfstein, R., Laron, Z., **Werner, H.** and Wertheimer, E. (2015) Insulin analogues display atypical differentiative

activities in skin keratinocytes. Arch. Physiol. Biochem., 121:32-39.

Milanesi, E., Hadar, A., Maffioletti, E., **Werner, H**., Shomron, N., Gennarelli, M., Schulze, T., Costa, M., Del Zompo, M., Squassina, A. and Gurwitz, D. (2015) IGF-1 differentially affects lithium sensitivity of lymphoblastoid cell lines from lithium responder and non-responder bipolar disorder patients. J. Mol. Neurosci., 56:681-687.

Shinderman Maman, E., Cohen, K., Weingarten, C., Nabriski, D., Twito, O., Baraf, L., Hercbergs, A., Davis, P.J., **Werner, H.,** Ellis, M. and Ashur-Fabian, O. (2016) The thyroid hormone-avb3 integrin axis in ovarian cancer: regulation of gene transcription and MAPK-dependent proliferation. Oncogene 35:1977-1987.

Lapkina-Gendler, L., Rotem, I., Pasmanik-Chor, M., Gurwitz, D., Sarfstein, R., Laron, Z. and **Werner, H**. (2016) Identification of signaling pathways associated with cancer protection in Laron syndrome. Endocrine Related Cancer 23:399-410.

Meisel-Sharon, S., Pozniak, Y., Geiger, T. and **Werner, H.** (2016) TMPRSS2-ERG fusion protein regulates insulin-like growth factor-1 receptor (IGF1R) gene expression in prostate cancer: involvement of transcription factor Sp1. Oncotarget, 7:51375-51392.

Liu, Z., Cordoba-Chacon, J., Kineman, R.D., Cronstein, B.N., Muzumdar, R., Gong, Z., **Werner, H.**, Yakar, S. (2016) Growth hormone control of hepatic lipid metabolism. Diabetes 65:3598-3609.

Cohen-Sinai, T., Cohen, Z., **Werner, H**., Berger, R. (2017) Identification of BRCA1 as a potential biomarker for insulin-like growth factor-1 receptor targeted therapy in breast cancer. Front. Endocrinol. 8:148.

Solomon-Zemler, R, Basel-Vanagaite, L., Steier, D., Yakar, S., Mel, E., Phillip, M., Bazak, L., Bercovich, D., **Werner, H**. and de Vries, L. (2017) A novel heterozygous IGF1 receptor mutation associated with hypoglycemia. Endocrine Connect., 17:0038.

Solomon-Zemler, R. and **Werner, H**. (2017) Nuclear insulin-like growth factor-1 receptor (IGF1R) displays proliferative and regulatory activities in non-malignant cells. PLoS ONE, in press.

Somri, L., Sarfstein, R., Lapkina-Gendler, L., Nagaraj, K., Laron, Z., Bach, L.A and **Werner, H.** (2017) Differential expression of IGFBPs in Laron syndrome-derived lymphoblastoid cell lines: potential correlation with reduced cancer incidence. Growth Hormone & IGF Res., in press.

Reviews

Bentov, I. and **Werner, H.** (2013) Insulin-like growth factor-1. In: Handbook of Biologically Active Peptides, Second edition, ed. by Kastin, A., Elsevier Press, San Diego. pp. 1627-1632.

Werner, H. and Sarfstein, R. (2013) Insulin receptor family. In: The Receptor Tyrosine Kinase Handbook, ed. by Wheeler, D.L. and Yarden, Y., Springer Science, New York, in press.

Sarfstein, R. and **Werner, H.** (2015) Insulin-IGF1 receptors (INSR/IGF1R) family. In: The Receptor Tyrosine Kinase Handbook, ed. by Wheeler, D.L. and Yarden, Y., Springer Science, New York, pp. 297-320.

Bruchim, I. and **Werner, H.** (2013) Targeting IGF-I signaling pathwys in gynecologic malignancies. *Expert Opinion Ther Targets*. 17:307-320.

Sarfstein, R. and **Werner, H.** (2013) Nuclear insulin and insulin-like growth factor receptors: a novel paradigm in signal transduction. *Endocrinology* 154:1672-1679.

LeRoith, D. and **Werner, H.** (2014) Insulin and IGF1 receptors in the brain: Physiological and pathological aspects. *Eur. Neuropsychopharmacol*. 24:1947-1953.

Bruchim, I., Sarfstein, R. and **Werner, H.** (2014) The IGF hormonal network in endometrial cancer: functions, regulation, and targeting approaches. *Front Endocrinol***.** 5:76.

Werner, H. and Sarfstein, R. (2014) Transcriptional and epigenetic control of IGF1 receptor gene expression: implications in metabolism and cancer. *Growth Hormone & IGF Res.,* 24:112-118.

Werner, H., Sarfstein, R., LeRoith, D. and Bruchim, I. (2016) Insulin-like growth factor-1 (IGF1) signaling axis meets p53 genome protection pathways. *Front. Oncol*. 6:159.

Laron, Z., Kauli, R., Lapkina, L. and **Werner, H.** (2016) IGF-1 deficiency, longevity and cancer protection of patients with Laron syndrome. *Mutation Res. Rev., 772:123-133.*

Werner, H., Lapkina-Gendler, L. and Laron, Z. (2017) Fifty years on: New lessons from Laron syndrome. *Israel Med. Assoc. J*. 19:6-7.

Werner, H., Lapkina-Gendler, L., Nagaraj, K., Sarfstein, R. and Laron, Z. (2017) Genome-wide profiling of congenital IGF1 deficient patients: translational implications in cancer prevention and metabolism. *Translational Med. Reports* 1:6657.

Grants

2014-2018 "Mechanistic insights into IGF1-dependent longevity genes". U.S.-Israel Binational Science Foundation.

2014-2019 "Investigation of metabolic genes associated with cancer protection pathways in a rare congenital IGF1 deficiency". Israel Science Foundation.

2016-2017 "Nuclear IGF1R translocation adds a new layer of signaling control". Hendrik and Irene Gutwirth Fund for Diabetes Mellitus Research, Sackler School of Medicine, Tel Aviv University,

2017-2018 "Identification of thioredoxin-interacting protein (TXNIP) as a novel metabolic tumor suppressor gene". Israel Cancer Association.

Prof. Efrat Wertheimer, MD., PhD.

Department of Pathology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: effy@patholog.tau.ac.il

Role of the Insulin Receptor in Skin and Implications to Diabetes

Position

Senior Lecturer, Sackler Faculty of Medicine

Co-editor Diabetes/Metabolism Research and Reviews

D-Cure scientific committee

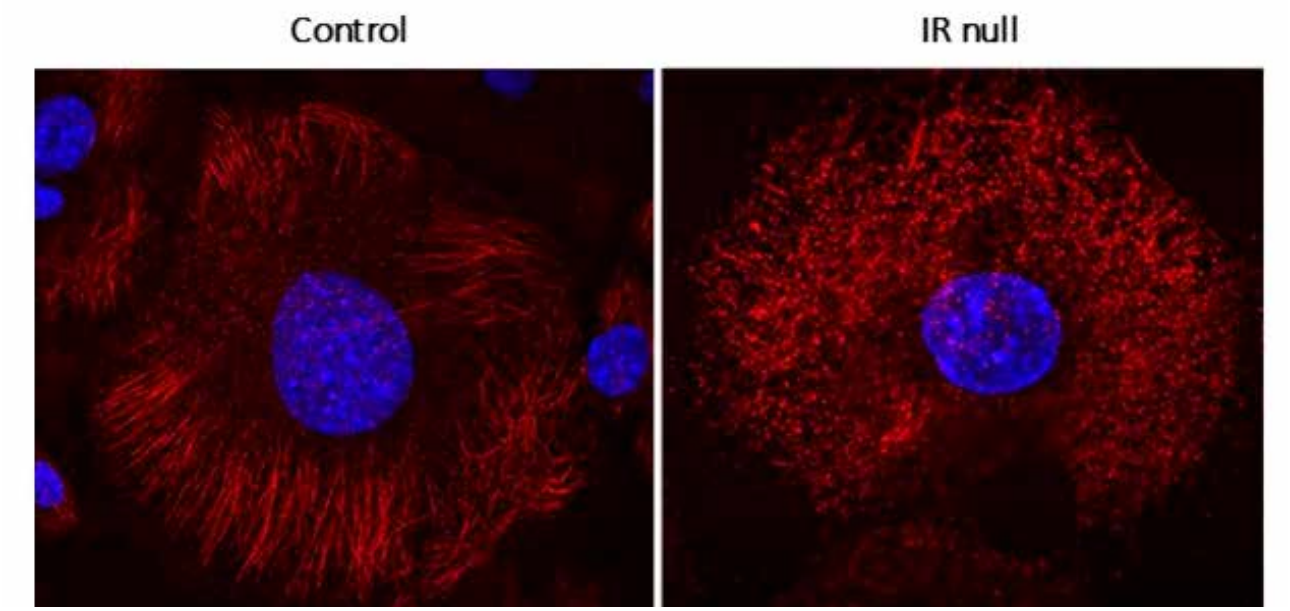
Research

The insulin receptor (IR) is one of the best-studied tyrosine kinase receptors. The receptor transmits insulin actions, and functions in the metabolic regulation of glucose in insulin sensitive tissues – muscle, liver and adipose tissue. In recent years, however, additional roles have emerged for the IR in various tissues including the regulation of transcription and translation, cell proliferation, differentiation and more.

Our research interests center on the role of insulin and the IR in skin. The importance of insulin and the IR in skin is evident when insulin action is impaired in insulin resistance and diabetes: One of the major known insulin resistance- and diabetes-associated skin complications is the impaired wound healing leading to amputations, increased illness and high mortality rates. Another skin complication associated with insulin resistance and diabetes is the marked increase in the risk, aggression, and recurrence of non-melanoma skin cancer.

We have identified a previously unknown unique signaling pathway in which insulin via the IR regulates the assembly of the cellular cytoskeleton in skin cells. As can be seen in the figure attached below, IR inactivation, mimicking insulin resistance, led to a striking abnormality in the structure and assembly of cytoskeleton filaments in the skin epithelial cells.

Such an abnormality in cytoskeleton assembly can explain the observed changes in cellular division, proliferation and migration of IR null skin cells. Furthermore, since these processes are involved in wound healing from one hand as well as in tumorigenesis on the other hand, the disassembled cytoskeleton could be part of the pathogenesis



leading to the development of the diabetes-associated skin pathologies.

In order to prove the importance of insulin and the IR in skin, and more specifically to wound healing and to skin tumorigenesis, we generated a skin-specific IR null mouse. In this mouse, the IR is inactivated only in the skin epidermis, without the development of hyperglycemia or other biochemical changes. By studying this mouse, we demonstrated that lack of epidermal IR by itself led to severely impaired wound healing. Furthermore, in another set of studies we demonstrated that IR inactivation in skin led to a marked decrease in transformation of skin cells *in vitro* as well as in skin tumorigenesis *in vivo*. Moreover, IR inhibition led to the reversal of transformation of transformed skin cells.

Our results indicate that the skin itself is abnormal in diabetes as a result of impaired insulin signaling, and that it should become an independent target for treatment and prevention of diabetes-associated skin pathologies. This research will lead to new means to reverse and prevent diabetes-associated skin complications from developing, effectively treat them, and halt their progression.

Publications

Solomon Zemler R, Weingarten G, Sarfstein R, Laron Z, Werner H, **Wertheimer E.** Insulin analogues display atypical differentiative activities in skin keratinocytes. Arch Physiol Biochem. 2015; 121:32-9.

Falik Zaccai TC, Kalfon L, Klar A, Elisha MB, Hurvitz H, Weingarten G, Chechik E, Fleisher Sheffer V, Haj Yahya R, Meidan G, Gross-Kieselstein E, Bauman D, Hershkovitz S, Yaron Y, Orr-Urtreger A, **Wertheimer E.** Two novel mutations identified in familial cases with Donohue syndrome. Mol Genet Genomic Med. 2014; 2:64-72.

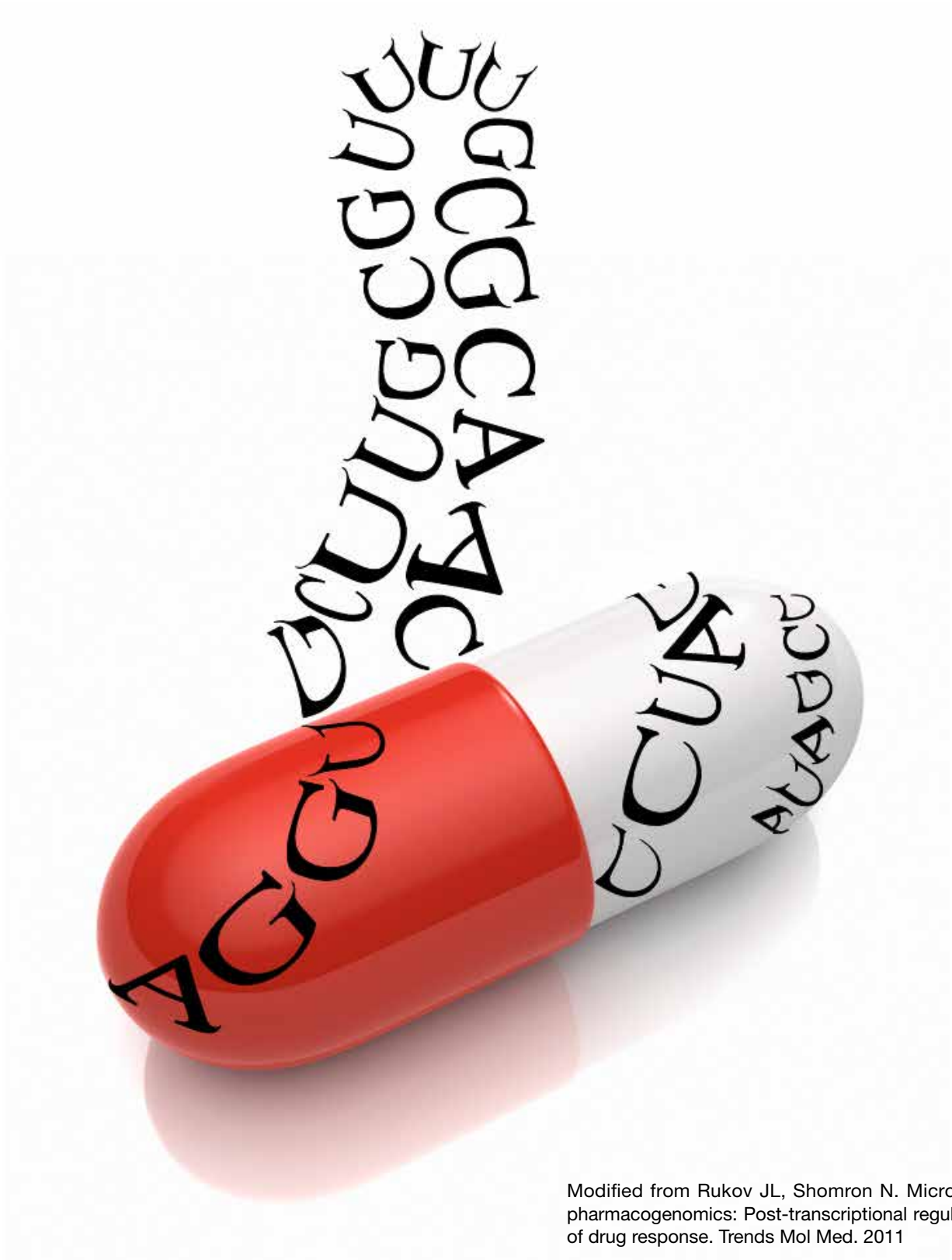
Grants

2016-2017 Industry – Ramot TAU Technology Transfer Company

Patent

US 14/521,494 Methods and Compositions for Treating Cancer

Genomics & Personalized Medicine



Modified from Rukov JL, Shomron N. MicroRNA pharmacogenomics: Post-transcriptional regulation of drug response. Trends Mol Med. 2011

Prof. Gil Ast, Ph.D.

Department of Human Molecular Genetics &
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: gilast@post.tau.ac.il
http://astlab.tau.ac.il/index.php

Alternative Splicing Generates Transcriptomic Diversity in Genetic Disorders & Cancer

Positions

Professor, Sackler Faculty of Medicine

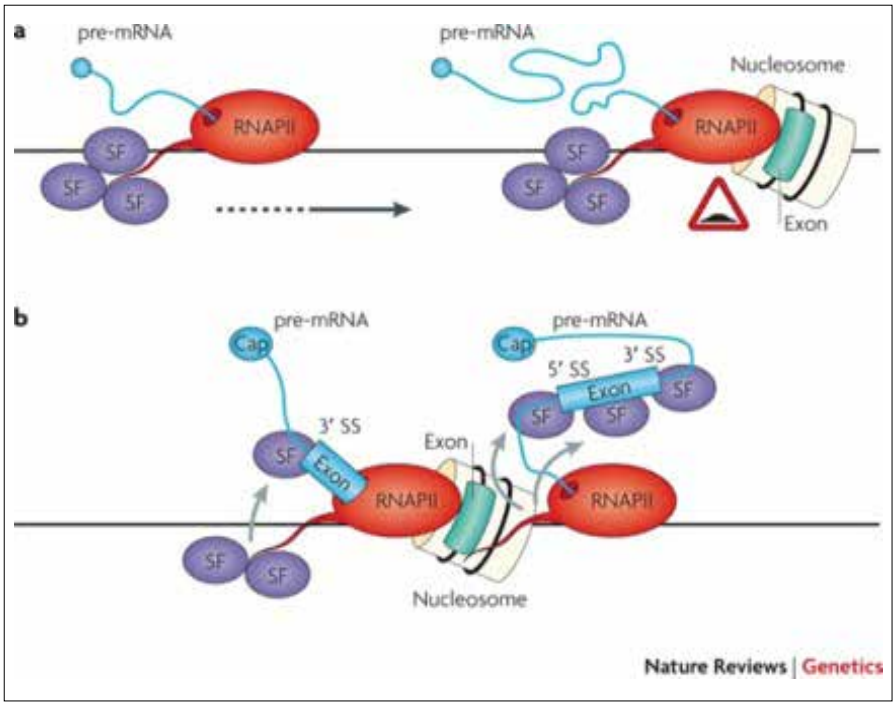
Boris Quentin Chair in Pathological Chemistry

Research

By utilizing the unique strengths of our research group in bioinformatic analyses as well as in genomic and advanced molecular biology methodologies, we are able to make groundbreaking discoveries in the field of alternative splicing. We study how alternative splicing generates higher level of organism complexity, especially in human. However, this comes with a price, and alternative splicing also inflicts many genetic disorders and cancer. Our research involves these two facets of alternative splicing. On one hand, we found how new functions evolved via the generation of new exons (mostly in human). We have also showed how different layers of gene expression affect each other, and found that chromatin organization and epigenetic markers (DNA methylation) mark the exon-intron structure. We also found that during the evolution of warm-blooded organisms two exon-intron gene architectures developed, and these also reflect the different effects of mutations on splicing in cancer and other genetic disorders. On the other hand, we study the impact of splicing abnormalities on colon and lung cancer, and we have recently discovered a new therapy for Familial Dysautonomia, a neurodegenerative disease caused by a splicing defect in the nervous system.

Publications

Naftelberg S, **Ast G***, Perlson E* (2017). Phosphatidylserine improves axonal transport by inhibition of HDAC and has potential in treatment of neurodegenerative diseases. *Neural Regen Res*. 12:534-537 *Co-corresponding author.



Nucleosome occupancy marks exons and is coupled to transcription. **a.** RNA polymerase II (RNAPII), associated with different splicing factors (SFs), travels along the gene and transcribes it. When RNAPII reaches an area with high nucleosome occupancy and encounters specific histone modifications that mark an exon, it is slowed down. **b.** This panel shows RNAPII and the nucleosome at the point at which their coupling marks the exon boundaries for the splicing machinery. RNAPII transcribes the exon and SFs detach from the carboxy-terminal domain of RNAPII and bind to the 3′ splice site (3′ SS) region of the precursor mRNA (pre-mRNA). During transcription elongation, additional SFs bind intronic and exonic splicing regulatory elements and the 5′ SS.

Bochner R, Samuelov L, Sarig O, Li Q, Adase CA, Isakov O, Malchin N, Vodo D, Shayevitch R, Peled A, Yu BD, Fainberg G, Warshauer E, Adir N, Erez N, Gat A, Gottlieb Y, Rogers T, Pavlovsky M, Goldberg I, Shomron N, Sandilands A, Campbell LE, MacCallum S, McLean WH, **Ast G**, Gallo RL, Uitto J, Sprecher E. Calpain 12 function revealed through the study of an atypical case of autosomal recessive congenital ichthyosis. *J Invest Dermatol*. 2017:137:385-393.

Naftelberg S, Abramovitch Z, Gluska S, Yannai S, Joshi Y, Donyo M, Ben-Yaakov K, Gradus T, Zonszain J, Farhy C, Ashery-Padan R, Perlson E, **Ast G**. Phosphatidylserine ameliorates neurodegenerative symptoms and enhances axonal transport in a mouse model of Familial Dysautonomia. PLoS Genet. 2016;12:e1006486.

Hollander D, Donyo M, Atias N, Mekahel K, Melamed Z, Yannai S, Lev-Maor G, Shilo A, Schwartz S, Barshack I, Sharan R, **Ast G**. A network-based analysis of colon cancer splicing changes reveals a tumorigenesis-favoring regulatory pathway emanating from ELK1. *Genome Res*. 2016;26:541-53.

Donyo M, Hollander D, Abramovitch Z, Naftelberg S, **Ast G**. Phosphatidylserine enhances IKBKAP transcription by activating the MAPK/ERK signaling pathway. *Hum Mol Genet*. 2016;25:1307-17.

Ekhilevitch N, Kurolap A, Oz-Levi D, Mory A, Hershkovitz T, **Ast G**, Mandel H, Baris HN. Expanding the MYBPC1 phenotypic spectrum: a novel homozygous mutation causes arthrogryposis multiplex congenita. *Clin Genet*. 2016;90:84-9.

Kfir N, Lev-Maor G, Glaich O, Alajem A, Datta A, Sze SK, Meshorer E, **Ast G**. SF3B1 association with chromatin determines splicing outcomes. *Cell Rep*. 2015;11:618-29.

Yearim A, Gelfman S, Shayevitch R, Melcer S, Glaich O, Mallm JP, Nissim-Rafinia M, Cohen AH, Rippe K, Meshorer E, **Ast G**. HP1 is involved in regulating the global impact of DNA methylation on alternative splicing. *Cell Rep*. 2015;10:1122-34.

Fuchs G, Hollander D, Voichek Y, Ast G, Oren M. (2014) Cotranscriptional histone H2B monoubiquitylation is tightly coupled with RNA polymerase II elongation rate. *Genome R*es. 24:1572-83.

Gelfman S, **Ast G**. When epigenetics meets alternative splicing. (2013) The roles of DNA methylation and GC architecture. *Epigenomics*. 2013:351-353.

Melamed Z, Levy A, Ashwal-Fluss R, Lev-Maor G, Mekahel K, Atias N, Gilad S, Sharan R, Levy C, Kadener S, **Ast G**. Alternative splicing regulates biogenesis of miRNAs located across exon-intron junctions. (2013). *Mol Cell*, 50:869-881.

Bochner R, Ziv Y, Zeevi D, Donyo M, Abraham L, Ashery-Padan R, **Ast G**. Phosphatidylserine increases IKBKAP levels in a humanized knock-in IKBKAP mouse model. (2013) *Hum Molec Genet*. 22: 2785-2794

Naftelberg S, Schor IE, **Ast G**, Kornblihtt AR. Regulation of alternative splicing through coupling with transcription and chromatin structure. *Annu Rev Biochem*. 2015;84:165-98.

Lev Maor G, Yearim A, **Ast G**. The alternative role of DNA methylation in splicing regulation. Trends Genet. 2015;31:274-80.

Gelfman S, Cohen N, Yearim A, **Ast G**. DNA-methylation effect on cotranscriptional splicing is dependent on GC architecture of the exon-intron structure. (2013) *Genome Res*. 23:789-799.

Reviews

Gelfman S, Ast G. (2013) When epigenetics meets alternative splicing: the roles of DNA methylation and GC architecture. *Epigenomics*. 5:351-3

Hollander D, Naftelberg S, Lev-Maor G, Kornblihtt AR, **Ast G**. How are short exons flanked by long introns defined and committed to splicing? *Trends Genet*. 2016.

Naftelberg S, **Ast G**, Perlson E. Phosphatidylserine improves axonal transport by inhibition of HDAC and has potential in treatment of neurodegenerative diseases. Neural Regen Res. 2017;12:534-537.

Grants

2013-2018	Israel Science Foundation, Identification of novel determinants of splicing regulation 2014-
2017	ISF-UGC (India) Binational Grant, Transcriptomic and proteomic analyses of colon cancer alternative splicing
2016-2017	ISF – Broad Institute, Site-specific DNA methylation
2016-2019	DKFZ-MOST, Network-based analysis of alternative splicing regulation
2017-2018	Israel Cancer Association (ICA), Analyses of alternative splicing aberrations in ovary cancer

Prof. Karen B. Avraham, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

Email: karena@post.tau.ac.il
URL: www.kbalab.com

Genomic Analysis of Hereditary Hearing Loss

Positions

Professor, Sackler Faculty of Medicine

Vice Dean for Preclinical Affairs, Sackler Faculty of Medicine

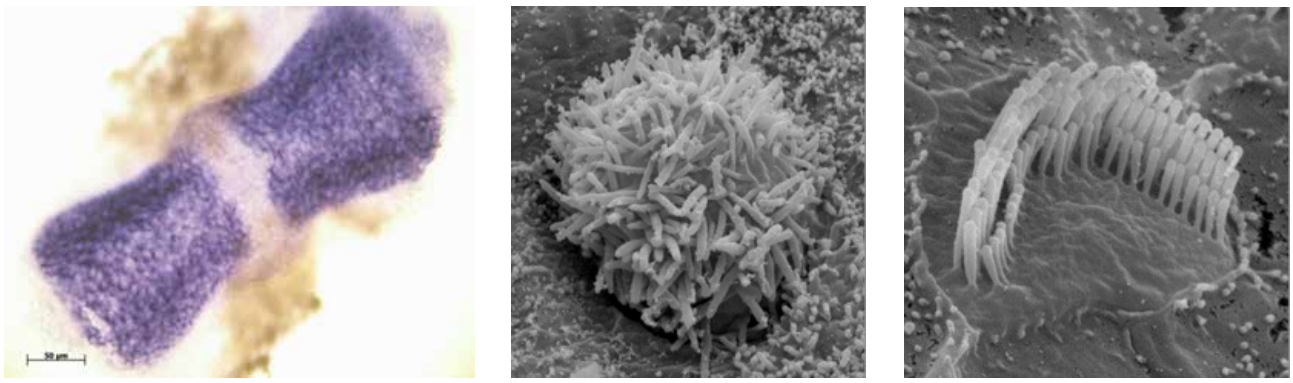
Drs. Sarah and Felix Dumont Chair for Research of Hearing Disorders

President, Israel Society of Auditory Research

Associate Editor, *European Journal of Human Genetics*

Research

Our primary interest is the genetic basis of hereditary hearing loss or deafness. Our group is working towards the identification, characterization and regulation of genes associated with hereditary hearing loss. For gene discovery, we focus on the Israeli Jewish and Palestinian Arab populations in the Middle East. Our studies have led to the identification of mutations in over 30 genes, since this is a genetically heterogeneous disease. We are employing deep sequencing, also known as massively parallel sequencing, to identify mutations using the latest genomic technology. Our work has provided the link between gene discovery and clinical diagnosis in genetic clinics in medical centers throughout Israel. In addition, we have studied the auditory and vestibular systems of a dozen mouse mutants, focusing on mutation identification, morphological and functional analysis of the organ of Corti and its cells, and behavioral analysis of hearing and balance disorders. This has allowed us to define the pathways leading to deafness in mouse models for human deafness. We have demonstrated that microRNAs are essential for development and function of inner ear hair cells in vertebrates through microRNA expression, mouse mutants and target identification. We have recently isolated long non-coding RNAs (lncRNAs) by RNA-seq from the cochlear and vestibular sensory epithelium. Reconstruction and filtering of the transcriptome of the inner ear led to 3,239 lncRNA genes, yielding 721 novel lncRNAs. We are now working on understanding their mechanisms in the auditory and vestibular systems. Finally, we are building epigenomic maps of DNA methylation, chromatin structure, and histone modifications of the auditory system and integrating them with transcriptomics to establish pathway-specific transcriptional regulatory networks (TRNs).



Wild type and mutant hair cell bundles in the PCKO mouse, lacking microRNAs in the inner ear, demonstrated by scanning electron microscopy (2 left panels). *In situ* hybridization reveals expression of the microRNA-182 in the inner ear crista (right).

Publications

Manuscripts

Horn, H.F.*, Brownstein, Z.*, Lenz, D.R., Shivatzki, S., Dror, A.A., Dagan-Rosenfeld, O., Friedman, L.M., Roux, K.J., Kozlov, S., Jeang, K.-T., Frydman, M., Burke, B., Stewart, C.L., and **Avraham, K.B.** (2013) The LINC complex is essential for hearing. *J. Clin. Invest.* 123:740-750

Parzefall T.*, Shivatzki, S.*, Lenz, D.R., Rathkolb, B., Ushakov, K., Karfunkel, D., Shapira, Y., Wolf, M., Mohr, M., Wolf, E., Sabrautzki, S.,Hrabé de Angelis, M., Frydman, M., Brownstein, Z., and **Avraham, K.B.** (2013) Cytoplasmic mislocalization of POU3F4 due to novel mutations leads to deafness in humans and mice. *Hum. Mut*. 34:1102-1110.

Ehmann, H., Hartwich, H., Salzig, C., Hartmann, N., Clément-Ziza, M., Ushakov, K., **Avraham, K.B**., Bininda-Emonds, O.R.P., Hartmann, A.K., Lang, P., Friauf, E., and Gerd Nothwang, H. (2013) Time-dependent gene expression analysis of the developing superior olivary complex. *J. Biol. Chem.* 288:25865-25879.

Brownstein, Z.*, Abu-Rayyan, A.*, Karfunkel-Doron, D., Sirigu, S., Davidov, B., Shohat, M., Frydman, M., Houdusse, A., Kanaan, M., **Avraham, K.B.** (2013) Novel myosin mutations for hereditary hearing loss revealed by targeted genomic capture and massively parallel sequencing. *Eur J Hum Genet*., 22:768-75.

Takada, Y., Beyer, L.A., Swiderski, D.L., O'Neal, A.L., Prieskorn, D.M., Shivatzki, S., **Avraham, K.B.**, and Raphael, Y. (2013) Connexin 26 null mice exhibit spiral ganglion degeneration that can be blocked by BDNF gene therapy. *Hear. Res*. 309C:124-135.

Behar, D.M., Davidov, B., Brownstein, Z., Ben-Yosef, T., **Avraham, K.B.**, and Shohat, M. (2014) The many faces of sensorineural hearing loss: one founder and two novel mutations affecting one family of mixed Jewish ancestry. *Genet. Test. Mol. Biomarkers*. 18:123-126.

Rudnicki, A., Shivatzki, S., Beyer, L.A., Takada, Y., Raphael, Y. and **Avraham, K.B**. (2014) microRNA-224 regulates Pentraxin 3, a component of the humoral arm of innate immunity, in inner ear inflammation. *Hum. Molec. Genet*. 23:3138-46.

Dror A.A., Lenz, D.R., Shivatzki, S., Cohen, K., Ashur-Fabian, O. and **Avraham, K.B.** (2014) Atrophic thyroid follicles and inner ear defects reminiscent of cochlear hypothyroidism in *Slc26a4*-related deafness. *Mamm. Genome*. 25:304-316.

Rudnicki, A., Isakov, O., Ushakov, K., Shivatzki, S., Weiss, I., Friedman, L.M., Shomron, N. and **Avraham, K.B.** (2014) Next-generation sequencing of small RNAs from inner ear sensory epithelium identifies microRNAs and defines regulatory pathways. *BMC Genomics*. 15:484.

Sokolov, M., Brownstein, Z., Frydman, M. and **Avraham, K.B.** (2014) Apparent phenotypic anticipation in autosomal dominant connexin 26 deafness. *J. Basic Clin. Physiol. Pharmacol.* 25:289-292.

Jones, C., Qian, D., Kim, S.M., Li, S., Ren, D., Knapp, L., Sprinzak, D., **Avraham, K.B.**, Matsuzaki, F., Chi, F. and Chen, P. (2014) Ankrd6 is a mammalian functional homolog of *Drosophila* planar cell polarity gene diego and regulates coordinated cellular orientation in the mouse inner ear. *Dev. Biol*. 395:62-72.

Shefer, S., Gordon, C., **Avraham, K.B.** and Mintz, M. (2015) Balance deficit enhances anxiety and balance training decreases anxiety in vestibular mutant mice. *Behav Brain Res*, 276:76-83.

Bhonker, Y., Abu-Rayyan, A., Ushakov, K., Amir-Zilberstein, A., Shivatzki, S., Yizhar-Barnea, O., Elkan-Miller, T., Tayeb-Fligelman, E., Kim, S.M., Landau, M., Kanaan, K., Chen, P., Matsuzaki, F., Sprinzak, D., **Avraham, K.B.** (2015) The GPSM2/LGN GoLoco motifs are essential for hearing. *Mamm*. Genome, 27:29-46.

Marcotti, W., Corns, L.F., Goodyear, R.J., Rzadzinska, A.K., **Avraham, K.B.**, Steel, K.P., Richardson, G. and Kros, C.J. (2016) The acquisition of mechano-electrical transducer current adaptation in auditory hair cells requires myosin VI. *J. Physiol*. 594:3667-3681.

Perl, K., Ushakov, K., Pozniak, Y., Yizhar-Barnea, O., Bhonker, Y., Shivatzki, S., Geiger, T., **Avraham, K.B.***, Shamir, R. (2016)* Reduced changes in protein compared to mRNA levels across non-proliferating tissues. *BMC Genomics*, 18:305. *Shared authorship.

Ushakov, K., Koffler-Brill, T., Rom, A., Perl, K., Ulitsky, I., **Avraham, K.B.** (2017) Genome-wide identification and expression profiling of long non-coding RNAs in auditory and vestibular systems. *Sci. Rep.*, 7:8637.

Reviews and Chapters

Brownstein, Z., Shivatzki, S. and **Avraham, K.B.** (2013) Molecular Etiology of Deafness and Cochlear Consequences. *In*: Deafness. (A. Kral, A.N. Popper, R.R. Fay, eds). Springer-Verlag, NY. 47:17-39.

Higashi, T., Lenz, D.R., Furuse, M. and **Avraham, K.B.** (2013) A "*Tric*" to tighten cell-cell junctions in the cochlea for hearing. *J. Clin. Invest*. 123:3712-3715.

Idan, N., Brownstein, Z., Shivatzki, S., and **Avraham, K.B.** (2013) Advances in genetic diagnosis for hereditary hearing loss. *J Basic Clin Physiol Pharmacol.* 24:165-170.

Avraham, K.B. (2013) Rescue from hearing loss in Usher's syndrome. *N Engl J Med.* 369:1758-1760.

Ushakov, K., Rudnicki, A., **Avraham, K.B**. (2013) MicroRNAs in sensorineural diseases of the ear. *Front Molec Neurosci*. 6:52.

Bhonker, Y., Ushakov, K., **Avraham, K.B**. (2014) Human Gene Discovery for Understanding Development of the Inner Ear and Hearing Loss. *In:* Development of Auditory and Vestibular Systems. Fourth Edition. (R. Romand, I. Varela, eds). Elsevier.

Karfunkel-Doron, D., Brownstein, Z. and **Avraham, K.B.** (2014) Genomic Applications in Audiological Medicine. In: Genomic Medicine Principals and Practice. Second Edition. (D. Kumar, C. Eng, eds). Oxford University Press. 663-682.

Koffler, T., Ushakov, K. and **Avraham, K.B.** (2015) Genetics of hearing loss – syndromic. *Otolaryngol Clin North Am*. 48:1041-1061.

Avraham, K.B. What's hot about otoferlin. (2016) *EMBO J.* 35:2502-2504.

Dror, A. and Avraham, K.B. (2017) The Slc26a4loop Mouse Model for Pendred's Syndrome and Nonsyndromic Deafness. In: The Role of Pendrin in Health and Disease. (S. Dossena, M. Paulmichl, eds). Springer International Publishing. 23-36.

Doetzlhofer, A. and **Avraham, K.B.** (2016) Insights into inner ear-specific gene regulation: epigenetics and non-coding RNAs in inner ear development and regeneration. Semin. *Cell Dev. Biol.* 65:69-79.

Yizhar-Barnea, O. and **Avraham, K. B.** (2017) Single cell analysis of the inner ear sensory organs. *Int J Dev Biol*. 61:205-213.

Grants

2011 – 2017	Gene Discovery for Hearing Loss in Middle East by Massively Parallel Sequencing, National Institutes of Health, Co-PI: Moien Kanaan
2014 – 2017	Epigenetic Regulation in the Mammalian Inner Ear. Binational Science Foundation. Co-PI: R. David Hawkins.
2016 – 2019	Identification of a Network of Short and Long Noncoding RNAs Controlling Mammalian Inner Ear Development. Israel Science Foundation. Foundation.
2018-2020	Function of microRNAs in the peripheral and central auditory system. German-Israeli Foundation for Scientific Research and Development (GIF). Co-PI: Hans Gerd Nothwang

Dr. Ran Elkon, Ph.D.

Department of Human Molecular Genetics and Biochemstry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: ranel@post.tau.ac.il
URL: http://www.elkonlab.tau.ac.il

Genomic-scale Bioinfomatics Exploration of Gene Regulation

Positions

Senior Lecturer, Sackler Faculty of Medicine

Research

Our research focuses on understanding mechanisms of gene regulation, which is an intricate multi-layer process. We apply bioinofrmatics methods to elucidate, on a genomic scale, how gene expression is regulated at the layers of gene transcription, transcript stability and protein translation. We aim at discovering how interruptions in these regulatory mechanisms contribute to the development of human pathological conditions, and how natural genomic variation affects our predisposition to common human diseases. Our analyses are based on novel deep-sequencing techniques that greatly boost our ability to systematically study gene regulation and decipher regulatory layers that were until recently largely unexplored.

Publications

Korkmaz G, Lopes R, Ugalde AP, Nevedomskaya E, Han R, Myacheva K, Zwart W, **Elkon R***, Agami R*. Functional genetic screens for enhancer elements in the human genome using CRISPR-Cas9. Nat Biotechnol. 2016, 34:192-8. (* Co-corresponding author)

Friedman-Mazursky O, **Elkon R**, Efrat S. Redifferentiation of expanded human islet β cells by inhibition of ARX. Sci Rep. 2016; 6:20698.

Creemers EE, Bawazeer A, Ugalde AP, van Deutekom HW, van der Made I, de Groot NE, Adriaens ME, Cook SA, Bezzina CR, Hubner N, van der Velden J, **Elkon R**, Agami R, Pinto YM. Genome-wide polyadenylation maps reveal dynamic mrna 3'-end formation in the failing human heart. Circ Res. 2016, 118:433-8.

Elkon R*, Loayza-Puch F*, Korkmaz G, Lopes R, Breugel PCv, Bleijerveld OB, Altelaar AFM, Wolf E, Lorenzin F, Eilers M, Agami R: Myc coordinates transcription and translation to enhance transformation and suppress invasiveness. *EMBO Rep. 2015, pii: e201540717*. (*Equal contribution).

Elkon R*, Milon B*, Morrison L, Shah M, Vijayakumar S, Racherla M, Leitch CC, Silipino L, Hadi S, Weiss-Gayet M, Barras E, Schmid CD, Ait-Lounis A, Barnes A, Song Y, Eisenman DJ, Eliyahu E, Frolenkov GI, Strome SE, Durand B, Zaghloul NA, Jones SM, Reith W, Hertzano R. RFX transcription factors are essential for hearing in mice. *Nat Commun 2015, 6:8549*. (*Equal contribution).

Rashi-Elkeles S*, Warnatz HJ*, **Elkon R***, Kupershtein A, Chobod Y, Paz A, Amstislavskiy V, Sultan M, Safer H, Nietfeld W, Lehrach H, Shamir R, Yaspo ML, Shiloh Y. Parallel profiling of the transcriptome, cistrome, and epigenome in the cellular response to ionizing radiation. *Sci Signal. 2014, 7:rs3*. (*Equal contribution).

Loayza-Puch F, Drost J, Rooijers K, Lopes R, **Elkon R***, Agami R*. p53 induces transcriptional and translational programs to suppress cell proliferation and growth. *Genome Biol. 2013, 14:R32.* (*co-corresponding authors).

Melo CA, Drost J, Wijchers PJ, van de Werken H, de Wit E, Oude Vrielink JA, **Elkon R**, Melo SA, Leveille N, Kalluri R, de Laat W, Agami R. eRNAs are required for p53-dependent enhancer activity and gene transcription. *Mol Cell. 2013, 49:524-35*.

Reviews

Elkon R, Ugalde AP, Agami R. Alternative cleavage and polyadenylation: extent, regulation and function. *Nat Rev Genet. 2013, 14:496-506*.

Prof. David Gurwitz, Ph.D.

Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

Email: gurwitz@post.tau.ac.il
URL:http://neuroscience-web.tau.ac.il/en/?post_type=portfolio&p=1757

Genomic Biomarkers for CNS Drug Response

Positions

Associate Professor, Sackler Faculty of Medicine
Director, National Laboratory for the Genetics of Israeli Populations

Senior Editor, *Pharmacogenomics*

Editorial Board: *Trends in Molecular Medicine, Genome Medicine, CNS Drugs, Drug Development Research, Pharmaceutical Biology Genomic Medicine*

Member of the NIH Pharmacogenomics Research Network (PGRN)

Research

Our lab, serving as the National Laboratory for the Genetics of Israeli Populations (http://nlgip.tau.ac.il), was established in 1995 by the Israeli Academy for Sciences and Humanities as the National Biobank of Israel. The biobank includes DNA samples and immortalized lymphoblastoid cell lines from over 2000 unrelated healthy donors representing the large genetic diversity of Jewish, Arab and Druze communities of Israel. This novel resource has been applied by hundreds of research groups in Israel and abroad.

Our primary interest is in finding genomic biomarkers for the response to CNS drugs – , for improving personalized medicine with respect to both treatment efficacy and safety. Our research is currently focused on drugs for treating major depression, bipolar disorder, and Alzheimer's disease. These CNS diseases inflict huge societal costs, and biomarkers are needed for better treatment. We use human immortalized lymphoblastoid cell lines from unrelated healthy donors for comparing drug response and searching for genomic biomarkers, including mRNA for genes, and non-coding RNAs such as microRNAs (miRNAs) and small nucleolar RNAs (snoRNAs).

Among genes that we identified as tentative genomic biomarkers for the response to anti-depressant drugs, two genes, CHL1 and ITGB3, have been replicated in clinical cohorts of major depression patients, lending support for our novel research approach.

A recent publication from our lab has been cited in a report by Scientific American: Unraveling the Mystery of How Antidepression Drugs Work:

http://www.scientificamerican.com/article/unraveling-the-mystery-of-ssris-depression/

In addition to the research on genomic biomarkers, we are involved in research on bioethics and societal aspects of human genomics research.

Publications

Gurwitz D. Data re-identification: protect the children. *Science*. 339(6123):1033 (2013).

Lunshof JE, **Gurwitz D**. Parental consent: Guarding children's genetic privacy. *Nature*. 494:430 (2013).

Morag A, Oved K, **Gurwitz D**. Sex differences in human lymphoblastoid cells sensitivities to antipsychotic drugs. *J Mol Neurosci*. 49:554-8 (2013).

Gurwitz D, McLeod HL. Genome-wide studies in pharmacogenomics: harnessing the power of extreme phenotypes. *Pharmacogenomics*. 14:337-339 (2013).

Gurwitz D. Expression profiling: a cost-effective biomarker discovery tool for the personal genome era. *Genome Med*. 5:41 (2013).

Oved K, Morag A, Pasmanik-Chor M, Rehavi M, Shomron N, **Gurwitz D**. Genome-wide expression profiling of human lymphoblastoid cell lines implicates integrin beta-3 in the mode of action of antidepressants. *Transl Psychiatry*. 3:e313 (2013).

Verhoef TI, Ragia G, de Boer A, Barallon R, Kolovou G, Kolovou V, Konstantinides S, Le Cessie S, Maltezos E, van der Meer FJ, Redekop WK, Remkes M, Rosendaal FR, van Schie RM, Tavridou A, Tziakas D, Wadelius M, Manolopoulos VG, Maitland-van der Zee AH; EU-PACT Group. A randomized trial of genotype-guided dosing of acenocoumarol and phenprocoumon. *N Engl J Med*. 369:2304-12 (2013).

Gurwitz D. Gene drives raise dual-use concerns. *Science*. 345:1010 (2014).

Gurwitz D. Computing: Keep files small to curb energy use. *Nature*. 514:305 (2014).

Gurwitz D. From transcriptomics to biological networks. *Drug Dev Res.* 75(5):267-70 (2014).

Gurwitz D., Milanesi E, Koenig T. Grant application review: the case of transparency. *PLoS Biology.* DOI: 10.1371/journal.pbio.1002010 (2014).

Chouchana L, Fernández-Ramos AA, Dumont F, Marchetti C, Ceballos-Picot I, Beaune P, **Gurwitz D**, Loriot MA. Molecular insight into thiopurine resistance: transcriptomic signature in lymphoblastoid cell lines. Genome Med. 7:37 (2015).

Markovič T, Gobec M, **Gurwitz D**, Mlinarič-Raščan I. Characterization of human lymphoblastoid cell lines as a novel in vitro test system to predict the immunotoxicity of xenobiotics. Toxicol Lett. 233:8-15 (2015).

Milanesi E, Hadar A, Maffioletti E, Werner H, Shomron N, Gennarelli M, Schulze TG, Costa M, Del Zompo M, Squassina A, **Gurwitz D**. Insulin-like Growth Factor 1 Differentially Affects Lithium Sensitivity of Lymphoblastoid Cell Lines from Lithium Responder and Non-responder Bipolar Disorder Patients. J Mol Neurosci. 56:681-7 (2015).

Fabbri C, Crisafulli C, **Gurwitz D**, Stingl J, Calati R, Albani D, Forloni G, Calabrò M, Martines R, Kasper S, Zohar J, Juven-Wetzler A, Souery D, Montgomery S, Mendlewicz J, Girolamo GD, Serretti A. Neuronal cell adhesion genes and antidepressant response in three independent samples. Pharmacogenomics J. 15:538-48 (2015).

Probst-Schendzielorz K, Scholl C, Efimkina O, Ersfeld E, Viviani R, Serretti A, Fabbri C, **Gurwitz D**, Lucae S, Ising M, Paul AM, Lehmann ML, Steffens M, Crisafulli C, Calabrò M, Holsboer F, Stingl J. CHL1, ITGB3 and SLC6A4 gene expression and antidepressant drug response: results from the Munich Antidepressant Response Signature (MARS) study. Pharmacogenomics. 16:689-701 (2015).

Lapkina-Gendler L, Rotem I, Pasmanik-Chor M, **Gurwitz D**, Sarfstein R, Laron Z, Werner H. Identification of signaling pathways associated with cancer protection in Laron syndrome. Endocr Relat Cancer. 23:399-410 (2016).

Rzezniczek S, Obuchowicz M, Datka W, Siwek M, Dudek D, Kmiotek K, Oved K, Shomron N, **Gurwitz D**, Pilc A. Decreased sensitivity to paroxetine-induced inhibition of peripheral blood mononuclear cell growth in depressed and antidepressant treatment-resistant patients. Transl Psychiatry. 6:e827 (2016).

Hadar A, Milanesi E, Squassina A, Niola P, Chillotti C, Pasmanik-Chor M, Yaron O, Martásek P, Rehavi M, Weisglass-Volkov D, Shomron N, Gozes I, **Gurwitz D**. RGS2 expression predicts amyloid-β sensitivity, MCI and Alzheimer's disease: genome-wide transcriptomic profiling and bioinformatics data mining. Transl Psychiatry 6:e909 (2016).

Breitfeld J, Scholl C, Steffens M, Brandenburg K, Probst-Schendzielorz K, Efimkina O, **Gurwitz D**, Ising M, Holsboer F, Lucae S, Stingl JC. Proliferation rates and gene expression profiles in human lymphoblastoid cell lines from patients with depression characterized in response to antidepressant drug therapy. Transl Psychiatry. 6:e950 (2016).

Milanesi E, Voinsky I, Hadar A, Srouji A, Maj C, Shekhtman T, Gershovits M, Gilad S, Chillotti C, Squassina A, Potash JB, Schulze TG, Goes FS, Zandi P, Kelsoe JR, **Gurwitz D**. RNA sequencing of bipolar disorder lymphoblastoid cell lines implicates the neurotrophic factor HRP-3 in lithium's clinical efficacy. World J Biol Psychiatry. 1-13 (2017).

Hadar A, Milanesi E, Squassina A, Niola P, Chillotti C, Pasmanik-Chor M, Yaron O, Martásek P, Rehavi M, Weissglas-Volkov D, Shomron N, Gozes I, **Gurwitz D**. RGS2 expression predicts amyloid-β sensitivity, MCI and Alzheimer's disease: genome-wide transcriptomic profiling and bioinformatics data mining. Transl Psychiatry. 7:e1035 (2017).

Reviews

Gurwitz D. Genetic privacy: trust is not enough. Science. 347:957-8 (2015).

Gurwitz D. Exosomal microRNAs in tissue crosstalk. Drug Dev Res. 76:259-62 (2015).

Gurwitz D. Human iPSC-derived neurons and lymphoblastoid cells for personalized medicine research in neuropsychiatric disorders. Dialogues Clin Neurosci. 18:267-276 (2016)

Gurwitz D. Peptide mimetics: Fast-forward look. Drug Dev Res. 78:231-235 (2017).

Gurwitz D. Peer review: Award bonus points to motivate reviewers. Nature. 542:414 (2017).

Grants

2014 – 2018 Deciphering beta-amyloid and tau neurotoxicity: Genome-wide expression profiling for sensitivity

biomarkers, Israel Science Foundation. Jointly with Illana Gozes

2014 – 2018 LITHOMICS: Lithium response biomarkers: comparative RNA sequencing of patients` lymphocytes and immortalized lymphoblastoid cell lines for personalized treatment of bipolar disorder, US – Israel Binational Science Foundation (BSF). Jointly with Peter Zandi, Thomas Schulze, Fernando Goes, James Potash, John Kelsoe

Prof. Carmit Levy, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler School of Medicine

TEL AVIV UNIVERSITY

Email: @post.tau.ac.il
Alternate email: @gmail.com
URL: http://www.carmitlevylab.com/

microRNA and DICER in Differentiation and Malignant Transformation of Melanocytes

Position

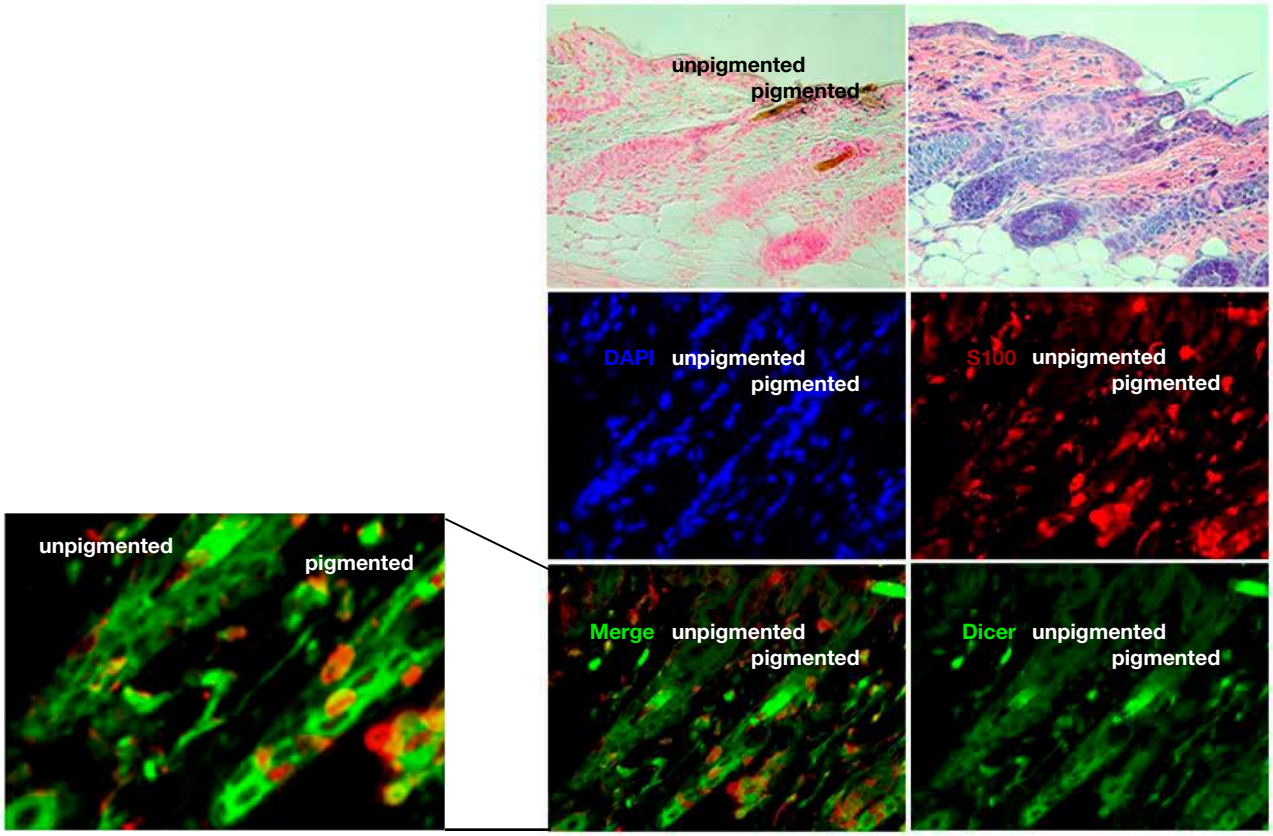
Associate Professor, Sackler Faculty of Medicine

Research

Our scientific interests involve the role of microRNAs in development, differentiation and malignant transformation. Focusing our studies on melanocytes will provide the foundation for developing novel approaches in the prevention, diagnosis, and treatment of skin cancer in general and melanoma in particular. In addition, we are intrigued by the possibility of using these systems as a model for exploring basic microRNA biogenesis beyond the cell specific context.

Publications

Brenner, R., **Levy, C.** and Kivity, S. (2017) Familial Mediterranean fever and incidence of cancer: An



Skin section, subject to H&E (left) and Fontana-Masson staining of melanin (right), shows pigmented and unpigmented regions of (floxed/floxed); Dct(Cre/Cre); Dct-lacZ; K14-scf mouse skin. Immunofluorescent staining of the skin section indicates expression of DICER (green) and S100 (red) (400x magnification). S100-stained epidermal and hair follicle melanocytes appear red; DAPI-stained nuclei appear blue. Merged image shows co-localization of DICER and S100 in the pigmented area of the skin (merge) compared to unpigmented region. Arrows in enlarged merge picture indicate the S100 and DICER co-localization.

analysis of 8534 patients with 258,803 person-years. *Arthritis & Rheumatology*.

Sheinboim, S., Maza, I., Dror, I., Parikh, S., Krupalnik, V., Bell, R.E., Zviran, A., Hakim, O., Mandel Gutfreund, Y., Khaled, M., Hanna, J.H. and **Levy C.** (2017) Oct4 impedes cell fate redirection by the melanocyte lineage master regulator Mitf in mouse ESCs. *Nature Communications*. In press.

Dror S, Sander L, Schwartz H, Sheinboim D, Barzilai A, Dishon Y, Apcher S, Golan T, Greenberger S, Barshack I, Malcov H, Zilberberg A, Levin L, Nessling M, Friedmann Y, Igras V, Barzilay O, Vaknine H, Brenner R, Zinger A, Schroeder A, Gonen P, Khaled M, Erez N, Hoheisel JD, **Levy C**. Melanoma miRNA trafficking controls tumour primary niche formation. *Nat Cell Biol*. 2016`

Levin L, Srour S, Gartner J, Kapitansky O, Qutob N, Dror S, Golan T, Dayan R, Brener R, Ziv T, Khaled M, Schueler-Furman O,Samuels Y, Levy C. Parkin aomatic mutations link melanoma and Parkinson's Disease. *J Genet Genomics*. 2016;43:369-79.

Bell RE*, Golan T*, Salamon A, Liron T, Sheinboim D, Gelfman S, Gabet Y, Shamir R, Levy C. Enhancer methylation dynamics contribute to cancer plasticity and patient mortality. *Genome Res*, 26:601-11. 2016.

Golan T, Messer AR, Amitai-Lange, A, Melamed Z, Ohana R, Bell RE, Kapitansky O, Lerman G, Greenberger S, Khaled M, Amar N, Albrengues J, Gaggioli C, Gonen P, Tabach Y, Sprinzak D, Shalom-Feuerstein R & Levy C. Interactions of melanoma cells with distal keratinocytes trigger metastasis via notch signaling inhibition of MITF. *Mol Cell* 59, 664-676. 2015.

Bell RE, Khaled M, Netanely D, Schubert S, Golan T, Buxbaum A, Janas MM, Postolsky B, Shamir R, **Levy C***. Transcription factor/microRNA axis blocks melanoma adhesion program by miR-211 targeting NUAK1. *J Invest Dermatol,* 134:441-512013. 2014.

Tabach Y, Golan T, Hernández-Hernández A, Messer AR, Fukuda T, Kouznetsova A, Liu J-G, Lilienthal I, **Levy C*,** Ruvkun G*. Human disease locus discovery and mapping to molecular pathways through phylogenetic profiling. *Mol Syst Biol*, 9:692. 2013.

Shaham O, Gueta K, Mor E, Oren-Giladi P, Grinberg D, Xie Q, Cvekl A, Shomron N, Davis N, Keydar-Prizant M, Raviv S, Pasmanik-Chor M, Bell R, **Levy C**, Avellino R, Banfi S, Conte I, Ashery-Padan R. Pax6 regulates gene expression in the vertebrate lens through miR-204. *PLoS Genet,* 9:e1003357. 2013.

Melamed Z, Levy A, Ashwal-Fluss R, Lev-Maor G, Mekahel K, Atias N, Gilad S, Sharan R, **Levy C**, Kadener S*, Ast G*. Alternative splicing regulates biogenesis of miRNAs located across exon-intron junctions. *Mol Cell* 50: 869-881, 2013.

Reviews

Levy, C. and Khaled M. (2015). Ecad vitiliGONE. *Pigment Cell Melanoma Res* doi: 10.1111/pcmr.12377.

Grants

2016-2019 Melanoma Research Alliance (MRA)

2016-2021 European Research Council (ERC)

Prof. Zvi (Gregory) Livshits, Ph.D.

Department of Anatomy and Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: gregl@post.tau.ac.il
URL: http://www.tau.ac.il/medicine/anatomy/anatomy.html

Genetic and Metabolic Research of Age-Dependent Chronic Degenerative Disease

Positions

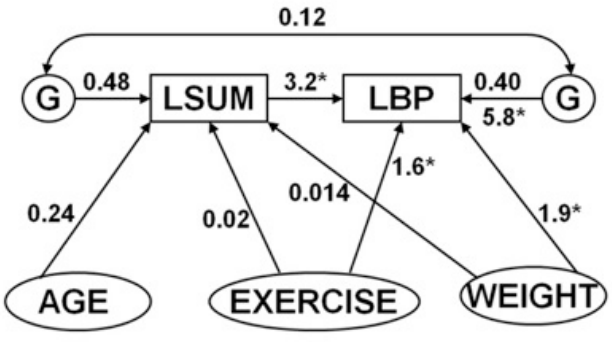
Professor Emeritus, Sackler Faculty of Medicine

Pollak Chair of Biological Anthropology

Honorary Research Fellow, King's College Medical School, London, UK

Research

Our research is focused on age-related chronic degenerative disease, such as osteoporosis, osteoarthritis, including disc degeneration disease and muscle mass loss – sarcopenia. The prevalence of sarcopenia is as high as 30% for those above 60 years old. In the elderly, the loss of muscle mass is correlated with profound physical impairment and disability with severe clinical consequences, including mobility loss, osteoporosis, osteoarthritis, increased fracture risk, dyslipidemia, insulin resistance, and increased mortality. However, it is also often developed at a much younger age. Despite the above clinical significance and despite the fact that a strong familial component in muscular mass variation is well established, there is almost a total lack of molecular genetic studies of this trait. This is in a great contradiction to studies concerning the other two body composition components: bone and fat mass, for each of which many dozens of studies have been published during the past two decades. It is therefore timely and imperative to invest extensive scientific research n the genetic and metabolic mechanisms of early and rapid muscle mass loss. The other important subject of our current research is low back pain, representing most common musculoskeletal disorder in general human population. However, it is still unclear which individuals develop it. We examine the contribution of genetic factors, lumbar disc degeneration and other potential risk factors in a general human population.



Path diagram of the main risk factors for low back pain (LBP) in middle-age women. The figure shows contribution of various factors to LBP, including genetic effects (G) and lumbar disc degeneration (LSUM). The results presented as variance components (portions) and odds ratios (marked by *). According to Livshists et al 2011, Ann Rheumat Dis.

Publications

Orit Blumenfeld, Frances MK Williams, Debora J Hart, Nigel K Arden, Timothy D Spector, Gregory **Livshits**. Lower limbs composition and radiographic knee osteoarthritis (RKOA) in Chingford sample – a longitudinal study. *Arch Gerontol Geriat*, 2013; 56:148-54.

Ruth Z. Birk, Sergey Ermakov, Gregory **Livshits**. Common fSNP variants of fourteen Bardet-Biedl syndrome genes and adult body mass. *Obesity*, 2013, 21:1684-9

Liran Franco, Frances MK Williams, Svetlana Trofimov, Tim D Spector, Gregory **Livshits**. Contribution of putative genetic factors and candidate gene variants to inter-individual variation of circulating fractalkine (CX3CL1) levels in a large UK twins' sample. *Hum Immunol*, 2013; 74:358-63.

Liran Franco, Frances MK Williams, Svetlana Trofimov, Tim D Spector, Gregory **Livshits**. Elevated plasma fractalkine levels are associated with higher levels of IL-6, Apo-B, LDL-C and insulin, but not with body composition. *Metabolism*, 2013; 62:1081-87.

Orit Blumenfeld, Frances MK Williams, Debora J Hart, Nigel K Arden, Timothy D Spector, Gregory **Livshits**. Association between cartilage and bone biomarkers and incidence of radiographic knee osteoarthritis (RKOA) in UK females: A prospective study. *Osteoarthritis Cartil,* 2013;21:923-9.

Liran Franco, Frances MK. Williams, Svetlana Trofimov, Ida Malkin, Gabriela Surdulescu, Timothy Spector, **Gregory Livshits**. Changes in heritability and IGF-1 gene effect on IGF-1circulating levels variation, *AGE*, 2014; 36:9622.

Orit Blumenfeld, Frances MK Williams, Ana Valdes, Debora J Hart, Ida Malkin, Timothy D Spector, **Gregory Livshits**. Association of interleukin-6 gene polymorphisms with hand osteoarthritis and osteoporosis. Cytokine, 2014; 69:94-101.

Ida Malkin, Frances MK Williams, Genevieve LaChance, Timothy Spector, Alex J MacGregor, **Gregory Livshits**. Low back and common widespread pain share common genetic determinants. *Ann Hum Genet* 2014; 78:357-66.

Tasbulat Dosaev, Jai Prakash, **Gregory Livshits**. Contribution of body composition components and biochemical factors related to fat and muscle tissues metabolism to body mass index variation, *Am J Hum Biol* 2014; 26:760-7.

Adina Bachar, Doron Hermony, **Gregory Livshits**. Ruth Birk. Late successful weight reduction and maintenance among overweight and obese adults – a two year retrospective study. *Diabetes Res Clinical Practice*. 2014; 106:511-21.

Alina German, **Gregory Livshits**, Inga Peter, Ida Malkin, Jonathan Dubnov, Hannah Akons, Michael Shmoish, Ze'ev Hochberg. Environmental rather than genetic factors determine the variation in age of the infancy to childhood transition (ICT): a twins study. *J Pediatr* 2015; 166:731-5.

Prakash J, Pichchadze G, Trofimov S, **Livshits G**. Age and genetic determinants of variation of circulating levels of the receptor for advanced glycation end products (RAGE) in the general human population. Mech Aging Devel 2015; 145:18-25.

Korostishevsky M, Williams FMK, Malkin I, Spector T, Macgregor AJ, **Livshits G**. Genetics and metabolomics of muscular mass. Eur J Hum Genet 2015.

Momi SK, Fabiane SM, Lachance G, **Livshits G**, Williams FM. Neuropathic pain as part of chronic widespread pain: environmental and genetic influences. Pain, 2015; 156:2100-6.

Livshits G, Macgregor AJ, Gieger C, Malkin I, Moayyeri A, Grallert H, Emeny RT, Spector TD, Kastenmüller G, Williams FMK. An omics investigation of chronic widespread musculoskeletal pain reveals potential biomarker. Pain, 2015; 156:1845-51.

Livshits G, Gao F, Malkin I, Needhamsen M, Xia Y, Yuan W, Bell CG, Ward K, Liu Y, Wang J, Bell JT, Spector TD. Contribution of heritability and epigenetic factors to skeletal muscle mass variation in United Kingdom twins. J Clin Endocrinol Metab. 2016; 101:2450-9.

Prakash J, Williams FM, Trofimov S, Surdulescu G, Spector T, **Livshits G.** Quantitative genetics of circulating Dickkopf-related protein 1 (DKK1) in community-based sample of UK twins. Osteoporos Int. 2016; 27:2065-75.

Burri A, Ogata S, **Livshits G**, Williams F. the association between chronic widespread musculoskeletal pain, depression and fatigue is genetically mediated. PLoS One. 2015; 10:e0140289.

Momi SK, Fabiane SM, Lachance G, **Livshits G**, Williams FM. Neuropathic pain as part of chronic widespread pain: environmental and genetic influences. Pain. 2015; 156:2100-6.

Burri A, Marinova Z, Robinson M, Kuehnel B, Waldenberger M, Wahl S, Kunze S, Geiger C, **Livshits G**, Williams F. Are epigenetic factors implicated in chronic widespread pain? PLoS One, 2016; 11:e0165548.

Ghosh S, Dosaev T, Malkin I, **Livshits G**. Comparative quntitative genetic analysis of the reltaionship between the body composition, somatotypes and arterial blood pressure in two ethnically differnet human populations. Am J Phys Anthrop, 2017; 162:701-714.

Livshits G, Malkin I, Freidin M, MacGregor A, Bell JT, Williams F. A genome-wide methylation analysis of a large population sample suggests neurological pathways involvement in chronic widespread pain. Pain, 2017; 158:1053-1062.

Prakash J, Gabdulina G, Trofimov S, **Livshits G.** Quantitative genetics of circulating hyaluronic acid (HA) and its correlation with age, body composition and hand osteoarthritis in community based sample. Ann Hum Biol 2017.

Zillikens MC, Demissie S, Yerges L, Hsu Y-H, Stolk L, Ward L, **Livshits G,** Chou, Ward LD, Broer L, Johnson T, Koller DL et al. Kiel D. A large meta-analysis of genome wide association studies identifies five significant loci for lean body mass. Nat Comm 2017; 8:80.

Livshits G, Ni Lochlainn M, Malkin I, Bowyer R, Verdi S, Staves C, Williams F. Shared genetic influence on frailty and chronic widespread pain: a study from TwinsUK. Age Ageing (in press).

Reviews

Sapir-Koren R, and **Livshits G**. Are estrogen and estrogen receptors essential to mechanical stimulation of bone formation? *Osteoporos Int*. 2013; 24:1771–89.

Sapir-Koren R, and **Livshits G**. Osteocyte control of bone remodeling: Is sclerostin a key molecular coordinator of the coupled bone resorption-formation cycles? *Osteopor Int*. 2014; 25:2685-700.

Sapir-Koren R, and **Livshits G**. Association of systemic hormones with FGF23 levels and their combined effect on bone remodeling. *BioFactors* 2014; 40:555-68.

Kalinkovich A and **Livshits G**. Sarcopenia – the search for emerging biomarkers. Aging Research Reviews, 2015, 22:58-71.

Sapir-Koren R, **Livshits G**. Rheumatoid arthritis onset in postmenopausal women: Does the ACPA seropositive subset result from genetic effects, estrogen deficiency, skewed profile of CD4(+) T-cells, and their interactions? Mol Cell Endocrinol. 2016; 431:145-63.

Kalinkovich A, **Livshits G**. Sarcopenic obesity or obese sarcopenia: A cross talk between age-associated adipose tissue and skeletal muscle inflammation is a main mechanism of the pathogenesis. Age Res Rev, 2016; 35:200-221.

Sapir-Koren R, **Livshits G**. Postmenopausal osteoporosis in rheumatoid arthritis: the estrogen deficiency–immune mechanisms link. Bone, 2017; 103: 102–115.

Grants

2013-2017 Genetics, Genomics and Metabolomics of the Low Back Pain and Spinal Disc Degeneration in Complex Arab Pedigrees in Israel. Israel Science Foundation (ISF).

Dr. Noam Shomron, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: @post.tau.ac.il
URL: http://www.tau.ac.il/~n-shomron

Genomics and Gene Regulation by Small RNAs

Positions

Senior Lecturer, Sackler Faculty of Medicine

Academic Director, ScienceAbroad

Editor-in-Chief, *Genetics Research*

Research

Our laboratory focuses on the analysis of regulation of gene expression aimed at understanding human disease. Combining high-throughput methods and bioinformatics, one aspect of our team's research explores microRNA regulation in order to reach a global, systems perspective of the mechanistic roles microRNAs play during disease development. Among our projects:

- Identification of a microRNA molecule that controls several oncogenes. Their discovery is paving the way for a potentially revolutionary drug for cancer treatment.
- Revealing the influence of microRNAs on pharmacogenomics and personalized medicine, thus leading to tailored drugs for cancer treatment.
- Exposing pathogens in human tissues based on deep sequencing of small RNA molecules followed by subtraction and assembly of the various genomes.

Publications

Pillar N, Pleniceanu O, Fang M, Ziv L, Lahav E, Botchan S, Cheng L, Dekel B, **Shomron N**. A rare variant in the FHL1 gene associated with X-linked recessive hypoparathyroidism. *Hum Genet.* 2017;136(7):835-845.

Eskin-Schwartz M, Drozhdina M, Sarig O, Gat A, Jackman T, Isakov O, **Shomron N**, Samuelov L, Malchin N, Peled A, Vodo D, Hovnanian A, Ruzicka T, Koshkin S, Harmon RM, Koetsier JL, Green KJ, Paller AS, Sprecher E. Epidermolytic Ichthyosis Sine Epidermolysis. *Am J Dermatopathol.* 2017;39(6):440-444.

Einhorn Y, Weissglas-Volkov D, Carmi S, Ostrer H, Friedman E, **Shomron N**. Differential analysis of mutations in the Jewish population and their implications for diseases. *Genet Res (Camb).* 2017;99:e3.

Gilam A, Shai A, Ashkenazi I, Sarid LA, Drobot A, Bickel A, **Shomron N**. MicroRNA regulation of progesterone receptor in breast cancer. *Oncotarget.* 2017;8(16):25963-25976.

Basel-Vanagaite L, Pillar N, Isakov O, Smirin-Yosef P, Lagovsky I, Orenstein N, Salmon-Divon M, Tamary H, Zaft T, Bazak L, Meyerovitch J, Pelli T, Botchan S, Farberov L, Weissglas-Volkov D, **Shomron N**. X-linked elliptocytosis with impaired growth is related to mutated AMMECR1. *Gene*. 2017;606:47-52.

Bochner R, Samuelov L, Sarig O, Li Q, Adase CA, Isakov O, Malchin N, Vodo D, Shayevitch R, Peled A, Yu BD, Fainberg G, Warshauer E, Adir N, Erez N, Gat A, Gottlieb Y, Rogers T, Pavlovsky M, Goldberg I, **Shomron N**, Sandilands A, Campbell LE, MacCallum S, McLean WH, Ast G, Gallo RL, Uitto J, Sprecher E. Calpain 12 Function Revealed through the Study of an Atypical Case of Autosomal Recessive Congenital Ichthyosis. *J Invest Dermatol.* 2017;137(2):385-393.

Gilam A, Conde J, Weissglas-Volkov, Oliva N, Friedman E, Artzi N, **Shomron N**. Local microRNA delivery targets Palladin and prevents metastatic breast cancer. *Nat Commun*. 2016;7:12868.

Hadar A, Milanesi E, Squassina A, Niola P, Chillotti C, Pasmanik-Chor M, Yaron O, Martásek P, Rehavi M, Weisglass-Volkov D, **Shomron N**, Gozes I, Gurwitz D. RGS2 expression predicts amyloid-β sensitivity, MCI and Alzheimer's disease: genome-wide transcriptomic profiling and bioinformatics data mining. *Transl Psychiatry*. 2017;7(2):e1035.

Rzezniczek S, Obuchowicz M, Datka W, Siwek M, Dudek D, Kmiotek K, Oved K, **Shomron N**, Gurwitz

D, Pilc A. Decreased sensitivity to paroxetine-induced inhibition of peripheral blood mononuclear cell growth in depressed and antidepressant treatment-resistant patients. *Transl Psychiatry*. 2016;31;6(5):e827.

Peled A, Sarig O, Samuelov L, Bertolini M, Ziv L, Weissglas-Volkov D, Eskin-Schwartz M, Adase CA, Malchin N, Bochner R, Fainberg G, Goldberg I, Sugawara K, Baniel A, Tsuruta D, Luxenburg C, Adir N, Duverger O, Morasso M, Shalev S, Gallo RL, **Shomron N**, Paus R, Sprecher E. Mutations in TSPEAR, Encoding a Regulator of Notch Signaling, Affect Tooth and Hair Follicle Morphogenesis. *PLoS Genet.* 2016;12(10):e1006369.

Ben-Shachar S, Yanai H, Sherman Horev H, Elad H, Baram L, Isakov O, Tulchinsky H, Pasmanik-Chor M, **Shomron N**, Dotan I. MicroRNAs Expression in the Ileal Pouch of Patients with Ulcerative Colitis Is Robustly Up-Regulated and Correlates with Disease Phenotypes. *PLoS One*. 2016;11(8):e0159956.

Knirsh R, Ben-Dror I, Modai S, **Shomron N**, Vardimon L. MicroRNA 10b promotes abnormal expression of the proto-oncogene c-Jun in metastatic breast cancer cells. *Oncotarget*. 2016;7(37):59932-59944.

Hilly O, Pillar N, Stern S, Strenov Y, Bachar G, **Shomron N**, Shpitzer T. Distinctive pattern of let-7 family microRNAs in aggressive carcinoma of the oral tongue in young patients. *Oncol Lett*. 2016;12(3):1729-1736.

Conde J, **Shomron N**, Artzi N. Biomaterials for Abrogating Metastasis: Bridging the Gap between Basic and Translational Research. *Adv Healthc Mater.* 2016;5(18):2312-9.

Hillman Y, Mazkereth N, Farberov L, **Shomron N**, Fishelson Z. Regulation of complement-dependent cytotoxicity by microRNAs miR-200b, miR-200c, and miR-217. *J Immunol*. 2016;196(12):5156-65.

Lin T, Simchovitz A, Shenhar-Tsarfaty S, Vaisvaser S, Admon R, Hanin G, Hanan M, Kliper E, Bar-Haim Y, **Shomron N**, Fernandez G, Lubin G, Fruchter E, Hendler T, Soreq H. Intensified vmPFC surveillance over PTSS under perturbed microRNA-608/AChE interaction. *Transl Psychiatry.* 2016;3;6:e801.

Eskin-Schwartz M, Metzger Y, Peled A, Weissglas-Volkov D, Malchin N, Gat A, Vodo D, Mevorah B, **Shomron N**, Sprecher E, Sarig O. Somatic mosaicism for a "lethal" GJB2 mutation results in a patterned form of spiny hyperkeratosis without eccrine involvement. *Pediatr Dermatol*. 2016;33(3):322-6.

Ivancic-Jelecki J, Forcic D, Jagusic M, Kosutic-Gulija T, Mazuran R, Lang Balija M, Isakov O, **Shomron N**. Influence of population diversity on neurovirulence potential of plaque purified L-Zagreb variants. *Vaccine*. 2016; 34(20):2383-9.

Abramowitz Y, Roth A, Keren G, Isakov O, **Shomron N**, Laitman Y, Weissglas-Volkov D, Arbel Y, Banai S, Finkelstein A, Friedman E. Whole-exome sequencing in individuals with multiple cardiovascular risk factors and normal coronary arteries. *Coron Artery Dis.* 2016;27(4):257-66.

Menachem A, Makovski V, Bodner O, Pasmanik-Chor M, Stein R, **Shomron N**, Kloog Y. Intercellular transfer of small RNAs from astrocytes to lung tumor cells induces resistance to chemotherapy. *Oncotarget*. 2016;7(11):12489-504.

Inberg S, Jacob E, Elkobi A, Edry E, Rappaport A, Simpson TI, Armstrong JD, **Shomron N**, Pasmanik-Chor M, Rosenblum K. Fluid consumption and taste novelty determines transcription temporal dynamics in the gustatory cortex. *Mol Brain*. 2016;9:13.

Tiram G, Segal E, Krivitsky A, Shreberk-Hassidim R, Ferber S, Ofek P, Udagawa T, Edry L, **Shomron N**, Roniger M, Kerem B, Shaked Y, Aviel-Ronen S, Barshack I, Calderón M, Haag R, Satchi-Fainaro R. Identification of dormancy-associated microRNAs for the design of osteosarcoma-targeted dendritic polyglycerol nanopolyplexes. *ACS Nano.* 2016;10(2):2028-45.

Stapleford KA, Moratorio G, Henningsson R, Chen R, Matheus S, Enfissi A, Weissglas-Volkov D, Isakov O, Blanc H, Mounce BC, Dupont-Rouzeyrol M, **Shomron N**, Weaver S, Fontes M, Rousset D, Vignuzzi M. Whole-genome sequencing analysis from the chikungunya virus caribbean outbreak reveals novel evolutionary genomic elements. *PLoS Negl Trop Dis*. 2016;10(1):e0004402.

Vaisvaser S, Modai S, Farberov L, Lin T, Sharon H, Gilam A, Volk N, Admon R, Edry L, Fruchter E, Wald I, Bar-Haim Y, Tarrasch R, Chen A, **Shomron N**, Hendler T. Neuro-Epigenetic Indications of Acute Stress Response in Humans: The case of microRNA-29c. *PLoS One*. 2016;11(1):e0146236.

Pillar N, Isakov O, Weissglas-Volkov D, Botchan S, Friedman E, Arber N, **Shomron N**. Actionable clinical decisions based on comprehensive genomic evaluation in asymptomatic adults. *Mol Genet Genomic Med*. 2015;3:433-9.

Pras E, Kristal D, Shoshany N, Volodarsky D, Vulih I, Celniker G, Isakov O, **Shomron N**, Pras E. Rare genetic variants in Tunisian Jewish patients suffering from age-related macular degeneration. *J Med Genet*. 2015;52:484-92.

Bordería AV, Isakov O, Moratorio G, Henningsson R, Agüera-González S, Organtini L, Gnädig NF, Blanc H, Alcover A, Hafenstein S, Fontes M, **Shomron N**, Vignuzzi M. Group selection and contribution of minority variants during virus adaptation determines virus fitness and phenotype. *PLoS Pathog*. 2015;11:e1004838.

Warshauer E, Samuelov L, Sarig O, Vodo D, Bindereif A, Kanaan M, Gat U, Fuchs-Telem D, **Shomron N**, Farberov L, Pasmanik-Chor M, Nardini G, Winkler E, Meilik B, Petit I, Aberdam D, Paus R, Sprecher E, Nousbeck J. RBM28, a protein deficient in ANE syndrome, regulates hair follicle growth via miR-203 and p63. *Exp Dermatol*. 2015;24:618-22.

Haer-Wigman L, Newman H, Leibu R, Bax NM, Baris HN, Rizel L, Banin E, Massarweh A, Roosing S, Lefeber DJ, Zonneveld-Vrieling MN, Isakov O, **Shomron N**, Sharon D, Den Hollander AI, Hoyng CB, Cremers FP, Ben-Yosef T. Non-syndromic retinitis pigmentosa due to mutations in the mucopolysaccharidosis type IIIC gene, heparan-alpha-glucosaminide N-acetyltransferase (HGSNAT). *Hum Mol Genet*. 2015;24:3742-51.

Smith EC, Case JB, Blanc H, Isakov O, **Shomron N**, Vignuzzi M, Denison MR. Mutations in coronavirus nonstructural protein 10 decrease virus replication fidelity. J Virol. 2015;89:6418-26.

Milanesi E, Hadar A, Maffioletti E, Werner H, **Shomron N**, Gennarelli M, Schulze TG, Costa M, Del Zompo M, Squassina A, Gurwitz D. Insulin-like growth factor 1 differentially affects lithium sensitivity of lymphoblastoid cell lines from lithium responder and non-responder bipolar disorder patients. *J Mol Neurosci*. 2015;56:681-7.

Farberov L, Herzig E, Modai S, Isakov O, Hizi A, **Shomron N.** MicroRNA-mediated regulation of p21 and TASK1 cellular restriction factors enhances HIV-1 infection. *J Cell Sci.* 2015;128:1607-16.

Isakov O, Bordería AV, Golan D, Hamenahem A, Celniker G, Yoffe L, Blanc H, Vignuzzi M, **Shomron N**. Deep sequencing analysis of viral infection and evolution allows rapid and detailed characterization of viral mutant spectrum. *Bioinformatics*. 2015;31:2141-50.

Hershkovitz-Rokah O, Modai S, Pasmanik-Chor M, Toren A, **Shomron N**, Raanani P, Shpilberg O, Granot G. Restoration of miR-424 suppresses BCR-ABL activity and sensitizes CML cells to imatinib treatment. *Cancer Lett*. 2015;360:245-56.

Isakov O, Lev D, Blumkin L, Celniker G, Leshinsky-Silver E, **Shomron N**. Crowdfunding effort identifies the causative mutation in a patient with nystagmus, microcephaly, dystonia and hypomyelination. *J Genet Genomics*. 2015;42:79-81.

Ninio-Many L, Grossman H, Levi M, Zilber S, Tsarfaty I, **Shomron N**, Tuvar A, Chuderland D, Stemmer SM, Ben-Aharon I, Shalgi R. MicroRNA miR-125a-3p modulates molecular pathway of motility and migration in prostate cancer cells. *Oncoscience*. 2014;1:250-61.

Pérez R, Calleros L, Marandino A, Sarute N, Iraola G, Grecco S, Blanc H, Vignuzzi M, Isakov O, **Shomron N**, Carrau L, Hernández M, Francia L, Sosa K, Tomás G, Panzera Y. Phylogenetic and genome-wide deep-sequencing analyses of canine parvovirus reveal co-infection with field variants and emergence of a recent recombinant strain. *PLoS One*. 2014; 9:e111779.

Hershkovitz-Rokah O, Modai S, Pasmanik-Chor M, Toren A, **Shomron N**, Raanani P, Shpilberg O, Granot G. MiR-30e induces apoptosis and sensitizes K562 cells to imatinib treatment via regulation of the BCR-ABL protein. *Cancer Lett*. 2014; 356(2 Pt B):597-60.

Rudnicki A, Isakov O, Ushakov K, Shivatzki S, Weiss I, Friedman LM, **Shomron N**, Avraham KB. Next-generation sequencing of small RNAs from inner ear sensory epithelium identifies microRNAs and defines regulatory pathways. *BMC Genomics*. 2014;15:484.

Brownstein CA, Beggs AH, Homer N, Merriman B, Yu TW, Flannery KC, DeChene ET, Towne MC, Savage SK, Price EN, Holm IA, Luquette LJ, Lyon E, Majzoub J, Neupert P, McCallie D Jr, Szolovits P, Willard HF, Mendelsohn NJ, Temme R, Finkel RS, Yum SW, Medne L, Sunyaev SR, Adzhubey I, Cassa CA, de Bakker PI, Duzkale H, Dworzyński P, Fairbrother W, Francioli L, Funke BH, Giovanni MA, Handsaker RE, Lage K, Lebo MS, Lek M, Leshchiner I, MacArthur DG, McLaughlin HM, Murray MF, Pers TH, Polak PP, Raychaudhuri S, Rehm HL, Soemedi R, Stitziel NO, Vestecka S, Supper J, Gugenmus C, Klocke B, Hahn A, Schubach M, Menzel M, Biskup S, Freisinger P, Deng M, Braun M, Perner S, Smith RJ, Andorf JL, Huang J, Ryckman K, Sheffield VC, Stone EM, Bair T, Black-Ziegelbein EA, Braun TA, Darbro B, DeLuca AP, Kolbe DL, Scheetz TE, Shearer AE, Sompallae R, Wang K, Bassuk AG, Edens E, Mathews K, Moore SA, Shchelochkov OA, Trapane P, Bossler A, Campbell CA, Heusel JW, Kwitek A, Maga T, Panzer K, Wassink T, Van Daele D, Azaiez H, Booth K, Meyer N, Segal MM, Williams MS, Tromp G, White P, Corsmeier D, Fitzgerald-Butt S, Herman G, Lamb-Thrush D, McBride KL, Newsom D, Pierson CR, Rakowsky AT, Maver A, Lovrečić L, Palandačić A, Peterlin B, Torkamani A, Wedell A, Huss M, Alexeyenko A, Lindvall JM,

Magnusson M, Nilsson D, Stranneheim H, Taylan F, Gilissen C, Hoischen A, van Bon B, Yntema H, Nelen M, Zhang W, Sager J, Zhang L, Blair K, Kural D, Cariaso M, Lennon GG, Javed A, Agrawal S, Ng PC, Sandhu KS, Krishna S, Veeramachaneni V, Isakov O, Halperin E, Friedman E, Shomron N, et al. An international effort towards developing standards for best practices in analysis, interpretation and reporting of clinical genome sequencing results in the CLARITY Challenge. *Genome Biol*. 2014;15:R53.

Stapleford KA, Coffey LL, Lay S, Bordería AV, Duong V, Isakov O, Rozen-Gagnon K, Arias-Goeta C, Blanc H, Beaucourt S, Haliloğlu T, Schmitt C, Bonne I, Ben-Tal N, **Shomron N**, Failloux AB, Buchy P, Vignuzzi M. Emergence and transmission of arbovirus evolutionary intermediates with epidemic potential. *Cell Host Microbe*. 2014;15:706-16.

Mor E, He L, Torchinsky A, **Shomron N**. MicroRNA-34a is dispensable for p53 function as teratogenesis inducer. *Arch Toxicol*. 2014;88:1749-63.

Nachmani D, Zimmermann A, Oiknine Djian E, Weisblum Y, Livneh Y, Khanh Le VT, Galun E, Horejsi V, Isakov O, **Shomron N,** Wolf DG, Hengel H, Mandelboim O. MicroRNA Editing Facilitates Immune Elimination of HCMV Infected Cells. *PLoS Pathog*. 2014, 10:e1003963.

Agranat-Tamir L, **Shomron N,** Sperling J, Sperling R. Interplay between pre-mRNA splicing and microRNA biogenesis within the supraspliceosome. *Nucleic Acids Res*. 2014.

Lustig Y, Barhod E, Ashwal-Fluss R, Gordin R, **Shomron N**, Baruch-Umansky K, Hemi R, Karasik A, Kanety H. RNA-Binding Protein PTB and MicroRNA-221 Coregulate AdipoR1 Translation and Adiponectin Signaling. *Diabetes*. 2014; 63:433-45.

Feinberg-Gorenshtein G, Guedj A, Shichrur K, Jeison M, Luria D, Kodman Y, Ash S, Feinmesser M, Edry L, **Shomron N**, Weizman A, Yaniv I, Avigad S. MiR-192 directly binds and regulates Dicer1 expression in neuroblastoma. *PLoS One*. 2013, 8:e78713.

Oved K, Morag A, Pasmanik-Chor M, Rehavi M, **Shomron N***, Gurwitz D*. Genome-wide expression profiling of human lymphoblastoid cell lines implicates integrin beta-3 in the mode of action of antidepressants. *Transl Psychiatry*. 2013; 3:e313. * Equal corresponding

Eytan O, Morice-Picard F, Sarig O, Ezzedine K, Isakov O, Li Q, Ishida-Yamamoto A, **Shomron N,** Goldsmith T, Fuchs-Telem D, Adir N, Uitto J, Orlow SJ, Taieb A, Sprecher E. Cole Disease Results from Mutations in ENPP1. *Am J Hum Genet*. 2013; 93:752-7.

Isakov O, Rinella ES, Olchovsky D, Shimon I, Ostrer H, **Shomron N**, Friedman E. Missense mutation in the MEN1 gene discovered through whole exome sequencing co-segregates with familial hyperparathyroidism. *Genet Res (Camb).* 2013; 95:114-20.

Barak B, Shvarts-Serebro I, Modai S, Gilam A, Okun E, Michaelson DM, Mattson MP, **Shomron N**, Ashery U. Opposing actions of environmental enrichment and Alzheimer's disease on the expression of hippocampal microRNAs in mouse models. *Transl Psychiatry*. 2013; 3:e304.

Samuelov L, Sarig O, Harmon RM, Rapaport D, Ishida-Yamamoto A, Isakov O, Koetsier JL, Gat A, Goldberg I, Bergman R, Spiegel R, Eytan O, Geller S, Peleg S, **Shomron N,** Goh CS, Wilson NJ, Smith FJ, Pohler E, Simpson MA, McLean WH, Irvine AD, Horowitz M, McGrath JA, Green KJ, Sprecher E. Desmoglein 1 deficiency results in severe dermatitis, multiple allergies and metabolic wasting. *Nat Genet*. 2013; 45, 1244–1248.

Ninio-Many L, Grossman H, **Shomron N**, Chuderland D, Shalgi R. microRNA-125a-3p reduces cell proliferation and migration by targeting Fyn. *J Cell Sci*. 2013; 126(Pt 13): 2867-76.

Gilam A, Edry L, Mamluk-Morag E, Bar-Ilan D, Avivi C, Golan D, Laitman Y, Barshack I, Friedman E, **Shomron N**. Involvement of IGF-1R regulation by miR-515-5p modifies breast cancer risk among BRCA1 carriers. *Breast Cancer Res Treat*. 2013; 138:753-60.

Mor E, Kano S, Colantuoni C, Sawa A, Navon R, **Shomron N**. MicroRNA-382 expression is elevated in the olfactory neuroepithelium of schizophrenia patients. *Neurobiol Dis*. 2013; 55:1-10.

Shaham O, Gueta K, Mor E, Oren-Giladi P, Grinberg D, Xie Q, Cvekl A, **Shomron N**, Davis N, Keydar-Prizant M, Raviv S, Pasmanik-Chor M, Bell RE, Levy C, Avellino R, Banfi S, Conte I, Ashery-Padan R. Pax6 regulates gene expression in the vertebrate lens through miR-204*. PLoS Genet*. 2013; 9:3.

Rukov JL, Wilentzik R, Jaffe I, Vinther J, **Shomron N**. Pharmaco-miR: linking microRNAs and drug effects. *Brief Bioinform*. 2013; Advance Access 10.1093/bib/bbs082.

Reviews

Conte J, **Shomron N**, Artzi N. Biomaterials for metastasis: Bridging the gap between basic and translational research. *Advanced Healthcare Materials.* In press.

Pillar N, **Shomron N**. Breast cancer genomics in the deep sequencing era. *Isr Med Assoc J*. 2014;16(12):783-4.

Modai S, **Shomron N**. Molecular Risk Factors for Schizophrenia. *Trends Mol Med.* 2016;22(3):242-53.

McGonigle I, **Shomron N.** Privacy, anonymity and subjectivity in genomic research. *Genet Re*s (Camb). 2016;98:e2.

Pillar N, **Shomron N**. Breast cancer genomics in the deep sequencing era. *Isr Med Assoc J.* 2014;16:783-4.

Shomron N. Prioritizing personalized medicine. *Genet Res (Camb).* 2014;96:e007.

Pillar N, Yoffe L, Hod M, Shomron N. The possible involvement of microRNAs in preeclampsia and gestational diabetes mellitus. *Best Pract Res Clin Obstet Gynaecol*. 2014 Aug 21. pii: S1521-6934(14)00169-2.

Pillar N, Isakov O, Shomron N. Sequencing your genome: your future is here, but are you sure you want to know it? *Genet Res (Camb).* 2014 Jan;96:e006.

Shomron N. Genetics research: jumping into the deep end of the pool. *Genet Res (Camb).* 2013; 95:1-3.

Mor E, **Shomron N**. Species-specific microRNA regulation influences phenotypic variability: Perspectives on species-specific microRNA regulation. *Bioessays*. 2013 35:881-8.

Shomron N. A personal perspective on personalized medicine. *Genet Res (Camb).* 2013; 95:51.

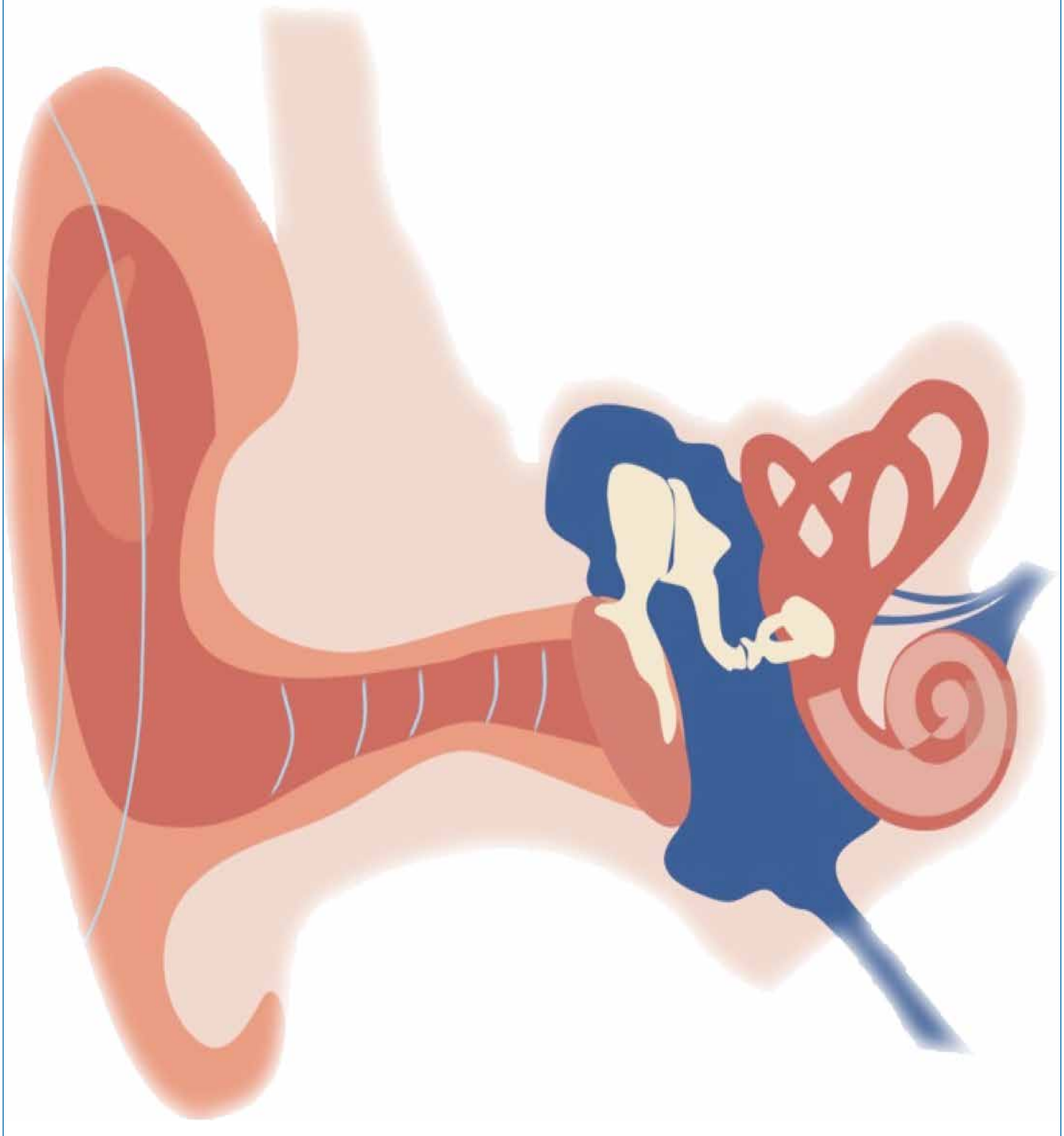
Isakov O, Perrone M, **Shomron N**. Exome sequencing analysis: a guide to disease variant detection. *Methods Mol Biol*. 2013; 1038:137-58.

Kol N, **Shomron N**. Assembly algorithms for deep sequencing data: basics and pitfalls. *Methods Mol Biol*. 2013; 1038:81-91.

Grants

2015-2018	Interdisciplinary grant of the Israeli Ministry of Science, Technology and Space on the Science, Technology and Innovation for the Third Age
2016-2018	Kamin
2016-2020	Israel Science Foundation

Hearing, Language & Speech Sciences and Disorders



Dr. Noam Amir, D.Sc.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: noama@post.tau.ac.il

Paralinguistic Communication, Phonetics and Psychoacoustics

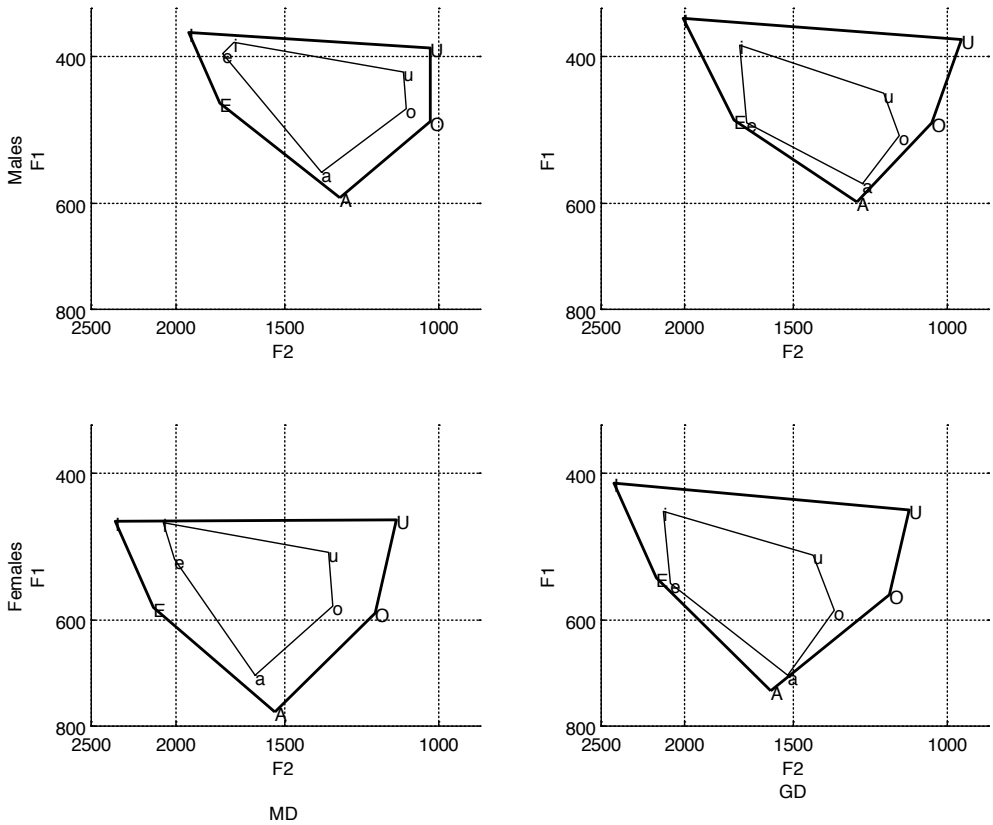
Positions

Senior Lecturer, Sackler Faculty of Medicine

Research

Our interests lie on the frontier between signal processing and human communication in both speech and music. One general field we have been involved in in recent years is the paralinguistic aspect of verbal communication. In this research my colleagues and we have been been exploring two main directions:

1. Emotion: Production and perception of emotions in speech, mostly in Hebrew, along with several excursions into cross lingual studies – Hebrew/German and Hebrew/Arabic. I've been looking at emotions as expressed in many different settings: films, event recollection, interviews, psychotherapy, and acted with conflicting textual and prosodic content.
2. Pragmatics: Production and perception of word stress (i.e. "I love my cat" vs. "I love my cat"), in Hebrew and Arabic, and lately also the manifestations of lexical stress in Hebrew.



Vowel spaces of Spoken Arabic in a Galilean Dialect (GD) and a "Muthallath Dialect" (MD) for men and women. External polygons are long vowels, internal polygons are short vowels. Note that short vowels are more centralized, and exhibit larger differences between dialects.

We have also been interested in signal processing aspects of music and musical acoustics for a very long time. Recent works we have participated in have been related to vibrato in the singing voice: quantifying it and relating it to factors such as singer proficiency, vocal warmup and singing style. Situated in the heart of the Middle East, we have become interested in acoustic phonetics of Hebrew and Spoken Arabic. Along with our colleagues, we have studied Hebrew vowels in everyday, connected speech, and in several dialects of Spoken Arabic, which have been studied very little. For example, vowel spaces of a Galilean dialect and the Kfar Kassem dialect are presented in the figure below.

Finally, the perceptual aspects of the subjects above have led us to examine their interaction with psychoacoustic thresholds. Starting with frequency perception thresholds, and now branching into intensity and spectral thresholds, our collaborators and we have been looking at their correlation to perception of of emotion and music.

Publications

M. Inspector, D. Manor, **N. Amir**, T. Kushnir, A. Karni. A word by any other intonation: FMRI evidence for implicit memory traces for pitch contours of spoken words in adult brains. *PLoS ONE*, 8(12) (2013).

E. Globerson, **N. Amir**, O. Golan, L. Kishon, M. Lavidor. Psychoacoustic abilities as predictors of vocal emotion recognition. *Attention Perception and Psychophysics*, 75, 1799 -1810 (2013).

Amir N, Amir O, Rosenhouse J. Colloquial Arabic vowels in Israel: a comparative acoustic study of two dialects. *J Acoust Soc Am*. 136:1895-907 (2014).

Globerson E, **Amir N**, Kishon-Rabin L, Golan O. Prosody recognition in adults with high-functioning autism spectrum disorders: from psychoacoustics to cognition. *Autism Res*. 8:153-63 (2015).

Kaplan-Neeman R, Muchnik C, **Amir N**. Listening to music with personal listening devices: monitoring the noise dose using a smartphone application. Int J Audiol. 2017;56:400-407.

Prof. Ofer Amir, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: oferamir@post.tau.ac.il

Voice, Speaking Rate, Stuttering and Fluency Disorders

Positions

Associate Professor, Sackler Faculty of Medicine

Research

Our research, as well as our clinical interest, focuses on two major fields: *Stuttering* and *Voice*. In the area of stuttering and other fluency disorders, we are interested in identifying and measuring various fluency charcteristics, providing normative data on speaking rate in Hebrew and exploring therapeutic approaches for stuttering, cluttering and other related fluency disorders. To this end, we are conducting studies on the perception of stuttering, and on the acoustic properties of speaking rate, normal disfluency and stuttering. In addition, we are currently collaborating with researchers in other research centers in a study that utilizes advanced methods for brain imaging related to stuttering and and language.

In the area of voice, we are highly interested in characterizing vocal properties related to different physical, physiological and emotional conditions, and on the professional voice. This line of research involves exploring and identifying acoustic, aerodynamic, percpetual and acoustic measures that differentiate, for example, between people with and without laryngeal pathologies, people who experience various emotional or social conditions, and women at different hormonal conditions and phases (e.g., using birth-control pills, pregnancy, menstrual cycle, etc.).

Publications

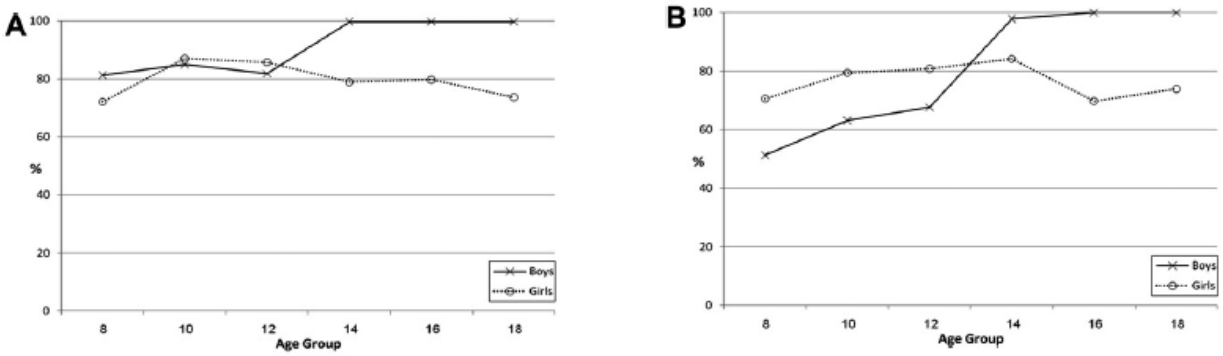
Amir, O., Primov-Fever, A., Kushnir, T., Kandelshine-Waldman, O. & Wolf M. (2013). Evaluating voice charcteristics of first-year acting-students in Israel: Factor analysis. *Journal of Voice.* 27, (1), 68-77.

Amir, O. & Levine-Yundof, R. (2013). Listeners' attitude toward people with dysphonia. Journal of Voice. 27, (4), 524.e1-524.e10.

Galili, L., **Amir, O**. & Gilboa-Schechtman, E. (2013). Acoustic Properties of Dominance and Request Utterances in Social Anxiety. Journal of Social & Clinical Psychology, 32, (6), 651-673.

Rochman, D. & **Amir O.** (2013). Examining in-session expressions of emotions with speech/vocal acoustic measures: An introductory guide. Psychotherapy Research, 23, (4), 381-393.

Finkelstein, M. & **Amir, O**. (2013). Speaking rate among professional newscasters: Hebrew speakers. Studies in Media and Communication, 1, 131-139.



Correct gender identification rates for boys and girls in the six age groups for (A) sentences and (B) vowels.

Amir, O., Lebi-Jacob, N. & Harari, O. (2014) The effect of In-Vitro Fertilization treatment on women's voice. Journal of Voice .pii: S0892-1997(13)00248-8

Gilboa-Schechtman, E., Galili, L., Sahar, Y. & **Amir, O**. (2014). Being "in" or "out" of the game: Subjective and acoustic reactions to exclusion and popularity in social anxiety. Frountiers in Human Neuroscience. 8:147, 1-13.

Civier O, Kronfeld-Duenias V, **Amir O**, Ezrati-Vinacour R, Ben-Shachar M. Reduced fractional anisotropy in the anterior corpus callosum is associated with reduced speech fluency in persistent developmental stuttering. Brain Lang. 2015;143:20-31.

Amir O, Wolf M, Mick L, Levi O, Primov-Fever A. Parents' evaluations of their children's dysphonia: The mamas and the papas. J Voice. 2015;29(4):469-75.

Kronfeld-Duenias V, Civier O, **Amir O**, Ezrati-Vinacour R, Ben-Shachar M. White matter pathways in persistent developmental stuttering: Lessons from tractography. J Fluency Disord. 2017, pii: S0094-730X(16)30078-X.

Freud D, Kichin-Brin M, Ezrati-Vinacour R, Roziner I, **Amir O**. The relationship between the experience of stuttering and demographic characteristics of adults who stutter. J Fluency Disord. 2017;52:53-63.

Mansour J, **Amir O**, Sagiv D, Alon EE, Wolf M, Primov-Fever A. The accuracy of preoperative rigid stroboscopy in the evaluation of voice disorders in children. J Voice. 2017;31(4):516.e1-516.e4.

Aharonson V, Aharonson E, Raichlin-Levi K, Sotzianu A, **Amir O**, Ovadia-Blechman Z. A real-time phoneme counting algorithm and application for speech rate monitoring. J Fluency Disord. 2017;51:60-68.

Halag-Milo T, Stoppelman N, Kronfeld-Duenias V, Civier O, **Amir O**, Ezrati-Vinacour R, Ben-Shachar M. Beyond production: Brain responses during speech perception in adults who stutter. Neuroimage Clin. 2016;11:328-38.

Kronfeld-Duenias V, **Amir O**, Ezrati-Vinacour R, Civier O, Ben-Shachar M. Dorsal and ventral language pathways in persistent developmental stuttering. Cortex. 2016;81:79-92.

Chapters and reviews

Amir, O. (2013). Current issues in voice assessment and intervention in Israel. In: *International Perspective on Voice Disorders*. Yiu, E. M-L. Bristol, UK: Multilingual Matters. Ch. 6. pp. 62-67.

Amir N, **Amir O**, Rosenhouse J. Colloquial Arabic vowels in Israel: a comparative acoustic study of two dialects. J Acoust Soc Am. 2014;136(4):1895-907.

Xu X, Biederman I, Shilowich BE, Herald SB, **Amir O**, Allen NE. Developmental phonagnosia: Neural correlates and a behavioral marker. Brain Lang. 2015;149:106-17.

Civier O, Kronfeld-Duenias V, **Amir O**, Ezrati-Vinacour R, Ben-Shachar M. Reduced fractional anisotropy in the anterior corpus callosum is associated with reduced speech fluency in persistent developmental stuttering. Brain Lang. 2015;143:20-31.

Halag-Milo T, Stoppelman N, Kronfeld-Duenias V, Civier O, **Amir O**, Ezrati-Vinacour R, Ben-Shachar M. Beyond production: Brain responses during speech perception in adults who stutter.

Kronfeld-Duenias **V, Amir O**, Ezrati-Vinacour R, Civier O, Ben-Shachar M. Dorsal and ventral language pathways in persistent developmental stuttering. Cortex. 2016;81:79-92.

Kronfeld-Duenias V, **Amir O**, Ezrati-Vinacour R, Civier O, Ben-Shachar M. The dorsal language pathways in stuttering: Response to commentary. Cortex. 2017;90:169-172.

Grants

2017-2012 Israel Science Foundation, Cerebral and cerebellar white matter pathways controlling Speech Rate

Dr. Daphne Ari-Even Roth, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: rothd@post.tau.ac.il

Learning and Plasticity and Early Detection of Hearing Loss – Clinical Implications

Positions

Lecturer, Sackler Faculty of Medicine

Research

Our research focuses on two main fields:

(a) Learning and plasticity in the auditory system:

Our research goal focuses on investigating perceptual learning and plasticity in the auditory system throughout the life span. Our interest in this area is motivated by the constant need in clinical practice to seek for better understanding of the learning characteristics and limitations of brain plasticity in the auditory modality which will in turn contribute to the better development of habilitation strategies in a variety of populations with hearing difficulties. We conduct behavioral studies in adults and children (i.e. single and multi-session training) using both non-verbal and verbal stimuli in order to explore the different characteristics of skill learning in the auditory system such as the time course of learning, the role of sleep for the establishment of delayed gains in performance, the generalization of the learning gains to untrained conditions etc. In order to provide evidence for functional plasticity in the neural encoding of sounds in the auditory system following training, we are currently also utilizing electrophysiological measures. Specifically, we record auditory brainstem responses to speech stimuli which provide us with a unique opportunity to follow changes in the neural signatures of the acoustic properties of the input signal (e.g., pitch tracking, harmonics, onset timing etc) that occur before and following training. We plan to explore the learning characteristics and limitations of brain plasticity in the auditory modality in different populations (e.g. middle-aged, elderly adults, hearing impaired, auditory processing disorders etc.) using both behavioral and electrophysiological measures.

(b) Early detection of hearing loss in neonates and its clinical limplications:

Our interest in this field is motivated by the growing evidence that early identification of hearing loss and intervention prior to six months of age can diminish the negative impact of hearing loss on speech and language acquisition. One line of research we conduct focuses on the prevalence and characteristics of hearing loss among different populations of infants such as infants with very low birth weight infants and congenital cytomegalovirus infection. Universal newborn hearing screening allows us not only identify special populations at risk for hearing loss but also, for the first time, to follow the developmental milestones of these children at a very young age and assess the communicative skills of infants with different types of hearing loss (e.g., unilateral hearing loss, mild hearing loss). These early communicative skills are known to be necessary to language and speech development. Thus, another line of research focuses on the effects of different degrees of hearing loss (e.g., unilateral hearing loss) on early auditory and pre-lexical productions. Learning the consequences of early detection and as a result early intervention provides insights to the ability to reverse the negative influence of auditory deprivation due to brain plasticity in young children.

Publications

G. Barkai, A. Barzilai, E. Mendelson, M. Tepperberg-Oikawa, **D. Ari-Even Roth**, J. Kuint. Newborn screening for congenital cytomegalovirus using real-time polymerase chain reaction in umbilical cord blood. Israel Medical Association Journal, 15(6), 279-283, 2013.

L. Kishon-Rabin, M. Avivi-Reich, **D. Ari-Even Roth**. Improved gap detection thresholds following auditory training: Evidence of auditory plasticity in older adults. The American Journal of Audiology, 22(2), 343-346, 2013.

C. Muchnik, **D. Ari-Even Roth**, M. Hildesheimer, M. Arie, Y. Bar-Haim, Y. Henkin. Abnormalities in auditory efferent activities in children with selective mutism. Audiology and Neurotology, 18(6), 353-361, 2013.

Y. Henkin, R. Taitelbaum-Swead, **D. Ari-Even Roth**, L. Kishon-Rabin, Y. Shapira, L. Migirov, M. Hildesheimer, R. Kaplan-Neeman. Evidence for a right cochlear implant advantage in simultaneous bilateral cochlear implantation. Laryngoscope, 124(8):1937-41, 2014.

G. Barkai*, **D. Ari-Even Roth***, A. Barzilai, M. Hildesheimer, M. Tepperberg-Oikawa, E. Mendelson, J. Kuint. Universal neonatal cytomegalovirus screening using saliva – report of clinical experience. Journal of Clinical Virology, 60(4):361-6, 2014. *equal contribution

Y. Zaltz, **D. Ari-Even Roth**, H. Gover, S. Liran, L. Kishon-Rabin. The effect of gender on a frequency discrimination task in children. Journal of Basic and Clinical Physiology & Pharmacology, 25, 293-299, 2014.

L. Kishon-Rabin, J. Kuint, M. Hildesheimer, **D. Ari-Even Roth**. Delay in auditory behaviour and preverbal vocalization in infants with unilateral hearing loss. Developmental Medicine and Child Neurology, 57, 1129-36, 2015.

O. Miron, **D. Ari-Even Roth**, L. Gabis, Y. Henkin, S. Shefer, I. Dinstein, R. Geva. Prolonged auditory brainstem responses in infants with autism. Autism Research, 9, 689-95, 2016.

D. Ari-Even Roth, L. Kishon-Rabin, M. Hildesheimer, A. Karni. Asymmetric interaural generalization of learning gains in a speech-in-noise identification task. Journal of the Acoustical Society of America, 138, 2627-2634, 2015.

Ari-Even Roth D, Hildesheimer M, Rosiner I, Henkin Y. Evidence for a right-ear advantage in newborn hearing screening results. Trends in Hearing, 20, 1-8, 2016.

Ari-Even Roth D, Lubin D, Kuint J, Tepperberg-Oikawa M, Mendelson E, Strauss T, Barkai G. Contribution of targeted saliva screening for congenital CMV-related hearing loss in newborns who fail hearing screening. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2017.

Dr. Katy Borodkin, Ph.D.

Department of Communication Disorders
School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

katyborodkin@tauex.tau.ac.il

Language Processing in Healthy and Brain Damaged Bilingual Speakers

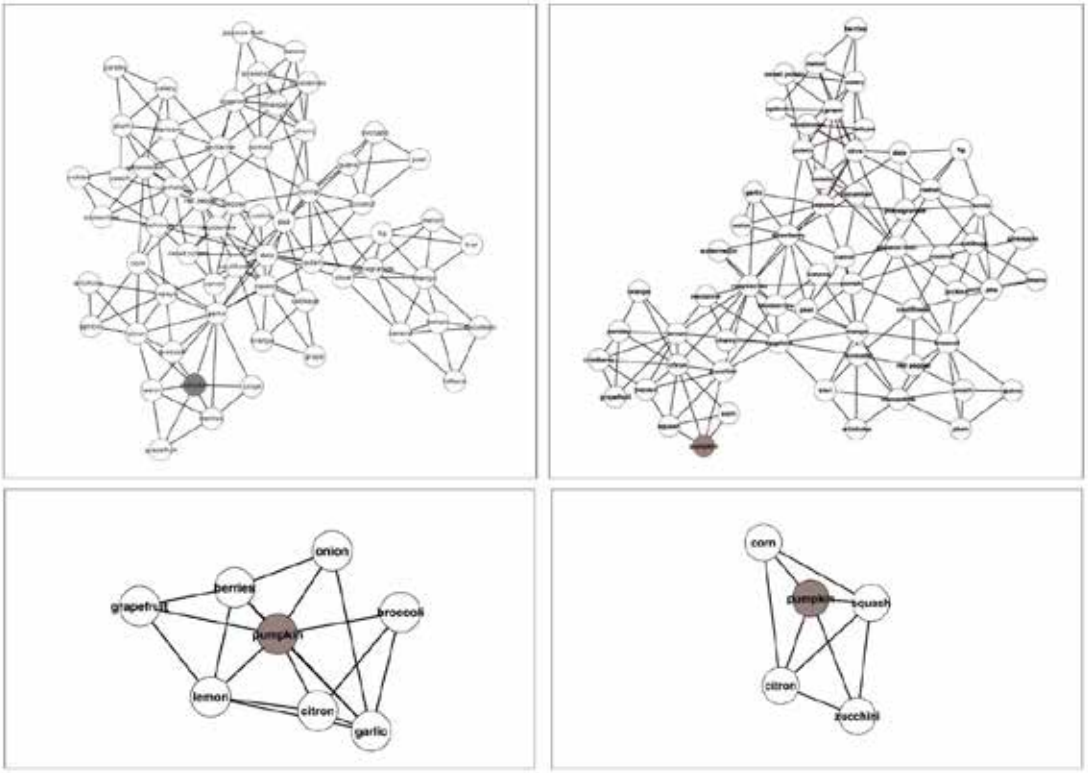
Position

Lecturer, Sackler Faculty of Medicine

Research

Many individuals in the contemporary society are required to use more than one language in everyday life. Research in our laboratory focuses on these speakers and explores how they process their languages. We apply behavioral and neuroimaging methods (fMRI and tDCS), both in healthy adults and in individuals with a language disorder following brain damage, such as aphasia. Current projects in the lab address the following questions:

1. What determines the differences among individuals in how successful they are in learning a second language? In one project, we look at the role of semantic processing and cognitive flexibility in vocabulary learning. In another, we study the interplay between auditory and motor systems in predicting the ability to acquire a foreign language pronunciation.
2. How using a language (to speak, listen, write or read) is different in native *vs* non-native language?



Organization of lexical networks in non-native language (Hebrew, left panels) and native language (English, right panels). Upper panels show the full network and the lower panels – the node *pumpkin* and its direct neighbors. The figures and the accompanying analyses suggest that non-native words are more densely connected to their neighbors and tend less to group into communities compared to native language words.

The conditions under which second language acquisition occurs are often less than ideal; for instance, second language is often acquired at an older age and used less frequently than the native language. In our lab, we have been investigating how these acquisition circumstances may affect the organization of lexical-semantic knowledge and the processing of words by the left and the right cerebral hemispheres.

3. What are the patterns and the mechanisms of language impairment and language recovery in bilingual and multilingual speakers? Some bilinguals with aphasia regain control of both languages in parallel, while in others language recovery is non-parallel (e.g., one language may be more impaired than the other, despite comparable premorbid proficiency). Our research aims at elucidating the factors predicting recovery patterns in these speakers and examines the cross-language effects of treatment on communicative abilities. We also study the interplay between neurobiological factors (such as the specific localization of the brain insult) and environmental factors (such as language proficiency) in determining spontaneous and treatment-induced neuroplasticity and its relevance to communicative abilities.

The research conducted in our laboratory can advance the current understanding of processes related to adult language learning, representation, processing, and breakdown.

Publications

Borodkin, K., & Faust, M. (2013). Tip-of-the-tongue (TOT) states and cross-linguistic transfer. *Bilingualism: Language and Cognition*, 16, 914-923.

Borodkin, K., & Faust, M. (2014). Native language phonological skills in low-proficiency second language learners. *Language Learning*, 64, 132-159.

Borodkin, K., & Faust, M. (2014). Naming abilities in low-proficiency second language learners. *Journal of Learning Disabilities*, 47, 237-253.

Mashal, N., **Borodkin, K.,** Maliniak, O., & Faust, M. (2015). Hemispheric involvement in native and non-native comprehension of conventional metaphors. *Journal of Neurolinguistics*, 35, 96-108.

Levy, T., Bloch, Y., Gat-Yablonski, G., Bar-Maisels, M., Djalovski, A., **Borodkin, K.,** Apter, A. S. (2015). Salivary oxytocin in adolescents with conduct disorder and callous-unemotional traits. *European Child & Adolescent Psychiatry*, 24, 1543-1551.

Borodkin, K., Kenett, Y., Faust, M., & Mashal, N. (2016). When pumpkin is closer to onion than to squash: The structure of the second language lexicon. *Cognition*, 156, 60-70.

Levy T, Apter A, Djalovski A, Peskin M, Fennig S, Gat-Yablonski G, Bar-Maisels **M, Borodkin K**, Bloch Y. (2017) The reliability, concurrent validity and association with salivary oxytocin of the self-report version of the Inventory of Callous-Unemotional Traits in adolescents with conduct disorder. *Psychiatry Res*, 256, 124-129.

Chapters

Borodkin, K., & Faust, M. (2012). Word retrieval in developmental language impairments: Application of the tip-of-the-tongue paradigm. In M. Faust (Ed.), *The handbook of the neuropsychology of language* (pp. 963-982). Oxford, UK: Wiley-Blackwell.

Dr. Yael Henkin, Ph.D.

Department of Communication Disorders
School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: henkin@post.tau.ac.il

Auditory Processing in the Normal and Impaired Auditory System

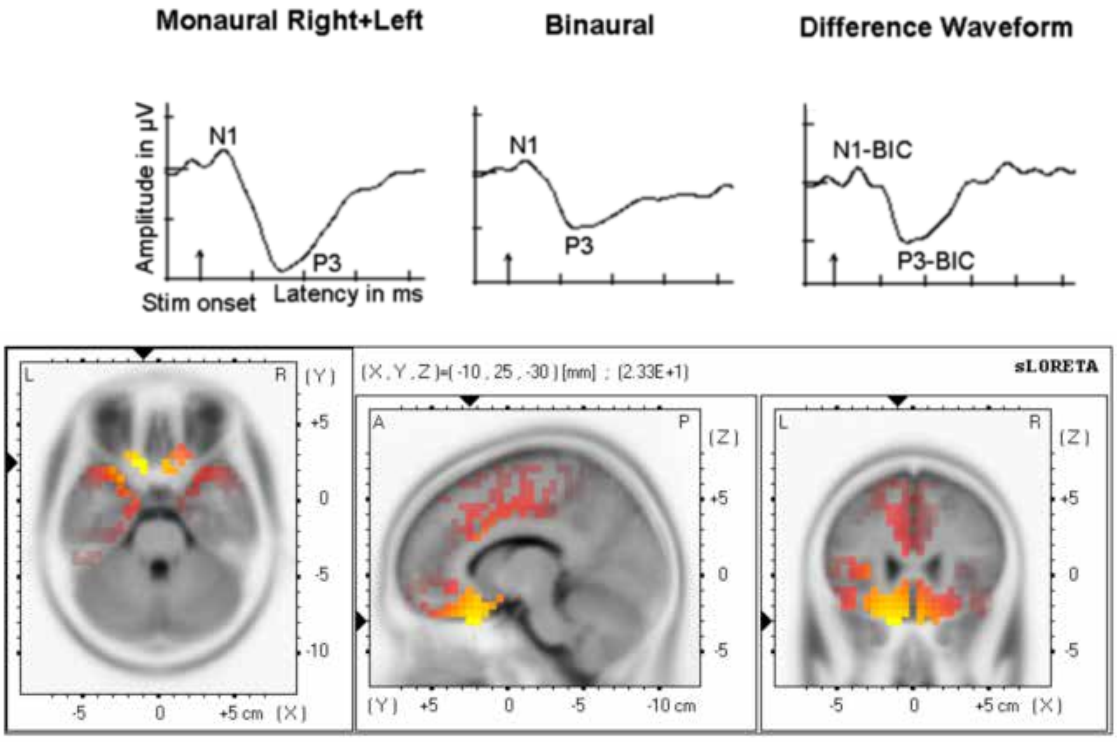
Positions

Senior Lecturer, Department of Communication Disorders, Sackler Faculty of Medicine

Head, Hearing, Speech, and Language Center, Sheba Medical Center, Tel Hashomer

Research

Research focuses on neurophysiologic and behavioral manifestations of auditory processing, as well as the relation between the two, in the normal and impaired auditory system. By means of event-related potentials (ERPs), voltage changes recorded from the scalp that trace events in time known to reflect discrete stages of neural processing, and a functional imaging technique (sLORETA), we study the time-course and cortical activation patterns during auditory (speech) processing. Of special interest are patients that have experienced bilateral and/or unilateral auditory deprivation and are habilitated by cochlear implants (CI) and/or hearing aids (HA). Currently under study are neurophysiologic processes that underlie: (1) Binaural processing in children that were sequentially or simultaneously implanted, in those using CI and HAs (bimodal hearing), and in those with HAs; and (2) Auditory-cognitive processing in elderly patients with CI.



Grand average waveforms of normal hearing children elicited during a speech discrimination task presented monaurally and binaurally. Shown are the sum of monaural right and left waveforms, the binaural response, and the difference waveform (Binaural interaction component=Sum of right+left –binarual response). Also shown are sLORETA images indicating the major site of activation during P3-BIC in the inferior and medial frontal gyri, (BA 11, 25) and orbital gyrus (BA 47) bilaterally.

Additional lines of research incorporate neurophysiologic and behavioral measures for studying: (1) The effect of auditory processing disorders (APD) on perceptual and post-perceptual stages of linguistic processing; and (2) The involvement of the peripheral and central auditory system in selective mutism and autism.

Understanding normal and impaired auditory processing contributes to the formation of rehabilitative technologies and approaches for auditory disorders.

Van de Heyning P, Távora-Vieira D, Mertens G, Van Rompaey V, Rajan GP, Müller J, Hempel JM, Leander D, Polterauer D, Marx M, Usami SI, Kitoh R, Miyagawa M, Moteki H, Smilsky K, Baumgartner WD, Keintzel TG, Sprinzl GM, Wolf-Magele A, Arndt S, Wesarg T, Zirn S, Baumann U, Weissgerber T, Rader T, Hagen R, Kurz A, Rak K, Stokroos R, George E, Polo R, Medina MDM, **Henkin Y**, Hilly O, Ulanovski D, Rajeswaran R, Kameswaran M, Di Gregorio MF, Zernotti ME. Towards a unified testing framework for single-sided deafness studies: A consensus paper. Audiol Neurootol. 2016;21(6):391-398.

Ari-Even Roth D, Hildesheimer M, Roziner I, **Henkin Y**. Evidence for a right-ear advantage in newborn hearing screening results. Trends Hear. 2016;20.

Publications

O. Miron, D. Ari-Even Roth, L. Gabis, **Y. Henkin**, S. Shefer, I. Dinstein, R. Geva. Prolonged auditory brainstem responses in infants with autism. Autism Research 9:689-95, 2016.

Y. Henkin, Y. Yaar-Soffer, L. Givon, M. Hildesheimer. Hearing with two ears: evidence for cortical binaural interaction during speech processing. Journal of the American Academy of Audiology 26: 384-392, 2015.

Y. Shapira, L. Migirov, Y. Yaar-Soffer, C. Muchnik, M. Hildesheimer, **Y. Henkin**. Pain in cochlear implant recipients – An uncommon, yet serious consequence of cochlear implantation. The Larynogoscope 125:1946-1951, 2015.

G. Nakache, L. Migirov, S. Trommer, M. Drendel, M. Wolf, **Y. Henkin.** Steroid based treatments for patients with total sudden sensorineural hearing loss. Acta Otolaryngologica 135:907-913, 2015.

D. Reznik, **Y. Henkin,** O. Levy, R. Mukamel. Perceived loudness of self-generated sounds is differentially modulated by expected sound amplitude.PLoS ONE 10:e0127651, 2015.

Y. Henkin, Y. Bar-Haim. An auditory-neuroscience perspective on selective mutism. Developmental Cognitive Neuroscience 12: 86-93, 2015.

K.A. Gordon, **Y. Henkin,** A. Kral. Asymmetric hearing during development: the aural preference syndrome and treatment options. Pediatrics 136: 141-53, 2015.

Y. Henkin, Y. Yaar-Soffer, M. Steinberg, C. Muchnik. Neural correlates of auditory-cogntive processing in older adults with cochlear implants. Audiology & Neurotology 19:S21-6, 2014.

D. Reznik, **Y. Henkin,** N. Schadel, R. Mukamel. Lateralized enhancement of auditory cortex activity and increased sensitivity to self-generated sounds. Nature Communications, 5:4059, 2014**.**

Y. Henkin, R. Taitelbaum-Swead, D. Ari-Even Roth, L. Kishon-Rabin, Y. Shapira, L. Migirov, M. Hildesheimer, R. Kaplan-Neeman. Evidence for a right cochlear implant advantage in simultaneous bilateral cochlear implantation. The Laryngoscope 124:1937-41, 2014

C. Muchnik, D. Ari-Even Roth, M. Hildesheimer, Y. Bar-Haim, **Y. Henkin.** Abnormalities in Auditory Efferent Activities in Children with Selective Mutism. Audiology & Neurootology 18:353-361, 2013

Prof. Minka Hildesheimer, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: hildeshe@post.tau.ac.il

Hearing Science and Clinical Audiology

Position

Professor Emeritus, Sackler Faculty of Medicine

Research

- Normal and abnormal auditory function
- Brain plasticity in cochlear Implants, Auditory Processing Disorders (APD)
- Clinical Audiology

Our research has been conducted in two areas:

A. Study of inner ear function in guinea pigs under three conditions: hypoxia, acoustic over-stimulation and differentiation. The study of these subjects has required the development of three special experimental techniques:

- A method of chronic implantation of an electrode into the facial nerve canal to enable longitudinal follow-up of hearing function in the awake state.
- A rheological model, which was developed for research on cochlear hypoxia in guinea pigs.
- A surgical method to completely eliminate the auditory efferent innervation to the cochlea while ensuring the animal's full recovery from this procedure. Thus it is possible to study the hearing function over time without the influence of the efferent system with the guinea pigs in an awake state.

B. Research on auditory plasticity in human subjects

The cochlear implant is a rehabilitative alternative in which an electrode inserted into the inner ear, directly stimulates the auditory nerve. Research is conducted in the area of programming the implant and speech perception using the implant. The research deals with the plasticity of the auditory system in acquisition of hearing and language skills and contributes basic theoretical and clinical knowledge about the importance of the auditory feedback to normal speech and hearing development and function.

Hearing in neonates and Auditory Processing Disorders: The Transient Evoked Oto-Acoustic Emission (TEOAE) is applied in hearing screening in neonates. Research was conducted to examine the reliability and validity of the test. We also investigated the development and activity of the efferent inhibitory system in newborns and premature babies using the suppression of the TEOAE test. We suggested the use of the test as a clinical tool for evaluation of auditory brain-stem function in neonates. We postulate that central auditory processing disorders (CAPD) manifested later in life can already be detected at this early stage of life using this method. We plan to continue to investigate the development of the efferent system and its importance for hearing throughout the life span, from childhood to old age, under difficult listening conditions and in subjects with communication disorders.

Publications

Muchnik, C., Ari-Even Roth, D., **Hildesheimer, M.**, Arie, M., Bar-Haim, Y. & Henkin, Y. (2013). Abnormalities in auditory efferent activities in children with selective mutism. *Audiology & Neurology*. 18:353–361

Henkin Y, Swead RT, Roth DA, Kishon-Rabin L, Shapira Y, Migirov L, **Hildesheimer M**, Kaplan-Neeman R. (2014) Evidence for a right cochlear implant advantage in simultaneous bilateral cochlear implantation. *Laryngoscope*. 124:1937-41

L. Kishon-Rabin, J. Kuint, **M. Hildesheimer**, D. Ari-Even Roth. Delay in auditory behaviour and preverbal vocalization in infants with unilateral hearing loss. Developmental Medicine and Child Neurology, 57, 1129-36, 2015.

D. Ari-Even Roth, L. Kishon-Rabin, **M. Hildesheimer**, A. Karni. Asymmetric interaural generalization of learning gains in a speech-in-noise identification task. Journal of the Acoustical Society of America, 138, 2627-2634, 2015.

Y. Henkin, Y. Yaar-Soffer, L. Givon, **M. Hildesheimer.** Hearing with two ears: Evidence for cortical binaural intraction during auditory processing. *J Am Acad Audiol*, 26:384-392, 2015.

Y. Shapira, Y. Yaar-Soffer, **M. Hildesheimer**, L. Migirov, Y. Henkin. (2015) Pain in cochlear implant recipients: An uncommon, Yet serious, Consequence of cochlear implantation. *Laryngoscope*, 125:1946-1951.

D. Ari-Even Roth, **M. Hildesheimer**, I. Roziner, Y. Henkin. (2016) Evidence for right-ear advantage in newborn hearing screening results. *Trends Hearing,* 20:1-8.

Prof. Liat Kishon-Rabin, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: lrabin@post.tau.ac.il

'Bottom-Up' and 'Top-Down' Processes in Human Auditory Perception and Recognition

Position

Professor, Sackler Faculty of Medicine

Head, Steyer School of Health Professions

Committee Member, Israel Auditory Society of Research

Research

Our research focuses on understanding the influence and relative contribution of sensory information ("bottom-up" processes) compared to cognitive capabilities and listening experience ("top-down" processes) on the perception of speech and language development. We test our hypotheses in a range of special populations including hearing-impaired infants, children and adults with cochlear implants and/or hearing aids, children on the autistic spectrum, bilingual and trilingual children and adults and middle-aged and elderly adults. We always compare performance with the typically developing population. We develop tests that are aimed to assess different levels of sensory, linguistic and cognitive processing. These include psychoacoustic tests of frequency, temporal and intensity resolution that involve non-speech auditory stimuli, linguistic tests that involve phonetic, word, and sentence material in optimal and degraded or difficult listening conditions (e.g. background noise, time-compressed speech, multi-talker, multi-accented) and cognitive tasks, such as, selective auditory attention using auditory adaptation of the 'stroop' task for attending relevant and irrelevant information (e.g. lexical-emotional stroop). In order to understand the influence of repeated exposure to auditory stimuli on performance, we train our subjects in single- or in multiple sessions thus providing us with insights to the auditory memory systems. We use different training tasks that involve the implicit and explicit memory systems that are assumed to be analogoues to language learing in infants and in older children. We utilze primarily behavioral measures that are occasionally supplemented with electriphysiological measures. Our studies are conducted in an infant speech perception/language lab which is unique of its kind in the country and is equipped to test different infant populations with behavioral techniques, and in an acoustically treated state-of-the art psychoacoustic lab. Understanding the factors that influence speech perception throughout the life span have important implications in the design of aural rehabilitation for the hearing impaired and intervention protocols in populations with developmental delays.

Publications

Globerson E, Amir N, Golan O, **Kishon-Rabin L**, Lavidor M. Psychoacoustic abilities as predictors of vocal emotion recognition. *Attention, Perception & Psychophysics*. 75:1799-810, 2013.

Kishon-Rabin L, Avivi-Reich M, Ari-Even Roth D. Improved gap detection thresholds following auditory training: Evidence of auditory plasticity in older adults. *The American Journal of Audiology*. 22:343-6, 2013.

Henkin Y, Taitelbaum-Swead R, Hildesheimer M, Ari-Even Roth D, **Kishon-Rabin L,** Kaplan-Neeman R. Evidence for a right cochlear implant advantage in simultaneous bilateral cochlear implantation. *Laryngoscope*. 124:1937-41, 2014.

Ben-Itzhak D, Greenstein T, **Kishon-Rabin L**. Parent report of the development of auditory skills in infants and toddlers who use hearing aids. *Ear & Hearing*. 2014. 35:e262-71.

Segal O, Kaplan D, Patael S, **Kishon-Rabin L**. Judging emotions in lexical-prosodic congruent and incongruent speech stimuli in adolescents on the ASD. *Folia Phonitrica*. Accepted for publication.

Y. Zaltz, D. Ari-Even Roth, H. Gover, S. Liran, **L. Kishon-Rabin**. The effect of gender on a frequency discrimination task in children. *Journal of Basic*

Clinical Physiology and Pharmacology, 25, 293-299, 2014.

E. Globerson, N. Amir, **L. Kishon-Rabin**, O.Golan. Prosody recognition in high functioning adults with autism spectrum disorders: From psychoacoustics to cognition. *Autism Research*, 8, 153-163, 2015.

L. Kishon-Rabin, J. Quint, M. Hildesheimer, D. Ari-Even Roth. Delay in auditory behavior and preverbal vocalization in infants with unilateral hearing loss. *Developmental Medicine & Child Neurology*. 57, 1129-1136, 2015.

D. Ari-Even Roth, M. Hildesheimer, Avi Karni, **L. Kishon-Rabin**. Asymmetric interaural generalization of learning gains in a speech-in-noise identification task. *Journal of the Acoustical Society of America*, 138. 138, 2627-2634, 2015.

Chordekar S, **Kishon-Rabin L**, Kriksunov L, Adelman C, Sohmer H. Experimental analysis of the mechanism of hearing under water. *BioMed Research International*, 526708, 2015.

O. Segal, D. Houston, **L. Kishon-Rabin**. Auditory discrimination of lexical stress patterns in hearing-impaired infants with cochlear implants compared to normal hearing: Influence of acoustic cues and listening experience to the ambient language. *Ear and Hearing*. 37, 225-34, 2016.

O. Segal, S. Heila, **L. Kishon-Rabin**. The effect of listening experience on the discrimination of /ba/ and /pa/ in Hebrew-learning and Arabic-learning infants. *Infant Behavior and Development*.42, 86-99, 2016.

Chordekar S, Adelman C, Sohmer H, **Kishon-Rabin L.** Non-osseous bone conduction as a possible contributor to the limited attenuation provided by hearing protection devices. *Noise and Health*. 18, 274-279, 2016.

Segal O, Kaplan D, Patael S, **Kishon-Rabin L.** Comprehension of 'narrow focus' by adolescents in the Autism Spectrum. *Folia Phoniatrica et Logopeadica*. 69, 67-77, 2017.

O. Segal, **L. Kishon-Rabin**. Recognition and comprehension of 'narrow focus' by young adults with prelingual hearing loss using hearing aids or cochlear implants. *Journal of Speech, Language and Hearing Research.* 60, 3609-3624, 2017.

Zaltz Y, Ari-Even Roth D, **Kishon-Rabin L**. (2017). Is the role of external and internal feedback in auditory skill learning age dependent? *Journal of Speech, Language and Hearing Research*, 60, 3656-3666.

Noam A, **Kishon-Rabin L**. (2017). Intelligibility of bandpass filtered speech: the effect of filter types. *Journal of the Acoustical Society of America*, 142 (6), 3813-3820.

Segal O, **Kishon-Rabin L**. (2017). Influence of the native language on sensitivity to lexical stress: Evidence from native Arabic and Hebrew speakers. *Studies of Second Language Acquisition* (in press).

Zaltz Y, Goldsworthy R, **Kishon-Rabin L**, Eisenberg L. (2018). Voice discrimination by adults with cochlear implants: the benefits of early implantation for vocal-tract length perception. *Journal of the Association for Research in Otolaryngology* (accepted).

Review

Kishon-Rabin L. Communication Disorders: A combined discipline of Audiology and Speech & Language Pathology - The Israeli Perspective. *ENT & Audiology News*, 25, 95-97. 2016.

Chapters in Books

Perez R, **Kishon-Rabin L**. Cochlear Implantation-Pediatric. In S. E. Kountakis (ed.): *Encyclopedia of Otolaryngology, Head and Neck Surgery*. Springer-Verlag Berlin Heidelberg, 2013.

Kishon-Rabin L. & Boothroyd A. The Role of Hearing for Speech and Language Acquisition and Processing. In D. Ravid and A. Baron, (eds): *Handbook of Communication Disorders: Theoretical, Empirical, and Applied Linguistic Perspectivess*. Mouton de Gruyter, Inc. In Press.

Kishon-Rabin L, Segal O. Beyond Hearing: Use of Parent Questionnaires for Assessing Auditory Functioning in Hearing-Impaired Infants. In L. Eisenberg (ed): *Clinical Management of Children with Cochlear Implants (2nd edition).* San Diego, Plural Publishing, Inc. In press.

Prof. Tova Most, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine
School of Education

TEL AVIV UNIVERSITY

E-mail: tovam@post.tau.ac.il
http://education.tau.ac.il/manage.asp?siteID=42&lang=1&pageID=4634

Speech and Hearing Sciences and Rehabilitative Audiology

Position

Professor, Sackler Faculty of Medicine and School of Education

Dean of Students, Tel Aviv University

Research

- Speech perception and production by the hearing impaired
- The implications of hearing loss on communication, cognitive and socio-emotional functionning in school, in the family and in general
- Educational Audiology
- Auditory rehabilitation of people with hearing loss

Our research focus is on evaluating the hearing and communication profile of individuals with a hearing loss and understanding the relationship between these functions and their functional management in various life environments. This research analysis expands the knowledge and understanding of theoretical models that examine the functioning of the individual with a hearing loss and constitutes a scientific basis for the development of intervention programs suited to the hearing and communication profile.

Our research activities focus on two main areas:

1. Research in the field of speech perception and communication through spoken language of individuals with a hearing loss.

   We focus on the perception of suprasegmental and paralinguistic features of the spoken message. These provide information on the communication intentions of the speaker (e.g. asking a question in comparison to stating a fact) as well as the speaker's emotional state.

2. Research of the ramifications of a hearing loss and communication difficulties on the individual's ability to function in various life environments: educational system, home and work environment, as well as the ramifications of the hearing loss and the communication difficulties on the people in the individual's environment.

   Our research focuses on the relationship between hearing loss and communication function through the use of spoken language in general and the speech intelligibility in particular.

   With the current trend to integrate children with a hearing loss into regular educational frameworks either individually or in a group, we also investigate the effect of hearing loss on the pupil's ability to function within these frameworks. This research is carried out in different sectors of the population (Jewish (secular & orthodox) and Arab), and on a range of age groups.

   Within the framework of the research examining the implications of hearing loss on the different aspects of a child's life, we investigate not only the individual's functioning but also those aspects that relate to the people in their environment such as their parents, siblings and teachers.

Publications

Michael, R. Cinamon R.G. & **Most, T**. (2013) The contribution of perceived parental support to the career self-efficacy of deaf, hard of hearing, and hearing adolescents. *JDSDE,* 18, 329-343.

Ziv, M., **Most, T**. & Cohen, S. (2013) Understanding of emotions and false beliefs among children with normal hearing versus children with hearing loss. *JDSDE* 18, 161-174.

Yehudai, N., Shpak, T., **Most, T**., Luntz, M (2013) Functional status of hearing aids in bilateral-bimodal users. *Otology & Neurotology*, 34, 675-681.

Luntz M., Yehudai N., Haifler, M., Sigal, G. & **Most T**. (2013) Clinical significance of sensorineural hearing loss in chronic otitis media. *Acta Oto-laryngologica*, 133, 1173-1180

Shpak, T., **Most, T.,** Luntz, M. (2014) Fundamental frequency information for speech recognition via bimodal stimulation: cochlear implant on one ear and hearing aid on the other. *Ear and Hearing*, 35, 97-109.

Bartov, T. & **Most, T**. (2014). Song recognition by young children with cochlear implants: comparison between unilateral, bilateral, and bimodal users. JSLHR, 1-13.

Luntz, M., Egra-Dagan, D., Attias, J., Yehudai, N., **Most, T**., & Shpak, T. (2014). From hearing with a cochlear implant and a contralateral hearing aid (ci/ha) to hearing with two cochlear implants (ci/ci): a within-subject design comparison. *Otology & Neurotology*, 35, 1682-1690.

Michael, R., **Most, T**., & Cinamon, R. G. (2015). Career-related parental support of adolescents with hearing loss: Relationships with parents' expectations and occupational status. *American Annals of the Deaf*, *160*, 60-72.

Michael, R., **Most, T**., & Cinamon, R. G. (2015). What shapes adolescents' future perceptions? The effects of hearing loss and career self-efficacy. *Journal of Deaf Studies and Deaf Education*. doi: 10.1093/deafed/env023.

Zaidman-Zait, A., **Most, T**. Haddad, E. Tarash, R. Brand, D. (2016). The Impact of childhood hearing loss on the family: Mothers and fathers stress and coping resources. JDSDE, 21, 23-33. Doi: 10.1093/deafed/env038

Most, T. & Ingbar, S. (2016). Effects of Exposure to Inclusion and Socioeconomic Status on Parental Attitudes towards the Inclusion of Deaf and Hard of Hearing Children. Deafness & Education International, 18, 124-133.

Zaidman-Zait, A., **Most, T**., Tarash, R., & Haddad, E. (2017). Mothers' and fathers' involvement in intervention programs for deaf and hard of hearing children. Disability and Rehabilitation,1-9.

Books

Most, T. & Ringvald, D. (Eds.) (2014). Theoretical and applied aspects in rehabilitation and education of deaf and hard of hearing individuals. MOFET Publishing House. Tel Aviv (In Hebrew).

Chapters

Levie, R., Ravid, R., Freud, T., and Most, T. (2014). Spelling Abilities in Hebrew-Speaking Children with Hearing Loss. In Barbara Arfe, Julie Dockrell and Virginia Berninger (Eds.**):** Writing Development in Children with Hearing Loss, Dyslexia or Oral Language Problems: Implications for Assessment and Instruction. Oxford University Press. New-York New-York. Chapter 6, pp. 70-84.

Most, T. (2016). Perception of the Prosodic Characteristics of Spoken Language by Individuals with Hearing Loss. In Marc Marschark and Pat Spencer (Eds.): The Oxford Handbook of Deaf Studies in Language: Research, Policy and Practice. Oxford University Press. Chapter 6, pp 79-93.

Tzach, N. & **Most, T**. (2016). The Inclusion of Deaf and Hard of Hearing Students in Mainstream Classrooms: Classroom Participation and its Relationship to Communication, Academic and Social Performance. In Marc Marschark, Venetta Lampropoulou, and Emmanouil Skordilis (Eds.): Diversity in Deaf Education, Oxford University Press. Chapter 13, pp 355-380.

Zaidman –Zait, A., & **Most, T**. Assessment of Pragmatic Abilities among Deaf and Hard of Hearing Learners in Relation to Social Skills. In Marc Marschark & Harry Knoors (eds.): Evidence-Based Practice in Deaf Education. Oxford University Press. Accepted for publication 20.6.17

Prof. Chava Muchnik, Ph.D.

Department of Communication Disorders
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: muchnik@post.tau.ac.il

Hearing Science and Clinical Audiology

Position

Professor, Sackler Faculty of Medicine

Chair, Department of Communication Disorders, Tel Aviv University

Senior Audiologist, Speech and Hearing Center, Sheba Medical Center

Research

One of our main research areas is related to the effect of noise on speech perception, in young, middle aged and elderly populations. A major complaint of hearing impaired and normal hearing adults is the difficulty to understand speech in the presence of noise. Our attempt to address this challenging problem encompasses several aspects:

a. Improving the signal to noise ratio in sensory aids (hearing aids and cochlear implants). Recently we demonstrated a significant beneficial effect of a single channel Cochlear-based Noise Reduction Algorithm (CNRA) in hearing aids users and cochlear implants recipients. Further investigation is required for improving CNRA performance at lower SNRs and in different noise spectra.

b. Investigating the influence of aging on the recognition of speech in background noise: Aging is known to induce physio-pathological changes in the entire auditory pathways. While there is a comprehensive documentation of this difficulty amongst elderly people aged 65 years and above, limited information is available on middle-aged listeners.

Another topic in our research is the estimation of the potential risk for hearing loss as a result of listening to music with Personal Listening Devices (PLDs). We are studying the function of the efferent auditory system in normal and pathological populations such as children and adults with Auditory Processing Disorders and Childhood Selective Mutism.

Cochlear Implants are another area of research interest. In particular we are studying the characteristic features of the electrical nerve response in cochlear implant recipients.

Publications

C. Muchnik, D. Ari-Even Roth, M. Hildesheimer, M. Arie, Y. Bar-Haim, Y. Henkin (2013) Abnormalities in auditory efferent activities in children with selective mutism. Audiology & Neurotology, 18:353-61, 2013.

Y. Shapira, L. Migirov, Y. Yaar-Soffer, **C. Muchnik**, M. Hildesheimer, Y. Henkin. Pain in cochlear implant recipients – An uncommon, yet serious consequence of cochlear implantation. The Larynogoscope 125:1946-1951, 2015.

Y. Henkin, Y. Yaar-Soffer, M. Steinberg, **C. Muchnik**. Neural correlates of auditory-cogntive processing in older adults with cochlear implants. Audiology & Neurotology 19:S21-6, 2014.

R. Kaplan-Neeman, **C. Muchnik**, N. Amir. Listening to music with personal listening devices: monitoring the noise dose using a smartphone application. International Journal of Audiology, 56:400-407, 2017.

Prof. Dorit Ravid, Ph.D.

Department of Occupational Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine
School of Education

TEL AVIV UNIVERSITY

Email: doritr@post.tau.ac.il
URL: http://doritravid.com

Language Acquisition and Development of Linguistic Literacy

Position

Professor, School of Education and Sackler Faculty of Medicine

Vice-President, International Association for the Study of Child Language

Member, Academie Europea

Research

We study the ways Israeli infants, toddlers, children and adolescents acquire the structures, meanings and functions of spoken and written Hebrew (and Arabic). Empirical and theoretical exploration of linguistic phenomena are conducted against general models of language and cognitive acquisition, on the one hand, and the typological properties and constraints of Hebrew (and Semitic) verbal expression, on the other. Human development is taken as the critical context within which native language learning can take place in children. Specific areas of current investigation are (inter alia) acquisition of Hebrew verb structure (root and *binyan*) and semantics in mother-child dyads, children's peer talk and children's storybooks; linguistic input (maternal talk) to children and the relationship to their development in different socio-economic contexts; the emergence of syntactic constructions in children's development language; prepositions and prepositional phrases in spoken and written Hebrew development; the development of written text production abilities across the school years; narrative acquisition and narrative theory; morpho-syntactic constructions in learning to spell Hebrew.

Publications

Schiff, D. & **D. Ravid**. 2013. Morphological processing in Hebrew-speaking reading-disabled students. *Journal of Learning Disabilities*, 46, 220-229.

Ravid, D. & R. Schiff. 2013. Different perspectives on the interface of dyslexia and language: Introduction to the special LLD issue on Dyslexia and Language. *Journal of Learning Disabilities,* 46, 195-199.

Ravid, D., Bar-On, A. & E. Dattner. 2014. Linguistics in the service of communications disorders: New frontiers. *AILA Review*, 26, 79-99.

Abugov, N. & **Ravid, D.** 2014. The impact of Israeli Hebrew on Yiddish: noun plurals in Sanz Ultra Orthodox Yiddish. International Journal of the Sociology of Language, 226, 189–211.

Uziel-Karl, U., F. Kanaan, N. Abugov, R. Yifat, I. Meir, **& D. Ravid**. 2014. Hebrew and Palestinian Arabic in Israel: Linguistic frameworks and SLP services. Special issue on "Global issues in language disorders: Processes, frameworks and policies", *Topics in Language Disorders*, 34, 133–154.

Schiff, R. & **D. Ravid**. 2014. Morpho-syntactic load in judging adjective plural agreement: comparing adults with and without ADD. *Communication Disorders Quarterly. 36, 79-89*.

Ravid D, Vered L. Hebrew verbal passives in Later Language Development: the interface of register and verb morphology. J Child Lang. 2017;44(6):1309-1336.

Chapters and books

Ravid, D. & Schiff, R. (Eds.) 2013. Journal of Learning Disabilities Special issue on Dyslexia and Language, 46.

Abugov, N. & **Ravid**, D. 2013. Assessing Yiddish plurals in acquisition: impacts of bilingualism. In Mueller Gathercole V. C (ed.) *Bilinguals and Assessment: State of the art guide to issues and solutions from around the world.* Bristol: Multilingual Matters, 90-110.

Ravid, D. 2013. Syntactic complexity in discourse production across different text types. In Catherine Bolly & Liesbeth Degand (eds), *Across the Line of Speech and Writing Variation*. Louvain-la-Neuve: Presses universitaires de Louvain, 51-66.

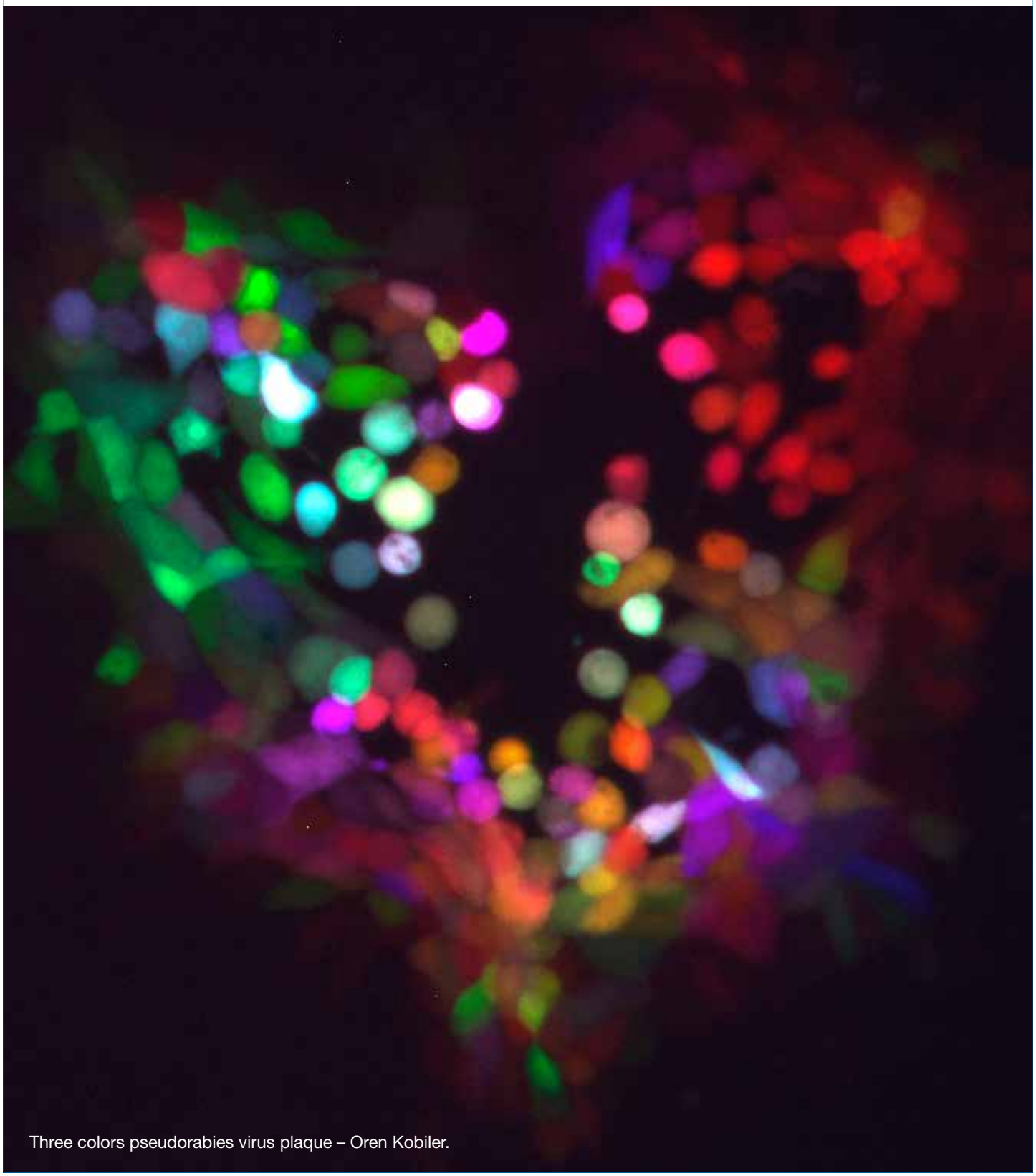
Ravid, D & G. Ginat-Heiman. 2014. L1 and L2 proficiency in Hebrew-English adolescent learners. In Adelheid Hu & Patrick Grommes (eds.), *Plurilingual Education: Policies – Practice – Language Development*. Amsterdam: Benjamins, 221-246.

Abugov, N. & **Ravid**, D. 2014. Noun plurals in Israeli Ultra-Orthodox Yiddish: a psycholinguistic perspective. In Aptroot, M. & Hansen, B. (eds.) *Yiddish Language Structures*. Berlin: Mouton De Gruyter, 9-39.

Grants

2013-2017	Verb structure and Semantics in Development. Israel Science Foundation.
2017-2021	Research grant, Israel Science Foundation

Infectious Diseases



Three colors pseudorabies virus plaque – Oren Kobiler.

Dr. Natalia T. Freund, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

nfreund@tauex.tau.ac.il
URL: http://www3.tau.ac.il/nfreund/

Human Antibody Responses in Health and Disease

Position

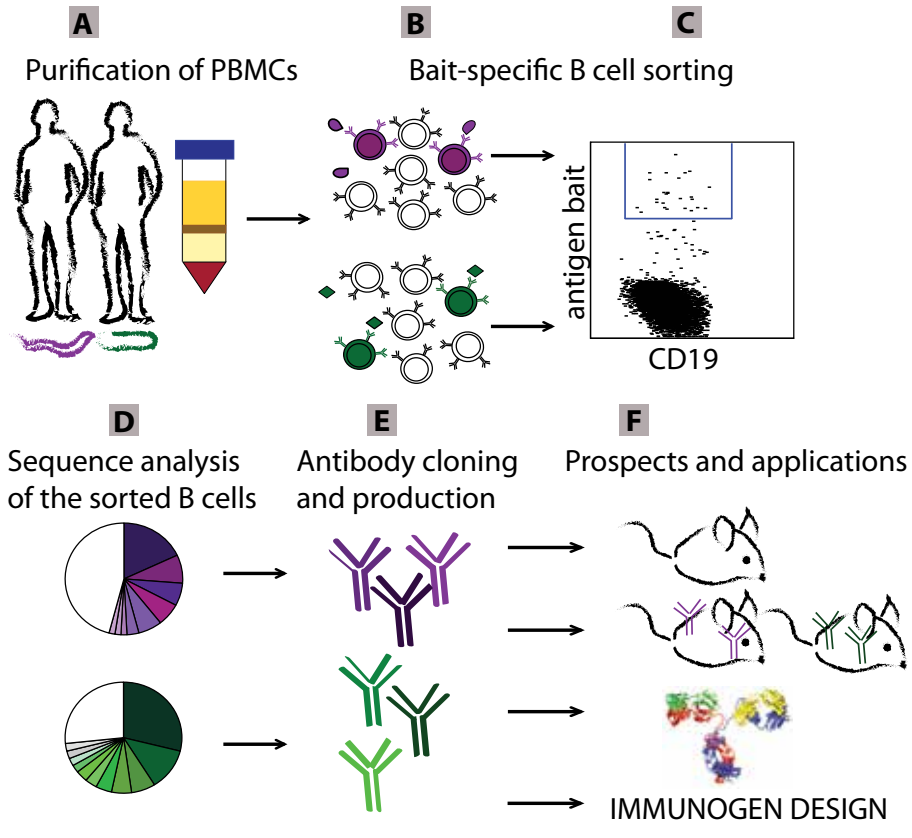
Senior Lecturer, Sackler Faculty of Medicine

Research

Antibodies are major players of the immune system and are the basis of most vaccines. Despite their important role, the mechanism by which they contribute to protection during disease, and how to elicit them, remains a mystery.

Each one of us possesses a diverse repertoire of naïve B cells, expressing one type of membrane antibody on each cell. This diversity allows us to respond to a variety of different invaders. When a naïve B cell encounters an antigen, it migrates to the secondary lymph organs, where it interacts with other cells of the immune system. There, B cells undergo affinity maturation, which is one of the most remarkable phenomena in nature. During affinity maturation, somatic mutations are introduced in antibody genes, and subsequently both antibody strength and affinity are improved, while weak and autoimmune antibodies are deleted. B cells then differentiate into antibody-secreting plasma cells and long-lived memory B cells.

We use molecular immunology and genetics, combined with innovative single cell methods, to isolate high-affinity disease-specific antibodies from memory B cells of infected patients. The ultimate goal of our lab is to study pathogen:host interactions, as well discover novel antibody-based drugs and vaccines.



ANTI-PATHOGEN ANTIBODY PURIFICATION FROM PATIENTS. (A) Whole blood will be collected from infected patients. (B) B cells are enriched and (C) stained with pathogen-specific antigens-baits. The positive cells are single cell sorted. (D) The heavy and light chain genes of the sorted cells will be amplified by PCR and the sequences analyzed for clonalty. (E) Antibodies that are part of expanded clones of antigen-specific B cells are cloned into expression vectors and produced recombinantly. (F) The antibodies are used in a variety of downstream applications.

Publications

Wang H, Gristick HB, Scharf L, West Jr. AP, Galimidi RP, Seaman MS, **Freund NT**, Nussenzweig MC, Bjorkman PJ Asymmetric recognition of HIV-1 Env trimer by V1V2 loop-targeting antibodies. *Elife* 2017, 26;6.

Freund NT, Haoqing H, Scharf L, Noguiera L, Horwitz JA, Sievers S, Sok D, Golijanin J, Halper-Stromberg A, West A, Lorenzi JC, Toth I, Piechocka-Torcha A, Wang LX, Seaman MS, Burton D, Gazumyan A, Walker BD, Bjorkman PJ; Nussenzweig MC. Co-existence of potent HIV-1 broadly neutralizing antibodies and antibody-sensitive viruses in a viremic controller. *Science Trans. Med.* 2017, 18;9(373).

Escolano A, Steichen J, Dosenovic P, Kulp D, Golijanin J, Sok D, **Freund NT**, Araki T, Lowe S, Chen S, Heinemann J, Oliveira T, Gitlin A, Hui-Yao K, Georgeson E, Karen L, Francisco S, Gazumyan A, Burton D, Schief W.R, Nussenzweig M.C Sequential Immunization Elicits broadly neutralizing anti-HIV- 1 antibodies in Ig knock in mice. *Cell.* 2016, 8;166:1445

Steichen J.M, Kulp D.W, Tokatlian, T, Escolano A, Docenovic, P, Stanfield RL, McCoy L.E, Ozorowski G, Xiaozhen H, Kalyuzhniy, O, Briney B, Schiffner T, Garces F, **Freund NT**, Gitlin, A, Georgeson E, Kubitz M, Adachi Y, Jones M, Mutafyan A, Yun D.S, Mayer C, Ward A, Burton D, Wilson IA, Irvine DJ, Nussenzweig MC, Schief WR. HIV vaccine design to target germline precursors of glycan-dependent broadly neutralizing antibodies. *Immunity* 2016, 20;45:483.

McGuire AT, Gray MD, Dosenovic P, Gitlin AD, **Freund NT**, Petersen J, Correnti C, Johnsen W, Kegel R, Stuart AB, Glenn J, Seaman MS, Schief WR, Strong RK, Nussenzweig MC, Stamatatos L. Specifically modified Env immunogens activate B-cell precursors of broadly neutralizing HIV-1 antibodies in transgenic mice. *Nat. Com.* 2016, 24;7:10618.

Freund NT, Horwitz JA, Nogueira L, Sievers SA, Scharf L, Scheid JF, Gazumyan A, Liu C, Velinzon K, Goldenthal A, Sanders RW, Moore JP, Bjorkman PJ, Seaman MS, Walker BD, Klein F, Nussenzweig MC. A new glycan-dependent CD4-binding site neutralizing antibody exerts pressure on HIV-1 In vivo. *PLoS Pathog.* 2015, 30;11:e1005238.

Freund NT, Roitburd-Berman A, Sui J, Marasco WA, Gershoni JM. Reconstitution of the receptor-binding motif of the SARS coronavirus *Protein Eng. Des. Sel*. 2015, 28:567-75.

Freund NT, Scheid JF, Mouquet H, Nussenzweig MC. Amplification of highly mutated human Ig lambda light chains from an HIV-1 infected patient. *J Immunol Methods.* 2015, 418:61-5.

Dosenovic P, von Boehmer L, Escolano A, Jardine J, **Freund NT**, Gitlin AD, McGuire AT, Kulp DW, Oliveira T, Scharf L, Pietzsch J, Gray MD, Cupo A, van Gils MJ, Yao KH, Liu C, Gazumyan A, Seaman MS, Björkman PJ, Sanders RW, Moore JP, Stamatatos L, Schief WR, Nussenzweig MC. Immunization for HIV-1 Broadly Neutralizing Antibodies in Human Ig Knockin Mice. *Cell.* 2015, 18;161(7):1505-15.

Prof. Fuad Iraqi, Ph.D.

Department of Human Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: fuadi@post.tau.ac.il

Genetic Bases of Host Response to Infections and Chronic Diseases

Position

Professor, Sackler Faculty of Medicine

Chair, Department of Clinical Microbiology and Immunology

Research

The research in my laboratory is focused on understanding the genetic bases of host response to infections and chronic diseases, which are important for human health. My team uses mouse model for speeding up the process of identifying such genes, which may involved of making some people resistant to a diseases while others are not. After finding the genes in mouse, it will be possible to identify the homologous genes in human. The product of our research can be used in developing new prevention and treatment tools for these diseases.

The main ongoing research projects at his lab are:

Identifying and characterizing genes involved in host response to bacterial infection by *Klebsiella Peumonia*.

Identifying and characterizing genes involved in host response to fungal infection by *Aspergillus Fumigatus* (Aspergillosis)

Identifying and characterizing genes involved in host response to bacterial that causes dental infection (periodontitis)

Identifying and characterizing genes involved in development of type-2 diabetes (T2D) in humans as a result of obesity and high fat-diet.

Identifying and characterizing genes involved in host immune response to infectious and chronic diseases.

Identifying and characterizing genes involved in development of colon cancer.

Publications

Shusterman A, Durrant C, Mott R, Schaefer A, Weiss EI, **Iraqi FA*** and Houri-Haddad Y* (2013) Host susceptibility to periodontitis: Mapping murine genomic regions. *J Dent Res* 92: 438-443.

Shusterman A, Salaymeh Y, Nashef A, Soller M, Wilensky A, Mott R, Weiss EI, Houri-Haddad Y and. **Iraqi FA** (2013) Genotype is an important determinant factor of host susceptibility to periodontitis in the Collaborative Cross and inbred mouse populations. *BMC Genet* 14: 68-79.

Iraqi FA, Athamni H, Dorman A, Salymah Y, Tomlinson I, Nashif A, Shusterman A, Weiss E, Houri-Haddad Y, Mott R, Soller M. (2014) Heritability and coefficient of genetic variation analyses of phenotypic traits provide strong basis for high-resolution QTL mapping in the Collaborative Cross mouse genetic reference population. *Mamm Genome*. 25:109-19.

Soller M and **Fuad Iraqi FA** (2014) The Collaborative Cross – a next generation mouse genetic resource population for high resolution genomic analysis of complex traits. *Livestock Sci J* 166: 19–25.

Chalfin L, Dayan M, Levy DR, Austad AN, Miller RA, **Iraqi FA,** Dulac C and Kimchi T (2014) Gene knockout in wild mice: a powerful tool for genetic mapping of ecologically-relevant social behaviors. *Nature Comm* 5:4569.

De Simone M, Spagnuolo L, Ivan Lorè N, Rossi G, De Fino I, Cigana C, **Iraqi FA** and Bragonzi A (2014) Host genetic background influences the response to the opportunistic Pseudomonas aeruginosa infection altering cell-mediated immunity and bacterial replication. *PLOS One* 9: e106873, 1-10.

Vered K, Durrant C, Mott R and **Iraqi FA** (2014) Susceptibility to *Klebsiella pneumonaie* infection in collaborative cross mice is a complex trait controlled by at least three loci acting at different time points. *BMC Genomics* 15:865.

Schaefer A, Bochenek G, Jochen As, Ellinghaus D, Dommisch H, Guzeldemir E, Graetz C, Harks I, Jockel-Schneide Y, Staufenbiel I, Eberhard J, Meyle J, Eickholz P, Linden G, Cine N, Nohutcu R, Yilmaz E, Weiss E, Houri-Haddad Y, Iraqi FA, Folwaczny M, Noack B, Strauch K, Gieger C, Waldenberger M, Peters A, Wijmenga C, Lieb W, Franke A, Rosenstiel P, Doerfer C, Bruckmann C, CARDIoGENICS, König I, Bruno G. Loos GB, Schreiber S (2014Genetic evidence for PLASMINOGEN as a shared genetic risk factor of coronary artery disease and periodontitis. *Circ Cardio Genet* 8:159-67.

Dorman A, Daria Baer, Tomlinson I, Mott R and **Iraqi FA** (2015) Intestinal polyp development in Collaborative Cross mice carrying the ApcMin/+ mutation. *Am Int J Cont Sci Res* 396: 1.

Lore' NI, **Iraqi FA** and Bragonzi A (2015) Host genotype an important determinant factor of *Pseudomonas aeruginosa* susceptibility in the Collaborative Cross mice. *BMC Genetics* 16 (106).

Levy R, Mott RF, **Iraqi FA**, Gabet Y (2015) Collaborative cross mice in a genetic association study reveal new candidate genes for bone microarchitecture. *BMC Genomics* 16:1013: 1-14.

Abu Toamih-Atamni HJ, Mott R, Soller M and **Iraqi FA** (2016) High-fat induced development of increased fasting glucose levels and impaired response to intraperitoneal glucose challenge in collaborative cross mouse reference population. *BMC Genetics* 17:10.

Dorman A, Daria Baer, Tomlinson I, Mott R and **Iraqi FA** (2016) Genetic analysis of intestinal polyp development in Collaborative Cross mice carrying the *ApcMin*/+ mutation. *BMC Genetics* 17:46.

De Simone M, Spagnuolo L, Ivan Lorè N, Cigana C, De Fino I, Broman KW, **Iraqi FA**, Bragonzi A (2016) Mapping genetic determinants of host susceptibility to *Pseudomonas aeruginosa* lung infection in mice**.** *BMC Genomics* 17(1).

Abu Toamih-Atamni H, Botzman M, Mott R, Gat-Vicks I, **Iraqi FA** (2016) Mapping Quantitative Trait Loci associated with host susceptibility to non-alcoholic fat liver accumulations using collaborative cross mouse genetic reference population. Mamm Genome.

Nashef A, Abu-Toamih Atamni HJ, Buchnik Y, Hasturk H, Kantarci A, Stephens D, Wiess EI, Houri-Haddad Y, Iraqi FA. (2017) Collaborative Cross mouse population for studying alveolar bone changes and impaired glucose tolerance comorbidity after high-fat diet consumption. *J Periodontol.* 88:e150-e158.

Nashef A, Agbaria M, Shusterman A, Lorè NI, Bragonzi A, Wiess E, Houri-Haddad Y, Iraqi FA. (2017) Dissection of host susceptibility to bacterial infections and its toxins. *Methods Mol Biol*. 1488:551-578.

Review and editorials

Schughart K, Libert C; **SYSGENET consortium**, Kas MJ. (2013) Controlling complexity: the clinical relevance of mouse complex genetics. *Eur J Hum Genet.* 21:1191-6.

Hernandez-Valladares M, **Rihet** P, Iraqi FA (2014) Host susceptibility to malaria in human and mice: compatible approaches to identify potential resistant genes. *Physiol Genomics* 46:1-16.

Meehan T, Blake A, Bottomley J, Castro A, Fessele S, Fray M, Kenyon J, Koscielny G, Mallon AM, Massimi M, Matteoni R, Relac M, Steinkamp R, Wilkinson P, Hrabe de Angelis M, Brown S, Tocchini-Valentini G, Herault Y, Ramirez-Solis R, Kollias G, Ulfhake B, Demengeot J, Fremond C, Bosch F, Montoliu L, Flicek RSP, Schughart K, Brakebusch C, Sedlacek R, Radislav T, McKerlie C, Malissen B, **Iraqi FA**, Jonkers J, Holger R, Huylebroeck D, Parkinson H, Raess M, Hagn M. (2015) INFRAFRONTIER- Providing mutant mouse resources as research tools for the international scientific community. *Nucleic Acid Res* 43: 1171-1175.

Rajilić-Stojanović M, Daisy M, Raes J, Hanevik K, Salonen A, Jalanka J, de Vos WM, Manichanh C, Golic N, Enck P, Philippou E, **Iraqi FA**, Clarke G, Spiller RC and Penders J. (2015) Intestinal microbiota and diet in IBS: causes, consequences or epiphenomena. *Am J Gastroent* doi: 10.1038/ajg.2014.427.

Abu-Hussein M, Watted N, Yehia M, Proff P and **Iraqi FA** (2015) Clinical genetic basis of tooth agenesis. *J Dent Med Sci* 14**:** 1-10.

Grants

2014-2018	German Research Foundation (DFG-TRIO)
2015-2018	Israeli-Science Foundations (ISF)
2016-2020	United States-Israel Binational Science Foundation (BSF)

Dr. Oren Kobiler, M.D., Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: okobiler@post.tau.ac.il
URL: http://www.tau.ac.il/~okobiler

Investigating Viral Genetic Diversity

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

Our research is focused on understanding how viruses generate and maintain genetic diversity. All virus populations display high genomic diversity, which provides opportunities for survival in the constantly changing environment. In many cases, such diversity results in failure of antiviral treatment (resistance to vaccines and antiviral drugs) and the emergence of zoonotic viral pathogens. DNA viruses and segmented RNA viruses exploit recombination and reassortment as mechanisms for diversity creation. We are interested in the mechanisms allowing DNA viral recombination and finding ways to inhibit these mechanisms.

Publications

Hadas Y, Etlin A, Falk H, Avraham O, **Kobiler O**, Panet A, Lev-Tov A, Klar A. (2014) A 'tool box' for deciphering neuronal circuits in the developing chick spinal cord. Nucleic Acids Res. 42:e148

Yamin D., Jones F.K., DeVincenzo J.P., Gertler S., **Kobiler O**., Townsend J.P. and Galvani A.P. (2016). Vaccination strategies against RSV. Proc Natl Acad Sci *USA.* 113 (46), 13239-44

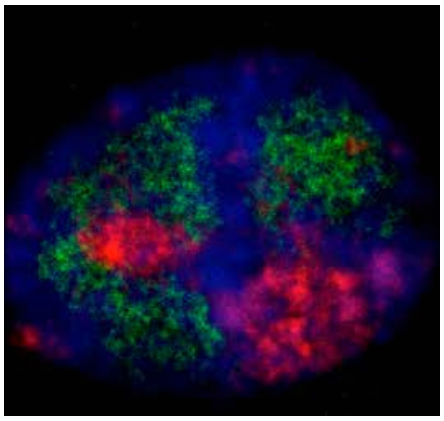
Cohen E. and **Kobiler O**. (2016). Herpes simplex virus-1 gene expression correlates with the number of viral genomes initiating infection in single cells. *PLoS Pathogens* 12 (12), e1006082

Shapira L., Ralph M., Tomer E., Cohen S. and **Kobiler O**. (2016). Histone Deacetylase inhibitors reduce the number of herpes simplex virus-1 genomes initiating expression in individual cells. *Front. Microbiol.* 7:1970.

Drayman N, Karin O, Mayo A, Danon T, Shapira L, Rafael D, Zimmer A, Bren A, **Kobiler O** and Alon U (2017). Dynamic proteomics of herpes simplex virus infection. *mBio* 8:e01612-17.

Grants

2014-2019	Grant, Israel Science Foundation (ISF)
2014-2019	Equipment Grant, Israel Science Foundation (ISF)
2016-2020	BSF, co-PI Dr. Weitzman Matthew



A. Spread of three alpha herpesviruses (each expressing a different XFP) from a single infected cell suggests that only a limited number of viral genomes are able to be expressed and replicated inside a single cell. B. Replication compartments in a single nucleus infected with two alphaherpesviruses suggest that genomes remain in separate territories in the nucleus.

Prof. Nir Osherov, Ph.D.

Department of Human Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: nosherov@post.tau.ac.il
URL: http://www.tau.ac.il/~nosherov/index.html

Human Mold Infections

Positions

Associate Professor, Sackler Faculty of Medicine

Chair, M.Sc. Committee, Sackler School of Medicine

Director, Ella Kodesz Institute of Host Defense against Infectious Diseases

Research

Aspergillus fumigatus is the most common mold pathogen of human beings, causing invasive diseases in immunocompromised (cancer after chemotherapy, bone marrow transplant etc) patients. Poor diagnostic tools and the ineffectiveness of antifungal drugs against established *Aspergillus* infections combine to result in high mortality following *A. fumigatus* infection. Left untreated, mortality rates from invasive pulmonary aspergillosis (IPA) exceed 90% and even following aggressive antifungal treatment fatality rates of 50-70% are common.

The goals of my lab are:

To understand what enables this mold to be such an effective and dangerous pathogen of immunocompromised patients

To develop novel modes of treatment including new antifungal compounds, targeted antibodies and nano medicines.

Publications

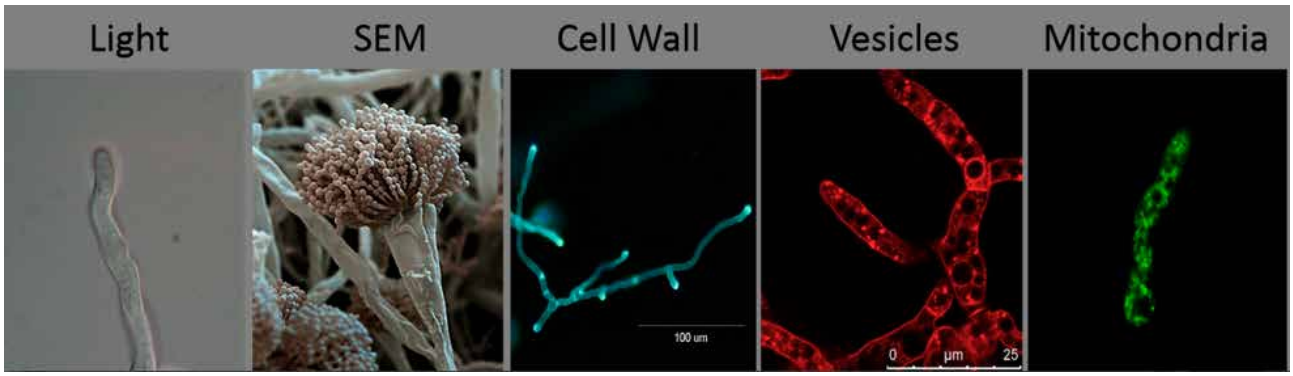
Wiemann P, Perevitsky A, Lim FY, Shadkchan Y, Knox BP, Landero Figueora JA, Choera T, Niu M, Steinberger AJ, Wüthrich M, Idol RA, Klein BS, Dinauer MC, Huttenlocher A, **Osherov N**, Keller NP. *Aspergillus fumigatus* copper export machinery and reactive oxygen intermediate defense counter host copper-mediated oxidative antimicrobial offense. *Cell Rep*. 2017;19:2174-2176.

Ben Yaakov D, Shadkchan Y, Albert N, Kontoyiannis DP, **Osherov N**. The quinoline bromoquinol exhibits broad-spectrum antifungal activity and induces oxidative stress and apoptosis in *Aspergillus fumigatus. J Antimicrob Chemother*. 2017;72:2263-2272.

Kaltdorf M, Srivastava M, Gupta SK, Liang C, Binder J, Dietl AM, Meir Z, Haas H,**Osherov N**, Krappmann S, Dandekar T. Systematic identification of anti-fungal drug targets by a metabolic network approach. *Front Mol Biosci*. 2016;3:22.

Osherov N, Ben-Ami R. Modulation of host angiogenesis as a microbial survival strategy and therapeutic target. *PLoS Pathog*. 2016;12:e1005479.

Vaknin Y, Hillmann F, Iannitti R, Ben Baruch N, Sandovsky-Losica H, Shadkchan Y, Romani L, Brakhage A, Kniemeyer O, **Osherov N**. Identification and characterization of a novel aspergillus fumigatus



The pathogenic mold *Aspergillus fumigatus*

rhomboid family putative protease, RbdA, Involved in hypoxia sensing and virulence. Infect Immun. 2016;84:1866-78.

Hover T, Maya T, Ron S, Sandovsky H, Shadkchan Y, Kijner N, Mitiagin Y, Fichtman B, Harel A, Shanks RM, Bruna RE, García-Véscovi E, **Osherov N**. Mechanisms of bacterial (*Serratia marcescens*) attachment to, migration along, and killing of fungal hyphae. *Appl Environ Microbiol*. 2016;82:2585-94.

Halperin A, Shadkchan Y, Pisarevsky E, Szpilman AM, Sandovsky H, **Osherov N**, Benhar I. Novel water-soluble amphotericin B-PEG conjugates with low toxicity and potent in vivo efficacy. *J Med Chem*. 2016;59:1197-206.

Ben Yaakov D, Rivkin A, Mircus G, Albert N, Dietl AM, Kovalerchick D, Carmeli S, Haas H, Kontoyiannis DP, **Osherov N**. Identification and characterization of haemofungin, a novel antifungal compound that inhibits the final step of haem biosynthesis. *J Antimicrob Chemother*. 2016;71:946-52.

Mircus G, Albert N, Ben-Yaakov D, Chikvashvili D, Shadkchan Y, Kontoyiannis DP, **Osherov N**. Identification and characterization of a novel family of selective antifungal compounds (CANBEFs) that interfere with fungal protein synthesis. *Antimicrob Agents Chemother*. 2015;59:5631-40.

Kroll K, Pähtz V, Hillmann F, Vaknin Y, Schmidt-Heck W, Roth M, Jacobsen ID, **Osherov N**, Brakhage AA, Kniemeyer O. Identification of hypoxia-inducible target genes of Aspergillus fumigatus by transcriptome analysis reveals cellular respiration as an important contributor to hypoxic survival. *Eukaryot Cell*. 2014;13:1241-53.

Vaknin Y, Shadkchan Y, Levdansky E, Morozov M, Romano J, **Osherov N**. The three Aspergillus fumigatus CFEM-domain GPI-anchored proteins (CfmA-C) affect cell-wall stability but do not play a role in fungal virulence. *Fungal Genet Biol*. 2014;63:55-64.

Grants

2014–2017 Infect-ERA Net Joint European Grant

Prof. Udi Qimron, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: ehudq@post.tau.ac.il
URL: http://www.tau.ac.il/~e-hudq/

Host-Virus Interactions in Bacterial Systems

Position

Professor, Sackler Faculty of Medicine

Research

Our laboratory studies basic aspects of bacteriophage growth with emphasis on phage interactions with their bacterial hosts, and particularly, the recently identified bacterial defense system, the CRISPR. Our ultimate objective is to identify novel phage products and strategies that will assist in overcoming drug resistant pathogens.

We combine genetic and biochemical approaches to identify and characterize interactions of phage proteins with other phage or host proteins. Specifically, we employ the T7 phage and its *Escherichia coli* host as models. We use high throughput screening systems, transposon mutagenesis, tandem affinity purification, mass spectrometry, and classical as well as modern bacterial genetic methods to identify and characterize these viral-host interactions.

Publications

Sberro H*, Leavitt A*, Kiro R*, Koh E, Peleg Y, **Qimron U**, and Sorek R. Novel families of toxin/immunity modules confer phage resistance in bacteria. *Molec Cell*, 50:136-48, 2013. *contributed equally. *Recommended by F1000*

Kiro R, Goren MG, Yosef I, and **Qimron U**. CRISPR adaptation in *Escherichia coli* type I-E system. *Biochem Soc Trans*, 41:1412-5, 2013.

Yosef I, Shitrit D, Goren MG, Burstein D, Pupko T, and **Qimron U**. DNA motifs determining the efficiency of adaptation into the *Escherichia coli* CRISPR array. *Proc Natl Acad Sci USA*, 110:14396-401, 2013. *Recommended by F1000*

Kiro R, Molshanski-Mor S, Yosef I, Milam SL, Erickson HP, and **Qimron U**. Gene-product 0.4 increases phage competitiveness by inhibiting host cell division. *Proc Natl Acad Sci USA*, 2013. 110:19549-54; Recommended by F1000.

Kiro R, Shitrit D, and **Qimron U.** Efficient engineering of a bacteriophage genome using the type I-E CRISPR-Cas system. *RNA Biol*, 11:42-4, 2014.

Yosef I, Kiro R, Molshanski-Mor S, Edgar E, and **Qimron U.** Different approaches for using bacteriophages against antibiotic-resistant bacteria. *Bacteriophage,* 4:e2849, 2014.

Molshanski-Mor S, Yosef I, Kiro R, Edgar R, Manor M, Gershovits M, Laserson M, Pupko T, and **Qimron U**. Revealing bacterial targets of growth inhibitors encoded by bacteriophage T7. *Proc Natl Acad Sci USA*, 111:18715-20, 2014.

Yosef I, Manor M, Kiro, R, **Qimron U**. Temperate and lytic bacteriophages programmed to sensitize and kill antibiotic-resistant bacteria. *Proc Natl Acad Sci USA*, 112:7267-7272, 2015.

Levy A*, Goren MG*, Yosef I, Auster O, Manor M, Amitai G, Edgar R, **Qimron U**†, #, Sorek R†# Spacer acquisition biases explain preference for foreign DNA in CRISPR adaptation. *Nature*, 520, 505-510, 2015. Recommended by F1000.

Yosef I, Manor M, Kiro R and **Qimron U.** Temperate and lytic bacteriophages programmed to sensitize and kill antibiotic-resistant bacteria. *Proc Natl Acad Sci USA*, 112, 7267-7272, 2015.

Yosef I, Edgar R, Levy A, Amitai G, Sorek R, Munitz A, and **Qimron U.** Natural selection underlies apparent stress-induced mutagenesis in a bacteriophage infection model. *Nature Microbiol*, 1, article #16047, 2016.

Goren MG, Doron S, Globus R, Amitai G, Sorek R*, and **Qimron U**#. Repeat size determination by two molecular rulers in the type I-E CRISPR array. Cell Reports, 16(11):2811-8, 2016.

Yosef I, Goren MG, Globus R, Molshanski-Mor S, and **Qimron U.** Extending the host range of bacteriophage particles for DNA transduction. Molecular Cell, 66(5):721-728, 2017. Cover page – Molecular Cell June 1, 2017.

Manor M. and **Qimron U.** Selection of Genetically Modified Bacteriophages Using the CRISPR-Cas System. Bio-Protocol, in press.

Reviews

Yosef I and Qimron U. Microbiology News and Views: How bacteria get spacers from invaders. *Nature*, 519, 166-167, 2015.

Yosef I, Manor M, and Qimron U. Counteracting selection for antibiotic-resistant bacteria. *Bacteriophage*, in press.

Goren MG, Yosef I, and Qimron U. Programming bacteriophages by swapping their specificity determinants. *Trends Microbiol*, 23, 744-746, 2015.

Sternberg S, Richter H, Charpentier E, and Qimron U. Adaptation in CRISPR-Cas systems. *Molec Cell*, 61(6):797-808, 2016.

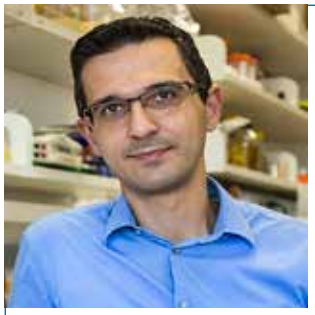
Yosef I, Edgar R, and **Qimron U.** Phenotypic heterogeneity in a bacteriophage population only appears as stress-induced mutagenesis. *Curr Genet,* 62(4):771-773.

Goren MG, Yosef I, and **Qimron U.** Sensitizing pathogens to antibiotics using the CRISPR-Cas system. *Drug Res Updates*, 30:1-6, 2017.

Globus R, and **Qimron U**. A Technological and Regulatory Outlook on CRISPR Crop Editing. *J Cell Biochem*, in press.

Grants

2014-2017	Israeli Ministry of Health Grant
2013-2018	ERC Starting Grant
2014-2019	Israel Science Foundation Grant
2016-2017	Momentum Fund



Dr. Dor Salomon, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: dorsalomon@mail.tau.ac.il
URL: http://www.dorsalomonlab.com

Bacterial Protein Secretion Systems and Toxins

Positions

Senior Lecturer, Sackler Faculty of Medicine

Research

Our lab is interested in the recently discovered Type VI Secretion Systems (T6SSs) and the toxins they deliver. We are pursuing discovery-driven research and translational approches to utilize the T6SS and its toxins as platforms for the development of novel antibacterial treatments.

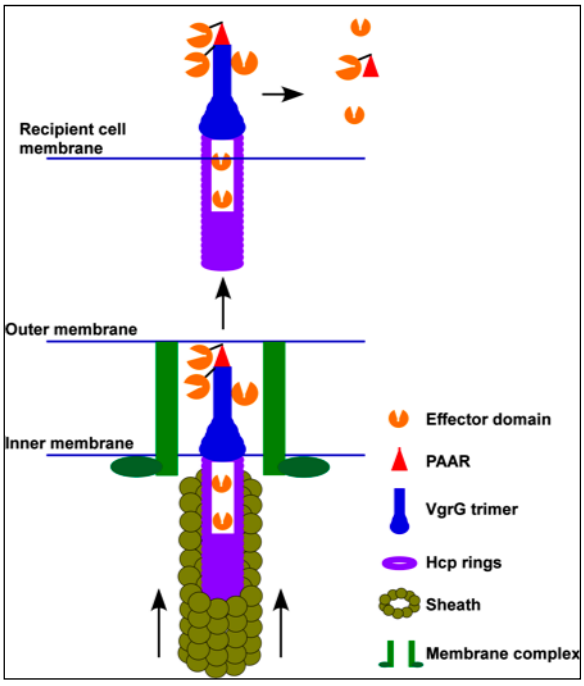
The T6SS is a contact-dependent protein delivery system that is found in many Gram-negative bacteria. It uses a contractile apparatus to propel an inner-tube, which is decorated with toxic effector proteins, outside of the bacterial cell and into an adjacent recepient cell, where effectors are deployed. The T6SS is unique as it can deliver toxins directly into eukaryotic host cells as well as into competing bacterial cells, and thus mediates both virulence and antibacterial toxicities.

We employ a multi-disciplinary approach to identify T6SSs activities and toxins in various bacterial pathogens. Using molecular biology, genetics, microbiology, biochemistry, microscopy, proteomics, and bioinformatic tools, we are identifying novel virulent and antibacterial toxins and determine their mechanism of action and their targets. In addition, we study T6SSs in pathogenic bacteria and determine their contibution to pathogenicity, inter-bacterial competition, and dissemination in the environment.

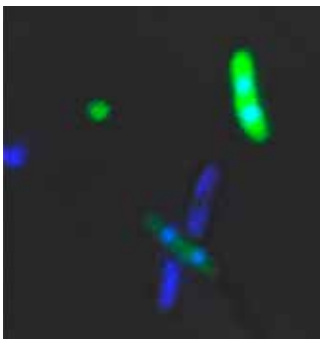
Publications

Ray A, Schwartz N, de Souza Santos M, Zhang J, Orth K, **Salomon D**. Type VI secretion system MIX-effectors carry both anti-bacterial and anti-eukaryotic activities. *EMBO Reports*. 2017, in press.

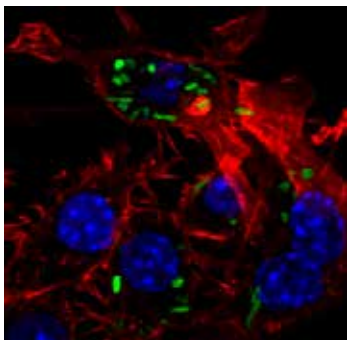
A



B



C



Type VI secretion systems (T6SSs) deliver effectors mediating antibacterial and virulence toxic activities. (A) A scheme of the T6SS. (B) Bacterial attackers (blue) using a T6SS with nuclease effectors to kill prey bacteria (green). (C) Bacteria (green) using a T6SS to allow survival and replication within a macrophage (red=actin cytoskeleton, blue = DNA).

Li P, Kinch LN, Ray A, Dalia AB, Cong Q, Nunen LM, Camilli A, Grishin NV, **Salomon D** #, Orth K #. Acute Hepatopancreatic Necrosis Disease (AHPND)-causing *Vibrio parahaemolyticus* strains maintain an antibacterial Type VI Secretion system with versatile effector repertoires. *Appl Environ Microbiol*. 2017, 83(13): e00737-17. # Corresponding authors

Ray A, Kinch LN, de Souza Santos M, Grishin NV, Orth K #, **Salomon D** #. Proteomics analysis reveals previously uncharacterized virulence factors in *Vibrio proteolyticus mBio*. 2016, 7(4):e01077-16. # Corresponding authors

Salomon D. MIX and match: mobile T6SS MIX-effectors enhance bacterial fitness. *Mob Genet Elements*. 2016, 6:e1123796.

Salomon D, Klimko JA, Trudgian DC, Kinch LN, Grishin NV, Mirzaei H, Orth K. Type VI secretion system toxins horizontally shared between marine bacteria. *PLoS Pathog*. 2015, 25;11:e1005128.

Salomon D, Klimko JA, Orth K. H-NS regulates the *Vibrio parahaemolyticus* type VI secretion system 1. *Microbiology*. 2014, 160:1867-73.

Salomon D, Kinch LN, Trudgian DC, Guo X, Klimko JA, Grishin NV, Mirzaei H, Orth K. Marker for type VI secretion system effectors. *Proc Natl Acad Sci USA*. 2014, 111:9271-6.

Salomon D, Gonzalez H, Updegraff BL, Orth K. *Vibrio parahaemolyticus* type VI secretion system 1 is activated in marine conditions to target bacteria, and is differentially regulated from system 2. *PLoS One*. 2013, 8:e61086.

Salomon D, Guo Y, Kinch LN, Grishin NV, Gardner KH, Orth K. Effectors of animal and plant pathogens use a common domain to bind host phosphoinositides. *Nat Commun*. 2013, 4:2973.

Salomon D, Orth K. What pathogens have taught us about posttranslational modifications. *Cell Host Microbe*. 2013, 14:269-79.

Grants

2016-2019	Alon Fellowship
2017-2022	European Research Council (ERC) Starting Grant
2017-2021	Israeli Science Foundation (ISF) Grant

Prof. Esther Segal, Ph.D.

Department of Clinical Microbiology and Immunology

TEL AVIV UNIVERSITY

Email: segale@post.tau.ac.il

Investigating the Pathogenesis of Candidiasis, Epidemiology of Dermatophytosis and Experimental Antifungal Drugs

Positions

Professor (Emeritus), Sackler Faculty of Medicine

President, Israel Society of Medical Mycology (ISMM)

Board Member (Treasurer), European Confederation of Medical Mycology (ECMM)

FECMM, Fellow of ECMM

Honorary Member of International Society of Human and Animal Mycology (ISHAM)

Research

We focus on studying phenotypic and genotypic characteristics of clinical *Candida albicans* strains from systemic and mucosal candidiasis in vitro and in vivo in experimental animal models, mice and Galleria mellonela.

We developed experimental antifungal drugs: the polyenes Amphotericin B (AMB) and Nystatin (NYT) associated with Intralipid (IL): AMB-IL and NYT-IL. Currently we assess susceptibility of the *C. albicans* clinical strains to AMB-IL and NYT-IL.

We investigate the epidemiology of dermatophytoses in Israel, in the general population and in the military.

Publications

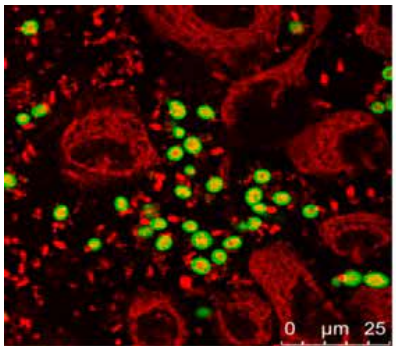
Semis R, Kagan S, Berdicevsky I, Polacheck I, **Segal E**. Mechanism of activity and toxicity of Nystatin-Intralipid. *Med Mycol*. 2013; 51:422-31

Alastruey-Izquierdo A, Mandelblat M, Ben Ami R, Perlin DS, **Segal E**. Multilocus sequence typing of Candida albicans isolates from candidemia and superficial candidiasis in Israel. *Med Mycol*. 2013 51:755-8.

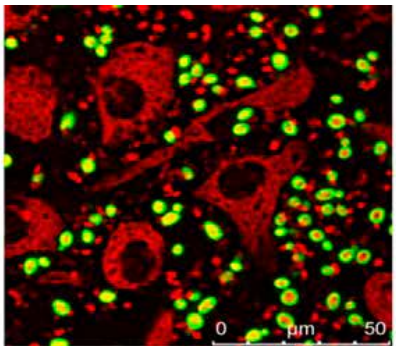
Segal E, Frenkel M. Dermatophyte infections in environmental contexts. *Res.Microbiol*. 2015; 166:564-9

Semis R, Nahmias M, Lev S, Frenkel M, **Segal E**. Evaluation of antifungal combinations of nystatin-intralipid against Aspergillus terreus using checkerboard and disk diffusion methods. *J Mycol Med*. 2015;25:63-70

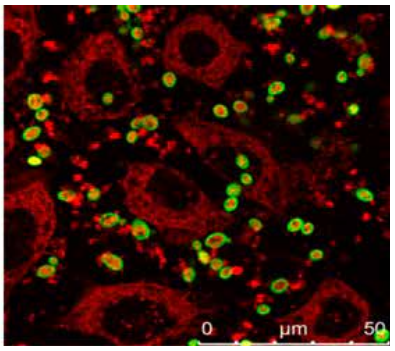
Segal R, Shemer A, Hochberg M, Keness Y, Shvarzman R, Mandelblat M, Frenkel M, **Segal E**.



CBS strain



S strain



M strain

Confocal microscopy of *C. albicans* strains adhering to HACAT cells showing strongly adherent strain from *Candida* blood-stream infection and weakly adherent strain from vaginal infection.

Onychomycosis in Israel: epidemiological aspects. *Mycoses*. 2015; 58: 133-9

Frenkel M, Mandelblat M, Alastruey-Izquierdo A, Mendlovic S, Semis R, **Segal E**. Pathogenicity of *Candida albicans* isolates from bloodstream and mucosal candidiasis assessed in mice and Galleria mellonella. *J Mycol Med*. 2016; 261-8

Mandelblat M, Frenkel M, Abbey D, Ben Ami R, Berman J, **Segal E**. Phenotypic and genotypic characteristics of Candida albicans isolates from bloodstream and mucosal infections. *Mycoses*. 2017 60:534-545

Segal E. Testing antifungal vaccines in an animal model of invasive candidiasis and in human mucosal candidiasis. *Methods Mol Biol*. 2017;1625:343-353

Grants

2018-2019 Maratier Fund

Dr. Ella Sklan, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: sklan@post.tau.ac.il

Viral Host Interactions of RNA Viruses

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

Our long-term goal is identification and characterization of the interactions of viruses with their host cells. Our current model systems include Ebola virus, Dengue virus and Hepatitis C and D viruses.

Current projects in the lab include:

1. Development of systems for the identification and characterization of new interactions between viral and host cell proteins.

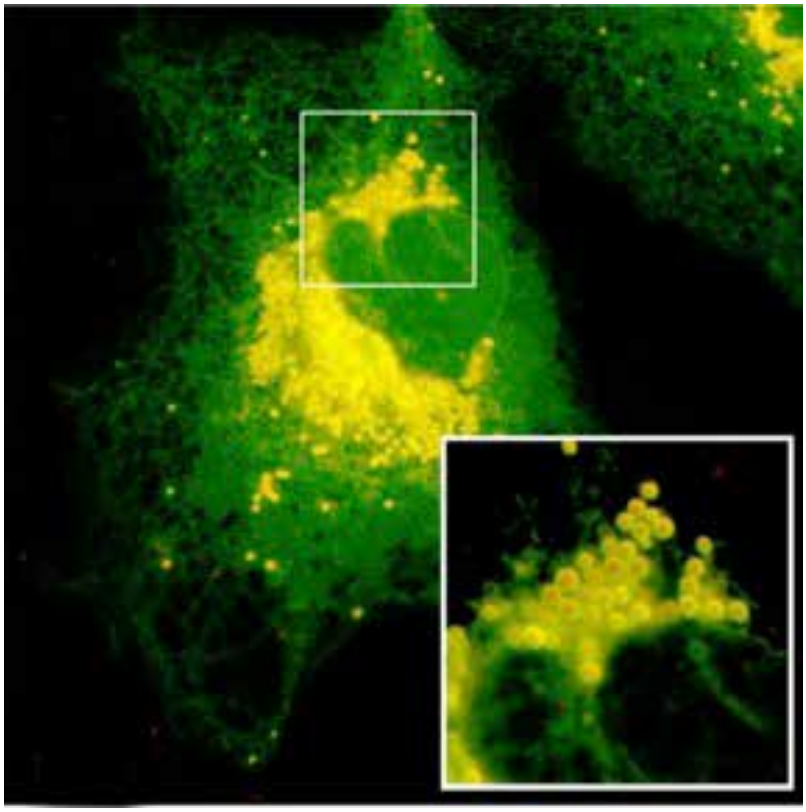
2. Using live cell imaging techniques to study viral-host interactions.

3. Identification of the mechanism of action of antiviral interferon stimulated genes.

Publications

Stern O, Hung YF, Valdau O, Yaffe Y, Harris E, Hoffmann S, Willbold D, **Sklan EH**. An N-terminal amphipathic helix in dengue virus nonstructural protein 4A mediates oligomerization and is essential for replication. (2013) *J Virol*. 87:4080-5.

Hanin G, Shenhar-Tsarfaty S, Yayon N, Hoe YY, Bennett ER, **Sklan EH**, Rao DC, Rankinen T, Bouchard



A live hepatoma cell (Huh7) expressing the viral non-structural protein 5A that localizes to the endoplasmic reticulum and lipid droplets.

C, Geifman-Shochat S, Shifman S, Greenberg DS, Soreq H. Competing targets of microRNA-608 affect anxiety and hypertension. (2014) *Hum Mol Genet*. 23:4569-80

David, N, Yaffe Y, Hagoel L, Elazar M, Glenn JS, Hirschberg K, **Sklan EH.** (2015) The interaction between the Hepatitis C proteins NS4B and NS5A is involved in viral replication. *Virology*, 475C:139-149.

Cho NJ, Lee C, Pang P, Pham EM, Fram B, Nguyen K, Xiong A, **Sklan EH**, Elazar M, Koytak ES, Kersten C, Kanazawa KK, Frank CW, Glenn JS. (2015) Phosphatidylinositol 4,5-bisphosphate is an HCV NS5A ligand and mediates replication of the viral genome. *Gastroenterology*, 148:616-25.

Hung Y, Schwartena M, Schünkea S, Thiagarajan-Rosenkranza P, Hoffmann S, **Sklan EH**, Willbold D, Koenig B. (2015) Dengue virus NS4A cytoplasmic domain binding to liposomes stabilizes membrane curvature. *BBA – Biomembranes*. 184:8 1119-1126.

Yaffe Y, Hagger I, Nevo Yassaf I, Shepshelovitch J, **Sklan EH**, Elkabetz Y, Yeheskel A, Pasmanik-Chor M, Benzing C, Macmillan A, Gaus K, Eshed-Eisenbach Y, Peles E, Hirschberg K. (2015) The myelin proteolipid Plasmolipin, forms oligomers and induces liquid ordered membranes in the Golgi apparatus. *J Cell Sci*, 128:2293-302.

Hung Y, Schwarten M, Hoffmann S, Willbold D, **Sklan EH**, Koenig B. (2015). Amino terminal region of Dengue virus NS4A cytosolic domain binds to highly curved liposome. *Viruses*, 7, 4119-4130.

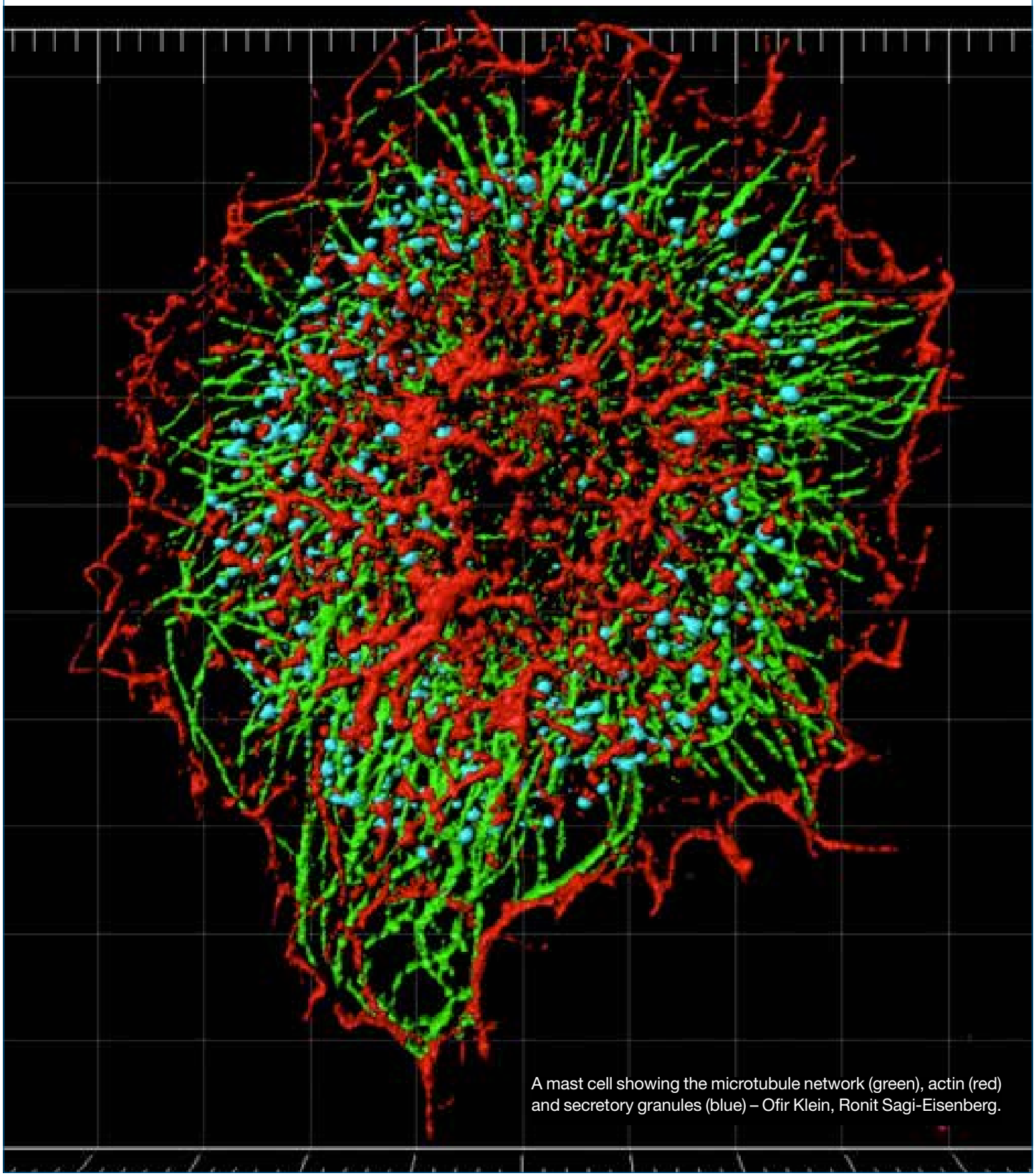
Levy G, Bomze D, Heinz S, Ramachandran SD, Noerenberg A, Cohen M, Shibolet O, **Sklan E,** Braspenning J, Nahmias Y. (2015) Long-term culture and expansion of primary human hepatocytes. *Nat Biotechnol*. 33:1264-1271.

Feldman M, Hershkovitz I, **Sklan EH**, Kahila Bar-Gal G, Pap I, Szikossy I, Rosin-Arbesfeld R. (2016). Detection of a tumor suppressor gene variant predisposing to colorectal cancer in an 18th century Hungarian mummy. *PLoS One*.11:e0147217.

Levy G, Habib N, Guzzardi M.A, Kitsberg D, Bomze D, Ezra E, Uygun B.E, Uygun K, Trippler M, Schlaak, J.F, Shibolet O, **Sklan EH**, Cohen M, Timm J, Friedman N, Nahmias Y. (2016) Nuclear receptors control pro- and anti-viral metabolic response to HCV infection. *Nature Chem Biol*. 12:1037-1045.

Nevo-Yassaf I, Lovelle M, Nahmias Y, Hirschberg K, **Sklan EH**. (2017) Live cell imaging and analysis of lipid droplets biogenesis in hepatatis C virus infected cells. *Methods*. 127:30-36.

Inflammatory and Autoimmune Diseases



A mast cell showing the microtubule network (green), actin (red) and secretory granules (blue) – Ofir Klein, Ronit Sagi-Eisenberg.

Prof. Ariel Munitz, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: arielm@post.tau.ac.il
URL: http://www.tau.ac.il/~ariel-elm/Ariel_Munitz,_PhD/Welcome.html

Regulatory Mechanisms in Mucosal Inflammation

Position

Associate Professor Sackler Faculty of Medicine

Associate Editor, *Journal of Allergy and Clinical Immunology*

Research

The gastrointestinal, respiratory and urogenital tracts are primary entry points of numerous pathogens and antigens. Therefore, complex immunological mechanisms evolved to efficiently and potently respond to such antigens. Notably, exaggerated immune responses such as those observed in asthma and inflammatory bowel disease are often harmful and may lead to substantial morbidity.

Our goal is to identify immunological mechanisms that can be pharmacologically targeted in diseases affecting the lung and gastrointestinal tract. We are specifically interested in defining the roles of immune inhibitory receptors in these mucosal sites. To achieve this goal we use a combination of novel in-vivo (unique gene targeted mice) and in-vitro approaches combining genomics, proteomics, molecular biology and biochemistry.

Publications

Reichman H, Moshkovits I, Itan M, Pasmanik-Chor M, Vogl T, Roth J, **Munitz A.** Transcriptome profiling of mouse colonic eosinophils reveals a key role for eosinophils in the induction of s100a8 and s100a9 in mucosal healing. *Sci Rep*. 2017;7:7117.

Rozenberg P, Reichman H, Zab-Bar I, Itan M, Pasmanik-Chor M, Bouffi C, Qimron U, Bachelet I, Fulkerson PC, Rothenberg ME, **Munitz A**. CD300f:IL-5 cross-talk inhibits adipose tissue eosinophil homing and subsequent IL-4 production. *Sci Rep*. 2017;7(1):5922.

Reichman H, **Munitz A**. Harnessing class II histone deacetylases in macrophages to combat breast cancer. *Cell Mol Immunol*. 2017;14(7):575-577.

Amit U, Kain D, Wagner A, Sahu A, Nevo-Caspi Y, Gonen N, Molotski N, Konfino T, Landa N, Naftali-Shani N, Blum G, Merquiol E, Karo-Atar D, Kanfi Y, Paret G, **Munitz A**, Cohen HY, Ruppin E, Hannenhalli S, Leor J. New role for Interleukin-13 Receptor β1 in myocardial homeostasis and heart failure. *J Am Heart Assoc*. 2017;6(5).

Elhaik Goldman S, Moshkovits I, Shemesh A, Filiba A, Tsirulsky Y, Vronov E, Shagan M, Apte RN, Benharroch DA, Karo-Atar D, Dagan R, **Munitz A,** Mizrachi Nebenzahl Y, Porgador A. Natural Killer Receptor

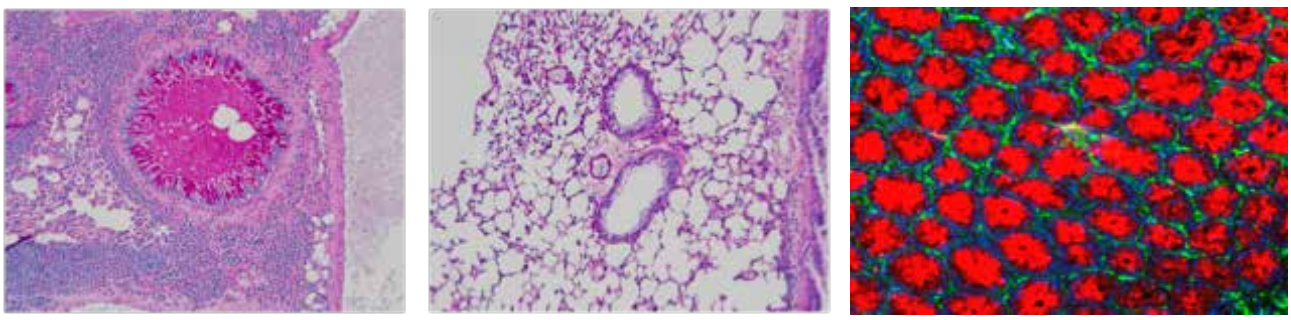


Figure legend: A photomicrograph of a normal lung displaying two large airways and a blood vessel (left). In many inflammatory conditions such as asthma and COPD, the airway is filled with mucus plugs (middle, pink stain). Right – an immunofluorescent stain of resistin-like molecule alpha (red), a proinflammatory, immunoregulatory molecule that is highly upregulated in gastointestinal epithelial in conditions such as inflammatory bowel disease (IBD).

1 dampens the development of allergic eosinophilic airway inflammation. *PLoS One*. 2016;11:e0160779.

Moshkovits I, Reichman H, Karo-Atar D, Rozenberg P, Zigmond E, Ziv-Haberman Y, Ben-Baruch-Morgenstern N, Lampinen M, Carlson M, Itan M, Denson LA, Varol C, **Munitz A**. A key requirement for CD300f in innate immune responses of eosinophils in colitis. *Mucosal Immunol*. 2016.

Yosef I, Edgar R, Levy A, Amitai G, Sorek R, **Munitz A**, Qimron U. Natural selection underlies apparent stress-induced mutagenesis in a bacteriophage infection model. Nat Microbiol. 1:16047, 2016.

Ben-Baruch-Morgenstern N, Mingler MK, Stucke EM, Besse JA, Wen T, Reichman H, Munitz A*, Rothenberg ME*. Paired immunoglobulin-like receptor B inhibits IL-13–driven eosinophil accumulation and activation in the esophagus. J Immunol (*-Equal contribution). 197:707-14, 2016.

Caspi M, Firsow A, Rajkumar R, Skalka N, Moshkovitz I, **Munitz A**, Pasmanik-Chor M, Greif H, Megido D, Kariv R, Rosenberg DW, Rosin-Arbesfeld R. A flow cytometry-based reporter assay identifies macrolide antibiotics as nonsense mutation read-through agents. *J Mol Med*. 2015

Knipper JA, Willenborg S, Brinckmann J, Bloch W, Maaß T, Wagener R, Krieg T, Sutherland T, **Munitz A**, Rothenberg ME, Niehoff A, Richardson R, Hammerschmidt M, Allen JE, Eming SA. Interleukin-4 Receptor α Signaling in Myeloid Cells Controls Collagen Fibril Assembly in Skin Repair. *Immunity*. 2015;43:803-16.

Moshkovits I, Karo-Atar D, Shik D, Reichman H, Itan M, Ejarque-Ortiz A, Hershko AY, Tian L, Coligan JE, Sayos J, **Munitz A**. CD300f associates with IL-4 receptor a and is required for IL-4-induced cellular responses. *Proc Natl Acad Sci USA*; 2015:112;8708-13.

Karo-Atar D, Bordowitz A, Wand O, Pasmanik-Chor M, Fernandez IE, Itan M, Frenkel R, Herbert DR, Eickelberg O, Munitz A. A protective role for IL-13 receptor a 1 in bleomycin-induced pulmonary fibrosis. *Mucosal Immunol*: 2014:9:240-53.

Karo-Atar D, Itan M, Pasmanik-Chor M, **Munitz A**. MicroRNA profiling reveals opposing expression patterns for miR-511 in alternatively and classically activated macrophages. *J Asthma*. 2014: 18:1-25

Shik D, Moshkovits I, Karo-Atar D, Reichman H, **Munitz A**. IL-33 requires CMRF35-like molecule-1 (CLM-1) expression for induction of myeloid cell activation. *Allergy***.** 2014, 69:719-29.

Baruch-Morgenstern NB, Shik D, Moshkovits I, Itan M, Karo-Atar D, Bouffi C, Fulkerson PC, Rashkovan D, Jung S, Rothenberg ME, **Munitz A**. Paired immunoglobulin-like receptor A is an intrinsic, self-limiting suppressor of IL-5-induced eosinophil development. *Nat Immunol*. 2014, 15:36-44.

Moshkovits I, Shik D, Itan M, Karo-Atar D, Bernshtein B, Hershko AY, van Lookeren Campagne M, **Munitz A**. CMRF35-like molecule 1 (CLM-1) regulates eosinophil homeostasis by suppressing cellular chemotaxis. *Mucosal Immunol,* 2013. 7:292-303.

Karo-Atar D, Moshkovits I, Eickelberg O, Königshoff M, **Munitz A.** PIR-B regulates pulmonary fibrosis by suppressing profibrogenic properties of alveoalar macrophages. *Am J Res Cell Mol Biol*; 2013: 48;456-464.

Reviews and Chapters

Reichman H, Karo-Atar D, **Munitz A**. Emerging roles for eosinophils in the tumor microenvironment. *Trends Cancer*. 2016;2:664-675.

Munitz A, Karo-Atar D, Foster PS. Asthma Diagnosis: miRNA's to the rescue. *J Allergy Clin Immunol*. 2016.

Grants

2014-2017	Israel Ministry of Health
2016-2017	The Teva Research Fund for Breakthroughs in Biomedicine; Title: Role of CD300f in eosinophils
2015-2020	The Israel Science Foundation Individual Research grant #95/11; Title: Regulation of GI eosinophils by CLM-1
2015-2018	The Israel Cancer Research Fund; Title: Molecular regulation of eosinophil activation in colorectal cancer

Dr. Mordechay (Motti) Gerlic, Ph.D.

Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: mgerlic@post.tau.ac.il
URL: http://med.tau.ac.il/profile/mgerlic

Cell Death and Immune Response: the Role of Necroptosis and Pyroptosis in Inflammation

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

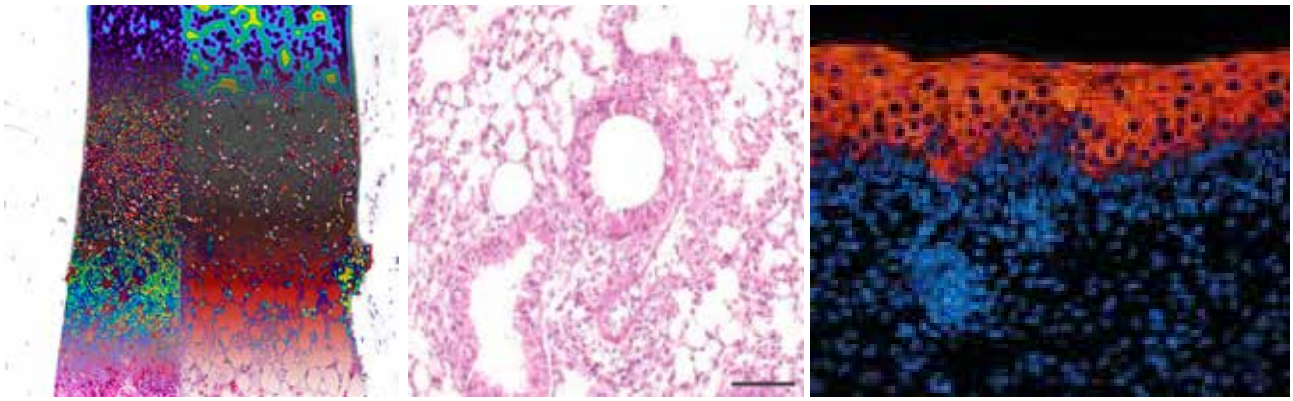
Cell death is an essential cellular process during development, but also facilitates the removal of damaged or infected cells, and is required for the resolution of innate and adaptive immune responses.

Our research focus is the understanding of the inflammatory response, with particular emphasis on novel NLRs (Nucleotide-binding domain and Leucine-rich repeat containing Receptors), and the non-apoptotic forms of cell death during infection. In particular we are interested in how pathogens (viruses and bacteria) are recognized by the innate immune system to facilitate these signals and how some pathogens evolve to target these mechanisms and prevent the host inflammatory response.

Recently, we discovered a physiological role for NLRP1 in driving a lethal, systemic inflammatory disease that is triggered by Caspase-1 activation and IL-1β production. Remarkably, active NLRP1 triggered a Caspase-1-dependent form of cell death, known as pyroptosis. This cell death affected hematopoietic stem and progenitor cells (HSPC), resulting in leukopenia at steady state, and cytopenia, bone marrow hypoplasia and immunosuppression, during periods of hematopoietic stress induced by chemotherapy or viral infection. Our recent research into how pathogens modulate complexes such as the NLRP1 inflammasome has defined mechanism by which *Vaccinia Virus* protein, F1L, target inflammasomes directly by binding and inhibiting the NLRP1 inflammasome formation. These findings reveal novel mechanism for viruses to evade host innate immune responses. Furthermore, we recently changed the thinking of necroptosis, which was thought to be RIPK1-dependent. We found the opposite, namely, that RIPK1 acts as a negative regulator of necroptosis, and loss of RIPK1 results in a lethal multi-organ systemic inflammatory response.

Publications

Sisquella X, Ofir-Birin Y, Pimentel MA, Cheng L, Abou Karam P, Sampaio NG, Penington JS, Connolly D, Giladi T, Scicluna BJ, Sharples RA, Waltmann A, Avni D, Schwartz E, Schofield L, Porat Z, Hansen D, Papenfuss AT, Eriksson EM, **Gerlic M**, Hill AF, Bowie AG, Regev-Rudzki N. Malaria parasite DNA-



Non-apoptotic induce inflammation. Inflammasome dependent lung inflammation during *vaccinia virus* infection (Left panel); Pyroptotic dependent bone marrow failure after chemotherapy treatment (Middle panel): Necroptotic dependent skin inflammation (Right panel).

harbouring vesicles activate cytosolic immune sensors. *Nat Comm*, in press, Oct, 2017.

Zargarian S, Shlomovitz I, Erlich Z, Hourizadeh A, Ofir-Birin Y, Croker BA, Regev-Rudzki N, Edry-Botzer L, **Gerlic M**. Phosphatidylserine externalization, "necroptotic bodies" release, and phagocytosis during necroptosis. *PLoS Biol*, June 2017.

McArthur K, D'Cruz AA, Segal D, Lackovic K, Wilks AF, O'Donnell JA, Nowell CJ, **Gerlic M**, Huang DCS, Burns CJ, Croker BA. Defining a therapeutic window for kinase inhibitors in leukemia to avoid neutropenia. *Oncotarget*, Accepted June 9 2017.

Murphy AJ, Kraakman MJ, Kammoun HL, Dragoljevic D, Lee MK, Lawlor KE, Wentworth JM, Vasanthakumar A, **Gerlic M**, Whitehead LW, DiRago L, Cengia L, Lane RM, Metcalf D, Vince JE, Harrison LC, Kallies A, Kile BT, Croker BA, Febbraio MA, Masters SL. IL-18 Production from the NLRP1 inflammasome prevents Obesity and Metabolic Syndrome. *Cell Metab*, 2016.

Uboldi AD, McCoy JM, Blume M, **Gerlic M**, Ferguson DJ, Dagley LF, Beahan CT, Stapleton DI, Gooley PR, Bacic A, Masters SL, Webb AI, McConville MJ, Tonkin CJ. Regulation of starch stores by a Ca(2+)-dependent protein kinase is essential for viable cyst development in *Toxoplasma gondii*. Cell Host Microbe. 18:670-681. 2015.

Lawlor KE, Khan N, Mildenhall A, **Gerlic M**, Croker BA, D'Cruz AA, Hall C, Spall SK, Anderton H, Masters SL, Rashidi M, Wicks IP, Alexander WS, Mitsuuchi Y, Benetatos CA, Condon SM, Wong WWL, Silke J, Vaux DL, Vince JE. RIPK3 promotes cell death, NLRP3 inflammasome and interleukin-1 activation in the absence of MLKL. *Nature Comm*, 6, 6282, 2015.

Murphy AJ, Kraakman MJ, Kammoun HL, Dragoljevic D, Lee MKS, Lawlor KE, Wentworth JM, Vasanthakumar A, **Gerlic M**, Whitehead LW, DiRago L, Cengia L, Lane RM, Metcalf D, Vince JE, Harrison LC, Kallies A, Kile BT, Croker BA, Febbraio MA, Masters SL. IL-18 Production from the NLRP1 inflammasome prevents obesity and metabolic syndrome. *Cell Metabolism*, DOI:*http://dx.doi.org/10.1016/j.cmet.2015.09.024*, 2015.

Blume M, Nitzsche R, Sternberg U, **Gerlic M**, Masters SL, Gupta N, McConville MJ. A *Toxoplasma gondii* gluconeogenic enzyme contributes to robust central carbon metabolism and is essential for replication and virulence. *Cell Host & Microbe*, 18, 210-220, 2015.

O'Donnell JA, Kennedy CL, Pellegrini1 M, Nowell CJ, Cengia1 L, Masters SL, Hartland EL, Roberts AW, **Gerlic M**, Croker BA. Fas controls neutrophil lifespan during viral and bacterial infection. *J Leukoc Biol*, December 3, 2014, doi: 10.1189/jlb.3AB1113-594RR.

Rickard JA*, O'Donnell JA*, Evans JM*, Lalaoui N, Poh AR, Rogers T, Vince JE, Lawlor KE, Ninnis RL, Anderton H, Hall C, Spall SK, Phesse TJ, Abud HE, Cengia LH, Corbin J, Mifsud S, Di Rago L, Metcalf D, Ernst M, Dewson G, Roberts AW, Alexander WS, Murphy JM, Ekert PG, Masters SL, Vaux DL, Croker BA*, **Gerlic M*#**, Silke J*#. RIPK1 regulates RIPK3-MLKL-driven systemic inflammation and emergency hematopoiesis. *Cell,* 157, 1175-1188, 2014 *These authors contributed equally to this work. # Corresponding authors.

Correa RG, Krajewska M, Ware CF, **Gerlic M**, Reed JC. The novel NLR-related protein NWD1 is associated with prostate cancer progression and impacts androgen receptor signalling. *Oncotarget.* March 26, 2014.

Gerlic M, Croker BA, Cengia LH, Moayeri M, Kile BT, Masters SL. NLRP1a expression in Srebp1a deficient mice. *Cell Metabolism***,** March 4, 2014.

Gerlic M*, Faustin B*, Postigo A, Yu ECW, Gombosuren N, Krajewska M, Flynn R, Croft M, Way M, Satterthwait A, Liddington RC, Salek-Ardakani S, and Reed JC. Vaccinia Virus F1L protein promotes virulence by inhibiting NLR inflammasome activation. *Proc Natl Acad Sci USA***,** 2013; 110:7808-13. *These authors contributed equally to this work..

Reviews

Liat Edry-Botzer L, **Gerlic M**. Exploding the necroptotic bubble. *Cell Stress.* 2017. DOI: 10.15698/cst2017.11.112

Gerlic M*, Croker BA*. Myelopoiesis embraces its inner weakness. *Nat Immunol*. Sep, 2017.

Shlomovitz I, Zargrian S, **Gerlic M***. Mechanisms of RIPK3-induced inflammation. *Immunol Cell Biol,* December, 2016.

Silke J, Rickard JA, **Gerlic M**. The diverse role of RIP kinases in necroptosis and inflammation. *Nature Immunol* 16, 689-697, 2015.

Croker BA, Silke J, **Gerlic M**. Fight or flight: regulation of emergency hematopoiesis by pyroptosis and necroptosis, *Curr Opin Hematol*, 22, 293-301, 2015.

Gerlic M, Masters SL. A healthy appetite for Toxoplasma at the cellular level**.** *Immunol Cell Biol*, 92, 813–814, 2014.

Haneklaus M*, **Gerlic M***, O'Neill LA, Masters SL. miR-223: infection, inflammation and cancer, *J Int*

Med, 274:215-26, 2013. *These authors contributed equally to this work.

Croker BA, O'Donnell JA, **Gerlic M**. Pyroptotic death storms and cytopenia. *Current Opinion in Immunology*, October 21, 2013.

Grants

2016-2018 Israel Society Foundation (ISF), Individual Research grant, *Mechanisms and physiological consequences of necroptosis*

2016-2018 Alpha-1 Foundation, Research grant, *The role of Necroptosis and IL-33 in lung pathology of A1AT deficiency*

Prof. Ronit Sagi-Eisenberg, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: histol3@post.tau.ac.il

Molecular Basis of Allergic Diseases: Genomic and Functional Analyses

Positions

Professor, Sackler Faculty of Medicine

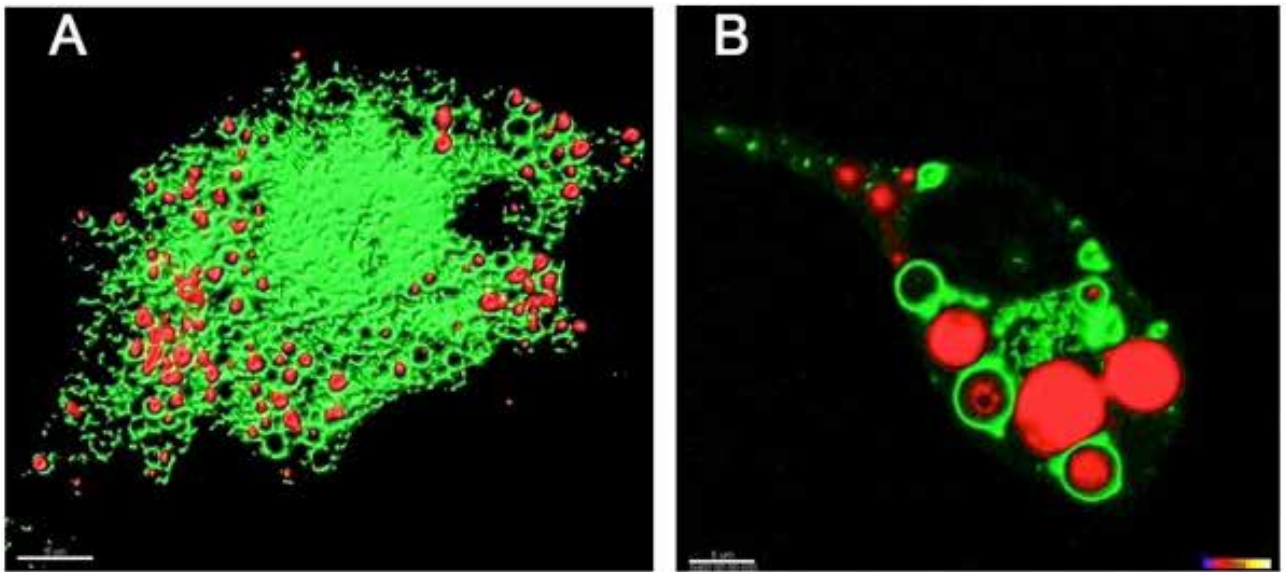
Chair, Department of Cell and Developmental Biology

Research

Our primary interest is the molecular basis of allergic and allergy related diseases, including skin allergy and asthma. Specifically, we explore the mechanisms underlying release of allergic (i.e. histamine) and inflammatory (i.e. cytokines) mediators from activated mast cells. Our research focuses on deciphering the signaling networks that link mast cell activation with mediator release and characterization of genes that could serve as cellular targets for the future development of anti allergic and asthma drugs. To this end, we combine functional genomics and phenotype driven screens of mast cells, activated by multiple stimuli, in order to recapitulate human pathophysiologic conditions. Research methods used include confocal microscopy in live and fixed cells; gene cloning; quantitative RT-PCR, pull down-assay; mass spectrometry, and bioinformatics.

Current projects in the lab include:

1. Revealing he secrets of mast cell secretion.
2. Mast cells and cancer – the good, the bad and the ugly.
3. Decoding the Rab networks that control mast cell function.



Cell imaging of mast cells (RBL-2H3 mast cell line), which were co-transfected with NPY-mRFP (red), as reporter for the secretory granules, and GFP-tagged wild type (A) or active mutant (B) of the small GTPase Rab5A (green) reveals a dramatic effect of this Rab active mutant on the secretory granules size.

Publications

Klein O, Roded A, Zur N, Azouz NP, Pasternak O, Hirschberg K, Hammel I, Roche PA, Yatsu A, Fukuda M, Galli SJ, **Sagi-Eisenberg R.** Rab5 is critical for SNAP23 regulated granule-granule fusion during compound exocytosis. *Sci Rep*. 2017;7,15315.

Gaudenzio, N., Sibilano, R., Marichal, T., Starkl, P., Reber, L.L., Cenac, N., McNeil, B.D., Dong, X., Hernandez, J.D., **Sagi-Eisenberg, R.**, Hammel, I., Roers, A., Valitutti, S., Tsai, M., Espinosa. E., and Galli, S.J. Different activation signals induce distinct mast cell degranulation strategies. *J Clin Invest. 2016;* 196, 3981-3998.

Gorzalczany, Y., Akiva E, Klein, O., Merimsky, O., and **Sagi-Eisenberg, R**. Mast cells are directly activated by contact with cancer cells by a mechanism involving autocrine formation of adenosine and autocrine/paracrine signaling of the adenosine A3 receptor. *Cancer Lett. 2017;* 397, 23-32.

Efergan A, Azouz NP, Klein O, Noguchi K, Rothenberg ME, Fukuda M, **Sagi-Eisenberg R**. Rab12 regulates retrograde transport of mast cell secretory granules by interacting with the rilp-dynein complex. *J Immunol*. 2016;196:1091-101.

Azouz NP, Fukuda M, Rothenberg ME, **Sagi-Eisenberg R**. Investigating mast cell secretory granules; from biosynthesis to exocytosis. J Vis Exp. 2015;95:52505.

Rudich N, Dekel O, **Sagi-Eisenberg R**. Down-regulation of the A3 adenosine receptor in human mast cells upregulates mediators of angiogenesis and remodeling. Mol Immunol. 2015;65:25-33.

Azouz NP, Hammel I, **Sagi-Eisenberg R**. Characterization of mast cell secretory granules and their cell biology. *DNA Cell Biol*. 2014; 33:647-51.

Azouz, N.P., Zur, N., Efergan, Ohbayashi, N., Fukuda, M., Amihai, D., Hammel, I., Rothenberg, ME and **Sagi-Eisenberg, R.** Rab5 is a novel regulator of mast cell secretory granules: impact on size, cargo and exocytosis. *J Immunol*. 192:4043-53 (2014)

Bar-Gill-Benado, A., Efergan, A., Seger, R., Fukuda, M., and **Sagi-Eisenberg R.** The extra-cellular signal regulated kinases ERK1 and ERK2 segregate displaying distinct spatiotemporal characteristics in activated mast cells. *Biochim Biophys Acta*. 1833, 2070-2082, (2013).

Bernstein-Molho R., Kollender, Y., Issakov, J., Bickels, J., Dadia S., Flusser, G., Meller, I., **Sagi-Eisenberg. R**. and Merimsky O. Clinical activity of mTOR inhibition in combination with cyclophosphamide in the treatment of recurrent unresectable chondrosarcomas. *Cancer Chemother Pharmacol*. 70, 855-860, (2012).

Azouz NP, Matsui, T., Fukuda, M. and **Sagi-Eisenberg, R.** Decoding the regulation of mast cell exocytosis by networks of Rab GTPases. *J Immunol*. 189, 2169-2180. (2012).

Reviews

Rudich N, Ravid K, and **Sagi-Eisenberg R**. Mast cell adenosine receptors function: a focus on the A3 adenosine receptor and inflammation. *Front Immunol*. 3:134. (2012).

Siebenhaar F, Falcone FH, Tiligada E, Hammel I, Maurer M, **Sagi-Eisenberg R**, Levi-Schaffer F. The search for Mast Cell and Basophil models – Are we getting closer to pathophysiological relevance? *Allergy* 2015;70:1-5.

Medical Education and Ethics

Dr. Oren Asman, LL.D., Adv.

Department of Nursing
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email:asman@post.tau.ac.il
URL: http://orenasman.com

Bioethics, Health Law and Medical Humanities

Positions

Visiting Lecturer, Sackler Faculty of Medicine

Executive Vice President, World Association for Medical Law - WAML

Program Chair, 24th World Congress on Medical Law and Ethics, Tel Aviv – WCML2018

Research

Our research focuses on ethical and legal aspects of biomedicine and health professions. Some studies are based on a normative-polemical analysis, while others use quantitative research methods or mixed methods. A large portion of this work is done in collaboration with professionals and researchers from different disciplines.

Our multicultural society and the interprofessional nature of current clinical practice, along with the developments in biomedical research, treatment methods and technology are all a setting for our bioethical deliberation and research. We are particularily interested in the ethical and legal implications of psychiatric and neurological conditions that influence one's thoughts, feelings and behabiours. The legal concept of competence which we focus on in our research brings to the fore some of the shortcomings of current medicine in realms where spirituality, philosophy and epistemology meet; the extent of respect for patients' autonomy during periods of lesser cognitive function is the main ethical focal point in this regard.

The empirical bioethics branch of our research focuses on thoughts, intentions and/or actual behaviors of health care professionals regarding activities of bioethical relevance, such as clinical research or interaction of professionals with the media. While some view normative bioethics to be the main or the only real bioethics research; we believe that combining both approaches provides a better basis for decision making and policy adaptation, as the empirical informs and influences the normative discussion.

Our primary research and teaching topics:

- Clinical research ethics
- Ethical and legal aspects of mental health and brain science
- Ethical and legal aspects of nursing and nursing education
- Public discourse on health issues, ethics and law
- Islamic law and bioethics

Publications

Bergman-Levy T, **Asman O**, Dahan E, Greenberg B, Hirshmann S & Strous R. Specific ethical codes for mental health care professionals –Do we need to annotate. Israeli Medical Association Journal. 2016,18(8), 454-460.

Asman O. Religion, Bioethics and Health Law in Israel. in *Health Law – A book in honor of Prof. Guilherme de Oliveira*, Vol I (Centro Direito Biomedico, Portugal, 2016) 107-130.

Asman O & Barilan YM. The songs of the sirens and the wax in the ears – An autonomy-based tool for DBS device users. American Journal of Bioethics – Neuroscience. 2017, 8(2), 120-122.

Asman O, Barnoy S, Menlinkov S, Tabak N. Research misconduct in Nursing – an Israeli survey. Nursing Ethics. 2017 DOI: 10.1177/0969733017727152.

Barilan YM & **Asman O**. Research Ethics, Military Medical Ethics and the Challenges of International Law. American Journal of Bioethics. 2017. 17(10) 54-56.

Asman O, Tabak N, Professional Standards Expected of Nurses from an Israeli Legal Perspective. Medicine and Law. 2017. 36(4) 53-72.

Asman O, Bergman-Levy T, Greenberg B & Strauss R. Psychiatrists' Media Involvement: A survey of attitudes. Israeli Journal of Psychiatry and Related Sciences. 2018.

Grants

2017-2019 The Israel National Institute for Health Policy Research

Prof. Yechiel Michael Barilan, M.D., M.A.

Department of Medical Education
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: barilanm@post.tau.ac.il

Bioethics, Biolaw and Medical Humanities

Position

Associate Professor, Sackler Faculty of Medicine

Research

The research area of our group is Medical Humanities, relying on theoretical methods with the occasional excrusion to qualitative research.

My own personal interests encompass moral theory and the intersections among bioethics, social history and related normative domains, such as law and religion, especially Halakhah (Jewish religious law). I explore human rights law and international humanitarian law in the light of the contemporary ethical and meta-ethical discourse. Another aspect of my work aims at developing better understanding and tools of deliberation in bioethics as a psycho-moral process and as socially constructed events of legitimization and education. I am intrigued by the incorporation of the history and philosophy of ideas such as conscience, responsibility, hope and doubt in clinical reality and medical education.

Another branch of research is the socio-historical and moral ideas in the representation of illness and medicine in Western visual art, since the late middle ages through contemporary and experimental art.

Ongoing research projects are:

1. Moral psychology and the notion of ethical expertise in medical education.

2. The history of karyotyping exams in questions of gender (e.g. gender verification in sport).

3. Ethics and law of military, humanitarian and disaster medicine.

4. The regulation of cloning in international law.

5. New born screening and the regulation of large, public-health data banks.

6. Human rights and international humanitarian law.

Our group's chief aim is to integrate deep theoretical knowledge and creativity with applied problems, contextualizing their ethical dimensions historically and socially. Efforts are made in the direction of cross-disciplinary work, especially through participation in the activities of the new **Edmund J. Safra Center for Ethics**, Tel Aviv University.

Monographs

Barilan, YM. Human dignity, human rights and responsibility: the new language of global bioethics ad biolaw. Cambridge (MA): MIT Press. 2012.

Barilan, YM. Jewish bioethics: rabbinic law and theology in their social and historical contexts. Cambridge University Press. 2017

Publications

Barilan YM. Bedside rationing or rational planning: in search for perspective on medical need and safety. In: Masin M, Fleck L, Hurst S. (eds.) Towards fair rationing at the bedside. Oxford: Oxford University Press, 2013.

Barilain YM, Barnea R. Routine medical care in the military. In: Siegal G, Kasher A. (eds.) Bioethics blue and white. Ha'kibbutz Ha'Me'uhad Press, 2014. [Hebrew]

Barilan YM. Rethinking the withholding / withdrawing distinction" the cultural construction of "life support" and the framing of end-of-life decisions". Multidisciplinary Respiratory Medicine 2015; 10:10

Barilan YM. Moral enhancement, gnosticism and some philosophical paradoxes. Cambridge Quarterly of Healthcare Ethics 2015; 24:75-85.

Lehmann J, Barilan YM. De-contructing de-mentia: a personal and person oriented perspective of de-personalization and moral status. Medicine Healthcare and Philosophy 2015; 18:153-158.

Barilan YM. and Brusa M. Triage. Encyclopedia of Global Bioethics. H. Ten Have (ed.) New York: Springer. Forthcoming 2016.

Barilan YM. and Brusa M. Bioethics Education. Encyclopedia of Global Bioethics. H. Ten Have (ed.) New York: Springer. Forthcoming 2016.

Barilan YM. Terror and the Leviathan. Pragmatics and Cognition. 2016; 23:461-472.

Asman O and **Barilan YM**. The songs of the sirens and the wax in the ears: an autonomy-based tool for DBS device users. AJOB Neuroscience 2017; 8:120-122

Barilan YM. The role of doctors in hunger strikes. Kennedy Institute of Ethics Journal. 2017; 27:341-369.

Barilan YM and Asman O. Research ethics, military medical ethics and the challenges of International humanitarian law. American Journal of Bioethics. 2107; 17:53-55.

Chapters

Brusa M and **Barilan YM**. Newborn screening on the cusp of genetic screening. From solidarity in public health to personal counseling. In Peterman HI, Harper PS, and Doetz S. (eds). History of Human Genetics: Aspects of its Development in Global Perspectives. New York: Springer, 2017. pp. 503-522.

Brusa M. and **Barilan YM**. Childbirth in Israel with special attention to home birth and newborn screening. In Lavi. S. and Boas H. (eds.) Bio-Israel. Cambridge University Press. 2017. pp. 180-201.

Dr. Orit Karnieli-Miller, Ph.D.

Department of Medical Education
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: oritkm@post.tau.ac.il

Studying Doctor-Patient Relationships, Communication and Medical Professionalism

Positions

Senior Lecturer, Sackler Faculty of Medicine

Board of Directors member, American Academy of Communication in Healthcare – AACH

Member, Research Committee, European Association of Communication in Healthcare (rEACH)

Member, Founding Committee, Society of Medical Education in Israel (Healer)

Research

Our primary research and teaching interests are focused on:

- Professionalism and humanism in medical schools. Understanding what students experience, how they interpret it and what we should do to help their development as humanistic professionals.
- Developing communication skills for handling and assessing multi-participant conversations (triadic communication) physician-patient-companion. Understanding how we should and could involve family members.
- Teaching medical students and professionals how to break bad news, including assessing how their personal difficulties and biases affect their communication.
- Enhancing medical students self-awareness (e.g., by using reflective diaries and narratives in medical education).
- Defining and applying Shared Decision Making in healthcare.

Publications

Bril-Barniv, S., Moran, G. S., Naaman, A., Roe, D., **Karnieli-Miller, O.** (2017). A qualitative study examining experiences and dilemmas in concealment and disclosure of people living with serious mental illness. *Qualitative Health Research*, 27(4) 573–583.

Naaman, A., Roe, D., Karni-Weiser, N., & **Karnieli-Miller, O.** (2017). Exploring the process of self-disclosure from the perspective of people coping with Schizophrenia. *Society and Welfare*, 37 (Hebrew).

Goldberg, M., Hadas-Lidor, N., & **Karnieli-Miller, O.** (2017). Professional development of social work students coping with mental illness. *Society and Welfare*, 37 (Hebrew).

Karnieli-Miller, O., Miron-Shatz, T., Siegal, G., & Zisman-Ilani, Y. (2017). On the verge of implementing shared decision making in Israel: An overview and future directions. Z. Evid. Fortbild. Qual. Gesundh. Wesen (ZEFQ), http://dx.doi.org/10.1016/j.zefq.2017.05.007

Hart, Y., Czerniak, E., **Karnieli Miller, O**., Mayo, A., Ziv, A., Biegon, A., Citron, A., & Alon, U. (2016). Automated video analysis of non-verbal communication in a medical setting. *Frontiers in Psychology*. 7, 130

Zisman-Ilani, Y., Roe, D., Scholl, I., Härter, M., **Karnieli-Miller, O.** (2016). Shared decision-making during active psychiatric hospitalization: assessment and psychometric properties. *Health Communication.* 32(1), 126-130 .

Czerniak, E., Biegon, A., Ziv, A., **Karnieli-Miller, O.**, Weiser, M., Alon, U., & Citron, A. (2016). Manipulating the placebo response in experimental pain by altering doctor's performance style. *Frontiers in Psychology* 7, 874

Goldberg, M., Hadas-Lidor, N., **Karnieli-Miller, O**. (2015). From patient to Therapatient: Social work students coping with mental illness. *Qualitative Health Research.* 25, 887–898. 2015

Zisman-Ilani, Y., Roe, D., **Karnieli-Miller, O.** (2015) Involving patients in decision making: understanding

the past and planning the future. Quality in Medicine, 3, 10-12. 2015 (Hebrew)

Michael K., Solenko L., **Karnieli-Miller, O.** (2015). Perspectives of significant life events among at-risk youth. *Society and Welfare*, 35, 537-562 (*Hebrew*).

Karnieli-Miller, O. Nissim, G., Goldberg, M. (2015). "It's In the Cards:" The contribution of illustrated metaphor cards to exploring values within narratives. *Qualitative Health Research,* 1-14.

Karnieli-Miller, O., Zisman-Ilani, Y., Meitar, D. & Mekori, Y. (2014) The role of medical schools in promoting social accountability through shared decision-making. Isra*eli Journal of Health Policy, Israel Journal of Health Policy Research* 4-1 ,3 ,2014.

Moran, G., Oz, G., & **Karnieli-Miller**, O. (2014) Psychiatrists' challenges in considering disclosure or schizophrenia diagnosis in Israel. *Qualitative Health Research*. 24, 1368–1380.

Karnieli-Miller, O., Frankel, R.M., & Inui, T.S. (2013). Cloak of compassion or evidence of elitism? an empirical analysis of white coat ceremonies? *Medical Education,* 43, 97-108.

Karnieli-Miller, O., Perlick, D. A., Nelson, A., Mattias, K., Corrigan, P., & Roe, D. (2013). Family members' of persons living with a serious mental illness: Experiences and efforts to cope with stigma. *Journal of Mental Health,* 22, 254-262.

Reviews

Yamin, A., Roe, D., **Karnieli-Miller, O**. (2017). Reviewing from the inside and out – the processes of parents of people coping with a mental illness enrolled in a group intervention to reduce self-stigma. In A. Shalev and N. Lidor-Hadass (Eds.,) *From Invisibility to Partnership: Paths to Recovery and Coping with Mental Illness in the Family* (Hebrew). Kiryat Ono: Ono Academic College, pp 117-130 (vol 2).

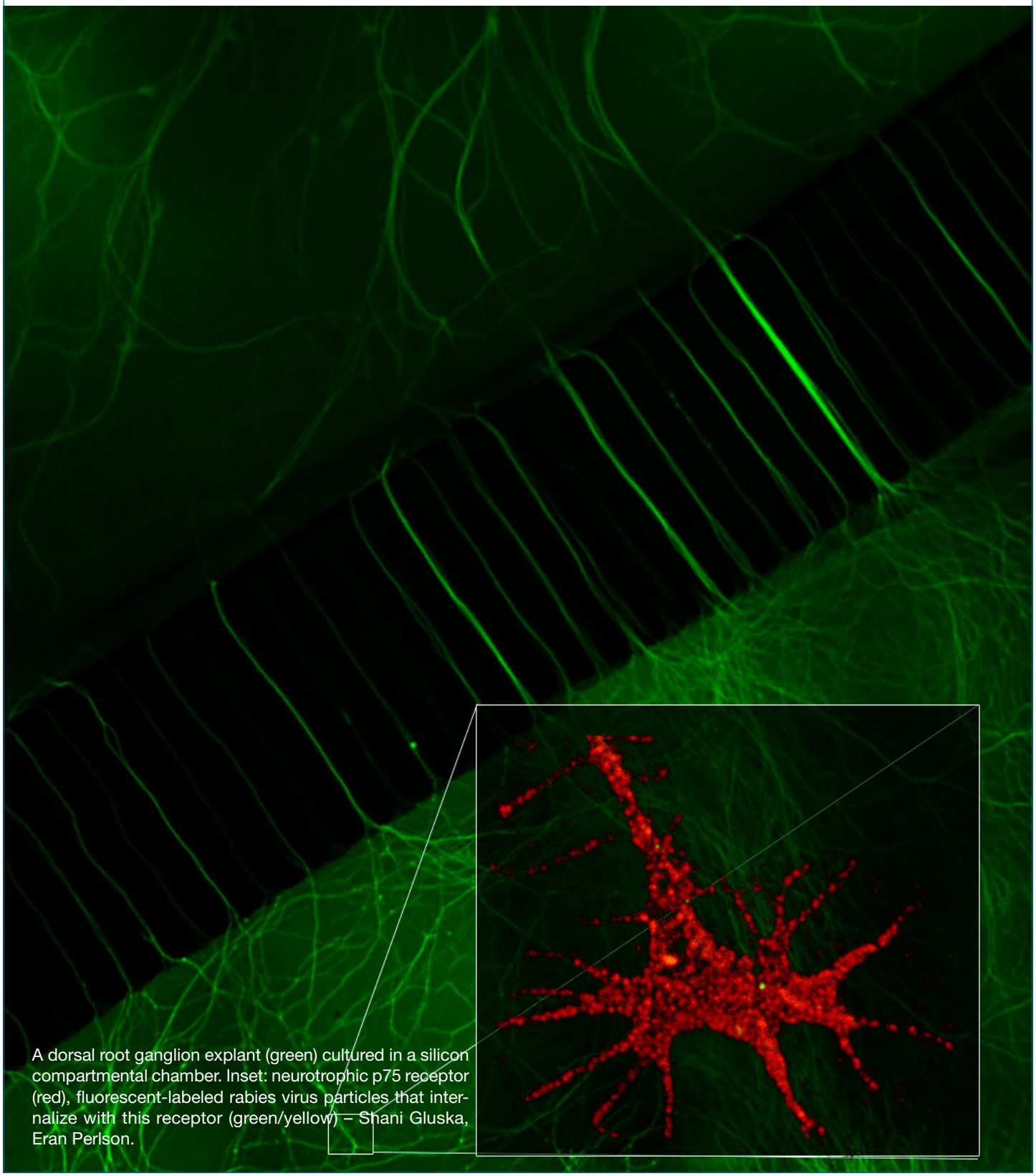
Shalev, A. Goldberg M., & **Karnieli-Miller O**. (2017). Building relationships, promoting communication and partnership with families of people coping with a mental Illness. In A. Shalev and N. Lidor-Hadass (Eds.,) *From Invisibility to Partnership: Paths to Recovery and Coping with Mental Illness in the Family* (Hebrew). Kiryat Ono: Ono Academic College, pp 235-272 (vol 2).

Werner, P., **Karnieli-Miller, O.,** Eidelman, S. (2013). Current knowledge and future directions about the diagnostic disclosure of dementia: A systematic review of the first decade of the 21st century. *Alzheimer's & Dementia, 9*, e74–e88.

Grants and Chapters

2016-2018	Preventing burnout and enhancing professionalism in the surgical unit care and medical teams
2017-2019	*Israel National Institute for Health Policy Research*, Enhancing Patient Centered Care through Understanding Barriers and Promotors to Implementing Shared Decision Process in Diabetes

Nervous System and Brain Disorders



A dorsal root ganglion explant (green) cultured in a silicon compartmental chamber. Inset: neurotrophic p75 receptor (red), fluorescent-labeled rabies virus particles that internalize with this receptor (green/yellow) – Shani Gluska, Eran Perlson.

Prof. Ruth Ashery-Padan, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: ruthash@post.tau.ac.il
URL: http://asherypadanlab.com

Investigating the Molecular Basis of Visual System Development

Positions

Professor, Sackler Faculty of Medicine

Committee Member, Israel Society of Developmental Biology

Research

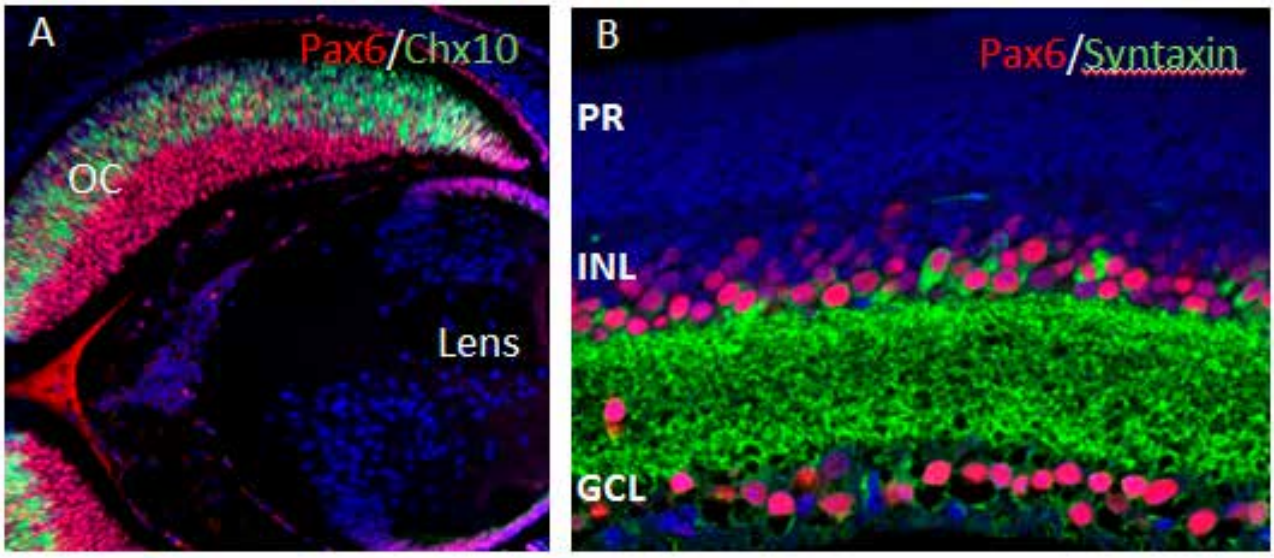
We study the gene networks that transform the embryonic cells into a complex, differentiated organ. We focus on exploring this question by studying the process of eye development as a model for organogenesis. We apply cutting-edge technologies including mouse genetic tools (Cre/loxP), molecular biology, and microarray analysis to identify and functionally characterize genes that regulate the development of the eye in mammals. Understanding the normal developmental regulation of the different eye structures is essential for understanding visual disorders and designing treatments for ocular phenotypes including retinal degeneration, glaucoma and cataracts, all of which are leading causes of blindness.

Publications

Remez LA, Onishi A, Menuchin-Lasowski Y, Biran A, Blackshaw S, Wahlin KJ, Zack DJ, **Ashery-Padan R**. Pax6 is essential for the generation of late-born retinal neurons and for inhibition of photoreceptor-fate during late stages of retinogenesis. *Dev Biol*, 2016; doi:10.1016/j.ydbio.2017.09.030.

Swisa A, Avrahami D, Eden N, Zhang J, Feleke E, Dahan T, Cohen-Tayar Y, Stolovich-Rain M, Kaestner KH, Glaser B, **Ashery-Padan R**, Dor, Y. PAX6 maintains beta cell identity by repressing genes of alternative islet cell types. *J Clin Invest* 2017;127, 230-243.

Menuchin-Lasowski Y, Oren-Giladi P, Xie Q, Ezra-Elia R, Ofri R, Peled-Hajaj S, Farhy C, Higashi Y, Van de Putte T, Kondoh H, Huylebroeck D, Cvekl



Developmental genes play role in adult neurons. Immunofluorescence analysis reveals the expression pattern of developmental transcription factors (A) in the retinal progenitor cells located in the embryonic mouse optic cup (OC). (C) In the adult retina the developmental gene Pax6 is expressed in subtypes of retinal interneurons that co-express the synaptic protein syntaxin.

A, **Ashery-Padan R**. Sip1 regulates the generation of the inner nuclear layer retinal cell lineages in mammals. *Development*. 2016;143:2829-41.

Raviv, S., K. Bharti, S. Rencus-Lazar, Y. Cohen, R. Schyr, N. Evantal, E. Meshorer, A. Zilberberg, M. Idelson, B. Reubinoff, R. Grebe, R. Rosin-Arbesfeld, B.E. Lauderdale, G. Lutty, H. Arnheiter, and **R. Ashery-Padan.** PAX6 regulates melanogenesis in the retinal pigmented epithelium through feed-forward regulatory interactions with MITF. *PLoS Genet*, 2014. 10:1004360.

Wolf, L., W. Harrison, J. Huang, Q. Xie, N. Xiao, J. Sun, L. Kong, S.A. Lachke, M.R. Kuracha, V. Govindarajan, P.K. Brindle, **R. Ashery-Padan**, D.C. Beebe, P.A. Overbeek, and A. Cvekl, Histone posttranslational modifications and cell fate determination: lens induction requires the lysine acetyltransferases CBP and p300. *Nucleic Acids Res*, 2013. 41:10199-214

Wolf, L., C.S. Gao, K. Gueta, Q. Xie, T. Chevallier, N.R. Podduturi, J. Sun, I. Conte, P.S. Zelenka, **R. Ashery-Padan**, J. Zavadil, and A. Cvekl. Identification and characterization of fgf2-dependent mRNA:microRNA networks during lens fiber cell differentiation. *G3*, 2013. 3:2239-2255.

Farhy, C., M. Elgart, Z. Shapira, V. Oron-Karni, O. Yaron, Y. Menuchin, G. Rechavi, and **R. Ashery-Padan**, Pax6 is required for normal cell-cycle exit and the differentiation kinetics of retinal progenitor cells. *PLoS One*, 2013. 8:e76489.

Zembrzycki A, Chou SJ, **Ashery-Padan R**, Stoykova A, O'Leary DD. Sensory cortex limits cortical maps and drives top-down plasticity in thalamocortical circuits. *Nat Neurosci*. 2013, 16:1060-7.

Shaham O, Gueta K, Mor E, Oren-Giladi P, Grinberg D, Xie Q, Cvekl A, Shomron N, Davis N, Keydar-Prizant M, Raviv S, Pasmanik-Chor M, Bell R, **Levy C**, Avellino R, Banfi S, Conte I, Ashery-Padan R. Pax6 regulates gene expression in the vertebrate lens through miR-204. *PLoS Genet,* 2013, 9:e1003357.

Bochner R, Ziv Y, Zeevi D, Donyo M, Abraham L, Ashery-Padan R, **Ast G**. Phosphatidylserine increases IKBKAP levels in a humanized knock-in IKBKAP mouse model. *Hum Molec Genet*. 2013, 22: 2785-2794

Grants

2014-2018	Binational Science Foundation (with Ales Cveki, Albert Einstein School of Medicine)
2014-2019	Israel Science Foundation
2016-2018	ISF-China (with Naihe Jing, Chinese Academy of Sciences, Shanghai)

Prof. Hagit Eldar-Finkelman, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: heladr@post.tau.ac.il
URL: http://www.tau.ac.il/~heldar/

GSK-3 Signaling in Health and Disease

Position

Professor, Sackler Faculty of Medicine

Chair, Sackler Committee for Ph.D. Graduate Studies

Research

Our research is focused on the molecular mechanisms regulating the protein kinase GSK-3 and their implications in human disease. GSK-3 is a central player in diabetes, neurodegenerative and psychiatric disorders, and recently emerged as a promising drug discovery target. We propose that inhibition of GSK-3 should produce therapeutic benefits in treating these disorders. We develop selective substrate competitive GSK-3 inhibitors and evaluate their efficacy and therapeutic effects in relevant in vitro and in vivo systems. So far we could show that our leading compound inhibitors had therapeutic efficacy in CNS disorders models for Alzheimer's disease, mood disorders, and multiple sclerosis.

In recent work we identified the lysosome as a GSK-3 target. This implicated GSK-3 as a key player in protein degradation pathways, particularly autophagy ad endocytosis. Research methods combine cell biology, molecular biology and biochemistry disciplines together with bioinformatics and computational biology.

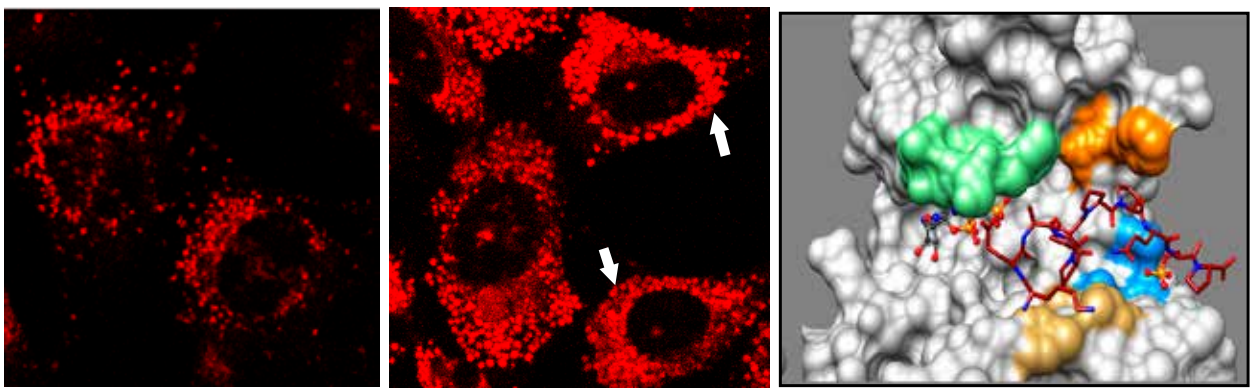
Publications

Monte, LM, Kramer, T., Gu, J., Brodecht, M., Fuertes, Dominguez, JM., Plotkin, B., **Eldar-Finkelman, H.,** Schmidt, B. 2013, Structure-based optimization of oxadiazole-based GSK-3 inhibitors. *Eur J Med Chem*. 61:26-40.

Avrahami, L., Farfara, D., Shaham-Kol, M., Vassar, R., Frenkel, D., **Eldar-Finkelman, H**. 2013, Inhibition of GSK-3 ameliorates β-amyloid (Ab) pathology and restores lysosomal acidification and mtor activity in the alzheimers disease mouse model. *In vivo* and *In vitro* studies. J Biol Chem 288:1295-1306.

Beurel, E., Kaidanovich-Beilin, O., Yeh, W., Song, L, Palomo, V., Michalek, SM., Woodgett, JR, Harrington, LE, **Eldar-Finkelman, H**., Martinez, A., Jope, RS. 2013, Regulation of Th1 cells and experimental autoimmune encephalomyelitis (EAE) by GSK-3. *J. Immunol*. 190:5000-5011.

La Pietra V., La Regina, G., Coluccia, A., Famiglini. V., Pelliccia, S., Plotkin, B., **Eldar-Finkelman, H**., Brancale, A., Ballatore, C., Crowe, A., Brunden, KR., Marinelli, L,, Novellino, E., Silvestri R. 2013. Design, synthesis, and biological evaluation of 1-Phenylpyrazolo[3,4-e]pyrrolo[3,4-g]indolizine-4,6(1H,5H)-diones as new glycogen synthase kinase-3β inhibitors. *J. Med Chem*. 56: 10066-10078.



Treatment with GSK-3 inhibitor restores lysosomal activity, lysosomes shown as red dots (left). Computational model of GSK-3 inhibitor –L803-mts-binding with the substrate binding site (right).

Azoulay-Alfaguter I, Elya R, Avrahami L, Katz A, **Eldar-Finkelman H**. 2014, Combined regulation of mTORC1 and lysosomal acidification by GSK-3 suppresses autophagy and contributes to cancer cells growth. *Oncogene*. 34:4613-23.

Azoulay-Alfaguter I, Elya R, Avrahami L, Katz A, **Eldar-Finkelman H.** (2014) Combined regulation of mTORC1 and lysosomal acidification by GSK-3 suppresses autophagy and contributes to cancer cells growth. *Oncogene*. *34: 4613-4623.*

Aloni, E., Shapira, M**., Eldar-Finkelman, H**., Barnea, A. (2015) GSK-3β inhibition affects singing behavior and neurogenesis in adult songbirds. *Brain, Behavior and Evolution*, *85:233-244.*

Klionsky, D.J., **Eldar-Finkelman,H**., et al (2016) Guidelines for the use and interpretation for assay for monitoring autophagy. *Autophagy,* 12:1-222.

Grieco, S.F., Velmeshev, D., Magistri, M., **Eldar-Finkelman, H**., Faghihi, M., Jope, R.S., Beurel, E. (2017) Ketamine up-regulates a cluster of intronic miRNAs within the serotonin receptor 2C gene by inhibiting glycogen synthase kinase-3. World J. Biol. Phsyc. 72:49-54.

Licht-Murava A, Paz R, Vaks L, Avrahami L, Plotkin B, Eisenstein M, **Eldar-Finkelman H**. (2016) A unique type of GSK-3 inhibitor brings new opportunities to the clinic. *Sci Signal*. 9:ra110.

Pardo M, Cheng Y, Velmeshev D, Magistri M, **Eldar-Finkelman H**, Martinez A, Faghihi MA, Jope RS, Beurel E. (2017) Intranasal siRNA administration reveals IGF2 deficiency contributes to impaired cognition in Fragile X syndrome mice. *JCI Insight.* 2:e91782.

Reviews

Avrahami, L., **Eldar-Finkelman, H**. 2013, GSK-3 and lysosomes meet in Alzheimer's disease. *Comm Integrat Biology*. 6:e251789.

Grants

2017-2020 Israel Science Foundation

Dr. Jason Friedman, Ph.D.

Department of Physical Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: jason@post.tau.ac.il
URL: http://www.curiousjason.com
URL: http://www.tau.ac.il/~-jason

Models and Rehabilitation of Grasping

Positions

Senior Lecturer, Sackler Faculty of Medicine

Associate Investigator, ARC Centre of Excellence in Cognition and its Disorders, Australia

Member, Sagol School of Neuroscience

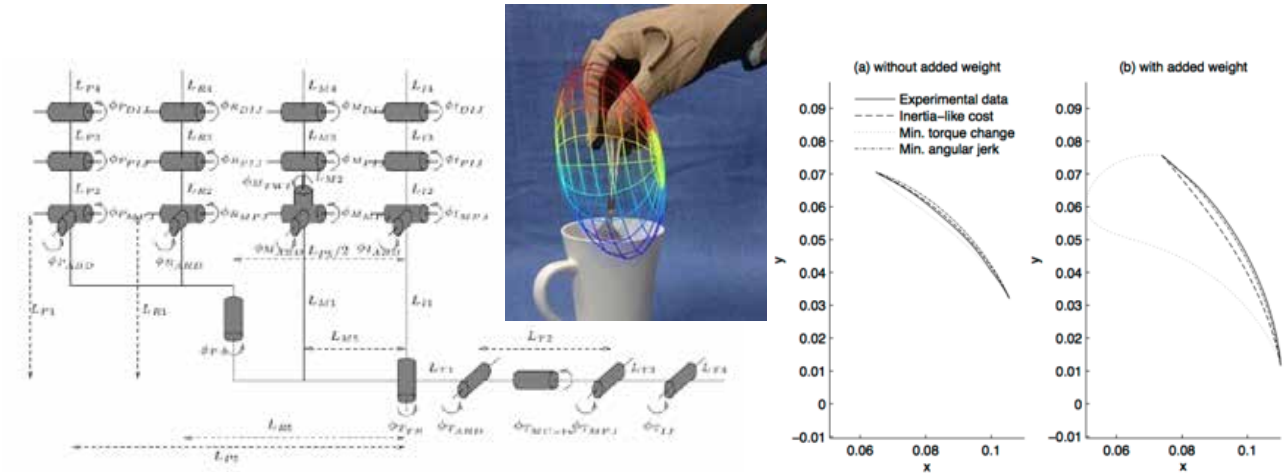
Research

We study human movement in typical and clinical populations, with a focus on grasping and finger movements. We are interesting in fundamental questions such as how we learn to make new movements, how children develop motor skills during development, and how our motor function is affected by disorders such as stroke, dystonia or cerebral palsy. We also study the interconnection between decision making and human movements. Our approach is to construct models that describe movement and force generation by the hand and arm, taking into account the biomechanics of the hand and the neural processes leading up to making movements. This approach gives us insights into the strategies behind the complex movements and force coordination required to successfully perform grasping and manipulation, as well as a greater understanding of the causes of differences in performance in individuals with motor disorders. A goal of this research is to improve rehabilitation of hand function through improving our knowledge of these strategies.

Publications

Shaklai S, Mimouni-Bloch A, Levin M, **Friedman J**. (2017) Development of finger force coordination in children. Exp Brain Res. 235:3709-3720.

Raveh E, **Friedman J**, Portnoy S. (2017) Visuomotor behaviors and performance in a dual-task paradigm with and without vibrotactile feedback when using a myoelectric controlled hand. Assist Technol. 1-7.



Left: We use a model of the hand with the finger joints modelled as revolute joints, with twenty degrees of freedom. **Middle:** Based on models such as these, we can determine the properties of grasps subjects select, for example, when stirring with a spoon, to determine what are the important factors used when generating these grasps. The ellipsoid shows that the subject selected the grasp to maximize the angular velocity about the up-down axis (i.e., to stir the coffee!). Figure from the cover of Cortex, 2007. **Right:** Comparing different models of finger movement to experimental data allowed us to adjudicate between different theoretical models of movement generation (from Friedman and Flash, Exp. Brain Res, 2009).

Noy L, Weiser N, **Friedman J**. (2017) Synchrony in joint action is directed by each participant's motor control system. Front Psychol. 8:531.

Awasthi, B., Williams, M. A., and **Friedman, J.** (2016). Examining the role of red background in magnocellular contribution to face perception. PeerJ, 4, e1617.

Noy, L., Alon, U., and **Friedman, J.** (2015). Corrective jitter motion shows similar individual frequencies for the arm and the finger. Experimental Brain Research, 233, 1307–1320.

Portnoy, S., Rosenberg, L., Alazraki, T., Elyakim, E., and **Friedman, J.** (2015). Differences in muscle activity patterns and graphical product quality in children copying and tracing activities on horizontal or vertical surfaces. Journal of Electromyography and Kinesiology, 25, 540–547.

Zopf, R., **Friedman, J.**, and Williams, M. A. (2015). The plausibility of visual information for hand ownership modulates multisensory synchrony perception. Experimental Brain Research, 233, 2311–2321.

Friedman, J., Brown, S. and Finkbeiner, M. (2014) Linking cognitive and reaching trajectories via intermittent movement control. Journal of Mathematical Psychology, 57:140-151.

Park, J., Pažin, N. **Friedman, J.**, Zatsiorsky, V.M. and Latash, M.L. (2014) Mechanical properties of the human hand digits: Age-related differences. Clinical Biomechanics, 29: 129-137.

Awasthi, B., Sowman, P., **Friedman, J.** and Williams, M.A. (2013) Distinct spatial scale sensitivities for early categorisation of Faces and Places: Neuromagnetic and Behavioural Findings. Frontiers in Neuroscience, 7:91.

Prof. Illana Gozes, Ph.D.

Department of Human Molecular Genetics and Biochemisty
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: igozes@post.tau.ac.il

Neuronal Plasticity and Nerve Cell Protection in Disease

Positions

Professor Emeritus of Clinical Biochemistry, Sackler Faculty of Medicine

Lily and Avraham Gildor Chair for the Investigation of Growth Factors

Director, Dr. Diana and Zelman Elton Laboratory for Molecular Neuroendocrinology

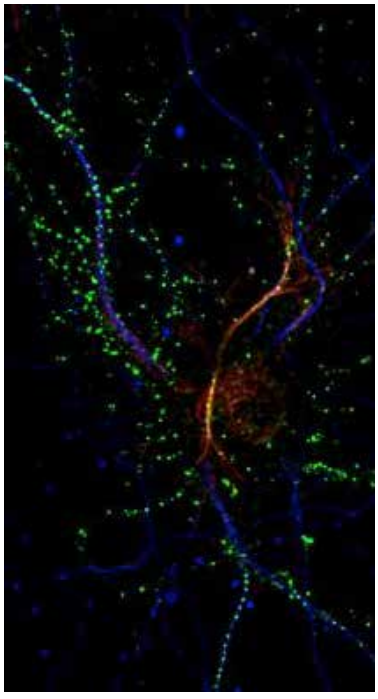
Editor-in-Chief, *Journal of Molecular Neuroscience*

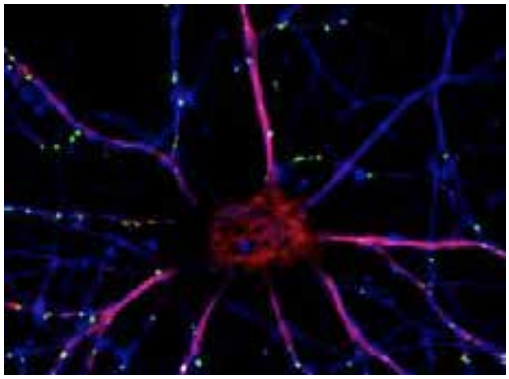
Member, MALAG (Israeli Council of Higher Education)

Research

Our research is characterized by a multi-level approach to the study of brain function, behavior, memory and drug discovery, from molecules to cures. Targeting autism, schizophrenia as well as Alzheimer's disease and related neurodegeneration and utilizing a multidisciplinary approach, our group investigates different aspects of neuronal plasticity and nerve cell protection, at the molecular, cellular and system level. A major focus in the laboratory is on nerve structure and transport mechanisms. We have discovered novel families of proteins associated with cross talk among nerve cells and their support cells, including activity-dependent neurotrophic factor (ADNF) and activity-dependent neuroprotetive proteins (ADNPs, with ADNP being a major gene mutated in autism). Small ADNF and ADNP derivatives are in clinical development. The lead compound, davunetide is planned for an advanced Phase II clinical trial with the biotech industry.

Davunetide has previously shown efficacy in several Phase II clinical trials (i.e. in patients suffering from mild cognitive impairment, preceding Alzheimer's disease and in schizophrenia patients, protecting activities of daily living).





The NAP-motif of activity-dependent neuroprotective protein (ADNP) regulates dendritic spines through Microtubule End Binding (EB) proteins.

Publications

Jouroukhin Y, Ostritsky R, Assaf Y, Pelled G, Giladi E, **Gozes I.** NAP (davunetide) modifies disease progression in a mouse model of severe neurodegeneration: Protection against impairments in axonal transport. *Neurobiol Dis.* 56C:79-94, 2013.

Esteves AR, **Gozes I**, Cardoso SM. The rescue of microtubule-dependent traffic recovers mitochondrial function in Parkinson's disease. *Biochim Biophys Acta*. 1842:7-21, 2014.

Merenlender-Wagner A, Malishkevich A, Shemer Z, Udawela M, Gibbons A, Scarr E, Dean B, Levine J, Agam G, **Gozes I**. Autophagy has a key role in the pathophysiology of schizophrenia. *Mol Psychiatry* 20: 126-132, 2015.

Gozes I, Schirer Y, Idan-Feldman A, David M, Furman-Assaf S. NAP alpha-aminoisobutyric acid (IsoNAP). *J Mol Neurosci*. 52:1-9, 2014

Schirer Y, Malishkevich A, Ophir Y, Lewis J, Giladi E, **Gozes I**. Novel marker for the onset of frontotemporal dementia: early increase in activity-dependent neuroprotective protein (ADNP) in the face of Tau mutation. *PLoS One*. 9:1, 2014

Gozes I, Iram T, Maryanovsky E, Arviv C, Rozenberg L, Schirer Y, Giladi E, Furman-Assaf S. Novel tubulin and TAU neuroprotective fragments sharing structural similarities with the drug candidate NAP (Davuentide). *J Alzheimers Dis*. 40 Suppl 1:S23-36.

Gozes I, Yeheskel A, Pasmanik-Chor M. activity-dependent neuroprotective protein (ADNP): a case study for highly conserved chordata-specific genes shaping the brain and mutated in cancer. *J Alzheimers Dis* 45: 57-73, 2015.

Korolkov VV, Allen S, Roberts CJ, **Gozes I**, Tendler SJ. Study of NAP adsorption and assembly on the surface of HOPG. *Peptides.* 62:55-8. 2014.

Oz S, Kapitansky O, Ivashco-Pachima Y, Malishkevich A, Giladi E, Skalka N, Rosin-Arbesfeld R, Mittelman L, Segev O, Hirsch JA, **Gozes I**. The NAP motif of activity-dependent neuroprotective protein (ADNP) regulates dendritic spines through microtubule end binding proteins. *Mol Psychiatry*. 19:1115-24, 2014.

Boxer A, Lang AF, Grossman M, Knopman DS, Miller BL, Schneider LS, Doody RS, Lees A, Golbe L, Williams DR, Corvol J-C, Ludolph A, Burn D, Lorenzl S, Litvan I, Roberson ED, Koestler M, Jack CR Jr., Van Deerlin, V, Randolph C, Lobach IV, **Gozes I**, Whitaker S, Hirman J, Stewart AJ, Gold M, Morimoto BH on behalf of the AL-108-231 investigators. Davunetide for Progressive Supranuclear Palsy: a multicenter, randomized, double-blind, placebo controlled trial. *Lancet Neurol*. 13:676-85, 2014.

Merenlender-Wagner A, Shemer Z, Touloumi O, Lagoudakib R, Giladi E, Andrieux A, Grigoriadis NC, **Gozes I.** New horizons in schizophrenia treatment: Autophagy protection is coupled with behavioral improvements in a mouse model of schizophrenia. *Autophagy* 10: 2324-2332, 2014.

Malishkevich A, Amram N, Hacohen-Kleiman G, Magen I, Giladi E, Gozes I. Activity-Dependent Neuroprotective Protein (ADNP) Exhibits Striking Sexual Dichotomy Impacting on Autistic and Alzheimer's Pathologies. *Transl Psychiatry* 5: e501, 2015.

Magen I, Ostritsky R, Richter F, Zhu C, Fleming SM, Lemesre V, Stewart AJ, Morimoto BH, **Gozes I**, Chesselet MF. Intranasal NAP (davunetide) decreases tau hyperphosphorylation and moderately improves behavioral deficits in mice overexpressing alpha-synuclein. *Pharmacol Res Perspect* 2, e00065, 2014.

Heimesaat MM, Fischer A, Kühl AA, Göbel UB, **Gozes I**, Bereswill S. Anti-Inflammatory properties of NAP in acute toxoplasma gondii-induced oleitis in mice. *Eur J Microbiol Immunol (Bp)*. 5: 210-220, 2015.

Hacohen Kleiman G, Barnea A, **Gozes I**. ADNP: A major autism mutated gene is differentially distributed (age and gender) in the songbird brain. *Peptides*. 72: 75–79, 2015.

Malishkevich A, Leyk J, Goldbaum O, Richter-Landsberg C, **Gozes I**. ADNP/ADNP2 expression in oligodendrocytes: implication for myelin-related neurodevelopment. *J Mol Neurosci* 57: 304-313, 2015.

Vaisburd S, Shemer Z, Yeheskel A, Giladi E, **Gozes I**. Risperidone and NAP protect cognition and normalize gene expression in a schizophrenia mouse model. *Scientific Reports*, 2015; 5:16300.

Malishkevich A, Marshall GA, Schultz AP, Sperling RA, Aharon-Peretz J, **Gozes I**. Blood-borne activity-depedent neuroprotective protein (ADNP) is correlated with premorbid inteligence, clinical stage and Alzheimer's disease biomarkers *J Alzheimers Dis*, 2015;50:249-60.

Gozes I, Sragovich S, Schirer Y, Idan-Feldman A. D-SAL and NAP: Two peptides sharing a SIP domain. *J Mol Neurosci*. 2016;59:220-31.

Amram N, Hacohen-Kleiman G, Sragovich S, Malishkevich A, Katz J, Touloumi O, Lagoudaki R, Grigoriadis NC, Giladi E, Yeheskel A, Pasmanik-Chor M, Jouroukhin Y, **Gozes I.** Sexual divergence in microtubule function: the novel intranasal microtubule

targeting SKIP normalizes axonal transport and enhances memory. *Mol Psychiatry.* 2016 . 21:1467-1476.

Hadar A, Milanesi E, Squassina A, Niola P, Chillotti C, Pasmanik-Chor M, Yaron O, Martásek P, Rehavi M, Weisglass-Volkov D, Shomron N, **Gozes I**, Gurwitz D. RGS2 expression predicts amyloid-b sensitivity, MCI and Alzheimer's disease: genomewide transcriptomic profiling and bioinformatics data mining. Transl Psychiatry 6:e909.

Licht-Murava A,* Paz R,* Vaks L, Avrahami L, Plotkin B, Eisenstein M, **Eldar-Finkelman H**. 2016 A unique type of GSK-3 inhibitor brings new opportunities to the clinic. Sci Signal 9, ra110.

Polanco MJ, Parodi S, Piol D, Stack C, Chivet M, Contestabile A, Miranda HC, Lievens PM-J, Espinoza S, Jochum T, Rocchi A, Grunseich C, Gainetdinov RR, Cato ACB, Lieberman AP, La Spada AR, Sambataro F, Fischbeck KH, **Gozes I**, Pennuto M (2016) Adenylyl cyclase activating polypeptide reduces phosphorylation and toxicity of the polyglutamine-expanded androgen receptor in spinobulbar muscular atrophy. Sci Trans Med 8, 370ra181.

Ivashko-Pachima, Y. Sayas, CL, Malishkevich A., **Gozes, I**. ADNP/NAP dramatically increase microtubule end binding protein-Tau interaction: A novel avenue for protection against tauopathy. Mol Psychiatry. 2017 doi: 10.1038/mp.2016.255.

Gozes I, Van Dijck A, Hacohen-Kleiman G, Grigg I, Karmon G, Giladi E, Eger M, Gabet Y, Pasmanik-Chor M, Cappuyns E, Elpeleg O, Kooy RF, Bedrosian-Sermone S. Premature primary tooth eruption in cognitive/motor-delayed ADNP-mutated children. Transl Psychiatry. 2017;7(2):e1043.

Gozes I, Patterson MC, Van Dijck A, Kooy RF, Peeden JN, Eichenberger JA, Zawacki-Downing A, Bedrosian-Sermone S. The eight and a half year journey of undiagnosed AD: gene sequencing and funding of advanced genetic testing has led to hope and new beginnings. Front Endocrinol (Lausanne). 2017;8:107.

Reviews

Gozes I, Baas P. Activity-Dependent Neuroprotective Protein (ADNP) and Davunetide (NAP). In: *Handbook of Biologically Active Peptides.* Edited by Abba J. Kastin, Second Edition, Section XVIII, section editor: Illana Gozes (section pp. 1611-1653). Academic Press, pp. 1611-1618, 2013.

Oz S, **Gozes I.** The cytoskeleton as a pharmacological target. In: The Cytoskeleton, imaging, isolation and interaction R. Dermietzel, Editor). *Neuromethods* 79: 151-169, 2013.

Magen I, **Gozes I**. Microtubule-stabilizing peptides and small molecules protecting axonal transport and brain function: focus on davunetide (NAP). *Neuropeptides*. 47:489-95, 2013.

Magen I, **Gozes I.** Davunetide: peptide therapeutic in neurological disorders. *Curr Med Chem*. 21:2591-8, 2014.

A. Del Carmen Alonso, E. Elakkad, C. Gong, F Liu, T. Tanaka, T. Kudo, Y. Tatebayashi, J. Pei, J. Wang, S. Khatoon, M. Flory, B. Ghetti, **I. Gozes**, M. Novak, M. Novak, N.K. Robakis, M. de Leon, M. Iqbal. Inge Grundke-Iqbal, Ph.D. (1937-2012): The discoverer of the abnormal hyperphosphorylation of Tau in Alzheimer's Disease. *J Mol Neurosci.* 49: 430-435. 2013.

Gozes I. Journal of molecular neuroscience: impacting our brains. *J Mol Neurosci*. 54:291-2. 2014

Gozes I. The cytoskeleton as a drug target for neuroprotection: the case of the autism-mutated ADNP. *Biol Chem*. 2016;397:177-84.

Gozes I, Baas PW, Richter-Landsberg C. International Meeting Molecular Neurodegeneration: News and Views in Molecular Neuroscience in Health and Disease. *J Mol Neurosci* 57: 153-159, 2015.

Gozes I, Helsmoortel C, Vandeweyer G, Van der Aa N, Kooy F, Sermone SB (2015) The compassionate side of neuroscience: Tony Sermone's undiagnosed genetic journey--ADNP mutation. *J Mol Neurosci* 56: 751-757, 2015.

Gozes I, Ivashko-Pachima, Y. ADNP: in search for molecular mechanisms and innovative therapeutic strategies for frontotemporal degeneration. *Front. Aging Neurosci*. 2015, 7:205.

Klionsky DJ et al., (including **Gozes I**) Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*. 2016;12:1-222.

Pennuto M, **Gozes I**. Introduction to the Special Issue on Spinal and Bulbar Muscular Atrophy. *J Mol Neurosci*. 2016;58:313-6.

Pachima YI, Zhou LY, Lei P, **Gozes I.** Microtubule-Tau Interaction as a Therapeutic Target for Alzheimer's Disease. *J Mol Neurosci*. 2016;58:145-52

Gozes I. Sexual Divergence in Activity-Dependent Neuroprotective Protein (ADNP) Impacting Autism, Schizophrenia and Alzheimer's Disease. J Neurosci Res. 2016, In press.

Gozes I. Neuroprotective Drug Development: The Story of ADNP, NAP (Davunetide), and SKIP. In: Neuroprotection in Alzheimer's Disease; I Gozes, Editor, Elsevier Press. 2016, in press.

Gozes I. PACAP, VIP, and ADNP: Autism and Schizophrenia. In: Pituitary Adenylate Cyclase Activating Polypeptide (Dora Reglodi and Andrea Tamas, Editors, Current Topics in Neurotoxicity 11, Springer) 2016 pp. 781-792.

Gozes I. Sexual divergence in activity-dependent neuroprotective protein impacting autism, schizophrenia, and Alzheimer's disease. J Neurosci Res. 2017;95(1-2):652-660.

Gozes I. (Editor) Neuroprotection in Alzheimer's Disease, Book 1-342, Introduction, pages 1-2, Academic Press (Elsevier), 2017.

Hadar A. **Gozes I**, Gurwitz D. RGS2 and SIRT1 Link Renin Angiotensin Aldosterone System to Alzheimer's Disease, in: **Gozes I.** (Editor) Neuroprotection in Alzheimer's Disease, Academic Press (Elsevier), Chapter 12, pages 239-251, 2017.

Gozes I. Neuroprotective Drug Development: The Story of ADNP, NAP (Davunetide), and SKIP, in: **Gozes I.** (Editor) Neuroprotection in Alzheimer's Disease, Academic Press (Elsevier), Chapter 13, pages 253-270, 2017.

Grants

2014-2018 Israel Science Foundation – Deciphering beta-amyloid and tau neurotoxicity: Genome-wide RNA sequencing for sensitivity biomarkers- with Dr. David Gurwitz

2016-2019 ERA-NET NEURON – Modelling syndromic autism caused by mutations in the ADNP gene (with Frank Kooy, Pierre-Luc Germain, Christopher E. Pearson)

Dr. Yoni Haitin, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

Email: yhaitin@post.tau.ac.il

The Molecular Basis of the Regulation of Immune and Cancer Cells by Ion Channels

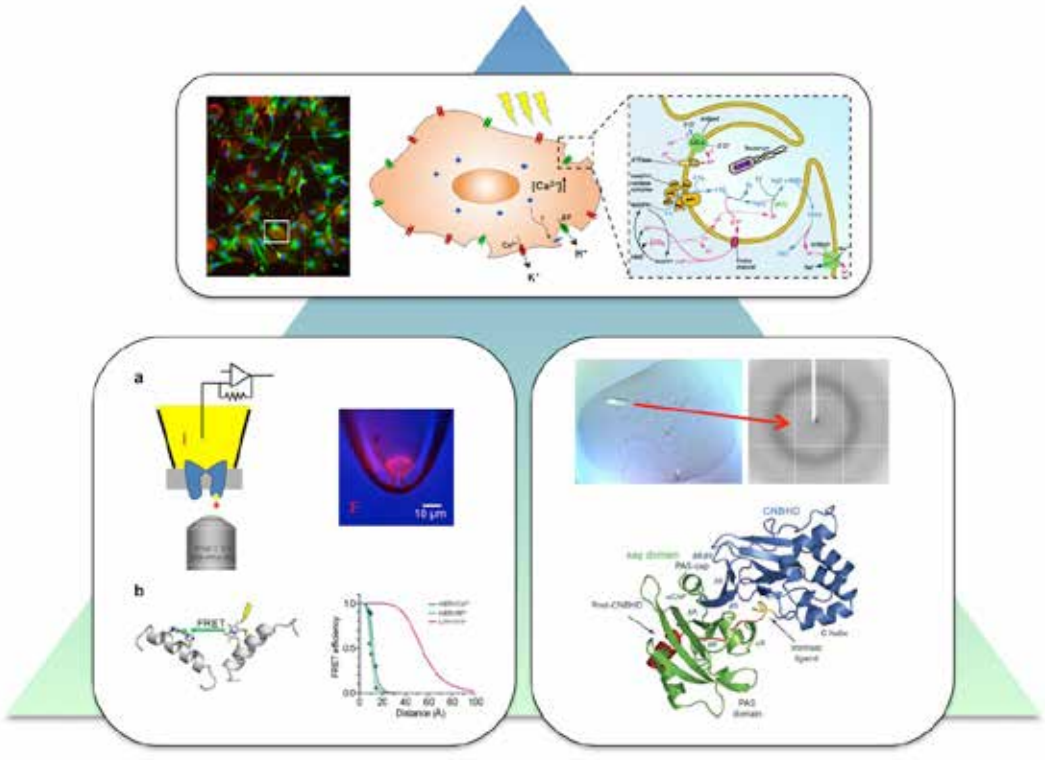
Position

Senior Lecturer, Sackler Faculty of Medicine

Research

Ion channels are membrane-embedded molecular machines that enable cells to communicate with their extracellular environment. Ion channels regulate a host of physiological processes such as neuronal excitability and immune cells activation. Consequently, genetic mutations that hamper their function can lead to severe pathologies, which include epilepsies, cardiac arrhythmias and transformation of cancer cells.

Our lab is interested in the utmost basic molecular and structural aspects of the emerging roles ion channels play in microglia, the resident immune cells of the brain. Any disturbance to brain homeostasis evokes rapid microglial transformation from a resting to an activated, phagocytic state. Ion channels, and other signalling cascades, orchestrate this activation. However, immune response in a central and delicate organ such as the brain can be a double-edged sword, exacerbating both acute conditions such as stroke and neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.



Our efforts for elucidating how ion channels contribute to microglial activity are equally supported by combining electrophysiological and fluorescence, which enable the characterization of ion channel dynamics, with x-ray crystallography for structural analysis at the atomic level.

Using a combined multidisciplinary approach, which includes fluorescence, x-ray crystallography, and electrophysiology, we pursue better understanding of the molecular mechanisms and protein dynamics governing the regulation of these channels and, in turn, elucidate how they contribute to microglial activity. Ultimately, unveiling the molecular basis of microglial ion channels modulation may prove beneficial for microglial-related brain pathologies.

Publications

Manuscripts

Padala P., Soudah N., Giladi M., **Haitin Y**., Isupov M.N., Wiener R. (2017) The crystal structure and conformations of an unbranched mixed tri-ubiquitin chain containing K48 and K63 linkages. *J Mol Biol.,* accepted for publication.

Tobelaim W.S., Dvir M., Lebel G., Cui M., Buki T., Peretz A., Marom M., **Haitin Y**., Logothetis D.E., Hirsch J.A., Attali B. (2017). Ca2+-Calmodulin and PIP2 interactions at the proximal C-terminus of Kv7 channels. *Channels*., accepted for publication.

Edri I., Goldenberg M., Lisnyansky M., Strulovich R., Newman H., Loewenstein A., Khananshvili D., Giladi M., **Haitin Y**. (2017) Overexpression and purification of human Cis-prenyltransferase in Escherichia coli. *J Vis Exp.,* **2017**.

Giladi M., Lee S.Y., Ariely Y., Teldan Y., Granit R., Strulovich R., **Haitin Y**., Chung K.Y. and Khananshvili D. (2017). Structure-encoded dynamics of regulatory diversity in sodium-calcium exchanger (NCX) isoforms. *Sci Rep.,* 7, 993.

James Z.M., Borst A.J., **Haitin Y**., Frenz B., Dimaio F., Zagotta W.N. and Veesler D. (2017). Allosteric Regulation of a Cyclic Nucleotide-Gated Ion Channel Visualized by *CryoEM. PNAS,* **114**, 4430-4435.

Giladi M.*, Edri I., Goldenberg M., Newman H., *Strulovich R.,* Khananshvili D., **Haitin Y.***, Loewenstein A. (2017). Purification and characterization of human dehydrodolychil diphosphate synthase (DHDDS) overexpressed in E. *coli. Protein Expr Purif.,* **132**, 138-142. *Co-corresponding author.

Tobelaim W.S., Dvir M., Lebel G., Cui M., Buki T., Peretz A., *Marom M.,* **Haitin Y**., Logothetis D.E., Hirsch J.A., Attali B. (2017). Competition of calcified calmodulin N lobe and PIP2 to an LQT mutation site in Kv7.1 channel. *PNAS*, **114**, E869–E878.

Dvir M., Strulovich R., Sachyani D., Ben-Tal Cohen I., **Haitin Y.**, Dessauer C., Pongs O., Kass R., Hirsch J.A. & Attali B. (2014). Long QT mutations at the interface between KCNQ1 helix C and KCNE1 disrupt I(KS) regulation by PKA and PIP2. *J Cell Sci*. 127, 3943-3955

Haitin Y., Carlson A.E. & Zagotta W.N. (2013). The structural mechanism of KCNH-channel regulation by the eag domain. *Nature* 501, 444-448

Reviews

Haitin Y. (2014). A “funny” cyclic dinucleotides receptor. Nat Chem Biol 10, 413-414

Dvir M., Peretz A., **Haitin Y.** & Attali B. (2014). Recent molecular insights from mutated IKS channels in cardiac arrhythmia. *Curr Opin Pharmacol* 15C, 74–82

Grants

2015 – 2019	Israeli Center for Research Excellence (I-CORE): Structural Biology of the Cell – Biophysics and medical technology
2016 – 2018	Recanati Foundation for Biomedical Research
2017 – 2018	German-Israeli Foundation for Scientific Research and Development (GIF), Young Scientists Program
2017 – 2020	Israel Science Foundation (ISF), Personal Grant
2017 – 2019	Israel Cancer Research Fund (ICRF), Research Career Development Award (RCDA)
2017 – 2018	INSTRUCT Pilot R&D Grant

Prof. Talma Hendler, M.D., Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine;
School of Psychological Sciences;
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

Email: hendlert@gmail.com
URL: http://www.fmri-tlv.org/

Brain Mechanisms of Human Emotion Generation & Regulation

Laboratory for Brain and Emotion Experience

Functional Brain Center, Wohl Institute for Advanced Imaging, Tel Aviv Sourasky Medical Center

Positions

Professor of Psychiatry and Psychology, Department of Physiology and Pharmacology, Sackler Faculty of Medicine, School of Psychological Sciences and Sagol School of Neuroscience

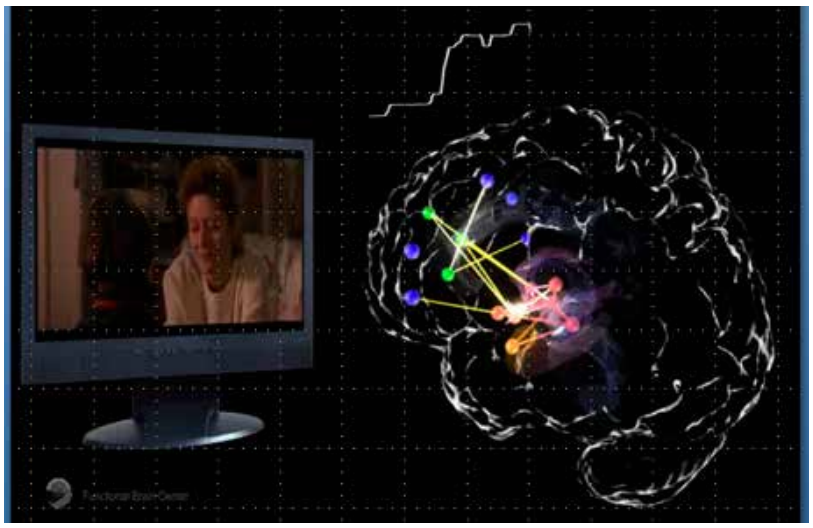
Director, The Sagol Center for Brain Functions, Wohl Institute for Advanced Imaging, Tel Aviv Sourasky Medical Center

Research

Investigating brain mechanisms underlie generation and regulation of the human emotional experience, in healthy and pathological states. The research is based on measuring indices of brain structure and functional dynamics via MRI (functional-MRI, DTI and Volumetric-MRI) and separate or simultaneous recording of electrical signals (scalp-EEG and intracranial-EEG). The characterization of individual brain response is based on correlating neural activity and connectivity with behavioral and physiological measurements of emotionality (e.g. heart rate, hormone secretion, genetic expression, skin conductance, eye movements and verbal output). Induction of emotional states is achieved via film and music media, inter-personal interactions, and interactive social games. Regulation of emotions is modulated via on-line feedback protocols from brain signals in a closed loop set-up (i.e. *NeuroFeedback*). The lab is also involved in studies aim to advance translation while focusing on neural markers of vulnerability and recovery with regard to post traumatic disorders (e.g. anxiety and depression), developmental disorders (e.g. schizophrenia and personality) and neurodegenerative disorders (e.g. parkinson disease). An essential part of this aspect of our work is the development of advanced new tools for acquiring and analyzing whole brain neural measurements; including applying multi-scale mapping for capturing dynamics of brain networks.

Publications

Ben-Simon, E., Podlipsky, I., Okon-Singer, H., Gruberger, M., Cvetkovic, D., Intrator, N., & **Hendler, T.** (2013). The dark side of the alpha rhythm:



A frame from Intra- and inter-Network Cohesion Index (NCI) mapping, obtained from 16 healthy individuals while viewing a sad inducing movie clip (*Stepmom).* The trace on top presents continuous reported sadness intensity indicating that the frame depicts a moment of enhanced sadness (adapted from Raz et al *Neuroimage* 2012).

fMRI evidence for induced alpha modulation during complete darkness. *European Journal of Neuroscience*. 37:795-803

Kinreich, S., Podlipsky, I., Intrator, N., & Hendler, T. (2012). Categorized EEG neurofeedback performance unveils simultaneous fMRI deep brain activation. *Machine Learning and Interpretation in Neuroimaging*, 108-115.

Esposito, N. Singer, I. Podlipsky , I. Fried, **T. Hendler**, R. Goebel (2013) Cortex-based inter-subject analysis of iEEG and fMRI data sets: Application to sustained task-related BOLD and gamma response. *NeuroImage*, 66, 457–468

Thaler, A., Mirelman, A., Helmich, R.C., van Nuenen, B.F., Rosenberg-Katz, K., Gurevich, T., Orr-Urtreger, A., Marder, K., Bressman, S., Bloem, B.R., Giladi, N., **Hendler, T**.; the LRRK2 Ashkenazi Jewish consortium (2013). Neural correlates of executive functions in healthy G2019S LRRK2 mutation carriers. *Cortex*, 00374-7.

Shapira-Lichter I, Oren N, Jacob Y, Gruberger M, & **Hendler T**. (2013). Portraying the unique contribution of the default mode network to internally-driven mnemonic processes .*Proc Natl Acad Sci USA*. 110:4950-5.

Raz, G., Jacob, Y., Gonen, T., Winetraub, Y., Soreq, E., Flash, T., **Hendler, T.** (2013) Cry for her or cry with her: Context-dependent dissociation of two modes of cinematic empathy reflected in network cohesion dynamics. *Soc Cogn Affect Neurosci*9:30-38 .

Admon, R., Milad, M. R., & **Hendler, T**. (2013). A causal model of post-traumatic stress disorder: disentangling predisposed from acquired neural abnormalities. *Trends in Cognitive Sciences*. 17: 337-47.

Raz, G., Jacob, Y., Gonen, T., Winetraub, Y., Flash, T., Soreq, E., & **Hendler, T**. (2014). Cry for her or cry with her: context-dependent dissociation of two modes of cinematic empathy reflected in network cohesion dynamics. *Social Cognitive and Affective Neuroscience*, 9, 30-38.

Gonen, T., Sharon, H., Pearlson, G., & **Hendler, T.** (2014). Moods as ups and downs of the motivation pendulum: revisiting reinforcement sensitivity theory (RST) in bipolar disorder. *Frontiers in Behavioral Neuroscience*, 8, 378.

Singer, N., Podlipsky, I., Esposito, F., Okon-Singer, H., Andelman, F., Kipervasser, S., ... & **Hendler, T**. (2014). Distinct iEEG activity patterns in temporal-limbic and prefrontal sites induced by emotional intentionality. Cortex, 60, 121-138.

Kinreich, S., Podlipsky, I., Jamshy, S., Intrator, N., & **Hendler, T.** (2014). Neural dynamics necessary and sufficient for transition into pre-sleep induced by EEG neurofeedback. *NeuroImage*, 97, 19-28.

Hendler, T., Gonen, T., Harel, E. V., & Sharon, H. (2014). From circuit activity to network connectivity and back: The case of obsessive-compulsive disorder. *Biological Psychiatry*, 75, 590-592

Raz, G., & **Hendler, T**. (2014). Forking cinematic paths to the self: neurocinematically informed model of empathy in motion pictures. Projections, 8, 89-114.

Abraham, E., **Hendler, T**., Shapira-Lichter, I., Kanat-Maymon, Y., Zagoory-Sharon, O., & Feldman, R. (2014). Father's brain is sensitive to childcare experiences. *Proc Natl Acad Sci USA*, 111, 9792-9797

Amar, D., Yekutieli, D., Maron-Katz, A., **Hendler, T**., & Shamir, R. (2015). A hierarchical Bayesian model for flexible module discovery in three-way time-series data. Bioinformatics, 31, i17-i26.

Ben Simon, E., Oren, N., Sharon, H., Kirschner, A., Goldway, N., Okon-Singer, H., Tauman, R., Deweese, M.M., Keil, A., & **Hendler, T.** (2015). Losing neutrality: The neural basis of impaired emotional control without sleep. *Journal of Neuroscience*, 35, 13194-13205.

Gilam, G., Lin, T., Raz, G., Azrielant, S., Fruchter, E., Ariely, D., & **Hendler, T**. (2015). Neural substrates underlying the tendency to accept anger-infused ultimatum offers during dynamic social interactions. *NeuroImage*, 120, 400-411.

Okon-Singer, H., **Hendler, T.,** Pessoa, L., & Shackman, A.J. (2015). The neurobiology of emotion–cognition interactions: fundamental questions and strategies for future research. *Frontiers in Human Neuroscience* 9, 58.

Glikmann-Johnston, Y., Oren, N., **Hendler, T**., & Shapira-Lichter, I. (2015). Distinct functional connectivity of the hippocampus during semantic and phonemic fluency. *Neuropsychologia*, 69, 39-49

Vaisvaser S., Modai S., Farberov L., Lin T., Sharon H., Gilam A., Volk N., Admon R., Edry L., Fruchter E., Wald I., Bar-Haim Y., Tarrasch R., Chen A., Shomron N., and **Hendler T.** (2016). Neuro-epigenetic indications of acute stress response in humans: the case of microRNA-29c. *PloS One* (accepted)

Keynan, J.N, Meir-Hasson, Y., Gilam, G., Cohen, A., Jackont, G., Kinreich, S., Ikar, L., Or-Borichev, A., Etkin, A., Gyurak, A., Klovatch, I., Intrator, N., & **Hendler, T**. (2016). Limbic activity modulation guided by fMRI-Inspired EEG improves implicit emotion regulation. *Biological Psychiatry* (accepted)

Gonen, T., Soreq, E., Eldar, E., Ben-Simon, E., Raz, G., & **Hendler, T**. (2016). Human mesostriatal response tracks motivational tendencies under naturalistic goal conflict. *Social Cognitive and Affective Neuroscience*, 11, 961-972.

Shapira-Lichter, I., Klovatch, I., Nathan, D., Oren, N., & **Hendler, T**. (2016). Task-specific aspects of goal-directed word generation identified via simultaneous EEG–fMRI. *Journal of Cognitive Neuroscience* 28, 1406-1418.

Meir-Hasson, Y., Keynan, J. N., Kinreich, S., Jackont, G., Cohen, A., … **Hendler, T**. & Intrator, N. (2016). One-Class FMRI-Inspired EEG Model for Self-Regulation Training. *PloS One*, 11, e0154968.

Gazit, T., Andelman, F., Glikmann-Johnston, Y., Gonen, T., Solski, A., Shapira-Lichter, I., ... & **Hendler, T**. (2016). Probabilistic machine learning for the evaluation of presurgical language dominance. *Journal of Neurosurgery*, 1-13.

Maron-Katz, A., Vaisvaser, S., Lin, T., **Hendler, T**., & Shamir, R. (2016). A large-scale perspective on stress-induced alterations in resting-state networks. *Scientific Reports*, 6.

Lin, T., Simchovitz, A., Shenhar-Tsarfaty, S., Vaisvaser, S., Admon, R., … **Hendler, T**. & Soreq, H. (2016) Intensified vmPFC surveillance over PTSS under perturbed microRNA-608/AChE interaction. *Translational Psychiatry*, 6, 1-8.

Raz, G., Touroutoglou, A., Wilson-Mendenhall, C., Gilam, G., Lin, T., ... **Hendler, T.** & Feldman Barrett, L. (2016). Functional connectivity dynamics during film viewing reveal common networks for different emotional experiences. *Cognitive, Affective, & Behavioral Neuroscience*, 1-15.

Singer S., Jacobi N., Lin T., Raz G., Shpigelman L., Gilam G., Granot R., **Hendler T.** (2016) Common modulation of limbic network activation underlies the unfolding of musical emotions and its temporal attributes. NeuroImage (accepted)

Raz G., Shpigelman L.,Jacob Y., Gonen T., Benjamini Y. and **Hendler T**. (2016) Psychophysiological whole-brain network clustering based on connectivity dynamics analysis in naturalistic conditions. *Human Brain Mapping* (accepted)

Yamin, H., Gazit, T., Tchemodanov, N., Raz, G., Jakont, G., Charles, F., ... **& Hendler, T.** (2016). Neurofeedback via intracranial depth electrodes. Proceeedings from the Sicth *International Brain Computer Interface Meeting.*

Yogev-Seligmann, G., Oren, N., Ash, E. L., **Hendler, T**., Giladi, N., & Lerner, Y. (2016). Altered topology in information processing of a narrated story in older adults with mild cognitive impairment. *Journal of Alzheimer's Disease,* 53(2), 517-533.

Bregman, N., Thaler, A., Mirelman, A., Gurevich, T., Gana-Weiss, M., Orr-Urtreger, A., **Hendler, T**., & Giladi, N. (2016). A cognitive fMRI study in non-manifesting LRRK2 and GBA carriers (P4. 105). *Neurology, 86*(16 Supplement), 94-105.

Sharon, H., Maron-Katz, A., Simon, E. B., Flusser, Y., **Hendler, T.,** Tarrasch, R., & Brill, S. (2016). Mindfulness meditation modulates pain through endogenous opioids. *The American Journal of Medicine*, 129(7), 755-758.

Shapira-Lichter, I., Weinstein, M., Lustgarten, N., Ash, E., Litinsky, I.,... **Hendler, T.**, & Paran, D. (2016). Impaired diffusion tensor imaging findings in the corpus callosum and cingulum may underlie impaired learning and memory abilities in systemic lupus erythematosus. *Lupus*, 25(11).

Domani, Y., Bleich-Cohen, M., Stoppelman, N., Tarrasch, R., **Hendler, T**., Meidan, R., ... & Sharon, H. (2016). Oral ketamine for treatment resistant major depression–A double blind randomized controlled trial. *European Psychiatry*, (33), S523.

Lerner, Y., **Hendler, T**., Levit-Binnun, N., & Golland, Y. (2016). Shared feelings: Investigating neural attunement to the emotions of others. *European Psychiatry*, (33), S457-S458.

Abraham, E., **Hendler, T.,** Zagoory-Sharon, O., & Feldman, R. (2016). Network integrity of the parental brain in infancy supports the development of children's social competencies. *Social Cognitive and Affective Neuroscience*, 11(11), 1707-1718.

Abend, R., Jalon, I., Gurevitch, G., Sar-El, R., Shechner, T., Pine, D. S., **Hendler, T.,** & Bar-Haim, Y. (2016). Modulation of fear extinction processes using transcranial electrical stimulation. *Translational Psychiatry, 6*(10), e913.

Jacob, Y., Winetraub, Y., Raz, G., Ben-Simon, E., Okon-Singer, H., Rosenberg-Katz, K., **Hendler, T.,** Ben Jacob, E. (2016). Dependency network anaylsis reveals context related influence of brain network nodes. *Scientific Reports, 6.*

Oren, N., Ash, E. L., Tarrasch, R., **Hendler, T.,** Giladi, N., & Shapira-Lichter, I. (2017). Neural patterns underlying the effect of negative distractors on working memory in older adults. *Neurobiology of Aging, 53,* 93-102.

Cohen, D., Perry, A., Gilam, G., Mayseless, N., Gonen, T., **Hendler, T.,** & Shamay-Tsoory, S. G. (2017). The role of oxytocin in modulating

interpersonal space: A pharmacological fMRI study. *Psychoneuroendocrinology, 76,* 77-83.

Lin, T., Gilam, G., Raz, G., Or-Borichev, A., Bar-Haim, Y., Fruchter, E., & **Hendler, T**. (2017). Accessible Neurobehavioral Anger-Related Markers for Vulnerability to Post-Traumatic Stress Symptoms in a Population of Male Soldiers. *Frontiers in Behavioral Neuroscience, 11.*

Gilam, G., Lin, T., Fruchter, E., & **Hendler, T.** (2017). Neural indicators of interpersonal anger as cause and consequence of combat training stress symptoms. *Psychological Medicine*, 1-12.

Ben Simon, E., Maron-Katz, A., Lahav, N., Shamir, R., & **Hendler, T.** (2017). Tired and misconnected: A breakdown of brain modularity following sleep deprivation. *Human Brain Mapping*, 38(6), 3300-3314.

Lin*, T., Gilam*, G., Raz, G., Or-Borichev, A., Bar-Haim, Y., Fruchter, E., & **Hendler, T.** Accessible neurobehavioral anger-related markers for vulnerability to post-traumatic stress symptoms in a population of male soldiers. *Frontiers in Behavioral Neuroscience,* 11(38). *equal contribution.

Golland, Y., Levit-Binnun, N., **Hendler, T.,** Lerner, Y. (2017). Neural dynamics underlying emotional transmissions between individuals. *Cognitive and Affective Neuroscience,* 12(8), 1249-1260.

Young, C. B., Raz, G., Everaerd, D., Beckmann, C. F., Tendolkar, I., **Hendler, T.,** ... & Hermans, E. J. (2017). Dynamic shifts in large-scale brain network balance as a function of arousal. *Journal of Neuroscience, 37*(2), 281-290.

Keynan, J., & **Hendler, T.** (2017). Amygdala-Neurofeedback Reduces Traumatic Stress Vulnerability. *Biological Psychiatry, 81*(10), S157-S158.

Abraham, E., Gilam, G., Kanat-Maymon, Y., Jacob, Y., Zagoory-Sharon, O., **Hendler, T.,** & Feldman, R. (2017). The human coparental bond implicates distinct corticostriatal pathways: longitudinal impact on family formation and child well-being. *Neuropsychopharmacology*, 42.

Hendler T, Raz G, Bleich M. (2017) Social affective context reveals altered network dynamics in schizophrenia patients. *Accepted for publication to Translational Psychiatry*

Artzi, M., Even-Sapir, E., Lerman Shacham, H., Thaler, A., Urterger, A.O., Bressman, S., Marder, K., **Hendler, T.,** Giladi, N., Ben Bashat, D., and Mirelman, A. (2017). DaT-SPECT assessment depicts dopamine depletion among asymptomatic G2019S LRRK2 mutation carriers. *Plos One*, 12(4).

Oren, N., Shapira-Lichter, I., Lerner, Y., Tarrasch, R., **Hendler, T.,** Giladi, N., Ash, E. (2017). Schema benefit vs. proactive interference: Contradicting behavioral outcomes and coexisting neural patterns. *NeuroImage*, 158, 271-281.

Chapters and Reviews

Y. Jacob, D. Papo, **T. Hendler** and E. Ben-Jacob (2012). Functional Holography and Cliques in Brain Activation Patterns, Advances in Brain Imaging, Dr. Vikas Chaudhary (Ed.), ISBN: 978-953-307-955-4, InTech, (pp.101-126).

Gruberger M., Ben-Simon E., & **Hendler T**. Neuroimaging Approaches to the Stream of Consciousness: Problems lost and found A book chapter in Consciousness: Its nature and functions. Edited By: S. Kreitler and O. Maimon. (pp. 311-324). Nova Publishers, Hauppage, NY. 2012.

Jamshy, S., Perez, O., Yeshurun, Y., **Hendler, T**., & Intrator, N. Searchlight based feature extraction. In Machine Learning and Interpretation in Neuroimaging, Lecture Notes in Computer Science, (pp. 17-25). Springer Berlin Heidelberg, 2012.

Raz, G., Hagin, B., & Hendler, T. "E-Motion Pictures of the Brain: Recursive Paths between Affective Neuroscience and Film Studies,"Arthur P. Shimamura (editor), Psychocinematics: Exploring Cognition at the Movies (pp. 285-313). (New York: Oxford University Press

Gilam, G., & Hendler, T. Deconstructing Anger in the Human Brain. In Current Topics in Behavioral Neurosciences. Springer Berlin Heidelberg, 2016.

Gilam, G., **Hendler, T**. (2016) With love, from me to you: Embedding social interactions in affective neuroscience. *Neuroscience and Biobehavioral Reviews* 68, 590-601.

Jacob Y., Papo D., Papo D., **Hendler T.** and Ben-Jacob E. (2012). Holography and cliques in brain activation patterns. Chapter in *Advances Brain Imaging edt*. (PP 101-126), Tech Publishing.

Raz G., Hagin B. and **Hendler T**. (2013) E-motion pictures of the brain: recursive paths between cinema and neuroscience. A *Shimamura (ed) Psychocinematics*: The Aesthetic Science of Movies. Oxford University Press.

Prof. Dario G. Liebermann, Ph.D.

Department of Physical Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: dlieberm@post.tau.ac.il
URL: http://www2.tau.ac.il/Person/medicine/Health-School/researcher.asp?id=aci-jhdjdl

Computational Motor Control and Clinical Applications to Upper-Limb Rehabilitation

Position

Professor, Sackler Faculty of Medicine

Movement Science Lab., Department of Physical Therapy

Associate Editor, Journal of Electromyography & Kinesiology

Research

Behavioral and computational motor control is our field of research. This is a main venue for understanding the motor system and its organization, in healthy and clinical populations. In the last years, we have dedicated major efforts in investigating methods and technologies (virtual reality, robot-based rehabilitation, neuro-stimulation) that can potentially enhance motor recovery and functional performance in clinical populations with a focus on upper-limb motion in stroke survivors. Mathematical model-based, as well as empirical neuromotor approaches, are used in our research for studying and understanding laws of motor control and sensorimotor integration.

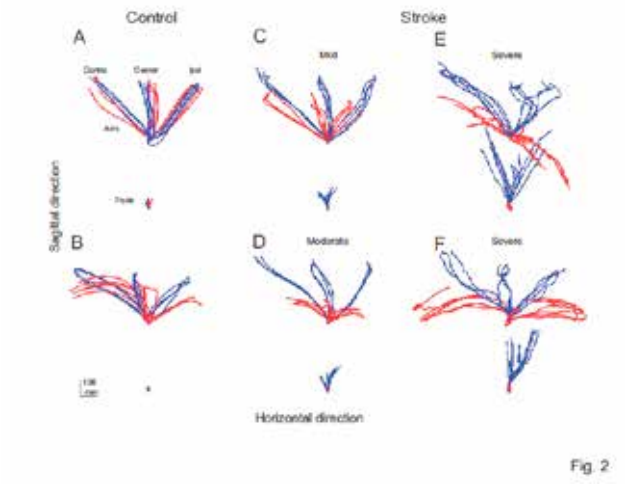
Publications

Frenkel-Toledo S, **Liebermann DG**, Bentin S, Soroker N. Dysfunction of the human mirror neuron system in Ideomotor Apraxia: Evidence from Mu suppression. J Cogn Neurosci. 2016, 28:775-91.

Levin MF, **Liebermann DG**, Parmet Y, Berman S. Compensatory versus noncompensatory shoulder movements used for reaching in stroke. Neurorehabil Neural Repair. 2016, 30:635-46.

Uri O, Pritsch M, Oran A, **Liebermann DG**. Upper limb kinematics after arthroscopic and open shoulder stabilization. J Shoulder Elbow Surg. 2015, 24:399-406.

Arzi H, Krasovsky T, Pritsch M, **Liebermann DG**. Movement control in patients with shoulder instability: a comparison between patients after open surgery



Top: Schematic view of arm and trunk rotation used in modeling arm-trunk coordination based on a geometric algebra approach**. Right**: Arm endpoint and trunk paths (horizontal plane view; i.e., from the above) during reaching movements to contra-, center and ipsilateral visual targets for two healthy controls (A, B) and four stroke patients with mild (C), moderate (D) and severe (E-F) hemiparesis. Center-out paths to targets in the physical environment are depicted in blue traces and 2D virtual environment in red traces.

and nonoperated patients. J Shoulder Elbow Surg. 2014, 23:982-92.

Berman S, **Liebermann DG**, McIntyre J. Constrained motion control on a hemispherical surface: path planning. J Neurophysiol. 2014, 111:954-68.

Frenkel-Toledo S, Bentin S, Perry A, **Liebermann DG**, Soroker N. Mirror-neuron system recruitment by action observation: effects of focal brain damage on mu suppression. Neuroimage. 2014, 87:127-37.

Arzi H, Krasovsky T, Pritsch (Perry) M, **Liebermann, D.G.** Movement Control in Patients with Shoulder Instability Before and After Open Surgery. Journal of Shoulder and Elbow Surgery 2013, pii: S1058-2746(13)00505-3.

Frenkel-Toledo S., Bentin S., Perry A., **Liebermann, D.G.**, Soroker N. Mirror-neuron system recruitment by action observation: Effects of focal brain damage on mu suppression. NeuroImage 2013, 87C, 127-137.

Berman S., **Liebermann D.G.**, McIntyre J., Constrained Motion Control on a Hemispherical Surface – Optimal Path Planning. J. of Neurophysiology 2014;111(5):954-68.

Frenkel-Toledo S., Bentin S., Perry A., **Liebermann D.G.**, Soroker N. Dynamics of the EEG Power in the Frequency and Spatial Domains During Observation and Execution of Manual Movements. Brain Research 2013, 1509, 43-57.

Merdler T., **Liebermann D.G.**, Levin M.F., Berman S. Arm-plane representation of shoulder compensation during pointing movements in patients with stroke. J. Electromyography & Kinesiology, 2013, 23:938-47.

Chapters

Levin, M.F., Deutsch J., Kafri M., **Liebermann D.G.** Validity of virtual reality environments for motor rehabilitation. In: Virtual Reality for Physical and Motor Rehabilitation, *Virtual Reality Technologies for Health and Clinical Applications,* P.L. (Tamar) (Series editor: P. Sharkey): Vol. 1: Virtual Reality for Physical and Motor Rehabilitation, Virtual Reality Technologies for Health and Clinical Applications, P.L. (Tamar) Weiss, E.A. Keshner, M.F. Levin (Eds.), Springer Science+Business Media, New York, 2014.

Liebermann, D.G. and Franks I.M. "Video-based technologies, substitution of reality and performance feedback"; In M. Hughes and I.M. Franks (Eds.), *The Essentials of Performance Analysis,* Routledge: London, Chapter 4, 2015.

Grants

2015-2017	Israeli Defense Forces
2015-2017	Nelly Horwitz Foundation
2015-2018	CIHR – ISF-Canada-Israel

Prof. Ilana Lotan, Ph.D.

Department of Physiology & Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: ilotan@post.tau.ac.il
Brain@tau: neuroscience.tau.ac.il/

Role of Potassium Channels in Neurotransmitter and Insulin Release in Diabetes

Position

Professor, Sackler Faculty of Medicine

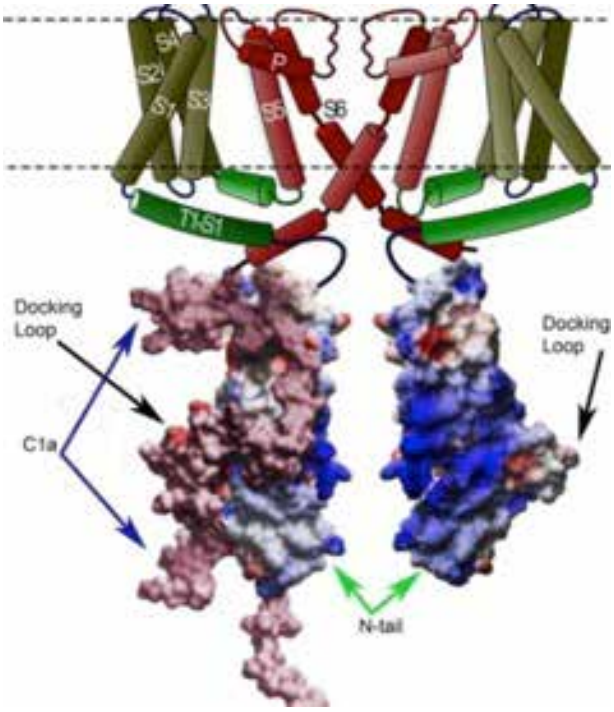
Research

We have a long standing interest in the study the molecular mechanisms of modulation of voltage gated K^+ (Kv) channels by interaction with signaling molecules. We were first to describe modulation of a brain Kv channel by major protein components of the exocytotic machinery. Since then our main focus is the role of Kv channels in transmitter release, finding that it may be far more than just repolarizing the membrane potential: independent of K^+ currents but mediated by protein-protein interactions with the exocytic SNARE proteins. The dual actions of the channel, through its currents and via its interaction with SNAREs, in combination, may reinforce the known activity dependence of dense core vesicle exocytosis.

Main research projects currently in the lab:

1) Study of the novel role of Kv2.1 potassium channel in insulin secretion from pancreatic islet β cells, as a target for novel drug design for the treatment of type-2 diabetes;

2) Study of structure-function and modulations by presynaptic modulators of Kv2.1 and other Kv channels, specifically KCNQ2 and KCNQ3, important in axonal and synaptic excitability.



Kv2.1-C terminal domain, C1a, wraps around the N terminus and is accessible for protein-protein interactions. Using biophysical and FRET analyses, combined with computational biology approach dealing with homology and ab initio modeling of protein structures, proteins docking simulations and molecular dynamics.

Kv2.1 (Lvov et al., J. Biol. Chem. (2009)

Research methods:

Biophysical: 1) Two-electrode voltage clamp and patch clamp techniques for the study of whole cell and single channel currents. 2) Membrane capacitance and amperometry measurements for the study of exocytosis.

Biochemical: co-immunoprecipitation, immunohystochemistry, recombinant protein purification, etc, for the study of *in vivo* and *in vitro* protein-protein interactions.

Imaging: 1) Fluorescence Resonance Energy Transfer (FRET) for the study of protein-protein interactions. 2) Total Internal Reflection Fluorescence Microscopy (TIRFM) for the study of neurotransmitter vesicles behavior.

Publications

Greitzer-Antes D, Barak-Broner N, Berlin S, Oron Y, Chikvashvili D, **Lotan I**. Tracking Ca2+-dependent and Ca2+-independent conformational transitions in syntaxin 1A during exocytosis in neuroendocrine cells. *J Cell Sci*. 2013;126:2914-23.

Singer-Lahat D, Barak-Broner N, Sheinin A, Greitzer-Antes D, Michaelevski I, **Lotan I.** The dual function of the polybasic juxtamembrane region of syntaxin 1A in clamping spontaneous release and stimulating Ca2+-triggered release in neuroendocrine cells. *J Neurosci* 2017, 1541-17.

Review

McCord MC, Kullmann PH, He K, Hartnett KA, Horn JP, **Lotan I**, Aizenman E. Syntaxin-binding domain of Kv2.1 is essential for the expression of apoptotic K+ currents. *J. Physiol*. 2014;592:3511-21.

Vertkin I, Styr B, Slomowitz E, Ofir N, Shapira I, Berner D, Fedorova T, Laviv T, Barak-Broner N, Greitzer-Antes D, Gassmann M, Bettler B, **Lotan I**, Slutsky I. GABAB receptor deficiency causes failure of neuronal homeostasis in hippocampal networks. *Proc. Natl Acad Sci USA*. 2015;112:E3291-9.

Siloni S, Singer-Lahat D, Esa M, Tsemakhovich V, Chikvashvili D, **Lotan I**. Regulation of the neuronal KCNQ2 channel by Src – a dual rearrangement of the cytosolic termini underlies bidirectional regulation of gating. *J Cell Sci*. 2015;128, 3489-3501.

Grants

2014-2018 Israel Science Foundation

Dr. Yuval Nir, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: ynir@post.tau.ac.il
URL: http://medicine.mytau.org/nir/

Sleep and Its Relation to Cognition

Position

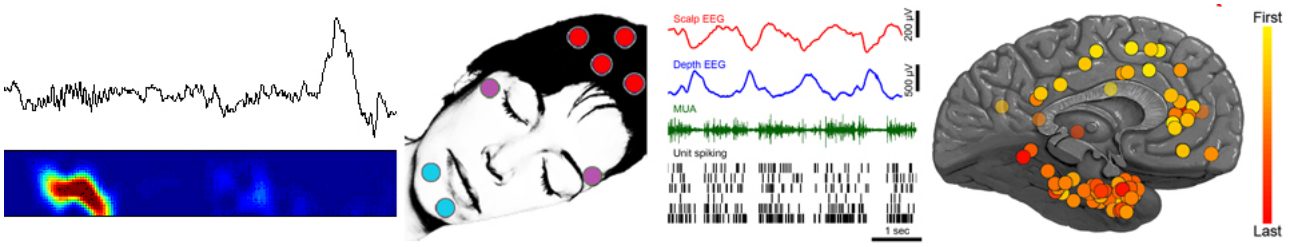
Senior Lecturer, Sackler Faculty of Medicine

Research

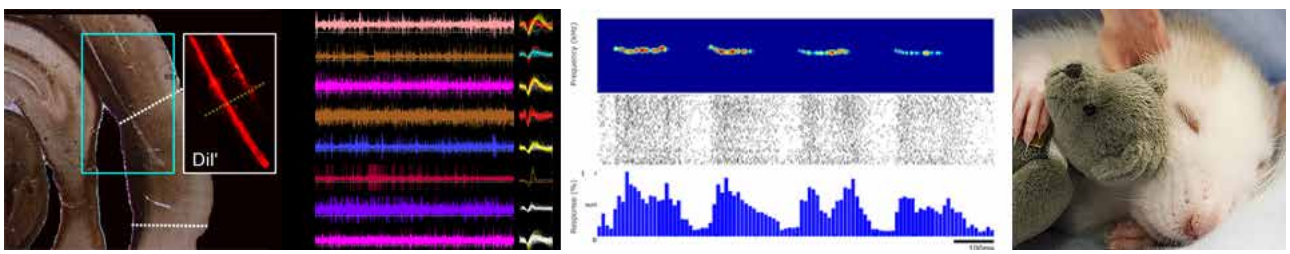
Sleep is a universal behavior that is present across the animal kingdom. We spend a third of our lives sleeping, disconnected from the world around us. Our sleep is closely regulated so that when we are sleep deprived, we ultimately compensate with longer, deeper sleep. Sleep helps our cognitive performance, promoting learning and memory consolidation. Lack of sleep immediately affects our cognition, mood, and health. All this suggests that sleep is essential, but what exactly is it about brain activity during sleep that is so crucial for restoring our normal cognition?

Sleep also involves dramatic changes to our perceptual awareness. Sometimes our consciousness fades altogether while at other times we experience vivid dreams. Although our brain continues to be active, we are mostly disconnected from sensory signals such as sounds, which would otherwise be perceived, trigger plasticity and result in behavior. How does the internal state of brain activity during sleep affect brain responsiveness and perceptual awareness?

Our goal is to understand how sleep relates to cognition and perception. Our research is guided by a belief that such studies require a combination of human and animal models. We therefore use multiple experimental techniques, focusing on the strengths of each setup to investigate the same key questions synergistically. Animal models are used to investigate underlying mechanisms, by performing detailed recordings of electrical activity and by manipulating neuronal activity with optogenetic, electrical and sensory stimulation. Human studies are carried out for careful investigation of cognitive factors and for studying large-scale brain activity (with fMRI, EEG, recordings in neurosurgical patients, and behavioral tests).



Intracranial sleep recordings in neurosurgical patients reveal that slow waves and sleep spindles – the hallmark EEG oscillations of sleep – occur mostly locally and have a tendency to propagate from medial prefrontal cortex to the medial temporal lobe. Therefore, intracerebral communication during sleep is constrained as sleep oscillations often occur out-of phase in different brain regions.



A comparison of single-unit and LFP responses in rat auditory across wakefulness and sleep states reveals comparable selectivity and response magnitudes of auditory-evoked responses across vigilance states.

Publications

Nir Y, Andrillon T, Marmelshtein A, Suthana N, Cirelli C, Tononi G, Fried I. Selective neuronal lapses precede human cognitive lapses following sleep deprivation. *Nat Med.* 2017, doi: 10.1038/nm.4433.

Makov S, Sharon O, Ding N, Ben-Shachar M, **Nir Y,** Zion Golumbic E. Sleep disrupts high-level speech parsing despite significant basic auditory processing. *J Neurosci.* 2017;37:7772-7781.

Sharon O, **Nir Y.** Attenuated fast steady-state visual evoked potentials during human sleep. *Cereb Cortex.* 2017;25:1-15.

Sela Y, Vyazovskiy VV, Cirelli C, Tononi G, **Nir Y**. Responses in rat core auditory cortex are preserved during sleep spindle oscillations. *Sleep*. 2016;39:1069-82.

Andrillon T, **Nir Y**, Cirelli C, Tononi G, Fried I.Single-neuron activity and eye movements during human REM sleep and awake vision. *Nat Commun*. 2015;6:7884.

Nir Y, Vyazovskiy VV, Cirelli C, Banks MI, Tononi G. Auditory responses and stimulus-specific adaptation in rat auditory cortex are preserved across NREM and REM sleep. *Cerebral Cortex*. 2015;25:1362-78.

Gilaie-Dotan S, Hahamy-Dubossarsky A, **Nir Y**, Berkovich-Ohana A, Bentin S, Malach R. Resting state functional connectivity reflects abnormal task-activated patterns in a developmental object agnosic. *Neuroimage*. 2013;70:189-98.

Grants

2014 – 2018 EU Marie Curie Career Integration Grant (CIG)

2013 – 2018 I-CORE Cognitive Neuroscience

2015-2020 Israel Science Foundation grant

Dr. Moshe Parnas, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

Email: mparnas@post.tau.ac.il

Neural Circuits and Olfactory Perception in Drosophila

Position

Senior Lecturer, Sackler Faculty of Medicine and Sagol School of Neuroscience

Research

We are exploring the various mechanisms by which neural circuits encode information and support behaviour, learning and memory. In addition, we are studying how the connectivity and activity of such circuits and neural networks are affected by molecular mechanisms underlying brain disorders. We use a multidisciplinary approach, with the *Drosophila* olfaction system as our model system. Our studies incorporate *in vivo* whole cell patch recordings, *in vivo* functional imaging, behaviour experiments, molecular biology, mathematical modelling and genetics.

Projects in the lab include:

1. Intensity and identity coding in a multidimensional sensory system – the *Drosophila* olfactory system.
2. Neuropeptidergic modulation of olfaction and its effect on odour perception.
3. The role of deregulated channel proteins and altered neuronal function in Frontotemporal Dementia.
4. A novel multifaceted approach to study the mechanisms underlying the effects of human genes associated with schizophrenia using *Drosophila*.

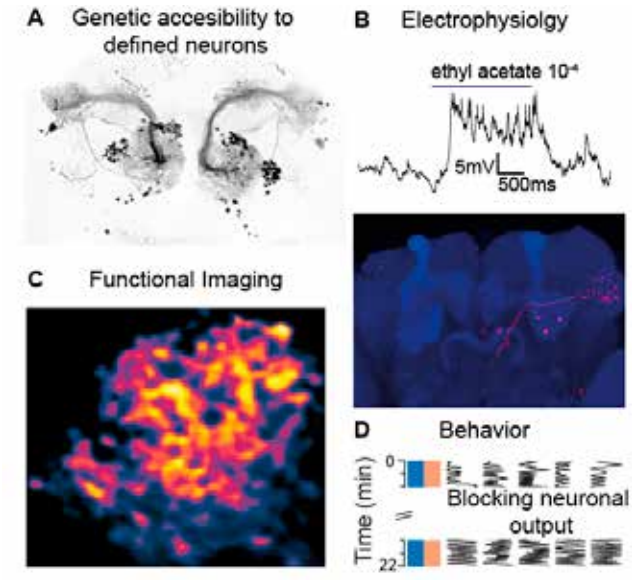
Publications

Manuscripts

Parnas, M., Lin, A.C., Huetteroth. W., and Miesenböck, G. (2013). Odor discrimination in *Drosophila*: From neural population code to behavior. *Neuron*, 79:932-944.

Grants

2016	NIPI – National Institute of Psychobiology in Israel
2017-2019	United States-Israel Binational Science Foundation
2016-2020	ERC Starting Grant



Drosophila as a model system for systems neuroscience. **A.** Using the genetic tools available for *Drosphila* there is accessibility for defined neurons. **B.** *In vivo* whole cell patch recording in awake behaving animals. **C.** *In vivo* functional imaging using genetically encoded sensors in awake behaving animals. D. Genetic access to defined neurons allows manipulatin of the activity of neural circuits in behaving animals.

Dr. Eran Perlson, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: eranpe@post.tau.ac.il
URL: http://www6.tau.ac.il/medicine/perlson/

Molecular Mechanisms of Neurodegeneration

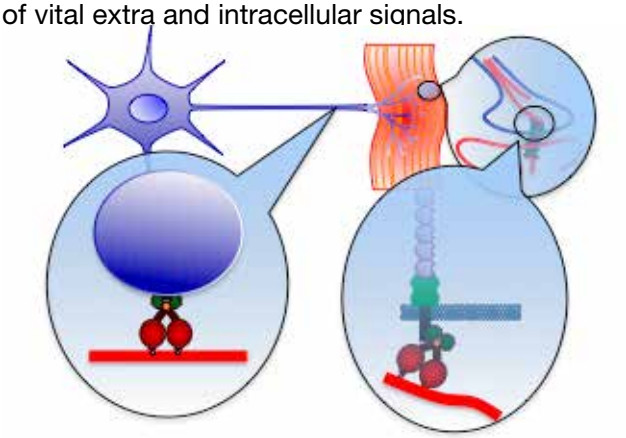
Position

Senior Lecturer, Sackler Faculty of Medicine

Research

The lab is a new multi-disciplinary molecular and cellular neurobiology lab. The lab uses state-of-the-art single molecule live imaging techniques on neuronal cultures, as well as biochemistry, cell biology and biophysics approaches on mouse model systems to study the role of axonal transport in neurodegenerative diseases, with an initial focus on ALS.

Neuronal survival and proper function depends on cell-cell communication mediated by ligand-receptor mechanisms. During neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS), there is considerable synapse/neuromuscular junction (NMJ) disruption and neuronal cell death. It is non-autonomous processes involve interactions between the neurons to its diverse extracellular microenvironments. The molecular basis for this neuronal dysfunction and death is still poorly understood. One possible reason is alterations in the nature, directed movement and spatial localization of vital extra and intracellular signals.



The dual role of dynein in spatiotemporal signaling. Dynein serve as a motor protein conducting long distance signaling process (left callout) or may play a role in receptors clustering and lateral movement in and out of membrane microdomain (right callout) for example in the neuromuscular junction. Alterations in its function leads to neurodegeneration.

The long-term research goal of the lab is to understand the vital molecular communications mechanisms between the neurons and its environment. More specifically, we seek to understand the role that retrograde signaling plays in (1) neuronal survival and (2) synapse stability.

We believe that our research will generate novel insights into neurodegenerative mechanisms and ultimately, provide a molecular basis for new drugs as well as delivery methods to treat a range of neurodegenerative diseases.

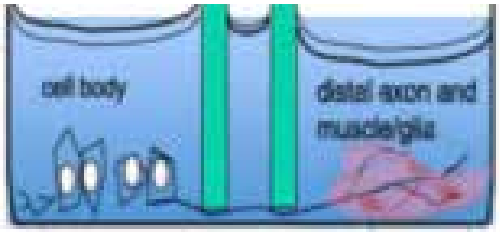
Publications

Naftelberg S, Ast G, **Perlson E.** (2017) Phosphatidylserine improves axonal transport by inhibition of HDAC and has potential in treatment of neurodegenerative diseases. *Neural Regen Res.* 12:534-537.

Zahavi EE, Maimon R, **Perlson E.** (2017) Spatial-specific functions in retrograde neuronal signalling. *Traffic* 18:415-424.

Rotem N, Magen I, Ionescu A, Gershoni-Emek N, Altman T, Costa CJ, Gradus T, Pasmanik-Chor M, Willis DE, Ben-Dov IZ, Hornstein E, **Perlson E**. (2017) ALS along the axons - expression of coding and noncoding RNA differs in axons of ALS models. Sci Rep. 7:44500.

Gershoni-Emek, N., Mazza A, Gradus T., Sharan R. and **Perlson E**. (2016) Proteomic analysis of dynein



In-vitro microfluidic platform with motor neuron cell bodies on one side and muscle cells on the other, creating a powerful system to study neurodegeneration mechanisms.

interactors in synaptosomes reveals a role for the RNA-binding protein Staufen1 in Amyotrophic Lateral Sclerosis. *Mol Cell Proteomics*. 15:506-22.

Ionescu A, Zahavi E, and **Perlson E.** (2016) A microfluidic system for studying muscle-neuron communication and neuromuscular junction maintenance. *Eur J Cell Biol.*95:69-88.

Gluska S, Chein M, Rotem N, Ionescu A and **Perlson E.** (2016) Tracking quantum-dot labeled neurotropic factors transport along primary neuronal axons in compartmental microfluidic chambers. *Methods Cell Biol.* 2016;131:365-87.

Zahavi E, Ionescu A, Ben-Yaakov K., Gluska S, and **Perlson E.** (2015) Spatial aspects of GDNF functions revealed in a compartmentalized microfluidic neuromuscular co-culture system. *J Cell Sci*, 128:1241-52.

Bauer A., Nolden T., Nemitz S., **Perlson E**. and Finke S. (2015) A dynein light chain 1 binding motif in RABV polymerase L protein plays a role in microtubule re-organization and viral primary transcription. *J Virol.* 89(18):9591-600.

Bornstein B., Zahavi E., Gelley S., Zoosman M., Yaniv S., Fuchs O., Porat Z., **Perlson E.** and Schuldiner O. (2015) Developmental axon pruning requires destabilizing of cell adhesion by JNK signaling. *Neuron*. 88:926-40.

Gluska S, Zahavi E, Chein M, Gradus T, Bauer A, Finke S and **Perlson E.** (2014). Rabies virus hijacks and accelerates the p75ntr retrograde axonal transport machinery. *Plos Pathogen.* 10:e1004348.

Bauer A., Nolden T., Römer-Oberdörfer A.,Gluska S., **Perlson E**. and Finke S (2014). Post-replicative glycoprotein dependent bi-directional rabies virus transport in dorsal root ganglion neurons. *J Virol.* 15;88.

Dadon-Nachum M, Ben-Yaacov K., Ben-Zur T. Barhum Y., Yaffe D. **Perlson E**. and Offen D. (2014). Transplanted modified muscle progenitor cells expressing a mixture of neurotrophic factors delay disease onset and enhance survival of ALS model SOD1 mice. *J Molec Neurosci*. [Epub ahead of print]

Bauer A., Nolden T., Römer-Oberdörfer A., Gluska S., **Perlson E**., and Finke S (2014). Post-replicative glycoprotein dependent bi-directional rabies virus transport in dorsal root ganglion neurons. *J Virol*. 15;88.

Gluska S, Zahavi E, Chein M, Gradus T, Bauer A, Finke S and **Perlson E**. (2014). Rabies virus hijacks and accelerates the p75NTR retrograde axonal transport machinery. *PloS Pathogen*. 10:e1004348.

Lilo E, Wald S, Solmesky L, Ben Yaakov K, Gershoni-Emek N, Gotkine M, Karosis D, Bulvik S, **Perlson E** and Weil M. (2013). Characterization of human sporadic ALS biomarkers in the familial transgenic mSOD1G93A mouse model. *Hum Mol Genet*. 22:4750-5.

Yashunsky V, Kharilker **L,** Zahavi E**,** Mercone S, Golosovskii M, **Perlson E**, Davidov D, Aroeti B (2013) Real-time sensing of enteropathogenic *E. coli*-induced effects on epithelial host cell height, cell-substrate interactions, and endocytic processes by infrared surface plasmon spectroscopy. *PLoS One*. 8:e78431

Perlson E, Hendricks AG, Wilson MH, Lazarus JE, Ben-Yaacov K, Zhang X, Xiang X, Holzbaur EL. (2013). Dynein interacts with NCAM180 to tether and stabilize synaptic microtubules. *J Biol Chem*. 27;288:27812-24

Castle M, **Perlson E**, Holzbaur EL, Wolf JH, (2013) Long-distance axonal transport of AAV9 is driven by dynein and kinesin-2 and is trafficked in a highly motile Rab7-positive compartment. *Mol Therapy*. 22:554-66.

Reviews and chapters

Guillermo MA., Gershoni-Emek, N., **Perlson E** and Bronfman FC. (2016). Neurodegeneration and Alzheimer's disease, What can proteomics tell us about the Alzheimer's brain?" Mol Cellular Proteomics. 15:409-25.

Gershoni-Emek, N., Zahavi EE., Gluska S., Slobodskoy Y and **Perlson E. (**2015) The Molecular Communication Mechanism of Neuron Survival and Synapse Maintenance. (Book chapter, University of Chicago Press), In press.

Gershoni-Emek, N., Chein, M., Gluska, S., **Perlson, E.** (2015). Amyotrophic Lateral Sclerosis as a Spatiotemporal Mislocalization Disease: Location, Location, Location. In: Jeon, K.W. (Ed.), International Review of Cell and Molecular Biology, pp. 23–71.

Gluska S, Finke S, **Perlson, E.** (2015) Rabies Express: Receptor-Mediated Increase in Rabies Virus Axonal Transport. Neuronal Regeneration Research. 10:883-4.

Grants

2013-2018 Molecular Communication Mechanism of Motor Neuron Survival and Synapse Maintenance, European Research Council (ERC) Starter Grant

Prof. Chaim G. (Chagi) Pick, Ph.D.

Department of Anatomy and Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: pickc@post.tau.ac.il

Brain Injuries: Cognitive, Behavioral and Cellular Outcome

Position

Professor, Sackler Faculty of Medicine

Chair, Department of Anatomy and Anthropology

Sagol School of Neuroscience faculty member

Dr Miriam and Sheldon G Adelson Chair in Biology of Addictive Diseases

Research

My group has a long history in mTBI research, not only in characterizing behavioral and biochemical sequelae of blunt head trauma, but also in developing preclinical models of mTBI of translational relevance to support the development of new treatment strategies and drugs. In order to look for answers regarding the blast induced traumatic brain injury, we have developed a blast injury model for mice that resembles, as much as possible, the conditions on the battlefield or at a terror-attack site. As such, the outcomes of the "real-life-like" exposure to the blast in our model may vary from severe to mild brain injury under controlled conditions for each mouse.

Publications

Rachmany, L., Tweedie D., Li, Y., Rubovitch, V., Holloway, H.W., Miller, J., Hoffer, B.J., Greig, N.H. and **Pick, C.G.** Exendin-4 Induced Glucagon-like Peptide-1 Receptor Activation Reverses Behavioral Impairments of Mild Traumatic Brain Injury in Mice. *Aging* 35:1621-36 (2013).

Tweedie, D,. Rachmany, L., Rubovitch, V., Lehrmann, E., Zhang, Y., Backer, K.G., Parez, E., Miller, J., Hoffer, B.J., Greig, N.H. and **Pick, C.G.** Exendin-4, a glucagon-like peptide-1 receptor agonist prevents mTBI-induced changes in hippocampus gene expression and memory deficits in mice. *Exp. Neurology*, 239:170-82 (2013).

Menachem, A., Chapman, J., Deri, Y., **Pick, G.C.** and Katzav, A. Immunoglobulin mediated neuro-cognitive impairment: review and preliminary experimental findings. Clinical Reviews in *Allergy & Immunology* 45:62-68 (2013).

Woods, A.S., Colsch, B., Jackson, S.N., Post, J., Baldwin, C., Roux, A., Hoffer, B.J., Cox, B., Hoffer M., Rubovitch,V. **Pick, C.G.** J.A., Schultz. and Balaban, C. Gangliosides and ceramides changes in a mouse model of a blast induced traumatic brain injury. ACS Chemical Neuroscience 17:594-600 (2013).

Domachevsky, L., **Pick, C. G.,** Peled, N., Gomori, J.M., Abramovich, A. and Tempel-Brami, C. MRI Findings after Hyperbaric Induced Seizures. *Epilepsy Res* 105: 62-68 (2013).

Tweedie, D., Rachmany, L., Rubovitch, V., Lehrmann, E., Zhang, Y., Becker, K.G., Perez, E., Hoffer, B.J., **Pick, C.G.** and Greig, N.H. Physical- versus Blast-Traumatic Brain Injury: commonalities in cognitive dysfunction and hippocampal gene transcriptome in mice. *Neurobiol Dis* 54:1-11 (2013).

Katzav, A., Ginsburg, D., Evert, T., Blank, M., **Pick, C.G.,** Shoenfeld, Y. and Chapman, J. Coagulopathy Triggered Autoimmunity: Experimental Antiphospholipid Syndrome in Factor V Leiden Mice. *BMC Medical* **11**:92 (2013).

Domachevsky, L., Rachmany, L., Barak, Y.,Rubovitch, V., Abramovich, A. and **Pick, CG.** Do hyperbaric oxygen-induced seizures cause a transient decrement in cognitive function. *Neuroscience*. 247: 328-334 (2013).

Rachmany, L., Tweedie, D., Rubovitch, V., Yu, Q., Wang, J.Y., Pick**, C.G.***, Greg, N.H*. Cognitive impairments accompanying rodent mild traumatic brain injury involve p53-dependent neuronal cell death and are ameliorated by the tetrahydrobenzothiazole PFT-a. *PLoS One* 28;8(11) (2013).

Schreiber, S., Hostovsky, A., Volis, I., Rubovitch, V. **Pick, CG**. The impact of antidepressant drugs on the antinociceptive properties of methadone in mice. *J. Molec Neurosci* 52: 598-604 (2014).

Benaroya-Milshtein, N., Apter, A., Yaniv, I., Oded, Y., Stern, B., Bengal, Y., Kodman, Y., Shemer, E., **Pick, G.C.,** Buchwald I. and Valevski A. Neuroimmunological function in parents of children suffering from cancer. *J Neural Transmission* 121: 299-306 (2014).

Itsekson, Z., Shavit-Stein, E., Weissberg, I., Katzav,A., Rubovich, V., Friedman, A., **Pick C.G.** and J. Chapman. Increased Levels of Thrombin and its Receptor PAR-1 in Minimal Traumatic Brain Injury in Mice. *J. Molec Neurosci* 53: 87-95 (2014).

Greg, N.H, Tweedie, D. Rachmany, L., Yu, Q., Rubovitch, V, Schreiber,S., Chiang, Y-H. Hoffer, B.J., Lahiri, D., Kumar Sambamurti, K., Becker,R.E., **Pick, C.G.** Incretin mimetics as pharmacological tools to elucidate and as a new drug strategy to treat traumatic brain injury. *Alzheimer's & Dementia* 10: S62-S75 (2014).

Eakin, K., Baratz-Goldstein, R., **Pick, C.G.,** Zindel, O., Hoffer, B.J., Balaban, C., Hoffer, M.E. Lockwood, M. Miller, and Hoffer, B.J. J. Efficacy of N-Acetyl Cysteine in Traumatic Brain Injury. *PLoS One* 16;9 (2014).

Katzav, A., Ben-Ziv, T., Blank M. **Pick, C. G.,** Shoenfeld Y and Chapman, J. Antibody-specific behavioral effects: Intracerebroventricular injection of antiphospholipid antibodies induces hyperactive behavior while anti-ribosomal-P antibodies induces depression and smell deficits in mice. *J Neuroimmunol*, 272:10-15(2014).

Schreiber, S., Lin, R., Haim, L., Baratz-Goldstien, R., Rubovitch, V., Waisman, N. and **Pick, C. G.** Enriched environment improves the cognitive effects from traumatic brain injury in mice. *Behav Brain Res* 271:59-64 (2014).

Lloyd, MC. Burke, N. Kalantapour, F. Niesen, MI. Hall, A. Pennypacker, K. Citron, B. **Pick, C. G.** Vernard A, V. Das, M. Mohapatra, S. Cualing, H and Blanck, G. Quantitative morphological and molecular pathology 1 of the human thymus correlate with infant cause of death. *Tech. Innovation* 16: 55-62 (2014).

Edut S., Rubovitch, V., Rehavi, M., Schreiber, S. and **Pick, C. G.** A study on the mechanism by which MDMA protects against dopaminergic dysfunction after minimal traumatic brain injury (mTBI) in mice. *J. Mol. Neurosci*. 54: 684- 697 (2014).

Katzav A., Menachem A., Maggio, N., Pollak, L., **Pick C. G.**, and Chapman J. IgG accumulates in inhibitory hippocampal neurons of experimental antiphospholipid syndrome. *J. Autoimm*. 55: 86-93 (2014).

Becker, M., Benromano, T., Shahar, A., Nevo, Z and **Pick, C. G.** Changes in the basal membrane of dorsal root ganglia Schwann cells explain the biphasic pattern of the peripheral neuropathy in streptozotocin

Benromano, T., Defrin, R., Ahn, A. H., Zhao, J., **Pick C. G** and Levy, D. Closed-head injury promotes a selective trigeminal hyper-nociception: implication for the acute emergence of post traumatic headache. *Eur. J. Pain* 19: 621-628 (2015).

Defrin, R., Riabinin, M., Feingold, Y., Schreiber, S and **Pick, C. G.** Deficient pain modulation systems in chronic post traumatic headache. *J. Neurotrauma* 32: 28-37 (2015).

Shavit-Stein, E., Itsekson, Z., Aronovich, A., Reisner, Y., **Pick C. G.**, Tanne, D., Chapman, J. and Maggio, N. Thrombin induces ischemic LTP (iLTP): implications for synaptic plasticity in the acute phase of ischemic stroke. *Sci. Rep*. 5: 7912 (2015).

Rubovitch, V., Baratz-Goldstein, R., Zilberstein, Y. and **Pick, C. G.** The involvement of the eIF2-alpha pathway in the neuroprotective effect of IGF-1 in mTBI. *NeuroMolecular Med*. 17:58-70 (2015).

Baratz, R., Tweedie, D., Rubovitch, V., Hoffer, B.J., Greig N. H. and **Pick, C. G.** Pathophysiological mechanisms of minimal traumatic brain injury (mTBI): TNF-a synthesis inhibitor as a potential neuroprotective therapy. J*. Neuroinflamm*. 12:45 (2015).

Yang, L-Y, Chu, Y-H, Tweedie, D., Yu, Q-S, **Pick, C. G.**, Hoffer, B.J., Greig N. H. and Wang, J-Y. Post-trauma administration of the pifithrin-α oxygen analogue improves histological and functional outcomes after experimental traumatic brain injury. *Exp. Neurol*. 269:56-66 (2015).

Ben Shimon, M., Lens, M., Ikenberg, B., Becker, D., Shavit Stein, E., Chapman, J. Tanne, D., **Pick, C. G.** Blatt, I., Neufeld, M., Vlachos A. and Maggio, N. Thrombin regulation of synaptic transmission and plasticity: implications for health and disease. *Front. Cell. Neurosci*. 21; 9:151(2015).

Defrin, R., Amanzio, M., Violeta Dimova, V., Filipovic, S., David Finn, D., Gimenez-Llort, L., Jensen-Dahm, C., Lautenbacher, S., Oosterman, J., Petrini, L., **Pick, C. G.**, Pickering, G., de Tommaso, M., Invitto, S., Vase, L. and Kunz,M. Experimental pain processing in individuals with cognitive impairment: state of the art. *Pain*, 156:1396-1408 (2015).

Li Y., Bader, M., **Pick C.G.** and Greig, N.H. Liraglutide is neurotrophic and neuroprotective in neuronal

cultures and mitigates mild traumatic brain injury in mice. *J. Neurochem* 135: 1203-1217 (2015).

Baeta-Corral, R., Defrin, R., **Pick C.G.** and Lydia Giménez-Llort L. Nociception response is preserved in 3xTg-AD mice. *Neurosci. Lett*. 600:158-163 (2015).

Tweedie, D., Rachmany, L., Rubovitch, V., Li, Y., Holloway, H.W., Lehrmann, E., Zhang, Y., Becker, K.G., Perez, E., Hoffer, B.J., **Pick C.G*.** and Greig, N.H. * Blast traumatic brain injury induced cognitive deficits associated with hippocampal neurodegeneration and changes in gene expression are attenuated by treatment with the glucagon-like peptide-1 receptor agonist, exendin-4. *Alzheimer Dement*. 12: 34-48 (2016). *Equal contribution.

Schreiber, S., Bader, M., Rubovitch, V. and **Pick, C.G**. Interaction between methylphenidate, methadone and different antidepressants drugs in mice, and possible clinical implications. World J. Biol. Psychiatry (2016).

Leśniak, A., Sacharczuk, M., Chaim G. **Pick, C.G.** and Lipkowski, A.W. Biphalin protects against cognitive deficits in a mouse model of mild traumatic brain injury (mTBI). *Neuropharmacol.* 101:506-518 (2016).

Levy D, Edut S., Baratz-Goldstein R., Rubovitch, V., Defrin, R., Zhao J. and **Pick C.G.** Responses of dural mast cells in concussive and blast models of closed-head mild traumatic brain injury: implications for post-traumatic headache. *Cephalalgia* (2016).

Itsekson-Hayosh, Z. Shavit-Stein, E., Katzav, A., Maggio, N., Harnof, S., Chapman, J. and **Pick C.G.** Minimal traumatic brain injury in mice – PAR-1 and thrombin related changes. *J Neurotrauma* (2016).

Deselms, H., Maggio, N., Rubovitch, V., Chapman, J. Schreiber, S., Tweedie, D., Kim, D.S, Greig, N.H Pick C.P. Novel pharmaceutical treatments for minimal traumatic brain injury and evaluation of animal models and methodologies supporting their development. *J Neurosci Meth*. (2016). doi:10.1016/j.jneumeth.2016.02.002.

Tweedie, D., Rachmany, L. Kim D.S., Rubovitch, V., Lehrmann, E., Zhang, Y., Becker, K.G., Perez, E., Hoffer, B.J., Pick C.G* and Greig, N.H. Mild traumatic brain injury-induced hippocampal gene expressions: the identification of target cellular processes for drug development. *J Neurosci Meth*. (2016). doi: 10.1016/j.jneumeth.2016.02.003. [Epub ahead of print]

Tweedie, D., Fukui, K., Li, Y., Barak, S., Tamargo, I., Rubovitch, V., Holloway, H.W., Hoffer, B.J. Becker, R.E., **Pick, C.G.** Greig, N.H. Cognitive impairments induced by concussive mild traumatic brain injury in mouse are ameliorated by treatment with phenserine via multiple non-cholinergic mechanisms. *PLoS One*. (2016). 11(6):e0156493.

Benromano, T., **Pick, C.G.** Merik, J. and Defrin, R. Objective and subjective indicators of pain among individuals with cerebral palsy and intellectual disability. *Pain Med* (In press).

Baratz-Goldstein, R., Deselms, H., Haim, L., Khomsky, L., Hoffer, B.J., Atlas, D. and **Pick, C.G.** Thioredoxin-mimetic-peptides protect cognitive function after mild traumatic brain injury (mTBI). *PLoS One* 2016;11(6):e0157064.

Ben Shimon M, Zeimer T, Shavit Stein E, Artan-Furman A, Harnof S, Chapman J, Eisenkraft A, **Pick CG**, Maggio N. Recovery from trauma induced amnesia correlates with normalization of thrombin activity in the mouse hippocampus. *PLoS One.* 12:e0188524 (2017).

Saykally JN, Ratliff WA, Keeley KL, **Pick CG**, Mervis RF, Citron BA. Repetitive mild closed head injury alters protein expression and dendritic complexity in a mouse model. *J Neurotrauma*. doi: 10.1089/neu.2017.5070 (2017).

Baratz-Goldstein R, Toussia-Cohen S, Elpaz A, Rubovitch V, **Pick CG**. Immediate and delayed hyperbaric oxygen therapy as a neuroprotective treatment for traumatic brain injury in mice. *Mol Cell Neurosci*. 83:74-82 (2017).

Rachmany L, Tweedie D, Rubovitch V, Li Y, Holloway HW, Kim DS, Ratliff WA, Saykally JN, Citron BA, Hoffer BJ, Greig NH, **Pick CG**. Exendin-4 attenuates blast traumatic brain injury induced cognitive impairments, losses of synaptophysin and in vitro TBI-induced hippocampal cellular degeneration. *Sci Rep*. 7:3735 (2017).

Heim LR, Bader M, Edut S, Rachmany L, Baratz-Goldstein R, Lin R, Elpaz A, Qubty D, Bikovski L, Rubovitch V, Schreiber S, **Pick CG**. The invisibility of mild traumatic brain injury: Impaired cognitive performance as a silent symptom. *J Neurotrauma.* 34:2518-2528 (2017).

Benromano T, **Pick CG**, Granovsky Y, Defrin R. Increased evoked potentials and behavioral indices in response to pain among individuals with intellectual disability. *Pain Med*. 18:1715-1730 (2017).

Lesniak A, Leszczynski P, Bujalska-Zadrozny M, **Pick CG**, Sacharczuk M. Naloxone exacerbates memory impairments and depressive-like behavior after mild traumatic brain injury (mTBI) in mice with upregulated opioid system activity. *Behav Brain Res.* 326:209-216 (2017).

Rubovitch V, Zilberstein Y, Chapman J, Schreiber S, Pick CG. Restoring GM1 ganglioside expression ameliorates axonal outgrowth inhibition and cognitive impairments induced by blast traumatic brain injury. *Sci Rep.* 7:41269 (2017).

Tamargo IA, Bader M, Li Y, Yu SJ, Wang Y, Talbot K, DiMarchi RD, **Pick CG**, Greig NH. Novel GLP-1R/*GIPR* co-agonist "twincretin" is neuroprotective in cell and rodent models of mild traumatic brain injury. *Exp Neurol.* 288:176-186 (2017).

Reviews

Hoffer BJ, **Pick CG**, Hoffer ME, Becker RE, Chiang YH, Greig NH. Repositioning drugs for traumatic brain injury - N-acetyl cysteine and Phenserine. *J Biomed Sci*. 24:71 (2017).

Prof. Moshe Rehavi, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: mrehavi@post.tau.ac.il

Molecular Mechanisms of Drugs for Neuropsychiatric Disorders

Positions

Professor Emeritus, Sackler Faculty of Medicine

Research

Main projects in the lab include:

1. Presynaptic monoamine transportes and the vesicular monoamine transporter as targets for neuropsychiatric drugs.
2. Anxiolytic effects of new herbal treatment: mice models of anxiety and biochemical studies.
3. Quaternary serotonin-reuptake inhibitors as novel anti-platelet drugs.
4. Methylphenidate (Ritalin): abuse potential and long-term effects.
5. Neuronal rescue by Rasagiline (MAO-B inhibitor) in thiamine deficiency.

Publications

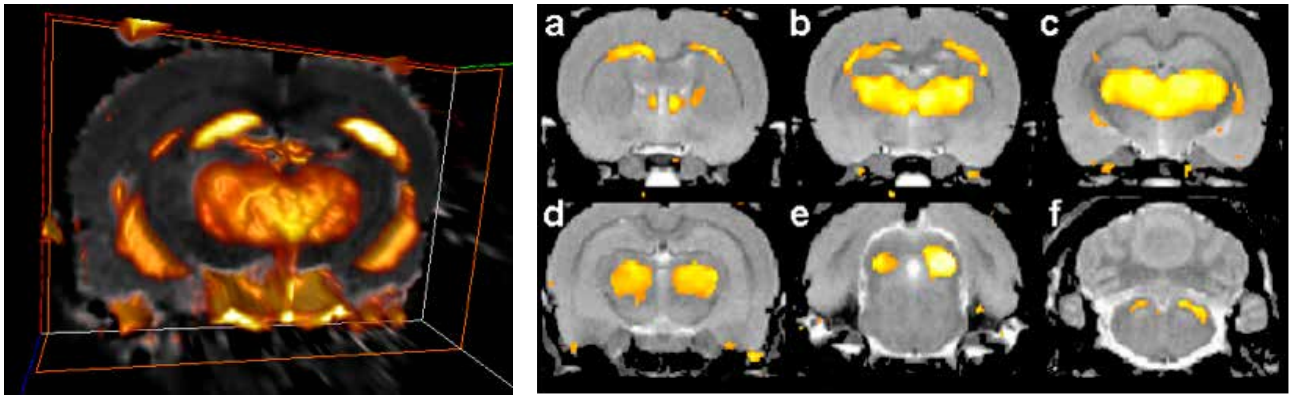
Oved K, Morag A, Pasmanik-Chor M, **Rehavi M**, Shomron N*, Gurwitz D*. (2013) Genome-wide expression profiling of human lymphoblastoid cell lines implicates integrin beta-3 in the mode of action of antidepressants. *Transl Psychiatry*. 3:e313.

Doron R, Lotan D, Einat N, Yaffe R, Winer A, Marom I, Meron G, Kately N, **Rehavi M** (2014) A novel herbal treatment reduces depressive-like behaviors and increases BDNF levels in the brain of stressed mice. *Life Sci*. 94:151-7

Dror V, **Rehavi M**, Biton IE, Eliash S. (2014) Rasagiline prevents neurodegeneration in thiamine deficient rats-A longitudinal MRI study. *Brain Res*. 1557:43-54

Kornilov P, Peretz A, Lee Y, Son K, Lee JH, Refaeli B, Roz N, **Rehavi M**, Choi S, Attali B. (2014) Promiscuous gating modifiers target the voltage sensor of Kv7.2, TRPV1, and Hv1 cation channels. *FASEB J*. 28:2591-602

Doron R, Lotan D, Versano Z, Benatav L, Franko M, Armoza S, Kately N, **Rehavi M** (2014) Escitalopram or novel herbal mixture treatments during or following exposure to stress reduce anxiety-like behavior through corticosterone and BDNF modifications. *PLoS One* 9:e91455



(A) Six representative coronal slices of T_2-weighted MR images from untreated thiamine-deficient rats on day 14. The yellow areas represent abnormalities characterized by a significant increase in signal intensity that occurred on day 14 as compared to day 0 (ANOVA, $p<0.01$). (a,b) thalamus and corpus callosum; (c,d) thalamus; (e) inferior colliculi; (f) superior cerebellar peduncle. (B) A Three-dimensional Maximum intensity projection (MIP) image of the T_2 maps, demonstrating the damaged thiamine-deficient areas on day 14.

Edut S, Rubovitch V, **Rehavi M**, Schreiber S, Pick CG. (2014) A study on the mechanism by which MDMA protects against dopaminergic dysfunction after minimal traumatic brain injury (mTBI) in mice. *J Mol Neurosci*. 54:684-97.

Simchon Tenenbaum Y, Weizman A, **Rehavi M**. (2015)The impact of chronic early administration of psychostimulants on brain expression of bdnf and other neuroplasticity-relevant proteins. *J Mol Neurosci*. 57.

Simchon-Tenenbaum Y, Weizman A, **Rehavi M**. (2015) Alterations in brain neurotrophic and glial factors following early age chronic methylphenidate and cocaine administration. *Behav Brain Res*. 282:125-32.

Hadar A, Milanesi E, Squassina A, Niola P, Chillotti C, Pasmanik-Chor M, Yaron O, Martásek P, **Rehavi M**, Weissglas-Volkov D, Shomron N, Gozes I, Gurwitz D. (2016) RGS2 expression predicts amyloid-β sensitivity, MCI and Alzheimer's disease: genome-wide transcriptomic profiling and bioinformatics data mining. *Transl Psychiatry* 6:e909.

Dr. Moran Rubinstein, Ph.D.

Department of Human Molecular Genetics and Biochemistry
Goldschleger Eye Research Institute

TEL AVIV UNIVERSITY

moranrub@post.tau.ac.il
URL: http://moranrub.wixsite.com/rubinsteinlab

The Molecular Basis of Epileptic Encephalopathies and Autism

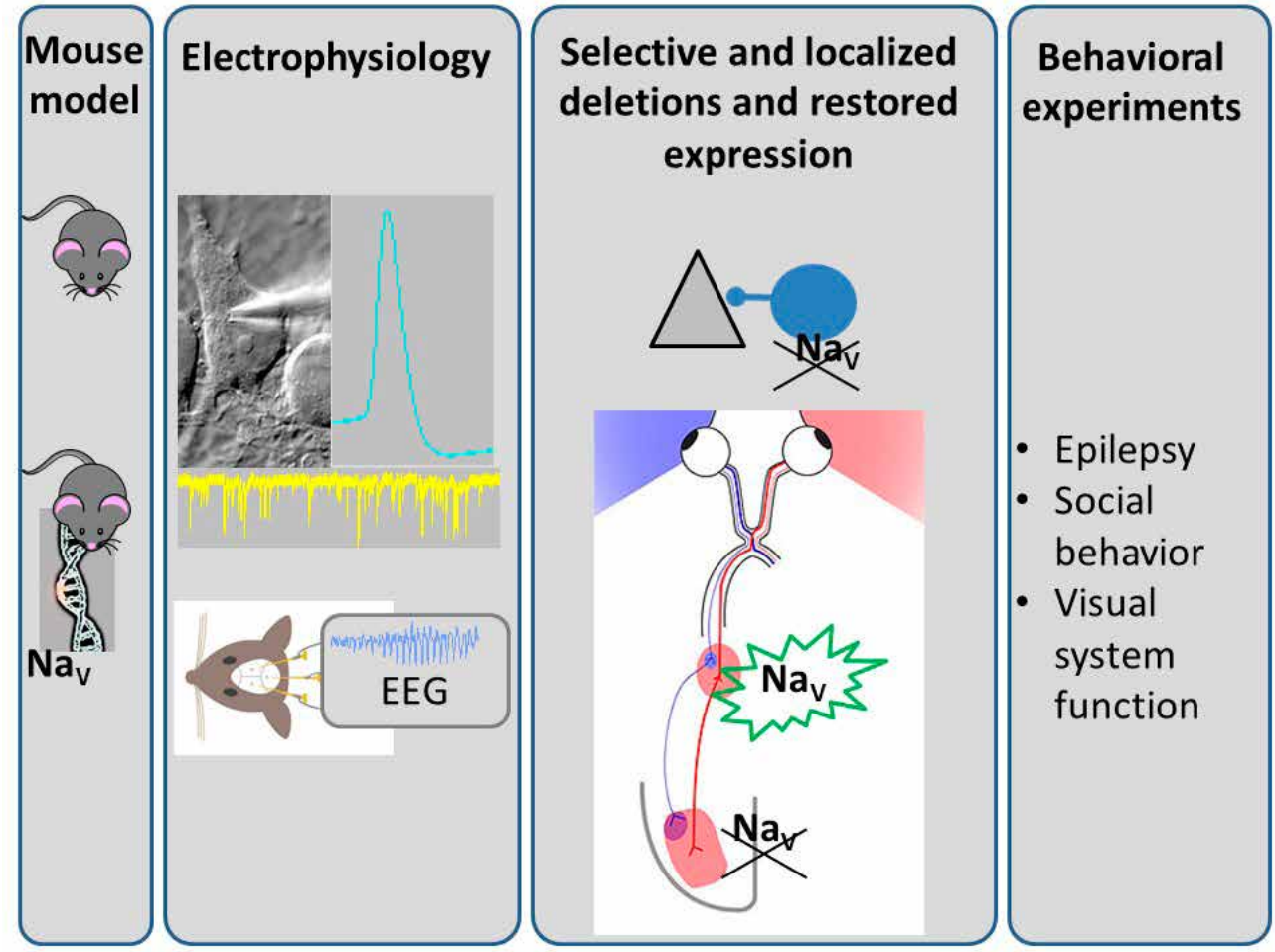
Position

Senior Lecturer, Sackler School of Medicine

Research

We study the neuronal and molecular basis of visual system abnormalities in severe epilepsy and autism. One out of every 68 children is diagnosed with an autism spectrum disorder, characterized by impaired social skills. Moreover, autistic features are observed in people suffering from epileptic encephalopathies, a group of severe disorders characterized by refractory seizures and cognitive deficit with limited treatment options and poor prognosis.

Visual system abnormalities are often observed in both disorders, ranging from lack of eye contact, through abnormal visual processing, to photosensitive seizures. The tremendous advancement in genetic studies helped to identify the involvement of many genes in the etiology of epilepsy and autism. However, our understanding of the pathways leading from a genetic mutation to abnormal brain function is still in its infancy.



Ion channels are molecular machines, crucial for transforming synaptic inputs into electrical response, controlling neuronal firing and neurotransmitter release. One of the pivotal families of ion channels are the voltage-gated sodium channels (Na_V). Indeed, mutations in multiple types of Na_V channels were identified in epilepsy and autism patients. However, connecting the dots between Na_V dysfunction and the resulting diseases have proven to be a formidable task.

In order to bridge this gap we harness the strength of mouse genetics, combined with electrophysiological recordings, to elucidate the molecular and neuronal basis of epilepsy and autism and to understand how genetic mutations in ion channels leads to these disorders. We use mouse models mimicking the human genetic mutation and unveil perturbations of neuronal function on cellular, network and behaving animal levels. Moreover, the contribution of different classes of neurons and different brain regions is tested using global and viral mediated localized selective genetic deletions. Finally, behavioral experiments are used to examine epilepsy, sociability and the function of the visual system.

Publications

Dascal, N., **Rubinstein, M**. Lithium reduces the span of G protein-activated K+ (GIRK) channels inhibition in hippocampal neurons. *Bipolar Disord*. In press.

Rubinstein, M., Patowary, A., Stanaway, I.B., McCord, E., Scheuer, T., Nickerson, D., Raskind, W.H., Wijsman, E.M., Bernier, R., Catterall, W.A. and Brkanac, Z. Association of rare missense variants in the second intracellular loop of NaV1.7 sodium channels with familial autism. *Mol Psych*. 2017.

Yakubovich, D., Berlin, S., Kahanovitch, U., **Rubinstein, M.**, Farhy-Tselnicker, I., Styr, B., Keren-Raifman, T., Dessauer, C.W., and Dascal, N. (2015). A quantitative model of the GIRK1/2 channel reveals that its basal and evoked activities are controlled by unequal stoichiometry of Gα and Gβγ. *PLoS Comp Biol* 11, e1004598.

Rubinstein, M., Han, S., Tai, C., Westenbroek, R.E., Hunker, A., Scheuer, T., and Catterall, W.A. (2015). Dissecting the phenotypes of Dravet syndrome by gene deletion. *Brain* 138, 2219-2233.

Rubinstein, M., Westenbroek, R.E., Yu, F.H., Jones, C.J., Scheuer, T., and Catterall, W.A. (2015). Genetic background modulates impaired excitability of inhibitory neurons in a mouse model of Dravet syndrome. *Neurobiol Dis* 73, 106-117.

Baek, J.H., **Rubinstein, M.**, Scheuer, T., and Trimmer, J.S. (2014). Reciprocal changes in phosphorylation and methylation of mammalian brain sodium channels in response to seizures. *J Biol Chem* 289, 15363-15373.

Kahanovitch, U., Tsemakhovich, V., Berlin, S., **Rubinstein, M.**, Styr, B., Castel, R., Peleg, S., Tabak, G., Dessauer, C.W., Ivanina, T., and Dascal, N. (2014). Recruitment of Gbetagamma controls the basal activity of G-protein coupled inwardly rectifying potassium (GIRK) channels: crucial role of distal C terminus of GIRK1. *J Physiol* 592, 5373-5390

Grants

2017 - 2022 ISF. Deciphering the neuronal and molecular basis of epileptogenesis and compensatory mechanisms in Dravet Syndrome

2017 - 2019 Fritz Thyssen Foundation. Unveiling the neuronal and network basis for visual system dysfunction in Dravet Syndrome

2017 – 2018 Jerome Lejeune Foundation. Unveiling the connection between epilepsy and intellectual disability in Dravet Syndrome.

Prof. Naphtali Savion, Ph.D.

Goldschleger Eye Research Institute
Department of Human Molecular Genetics and Biochemistry
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: eyeres@post.tau.ac.il
URL: http://www2.tau.ac.il/Person/medicine/researcher.asp?id=abfmlhgdk

Novel Antioxidant and Stem Cells for Treatment of Degenerative Diseases

Positions

Professor Emeritus, Sackler Faculty of Medicine

Director, Goldschleger Eye Research Institute

Chair, Maratier Institute for the Study of Blindness & Visual Disorders

Research

We are studying the potential of S-allylmercapto-N-acetylcysteine (ASSNAC) a newly developed derivative of allicin (the active component in garlic) to serve as a treatment for oxidative stress associated degenerative diseases. The research involves cell biology tools and animal models.

The following specific subjects are studied:

- Demonstrating the capacity of ASSNAC to activate the transcription factor Nrf2 resulting in up-regulation of the antioxidant cellular mechanisms that increases the protective capacity of cells against reactive oxygen species.
- Testing the potential of ASSNAC to modulate the bone marrow stem cells population and attenuate the clinical manifestations of neurodegenerative diseases, diabetes, and osteoporosis.
- Testing the potential of ASSNAC to attenuate ocular degenerative diseases such as cataract and light-induced retinal damage.

Publications

M. Tao, P. Yu, B.T. Nguyen, B. Mizrahi, **N. Savion**, G. Sukhova, F.D. Kolodgie, R. Virmani, C.K. Ozaki, J. Schneiderman. Locally applied leptin induces regional aortic wall degeneration in apoe deficient mice preceding aneurysm formation. Arterioscler. Thromb. Vasc. Biol. 33:311-20, 2013.

I. Ben Aharon, H. Bar Joseph, M. Tzabari, B. Shenkman, N. Farzam, M. Levi, R. Shalgi, S.M. Stemmer, **N. Savion**. Doxorubicin-induced vascular toxicity – Targeting potential pathways may reduce procoagulant activity. PLoS ONE, 8: e75157, 2013.

E. Asher, P. Fefer, M. Shechter, R. Beigel, D. Varon, B. Shenkman, **N. Savion**, H. Hod, S. Matetzky. Increased Mean Platelet Volume is Associated with Non-responsiveness to Clopidogrel. Thromb. Haemost. 112: 137-141, 2014

P. Fefer, R. Beigel, N. Rozenberg, M. Shechter, S. Gannot, D. Varon, **N. Savion**, S. Matetzky. Evaluation of Platelet Response to Different Clopidogrel Dosing Regimens in Patients with Acute Coronary Syndrome in Clinical Practice. Platelets, 26:126-131, 2015.

N. Savion, N. Izigov, M. Morein, S. Pri-Chen, S. Kotev-Emeth. S-Allylmercapto-N-acetylcysteine (ASSNAC) protects cultured nerve cells from oxidative stress and attenuates experimental autoimmune encephalomyelitis. **Neurosci. Lett.** 583:108-113, 2014.

I. Budnik, B. Shenkman, **N. Savion.** Synergistic effect of signaling from receptors of soluble platelet agonists and outside-in signaling in formation of a stable fibrinogen–integrin αIIbβ3–actin cytoskeleton complex. **Thromb. Res.**, 135:114-120, 2015.

M. Levi, M. Tzabari, **N. Savion**, S. M. Stemmer, R. Shalgi, I. Ben- Aharon. Dexrazoxane exacerbates doxorubicin-induced testicular toxicity. *Reproduction* 150:357–366, 2015.

I. Budnik, B. Shenkman, **N. Savion**. Role of G protein signaling in formation of the fibrin(ogen)–integrin αIIbβ3–actin cytoskeleton complex in platelets. Platelets, early online March 30, 2016.

M. Levi, A. Popovtzer, M. Tzabari, A. Mizrachi, **N. Savion**, S. M. Stemmer, R. Shalgi, I. Ben-Aharon. Cetuximab intensifies Cisplatin-induced testicular toxicity. Reprod Biomed Online 33:102-10, 2016.

D. Ben-Zvi, **N. Savion**, F. Kolodgie, A. Simon, S. Fisch, K. Schäfer, N. Bachner-Hinenzon, X. Cao,

A. Gertler, G. Solomon, E. Kachel, E. Raanani, J. Lavee, S. Kotev Emeth, R. Virmani, F.J. Schoen, J. Schneiderman. Local application of leptin antagonist attenuates Angiotensin II-induced ascending aortic aneurysm and cardiac remodeling. J. Am. Heart Assoc. 5:e003474; 2016.

Budnik I, Shenkman B, Hauschner H, Zilinsky I, **Savion N.** Role of heterotrimeric G proteins in platelet activation and clot formation in platelets treated with integrin αIIbβ3 inhibitor. Platelets. 13:1-5, 2017.

Prof. Inna Slutsky, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: islutsky@post.tau.ac.il

Regulation of Hippocampal Plasticity: Single Synapses to Alzheimer's Disease

Positions

Associate Professor, Sackler Faculty of Medicine

Editorial Board Member: *eLife*, *Scientific Reports*, *Frontiers in Cellular and Molecular Neuroscience*

Member, American Federation for Aging Research (AFAR) National Scientific Advisory Council

Member, Minerva grant committee

Member, Azrieli PhD fellowship committee;

Member, PhD program committee, Sagol School of Neuroscience

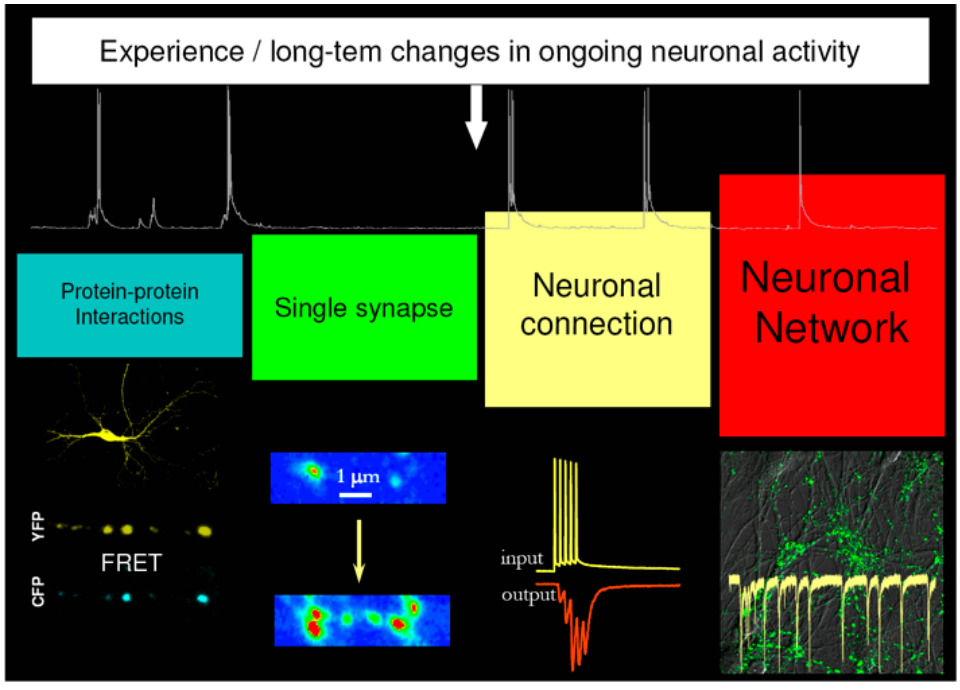
Member, Scientific Committee, Center of Nanoscience and Nanotechnology

Research

The research in the laboratory is focused on understanding the basic mechanisms underlying synaptic function and primary mechanisms initiating synaptic dysfunction at very early stages of Alzheimer's Disease. To achieve this goal, we developed an integrated system that enables simultaneous real-time visualization of structural reorganization in spatially-restricted signaling complexes and functional modifications of single synapses in brain circuits. Utilizing FRET spectroscopy, high-resolution optical imaging, electrophysiology, molecular biology, and biochemistry we explore experience-dependent mechanisms regulating the number and plasticity of hippocampal synapses under physiological and pathological conditions.

Publications

Wang Z, Jackson RJ, Hong W, Taylor WM, Corbett GT, Moreno A, Liu W, Li S, Frosch MP, **Slutsky I,** Young-Pearse T, Spires-Jones TL, Walsh DM. (2017) Human brain-derived Aβ oligomers bind to synapses and disrupt synaptic activity in a manner that requires APP. J Neurosci. pii: 2009-17.



Tao K, Xue B, Frere S, Slutsky I, Cao Y, Wang W, Gazit E. (2017) Multiporous supramolecular microspheres for artificial photosynthesis. Chem Mater. 29:4454-4460.

Milshtein-Parush H, Frere S, Regev L, Lahav C, Benbenishty A, Ben-Eliyahu S, Goshen I, **Slutsky I**. (2017) Sensory deprivation triggers synaptic and intrinsic plasticity in the hippocampus. Cereb Cortex. 27:3457-3470.

Segal-Gavish H, Gazit N, Barhum Y, Ben-Zur T, Taler M, Hornfeld SH, Gil-Ad I, Weizman A, **Slutsky I**, Niwa M, Kamiya A, Sawa A, Offen D, Barzilay R. (2017) BDNF overexpression prevents cognitive deficit elicited by adolescent cannabis exposure and host susceptibility interaction. Hum Mol Genet. 26:2462-2471.

Gazit N, Vertkin I, Shapira I, Helm M, Slomowitz E, Sheiba M, Mor Y, Rizzoli S, **Slutsky I**. (2016) IGF-1 receptor differentially regulates spontaneous and evoked transmission via mitochondria at hippocampal synapses, Neuron 89, 583-597.

Frere S., **Slutsky I**. (2016) Targeting PTEN interactions for Alzheimer's disease, Nature Neuroscience 19, 416-418.

Vertkin I, Styr B, Slomowitz E, Ofir N, Shapira I, Berner D, Fedorova T, Laviv T, Barak-Broner N, Greitzer-Antes D, Gassmann M, Bettler B, Lotan I, **Slutsky I**. (2015) GABAB receptor deficiency causes failure of neuronal homeostasis in hippocampal networks, Proc Natl Acad Sci USA 112, E3291-3299.

Slomowitz E, Styr B, Vertkin I, Milshtein-Parush H, Nelken I, Slutsky M, **Slutsky I**. (2015). Interplay between population firing stability and single neuron dynamics in hippocampal networks. Elife 4.

Fogel H, Frere S, Segev O, Bharill S, Shapira I, Gazit N, O'Malley T, Slomowitz E, Berdichevsky Y, Walsh Dominic M, Isacoff Ehud Y, Hirsch Joel A, **Slutsky I** (2014) APP homodimers transduce an amyloid-β-mediated increase in release probability at excitatory synapses. *Cell Reports*, 7: 1560-1576.

Becker W, Shcheslavkiy V, Frere S, **Slutsky I.** (2014) Spatially resolved recording of transient fluorescence-lifetime effects by line-scanning TCSPC. *Microsc Res Tech*. 77:216-24

Dolev I*, Fogel H*, Milshtein H, Berdichevsky Y, Lipstein N, Brose N, Gazit N, **Slutsky I** (2013) Spike bursts increase amyloid-beta 40/42 ratio by inducing a presenilin-1 conformational change. *Nature Neurosci*. 16: 587-595.

Review

Frere S, **Slutsky I.** (2016) Targeting PTEN interactions for Alzheimer's disease. Nat Neurosci. 19:416-8.

Grants

2013 – 2018 Israel Science Foundation

2014 – 2017 Heritage Legacy Fund and Israel Science Foundation

2014 – 2018 Binational US-Israel Science Foundation

2013 – 2018 Rosetrees Trust, UK

Prof. Arieh S. Solomon, M.D., Ph.D.

Goldschleger Eye Research Institute
Department of Ophthalmology
Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

E-mail: asolomon@post.tau.ac.il

Basic and Applicative Research of Eye Physiology, Diseases and Function

Positions

Associate Professor, Sackler Faculty of Medicine

Editorial Board, *Translational Vision Science & Technology (TVST)*

International Committee Member, ARVO

Research

The eye presents many challenges for research regarding unsolved conditions such as retinal and optic nerve assaults, damage to eye by surrounding conditions of work and every day activity.

The following specific subjects are studied:

- Optic nerve research: creating models of trauma and disease to investigate the mechanisms of degeneration and regeneration
- Investigate ways to treat corneal injury and diseases
- Ultraviolet light damage to the eye
- Research on the neovascular process in the eye and search ways to prevent it
- Occupational and environmental factors affecting eye and vision

Publications

Dvashi Z, Sar Shalom H, Shohat M, Ben-Meir D, Ferber S, Satchi-Fainaro R, Ashery-Padan R, Rosner M, **Solomon AS**, Lavi S. (2014) Protein phosphatase magnesium dependent 1a governs the wound healing-inflammation-angiogenesis cross talk on injury. Am J Pathol. 184:2936-2950.

Ohana R., Weiman-Kelman B., Shaul R.,Tamm E., Pasmanik-Chor M., Rinon A., Netanely D., Shamir R., **Solomon AS.,** Ashery-Padan R. MicroRNAs of the RPE arteial for RPE differentiation and photoreceptor maturation. Development, 2015;142:2487-98.

Tzameret A., Sher I., Belkin M, Treves AJ., Meir A., **Nagler A, Levkovicitch-Verbin H., Rotenstreich Y., Solomon AS.** Epiretinal transplantation of human bone marrow mesenchymal stem cells rescues retinal and vision function in a rat model of retinal degeneration. Stem Cell Res, 15:387-94.

Yuval C, Ben-Mair E, Rosenzweig E, Shechter- Amir D, **Solomon AS.** The effect of nocturnal CPAP therapy on the intraocular pressure of patients with Sleep Apnea Syndrome. Graephe's Arch Exp Clin Ophthal, 2015, 253:2263-2271.

Maharshak I, Salomon- Zimri S., Antes R,Liraz O., Nisgav Y., Livnat T., Weinberger D., Colton C., **Solomon AS,** Michaelson DM. The effect of the ApoE4 Genotype on the developing mouse retina. Exp Eye Res, 2015, 145:17-25.

Dr. Eran Stark, M.D., Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

www.eranstarklab.com
Email: eranstark@post.tau.ac.il

Spiking Network Mechanisms Underlying Cognition

Position

Senior Lecturer, Sackler Faculty of Medicine and Sagol School of Neuroscience

Research

We study the way neuronal networks give rise to function. There are many levels to approach this topic and we are interested at the spiking level, mainly in local circuits of free, behaving animals. We focus on short-term memory and spatial navigation in rodents. For this, we are continuously developing technologies to interface bi-directionally with the intact brain at the spatiotemporal resolution of a single neuron and a single spike. Our mechanistic approach involves high-density recording and manipulation of dozens to hundreds of neurons simultaneously, while freely moving rodents perform cognitive tasks. By erasing and writing individual spikes of multiple neurons in real time, we precisely modify network-spiking activity during specific epochs (for instance, short term memory maintenance), and study the effects on behavior (memory deterioration or boosting).

Publications

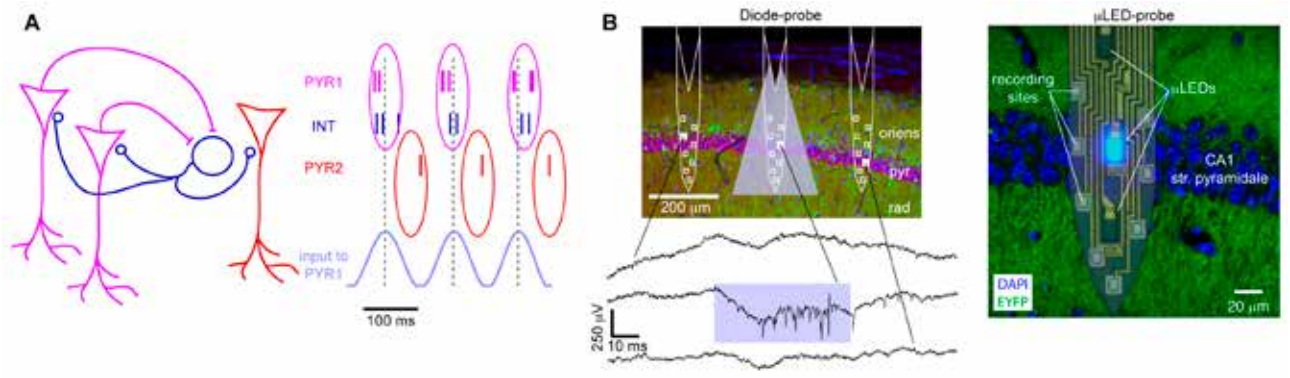
Roux L, Hu B, Eichler R, **Stark E**, Buzsáki G (2017) Sharp wave ripples during learning stabilize hippocampal spatial map. *Nat Neurosci*, 20(6):845-853.

Platkiewicz J, Stark E, Amarasingham A (2017) Spike-centered jitter can mistake temporal structure. *Neural Comp*, 29(3):783-803

Kampasi K, **Stark E**, Seymour J, Na K, Winful HF, Buzsáki G, Wise KD, Yoon E (2016) Fiberless multicolor neural optoelectrode for in vivo circuit analysis. *Scientific Reports*, 6:30961

Wu F*, **Stark E***, Ku P, Wise K, Buzsáki G, Yoon E (2015) Monolithically integrated µLEDs on silicon neural probes for high-resolution optogenetic studies in behaving animals. *Neuron*, 88:1136-1148.

Stark E, Roux L, Eichler R, Buzsáki G (2015) Local generation of multi-neuronal spike sequences in the hippocampal CA1 region. *Proc. Natl. Acad. Sci. USA* 112:10521-6.



A. Dynamic segregation of neuronal networks into cell assemblies. In the freely-moving mouse, external input is applied to one group of excitatory pyramidal cells (PYR1), which drive inhibitory cells (INT), which then inhibit a second group (PYR2). At certain input frequencies, inhibition actually *induces* spiking in PYR2. The activity of the PYR1 and PYR2 assemblies (each of which may represent a distinct memory) is thus linked and multiplexed in time. **B. Hardware for recording and manipulating circuit elements in freely moving animals.** A *diode-probe* device consists of multiple optical fibers, each coupled to a distinct light source and associated with a distinct electrode array. In animals that express light-senstive ion channels (opsins), light applied at one site induces spiking of multiple cells only at that site. *µLED-probes* take spatial resolution one step further by implanting neuron-sized diodes directly in the brain.

English D, Peyrache A, **Stark E**, Roux L, Vallentin D, Long M, and Buzsáki G (2014) Excitation and inhibition compete to control spiking during hippocampal ripples: intracellular study in behaving mice. *J. Neurosci.* 34:16509-16517.

Stark E*, Roux L*, Eichler R*, Senzai Y, Royer S, Buzsáki G (2014) Pyramidal cell-interneuron interactions underlie hippocampal ripple oscillations. *Neuron* 83:467-80.

Berenyi A, Somogyvari Z, Nagy A, Roux L, Long J, Fujisawa S, **Stark E**, Leonardo A, Harris T, Buzsáki G (2014) Large-scale, high-density (up to 512 channels) recording of local circuits in behaving animals. *J. Neurophysiol.* 111:1132-49.

Stark E, Eichler R, Roux L, Fujisawa S, Rotstein H, Buzsáki G (2013) Inhibition-induced theta resonance in cortical circuits. *Neuron* 80:1263-76.

Wu F, **Stark E**, Im M, Cho IJ, Yoon ES, Buzsáki G, Wise KD, Yoon E (2013) An implantable neural probe with monolithically integrated dielectric waveguide and recording electrodes for optogenetic applications. *J. Neural Eng.* 10:056012.

Reviews

Buzsáki G, **Stark E**, Berenyi A, Khodagholy D, Kipke DR, Yoon E, Wise K (2015) Tools for probing local circuits: high-density silicon probes combined with optogenetics. *Neuron* 86:92-105.

Roux L, **Stark E**, Sjulson L, Buzsáki G (2014) In vivo optogenetic identification and manipulation of GABAergic interneuron subtypes. *Curr. Opin. Neurobiol.* 26C:88-95.

Grants

2016-2021	ERC Starting Grant
2016-2020	CRCNS (NSF-BSF) Grant
2016-2020	ISF Grant
2017-2020	Rosetrees Grant
2017-2019	ISF Bikura Grant

Dr. Ido Tavor, Ph.D.

Department of Anatomy and Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: idotavor@post.tau.ac.il

Functional and Structural Brain Connectivity using MRI

Positions

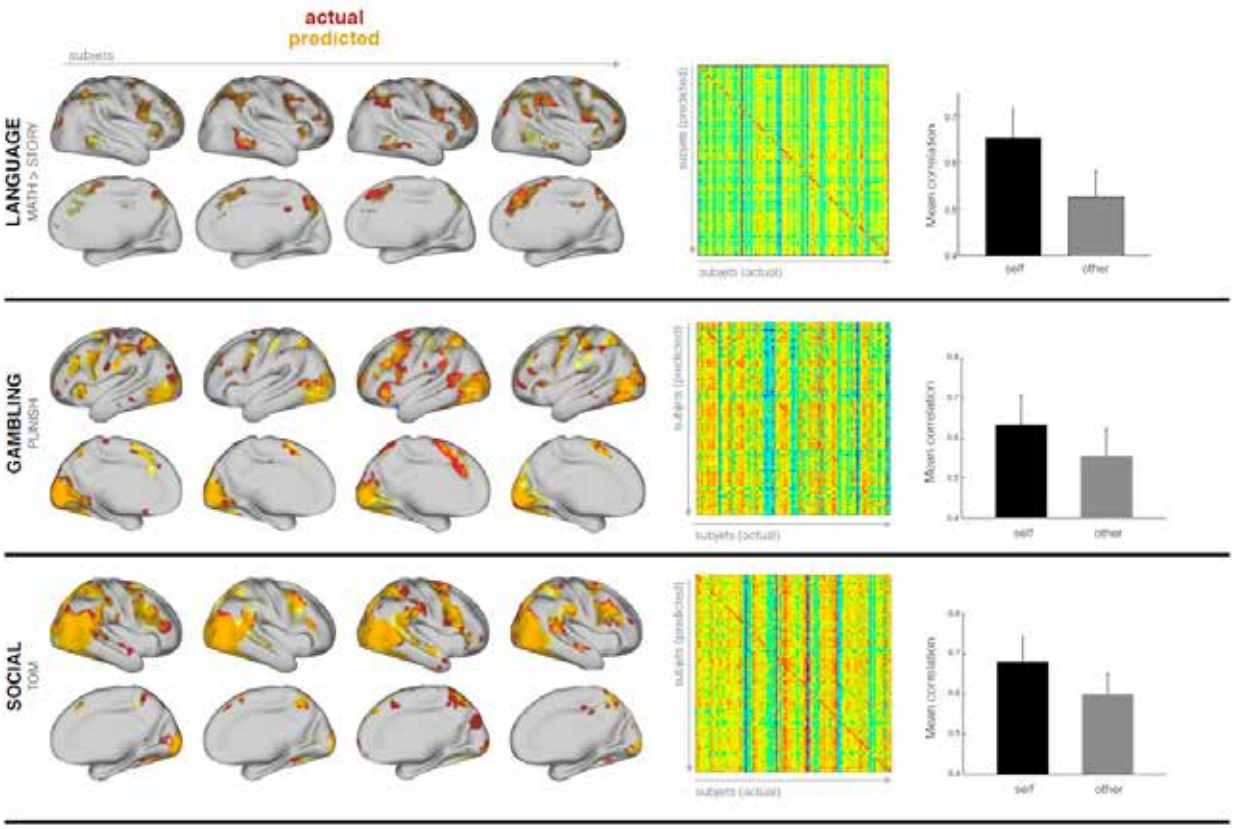
Senior Lecturer, Sackler Faculty of Medicine

Faculty member, Sagol School of Neuroscience

Research

Work in our lab is focused on exploring the relations between brain structure, function and behavior using magnetic resonance imaging (MRI). We're using state-of-the-art MRI methodologies to study inter- and intra- subject variability in brain connectivity and use behavioral experiments to study whole-brain neuroplasticity.

Specifically, we develop models to predict individual differences in brain activity and human behavior from brain structure and connectivity measurements. We also study learning-related brain plasticity by developing behavioral tasks that induce functional and structural brain modifications and investigate the underline mechanisms of functional neuroplasticity as measured with fMRI. We also work on advanced statistical modeling of MRI data.



Predicting individual differences in brain activation in a variety of tasks: Examples for tasks in the language, decision making and social domains are shown for 4 representative subjects, where actual activation is shown in red and predicted activation in yellow. The specificity of prediction is demonstrated by the connectivity matrix between true and predicted activation maps of 100 subjects (note the pronounced diagonality of the correlation matrix).

Publications

I. Tavor, S. Hofstetter, Y Assaf. Micro-structural assessment of short term plasticity dynamics. *NeuroImage* 81, 1-7, 2013

S. Hofstetter, **I. Tavor**, S. Tzur Moryosef, Y. Assaf. Short-Term Learning Induces White Matter Plasticity in the Fornix. *Journal of Neuroscience* 33, 12844-50, 2013

I. Tavor, M. Yablonski, A. Mezer. S. Rom, Y Assaf and G. Yovel. Separate parts of occipito-temporal white matter fibers are associated with recognition of faces and places. *NeuroImage* 86, 123-30, 2014

A. Horowitz, D. Barazany, **I. Tavor**, M. Bernstein, G. Yovel and Y. Assaf. In vivo correlation between axon diameter and conduction velocity in the human brain. *Brain Structure and Function* 220, 1-12, 2015

A. Horowitz, D. Barazany, **I. Tavor**, G. Yovel and Y. Assaf. Response to comments on the paper by Horowitz et al. *Brain Structure and Function* 220, 1791, 2015

D. Joel, Z. Berman, **I. Tavor**, N. Wexler, O. Gaber, Y. Stein, N. Shefi, J. Pool, S. Urchs, D.S. Margulies, F. Liem, J. Hänggi, L. Jäncke, Y. Assaf, 2015. Sex beyond the genitalia: The human brain mosaic. *Proc. Natl. Acad. Sci. USA* 15468-73, 2015

I. Tavor, O. Parker Jones, R.B. Mars, S.M. Smith, T.E. Behrens, S. Jbabdi. Task-free MRI predicts individual differences in brain activity during task performance. *Science* 352, 216-220, 2016

Nursing, Occupational and Physical Therapy

Dr. Michal Avrech Bar, Ph.D., O.T.

Department of Occupational Therapy
Steyer School of Health Professions

TEL AVIV UNIVERSITY

Email: michaavr@post.tau.ac.il

Occupational Science: Investigating Occupations, Health and Well-Being Among Women

Positions

Lecturer, Sackler Faculty of Medicine

Committee Member, Occupational Science Europe Research Committee

Research

Occupational Science is the study of human participation. Research in this area focuses on specific populations and their unique challenges to engage in meaningful occupations. Our primary area of research is exploring the relationship between engagement in occupations, health and well-being among women, especially as related to the role of motherhood. We focus on the effect of occupational performance on life satisfaction and perceived physical and mental health in various life-changing situations. The populations that we study include women who experienced a major change in their lives (such as transgender women or becoming a caregiver), women diagnosed with illness or having a disability, mothers of children who were diagnosed with Autism Spectrum Disorder (ASD) or Attention Deficit Hyperactivity Disorder (ADHD), and healthy mothers from different cultures/religions.

Our second area of research is developing and evaluating advanced teaching methods in occupational therapy, specifically, testing the contribution of Problem-Based Learning (PBL) to the development of students' learning skills, knowledge, communication skills and success in clinical fieldwork studies.

Publications

Avrech Bar, M., Rubin, V., Gavrieal-Tyjchman, G., & Jarus, T. (2013). The validity and reliability of the modified version of the Role Checklist (M-RCL). *Scandinavian Journal of Occupational Therapy*, *20*, 454-462.

Lipskaya-Velikovsky, L., **Avrech Bar, M.**, & Bart, O. (2014). Context and psychosocial intervention in mental health. *Scandinavian Journal of Occupational Therapy*, *21*, 136-144.

Avrech Bar, M., & Jarus, T. (2015). The effect of engagement in everyday occupations, role overload and social support on health and life satisfaction among mothers. *International Journal of Environmental Research and Public Health, 12*, 6045-6065.

Avrech Bar, M., Jlole Majadla, S. & Bart, O. (2015). Managing everyday occupations as a predictor of health and life satisfaction among mothers of children with ADHD. *Journal of Attention Disorders*, 1087054715601211.

Avrech Bar, M., Shelef, L., & Bart, O. (2016). Do participation and self-efficacy of mothers to children with ASD predict their children participation? *Research in Autism Spectrum Disorders, 24*, 1-10.

Avrech Bar, M., Jarus, T., Wada, M., Rechtman, L., & Noy, E. (2016). Male-to-female transitions: Implications for occupational performance history, health, and life satisfaction. *Canadian Journal of Occupational Therapy, 83*, 72-82.

Avrech Bar, M., Forwell, S., & Backman, C. (2016). Ascribing meaning to occupation: An example from healthy, working mothers. *OTJR: Occupation, participation and Health, 36, 148-158.*

Avrech Bar, M., Ratzon, N. Z. (2016). Enhancing occupational therapy students' knowledge, competence, awareness, and interest in accessibility. *Hong Kong Journal of Occupational Therapy*, *27*, 18-25.

Avrech Bar, M., Pade, M., Jarus, T., Gat, S., Kaufman Cohen, Y. & Lipskaya-Velikovsky, L. (2017). Problem-Based learning in occupational therapy curriculum – Implications and challenges. *Disability and Rehabilitation*, 10.1080/09638288.2017.1325942.

Rand, D., Givon, N., & **Avrech Bar, M**. (2017). A video-game group intervention: Experiences and perceptions of adults with chronic stroke and their therapists. *Canadian Journal of Occupational Therapy* (in press).

Dr. Tami Bar-Shalita, Ph.D., O.T.

Department of Occupational Therapy
School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: tbshalita@post.tau.ac.il

Investigating Sensory Modulation Disorder (SMD) Over Life Span

Positions

Lecturer, Sackler Faculty of Medicine

Research

SMD is a health condition in which abnormal responses to naturally occurring stimuli is demonstrated in a manner that interferes with daily life, affecting 10% of otherwise healthy individuals. Our lab studies a unique perspective associating SMD with pain. Our research is aiming to better understand the underlying mechanisms by identifying biomarkers that would specify this health condition, applying psychophysical and neurophysiological methodologies in children and adults. New biomarkers found guide new therapeutic modalities for this population, ameliorating intervention opportunities: Specifically we are developing a neurofeedback system for treating SMD, based on our findings of EEG components that characterize individuals with SMD.

Moreover, in trying to understand the potential role of SMD in neurodevelopmental and other disorders trajectories, we study SMD as a risk factor in other health conditions such as chronic pain, mental health, substance abuse, and neurodevelopmental disorders.

Research is performed in the Sensory Integration Laboratory at TAU and in hospitals.

Publications

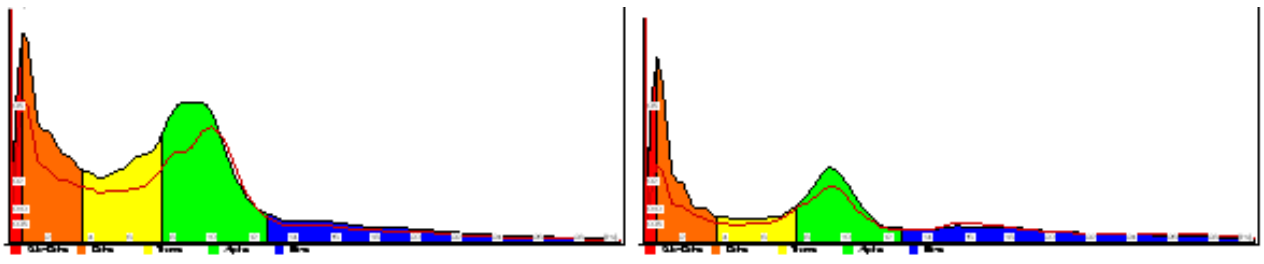
Weissman-Fogel I, Granovsky Y, **Bar-Shalita T**. Sensory over-responsiveness among healthy subjects is associated with a pronociceptive state. Pain Pract. 2017, doi: 10.1111/papr.12619.

Bart O, **Bar-Shalita T**, Mansour H, Dar R. Relationships among sensory responsiveness, anxiety, and ritual behaviors in children with and without atypical sensory responsiveness. Phys Occup Ther Pediatr. 2017, 37:322-331.

Bart O., **Bar-Shalita, T**., Darr, R. Relationships among sensory responsiveness, anxiety, and ritual behaviors in children with and without atypical sensory responsiveness. Phys Occ Ther Ped. 2016:1-10.

Bar-Shalita, T., Cermak, S. Atypical sensory modulation and psychological distress in the general population. Am J Occ Ther. 2016, 70: 1-9.

Lipskaya-Velikovsky, L., **Bar-Shalita, T.,** Bart, O. Sensory modulation and daily-life participation in people with schizophrenia. *Comp Psych*. 2015, 58:130-137



EEG of resting state (5 min) in controls and SMD adults recorded from frontal and central cortical sites demonstrated lower power cortical oscllations at δ (orange), β (yellow) and a (green)

Bar-Shalita, T., Deutsch, L., L Honigman, L., Weissman-Fogel, I. Ecological aspects of pain in sensory modulation disorder. Res Dev Disabil. 2015, 45–46: 157–167.

Bar-Shalita, T., Vatine, J.J., Yarnitsky, D., Parush, S., Weissman-Fogel, I. Atypical central pain processing in sensory modulation disorder: absence of temporal summation and higher after-sensation. Exp Brain Res. 2014, 232: 587-595.

Bar-Shalita, T., Vatine, J.J., Yanitsky, D., Parush, S., Weissman-Fogel, I. (2014) Atypical central pain processing in sensory modulation disorder: absence of temporal summation and higher after-sensation. Exp Brain Res 232, 587-595.

Bar-Shalita, T., Parush,S. Pain and sensory modulation disorder (abstracts from the Gerry Schwartz and Heather Reisman 3rd International Conference). Int J Child Health Hum Dev 2013;6:385

Bar-Shalita, T., Boni, O., Gevir, D., & Doryon, Y. (2013). The Israeli Occupational Therapy Code of Ethics. The Israeli Occupational Therapy National higher professional committee, Israel's Occupational Therapy Association.

Prof. Sivia Barnoy, R.N., Ph.D.

Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: sivia@post.tau.ac.il

Nursing Genetics and Information Technologies

Positions

Associate Professor, Sackler Faculty of Medicine

Research

Our research focuses on two main fields: 1. Genetics 2. Nursing and Information Technologies

In genetics our interest is in factors influencing individual decision-making on taking genetic tests. The decision whether or not to take a test may be influenced by factors relating to the illness tested for such as its severity or how far it can be controlled, or by personality factors such as risk-perception and optimism, or by the identity of the agent recommending the test (doctor or nurse) and their perceived epistemic authority. In a series of studies we are currently conducting we are trying to find linkages between these factors and the decision whether or not to take genetic tests.

Another issue being studied is the question "to whom does genetic information belong?" Genetic information is of importance to the tested individual's family as well as to them self. However, not all test subjects share the findings with their relatives. In a large-scale study, conducted together with Dr. Roy Gilbar of the Leicester University and funded by the Israel Cancer Association we examined the attitudes, opinions and behavioral intentions of genetic counselees regarding the disclosure of their genetic information to their families. We are planning a qualitative study to examine views of genetic counselors on this topic.

Information Technologies: Due to the rise of internet technology, medical information is no longer the exclusive property of medical service givers – it is now accessible to everybody— and this new situation has an effect on patient-caregiver relations. Among the research studies we are carrying out, we have investigated the attitudes of nurses towards patients who come forward with information found on the web, what affects those attitudes, and the reactions of nursing teachers to students who bring such information to class. Up to now, most research into this issue has concentrated on the professional caregiver's point of view. We wish to turn the spotlight onto the patient's point of view, and on how they feel after bringing Internet information to an appointment with their doctor or nurse.

Publications

Itzhaki, M., Bar-Tal, Y. & **Barnoy, S**. (2013). Staff and lay people's reactions to family presence during resuscitation: The effect of blood, resuscitation outcome and gender – a quasi-experimental study. *Journal of Advanced Nursing*

Itzhaki, M., Bluvstein, I., Raz, S. and **Barnoy, S**. (2013). Factors affecting the actions and emotional reactions of nursing teachers following encounters with students who present them with Internet Information. *Nursing Education Today*, 33, 8842–846.

Elkind, E Vaisid, T., Kornspan, J. D., **Barnoy, S**., Rottem, S. & Kosower, N.S. (2012)**.** Calpastatin upregulation in *Mycoplasma hyorhinis*-infected cells is promoted by the mycoplasma lipoproteins via the NF-kB pathway. *Cellular Microbiology,* 14:840-851.

Gilbar, R. & **Barnoy, S.** Disclosure of genetic information to relatives in Israel: between privacy and solidarity. (2012). *New Genetics and Society*, 31:391-407.

Skirton, H., **Barnoy, S**. Erdem, Y., Ingvoldstad, C., Pestoff, R., Teksen, F. & Williams, J. (2012). Suggested components of the curriculum for nurses and midwives to enable them to develop essential knowledge and skills in genetics. *Journal of Genetic Counseling*, 3:323-9.

Prows, C. A., Hopkin, R. J., **Barnoy, S.** & Van Riper, M. (2013). An update of childhood genetic disorders. *Journal of Nursing Scholarship,* 45, 34-42.

Tabak, N., Itzhaki, M., Sharon, D. and **Barnoy, S**. (2013). Intentions of nurses and nursing students to

tell the whole truth to patient and family members. *Journal of Clinical Nursing*, 22, 1434-1441.

Menshadi, N., Bar-Tal, Y. and **Barnoy, S.** (2013). The relationship between learned resourcefulness and cancer related fatigue in patients suffering from Non-Hodgkin's Lymphoma. *Oncology Nursing Forum*, 40, 133-138.

Kagan, I. and **Barnoy, S.** (2013). Organizational culture safety and medical error reporting by Israeli nurses. *Journal of Nursing Scholarship,* 45, 273-280.

Gilbar R, Shalev S, Spiegel R, Pras E, Berkenstadt M, Sagi M, Ben-Yehuda A, Mor P, Perry S, Zaccai TF, Borochowitz Z, **Barnoy S**. (2016) Patients' attitudes towards disclosure of genetic test results to family members: the impact of patients' sociodemographic background and counseling experience. *J Genet Couns*. 25, 314-324.

Itzhaki, M., Hildesheimer, G., **Barnoy, S**. & Katz, M. (2016) Family involvement in medical decision making: Perceptions of nursing and psychology students. *Nurse Education Today*, 40, 181-187.

Peles-Bortz, A., Bluvstein, I., Bergman, L. & **Barnoy, S.** (2016). Suspicion of gynecologic malignancy: Support resources for women before gynecological surgery. *Women & Health*, In press.

Itzhaki, M., Meridian, O., Schifter-Sagiv, T. & **Barnoy, S**. (2016). Nursing students' attitudes and intention to work with mentally ill patients before and after a planned intervention. *Academic Psychiatry*, In press.

Bar-Tal, Y. and **Barnoy, S**. Factors Influencing Participants' Decision to Comply with Nurse Recommendations. *Nursing Inquiry*. In press.

Warshawski, S., Barnoy, S. & Itzhaki, M. Factors associated with nursing students' resilience: communication skills course, use of social media and satisfaction with clinical placement. Journal of Professional Nursing, 33:157.

Niv, G., Bar-Josef, S., Ben Bassat, O., Avni, I., Lichtenshtein, L., Niv, Y., **Barnoy, S.** (2017). Quality of life and uncertainty in Crohn's disease. *Quality of Life Research*, 26(6),1609–1616.

Barnoy, S., Biton, A., Itzhaki, M. (2017). Social inclusion of children with Down syndrome: Jewish and Muslim mothers' knowledge, attitudes, beliefs, and behavioral intentions. *Journal of Pediatric Nursing*, 35, 50-56.

Kardosh, M., Bar-Tal, Y., **Barnoy, S**. (2017). The relationship between body image, gender, subjective norms and the decision to undergo preventive mastectomy among Arab and Jewish BRCA carriers. *Cancer Nursing*. In press.

Warshawski, S., **Barnoy, S**., Kagan, I. Generation, gender and professional differences in perception of organizational values. *Journal of Interprofessional Care*, In press.

Asman, O., Melnikov, S., **Barnoy, S**., Tabak, N. (2017). perceptions and experiences of registered nurses regarding research ethics and misconduct. *Nursing Ethics*. In press.

Dr. Orit Bart, Ph.D., OTR

Department of Occupational Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: oritbert@post.tau.ac.il

Co-Morbidity of Sensory-Motor and Cognitive Dysfunction and Psychosocial Problems

Positions

Senior Lecturer, Sackler Faculty of Medicine

Chair, Department of Occupational Therapy

Member, Israeli National Board for Certification of Occupational Therapy – Ministry of Health

Member, National Advisory Committee on Services for Child Development – Ministry of Health

Research

Our research is focused on the association between sensory-motor function and psychological aspects (anxiety, sense of coherence, hope, loneliness, etc.) of typically developed children and children with developmental problems such as Developmental coordination disorder (DCD), Attention Deficit Hyperactive Disorder (ADHD), and Sensory Processing Disorder (SPD). In the studies I conduct I try to learn and understand more about the mechanism behind the co-morbidity of sensory-motor dysfunctions and psychosocial problems. Further more, there are some studies where we assess the efficacy of sensory-motor intervention and its influence on the psychological behavior of the treated children.

Another related topic that is in the focus of my research is children's participation. According to the International Classification of Functioning, Disability and Health (ICF, 2001), Participation is relatively a new concept that reflects a new approach to functioning and serves as an outcome measure. Therefore we developed a questionnaire to assess pre-school children's participation. We are now developing additional questionnaires to assess infants, preschoolers and school age participation. We are running a few studies to assess differences in participation patterns of children with various developmental problems. Moreover I have started to investigate the influence of Occupational Therapy (OT) intervention and sensory-motor approaches on children's satisfaction and participation.

Publications

O. Bart, D. Tzafrir, S. Averbuch. Validation of the Israeli version of the rivermead behavioral memory test for children following acquired brain injury. *Journal of Head Trauma Rehabilitation*. 28, 419-425, 2013.

L. Rosenberg, **O. Bart**, N. Ratzon, T. Jarus. Personal and environmental factors predict participation of children with and without mild developmental disabilities. *Journal of Child and Family Stud*ies, 22, 658-671, 2013.

O. Bart, L, Liberman, N. Ratzon. The profile of performance skills and emotional factors in the context of participation among young children with Developmental Coordination Disorder. *Research in Developmental Disabilities*, 34, 87-94, 2013.

O. Bart, L. Daniel, Y. Bar-Haim. Influence of methylphenidate on motor performance in children with Developmental Coordination Disorder and Attention Deficit Hyperactive Disorder. *Research in Developmental Disabilities*, 34, 1922-1927, 2013.

I. Morag, **O. Bart**, R. Raz, S. Shayevitz, T. Strauss, S. Zangen, J. Kuint, L.Gabis. Developmental characteristics of late preterm infants at six and twelve months: a prospective study. Infant Behavior & Development, 36, 451– 456, 2013.

L. Rosenberg, **O. Bart**, NZ. Ratzon, T. Jarus. Complementary contribution of parents and therapists to child's assessment process. *Australian Occupational Therapy Journal*, 60, 410-415, 2013.

L. Lipskaya-Velikovsky, M. Avrech Bar, **O. Bart**. Context and psychosocial intervention in mental health. *Scandinavian Journal of Occupational Therapy.* 21, 136-144, 2014.

O. Bart, S. Raz, O. Dan. Reliability and validity of the online continuous performance test among children. *Assessment*. 21, 637-643, 2014.

L. Gabis, K. Hacham- Pilosof, O.Bar Yosef, G. Rabinovitz, G. Leshem, A. Shilon- Hadassa, Y. Biran, B. Reichmana, J. Kuint, **O. Bart**. The influence of a multi-sensory intervention for preterm infants, provided by parents, on developmental abilities and on parental stress levels. *Journal of Child Neurology*. 30, 896-903, 2015.

L. Lipskaya-Velikovsky**,** T. Bar-Shalita, **O. Bart**. Sensory modulation and daily-life participation in people with schizophrenia. *Comprehensive Psychiatry*. 58, 130-137, 2015.

M. Avrech Bar, L. Shelef, **O. Bart**. Do participation and self-efficacy of mothers to children with ASD predict their children's participation? *Research in Autism Spectrum Disorder.* 24, 1-10, 2016.

M. Avrech Bar, S. Jlole Majadla, **O. Bart**. Managing everyday occupations as a predictor of health and wellbeing among mothers of children with ADHD**.** *Journal of Attention Disorders,* 2015.

L. Rosenberg, **O. Bart**. Different pathways to children's enjoyment of participation in daily activities. *Scandinavian Journal of Occupational Therapy*, 2016.

O. Bart, T. Bar-Shalta, H. Mansour, R. Dar. Relationships among sensory responsiveness, anxiety and ritual behaviors in children with and without Atypical Sensory Responsiveness. *Physical and Occupational Therapy in Pediatrics,* 2016.

A. Mimouni Bloch, M. Tsadok-Cohen, **O. Bart.** Motor difficulties and their effect on participation in school-aged children**.** *Journal of Child Neurology,* 2016.

L. Rosenberg., A. Moran, **O. Bart**. The associations among motor ability, social-communication skills, and participation in daily life activities in children with low-functioning autism spectrum disorder. *Journal of Occupational Therapy, Schools & Early Intervention.*, 2017.

L. Rosenberg, Shani Jacobi, **O. Bart**. Executive functions and motor ability contribute to children's participation in daily activities. *Journal of Occupational Therapy, Schools, & Early Intervention*, 2017.

Bart O, Bar-Shalita T, Mansour H, Dar R. Relationships among sensory responsiveness, anxiety, and ritual behaviors in children with and without atypical sensory responsiveness. Phys Occup Ther Pediatr. 2017, 37:322-331.

Prof. Ruth Defrin, Ph.D.

Department of Physical Therapy
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: rutidef@post.tau.ac.il

Investigating Pain Perception and Mechanisms of Chronic Pain

Position

Professor, Sackler Faculty of Medicine

Director, Biomed@TAU Pain Research Hub

Research

We study the perception of pain among healthy subjects as well as among individuals with mental disorders and cognitive impairments. We are interested in the manner with which the brain processes various temporal and spatial aspects of painful evens and in inter-personal differences in pain perception.

We are also interested in the underlying mechanisms of chronic pain that develops after traumatic events. These include physical injuries such as spinal cord injury, brain injury and brain stroke as well as psychological traumas such as shell shock, captivity and torture. We are particularly interested in the effects of stress on the function of the pain system in these conditions and in healthy subjects.

We use state of the art devices such as computerized thermal stimulators, mechanical and electrical stimulators and a recording system for event related brain potentials. We perform experiments in the pain laboratory at TAU and in hospitals.

Publications

Levy D, Abdian L, Dekel-Steinkeller M, **Defrin R.** Experimental evidence for weaker endogenous inhibition of trigeminal pain than extra-trigeminal pain in healthy individuals. Cephalalgia. 2017:333102417735851.

Ginzburg K, Biran I, Aryeh IG, Tsur N, **Defrin R.** Pain perception and body awareness among individuals with borderline personality disorder. J Pers Disord. 2017; 13:1-18.

Tsur N, Shahar G, **Defrin R.** Lahav Y, Ginzburg K. Torturing personification of chronic pain among torture survivors. J Psychosom Res. 2017; 99:155-161.

Benromano T, Pick CG, Granovsky Y, **Defrin R.** Increased evoked potentials and behavioral indices in response to pain among individuals with intellectual disability. Pain Med. 2017.

Tsur N, **Defrin R.** Ginzburg K. Posttraumatic stress disorder, Orientation to pain, and pain perception in ex-prisoners of war who underwent torture. Psychosom Med. 2017;79(6):655-663.

Hadid A, Katz I, Haker T, Zeilig G, **Defrin R.** Epstein Y, Gefen A. Effect of load carriage on upper limb performance. Med Sci Sports Ex. 2017; 49:1006-1014.

Granovsky Y, Raz N, **Defrin R.** Electrophysiological and psychophysical correlates of spatial summation to noxious heat: the possible role of A-delta fibers. Ex Brain Res. 2017; 235:639-646.

Defrin R. Lahav Y, Solomon Z. Dysfunctional pain modulation in trauma survivors: the mediating effect of PTSD. J Pain 2017; 18:1-10.

Geva N, Pruessner J, **Defrin R.** Triathletes lose their advantageous pain modulation under acute psychosocial stress. Med Sci Sports Ex. 2017; 49:333-341.

Benromano T, Pick CG, Merick J, **Defrin R.** Physiological and behavioral responses to calibrated noxious stimuli among individuals with cerebral palsy and intellectual disability. Pain Med. 2017; 18:441-453.

de Tommaso M, Arendt-Nielsen L, **Defrin R.** Kunz M, Pickering G, Valeriani M. Pain assessment in neurodegenerative diseases. Behav Neurol. 2016; 2016:2949358.

de Tommaso M, Arendt-Nielsen L, **Defrin R.** Kunz M, Pickering G, Valeriani M. Pain in neurodegenerative disease: Current knowledge and future perspectives. Behav Neurol. 2016; 2016:7576292.

Gruener H, Zeilig G, Laufer Y, Blumen N, **Defrin R.** Differential pain modulation properties in central neuropathic pain after spinal cord injury. Pain. 2016;157:1415-24.

Zeilig G, Rivel M, Doron D, **Defrin R**. Does hemiplegic shoulder pain share clinical and sensory characteristics with central neuropathic pain? A comparative study. Eur J Phys Rehab Med. 2016.

Weissman-Fogel I, Dror A, **Defrin R**. Temporal and spatial aspects of experimental tonic pain: understanding pain adaptation and intensification Eur J Pain. 2015;19:408-18.

Defrin R, Riabinin M, Feingold Y, Schreiber S, Pick CG. Deficient pain modulatory systems in patients with mild traumatic brain and chronic post-traumatic headache: implications on its mechanism. J Neurotrauma. 2015;32:28-37.

Benromano T, **Defrin R**, Ahn AH, Zhao J, Pick CG, Levy D. Mild closed head injury promotes a selective trigeminal hyper-nociception: implications for the acute emergence of posttraumatic headache. Eur J Pain. 2015;19:621-8.

Raz N, Granovsky Y, **Defrin R**. Investigating the neural processing of spatial summation of pain: the role of A-delta nociceptors. Exp Brain Res. 2015;233:405-13.

Defrin R., Arad M., Pieck M. Ben-Sasson, K. Ginzburg. Attitudes towards pain and sensitivity to painful stimuli among people routinely engaging in masochistic behavior. Eur J Pain. 2015;19:1321-1330.

Baeta-Corral R, **Defrin R**, Pick CG, Giménez-Llort L. Tail-flick test response in 3xTg-AD mice at early and advanced stages of disease. Neurosci Let. 2015;600:158-63.

Defrin R, Schreiber S, Ginzburg K. Paradoxical pain perception in PTSD: The unique role of anxiety and dissociation. J Pain. 2015;16:961-970.

Levitan Y, Zeilig G, Bondi M, Ringler E, **Defrin R**. Predicting the risk for central pain using the sensory components of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). J Neurotrauma. 2015; 32:1684-92

Kucyi A, Sheinman A, **Defrin R**. Distinguishing feigned from genuine performance in psychophysical pain testing. J Pain. 2015;16:1044-1053

Defrin R. Compression at myofascial trigger points for the management of acute low back pain. Commentary. Eur J Pain. 2015 ;19:1057-8.

Ginzburg K, Tsur N, Karmin C, Speizman T, Tourgeman R, **Defrin R.** Body awareness and pain habituation: The role of orientation towards somatic signals. J Behavi Med. 2015;38:876-85.

de Knegt NC, **Defrin R**, Evenhuis HM, Lobbezoo F, Schuengel C, Scherder EJA. Quantitative sensory testing of temperature, pain, and touch in adults with Down syndrome. Res Dev Dis. 2015;47:306-31.

Levy D, Edut S, Baraz-Goldstein R, Rubovitch V, **Defrin R**, Bree D, Gariepy H, Zhao J, Pick CG. Responses of dural mast cells in concussive and blast models of mild traumatic brain injury in mice: Potential implications for post-traumatic headache. Cephalalgia. 2015 [epub ahead of print]

Andersen TE, Lahav Y, **Defrin R**, Mikulincer M, Solomon Z. Attachment security and pain--The disrupting effect of captivity and PTSS. J Psychosom Res. 2015;79:471-6.

Defrin R, Devor M, Brill S. Tactile allodynia in patients with lumbar radicular pain (sciatica). Pain. 2014;155:2551-9.

Geva N, Pruessner J, **Defrin R**. Acute psychosocial stress reduces pain modulation capabilities in healthy men. Pain. 2014;155:2418-2520.

Defrin R, Ginzburg K, Mikulincer M, Solomon Z. The long-term impact of tissue injury on pain processing and modulation: a study on ex-prisoners of war who underwent torture. Eur J Pain. 2014;18:548-58.

Geva N, **Defrin** R. Enhanced pain modulation among triathletes: a possible explanation for their exceptional capabilities. Pain. 2013;154:2317-23.

Ginzburg K, Tsur N, Barak-Nahum A, **Defrin** R. Body awareness: differentiating between sensitivity to and monitoring of bodily signals. J Behav Med. 2014;37:564-75.

Zeilig G, Rivel M, Weingarden H, Gaidoukov E, **Defrin** R. Evidence of a neuropathic origin in hemiplegic shoulder pain. Pain. 2013;154:959-60.

Defrin R, Lurie R. Indications for peripheral and central sensitization in patients with chronic scalp pain (trichodynia). Clin J Pain. 2013;29:417-24.

Zeilig G, Rivel M, Weingarden H, Gaidoukov E, **Defrin** R. Hemiplegic shoulder pain: evidence of a neuropathic origin. Pain. 2013;154:263-71.

Reviews and Chapters

de Tommaso M, Arendt-Nielsen L, **Defrin R,** Kunz M, Pickering G, Valeriani M. Pain in Neurodegenerative Disease: Current Knowledge and Future Perspectives. Behav Neurol. 2016.

Defrin R, Amanzio M, de Tommaso M, Dimova V, Filipovic S, Finn DP, Gimenez-Llort L, Invitto S, Jensen-Dahm C, Lautenbacher S, Oosterman J, Petrini L, Pick CG, Pickering G, Vase L, Kunz M. Experimental pain processing in individuals with cognitive impairment: Current state of the science. Pain. 2015;156:1396-1408.

Grants

2014-2017	National Insurance Association
2015-2017	IRP- International Foundation for research in Paraplegia
2015-2019	ISF-Israel Science Foundation

Dr. Michal Itzhaki, R.N., Ph.D.

Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: itzhakim@post.tau.ac.il

Emotional Management, Cultural Competence and Decision-Making

Positions

Lecturer, Sackler Faculty of Medicine

Head, Generic BA Nursing Program

Research

Qualitative and quantitative research methods are used to study nurses' and patients' attempts to structure their emotions through the process of emotional management. We focus on self-care research: understanding the interventions, correlates and outcomes of nurses' self care by International research on caritas as healing. Our research involves studying cultural competence, which enables nurses to care for and to communicate with patients from different cultural and ethnic backgrounds. Furthermore, the focus is on acculturation and job satisfaction among immigrant nurses from different countries. The theory of family-centered care is studied: the preferences of lay people regarding family involvement in medical decisions. Moreover, we research the attitudes of lay people and staff members to family presence during resuscitations and invasive procedures. Understanding these aspects is essential for creating caring environments for nurses, patients and families within today's complex health care organizations.

Publications

Kagan I, **Itzhaki M** & Melnikov S. Patriotism, organizational commitment and nurses' intention to report to work in emergencies *International Nursing Review*. 2017, in press.

Melnikov S, **Itzhaki M** & Koton, S. Age-group and gender differences in stroke knowledge in an Israeli Jewish adult population. *Journal of Cardiovascular Nursing*. 2017, DOI: 10.1097/JCN.0000000000000424

Barnoy S, Biton A & **Itzhaki M.** Social inclusion of children with Down syndrome: Jewish and Muslim mothers' knowledge, attitudes, beliefs, and behavioral intentions. *Journal of Pediatric Nursing*. 2017, 35, 50-56.

Warshawski S, Barnoy S & **Itzhaki M.** Factors associated with nursing students' resilience: Communication skills course, use of social media and satisfaction with clinical placement. *Journal of Professional Nursing.* 2017, DOI: 10.1016/j.profnurs.2016.08.006.

Itzhaki M, Melnikov S & Koton, S. Gender differences in feelings and knowledge about stroke. *Journal of Clinical Nursing*. 2016. 25, 2958–2966.

Coffey A, McCarthy G, Weathers E, Friedman M, Gallo K, Ehrenfeld M, Chan S, Li W, Poletti P, Zanotti R, Molloy D, McGlade C, Fitzpatrick J & **Itzhaki M**. Nurses' knowledge of advanced directives and perceived confidence in end-of-life care: A cross-sectional study in five countries. *International Journal of Nursing Practice*. 2016, 22, 247-257.

Itzhaki M, Hildsheimer G, Barnoy S & Katz M. Family involvement in medical decisions making: Perceptions of nursing and psychology students. *Nurse Education Today*. 2016, 40, 181-187, DOI: 10.1016/j.nedt.2016.03.002

Itzhaki M, Meridan O, Sagiv-Schifter T & Barnoy S. Nursing students' attitudes and intention to work with mentally ill patients before and after a planned intervention. *Academic Psychiatry*. 2016, DOI: 10.1007/s40596-016-0521-3

Itzhaki M, Peles Bortz A, Kostistky A, Barnoy D, Filshtinsky V & Bluvstein I. The exposure of mental health nurses to violence as associated with job stress, life satisfaction, staff resilience and posttraumatic growth. *International Journal of Mental Health Nursing*. 2015, 24, 403-412

Itzhaki M, Treacy M, Phaladze N, Rumeu C, Vernon R, Marshall B, Fealy G, Ehrenfeld M, Larkin P, McNamara M, Dignam D, Rollins-Ganz N, Nelson J. A 5-country

partnership to measure perception of nursing staffs' caring for self, burnout and compassion fatigue. *Interdisciplinary Journal of Partnership Studies.* 2015, 2(1), article 8.

Melnikov S, **Itzhaki M** & Koton, S. Differences between new immigrants from the Former Soviet Union and veteran residents in knowledge, perception and risk factors of stroke. *Journal of Cardiovascular Nursing.* 2015, DOI: 10.1097/JCN.0000000000000278

Itzhaki M & Koton S. Knowledge, perceptions and thoughts of stroke among Arab-Muslim Israelis. *European Journal of Cardiovascular Nursing*. 2014, 13, 78 – 85.

Koren A, Mintz A & **Itzhaki M**. Is this a mistake? Perception of nursing students' errors by clinical perceptors. *Body of Knowledge – The Israel Journal for Nursing Research* 2014, 11, 2-14. (Hebrew)

Melnikov S*, **Itzhaki M*,** Kagan I. Israeli nurses' intention to report for work in an emergency or disaster. *Journal of Nursing Scholarship* 2013, 46, 134-42 (*Equally contributing authors)

Itzhaki M & Koton S. Knowledge, perceptions and thoughts of stroke among Arab-Muslim Israelis. *European Journal of Cardiovascular Nursing* 2013, 13, 78-85

Coffey A, McCarthy G, Weathers E, Friedman M, Gallo K, Ehrenfeld M, **Itzhaki M,** Chan S, Li W, Poletti P, Zanotti R, Molloy D, McGlade C & Fitzpatrick J. Nurses' preferred end-of-life treatment choices in five countries. *International Nursing Review* 2013, 33, 842–846.

Itzhaki M, Ea E, Ehrenfeld M, Fitzpatrick J. Job satisfaction among immigrant nurses in Israel and in the United States. *International Nursing Review.* 2013, 60, 122-128.

Tabak N*/**Itzhaki M*** Sharon D, Barnoy S. Intentions of nurses and nursing students to tell the whole truth to patients and family members. *Journal of Clinical Nursing*. 2013, 22:1434-41 (*Equally contributing authors)

Itzhaki M, Bluvstein I, Raz S, Barnoy S. Factors affecting the actions and emotional reactions of nursing teachers following encounters with students who present them with internet information. *Nurse Education Today* 2013, 33:842-6.

Chapter

Ben Natan M, Ehrenfeld M & **Itzhaki M**. Applications of Transcultural Nursing Theory. In J. J. Fitzpatrick & A. L. Whall (Eds.), *Conceptual models of nursing: Global perspectives* (5th ed.). (pp. 148 -163). 2015, Englewood, NJ: Prentice Hall.

Dr. Ilya Kagan, R.N., Ph.D.

Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: kaganily@post.tau.ac.il

Quality of Care and Patient Safety

Positions

Lecturer, Sackler Faculty of Medicine

Head, Accelerated Program for Non-Nursing B.A. Graduates

Research

Peri-operative Factors and Their Impact on Post-operative Recovery

Our research area is developing in two tracks: a) discovering the factors that affect quality and safety behavior of healthcare workers (HCWs) and b) examination of psycho-social and bio-physiological factors before and after surgery and their impact on short-/long-term recovery and rehabilitation. The first research track focuses on both the "human element" variables and the systemic approach to the quality improvement, clinical risk management and patient safety issues such as medical error-reporting, safety culture, disclosure errors to patients, patient empowerment and more. The studies highlight the barriers that have to be addressed when planning and implementing changes to improve quality and patient safety in healthcare. The second track addresses the influence of variables such as personal self-efficacy, situational anxiety, health literacy, subjective readiness to surgery, gender, ethnicity etc., on post-operative recovery. These studies aim to identify variables that could have a positive or negative effect on readiness to leave hospital after surgery, to comply with the recommendations on discharge from hospital, to adhere rehabilitation programs and more.

Publications

Kagan, I. and Barnoy, S. (2013). Organizational safety culture and error-reporting by Israeli nurses. *Journal of Nursing scholarship,* 45, 273-80.

Melnikov, S., Itzhaki, M., **Kagan, I** (2013). Intention to report to work in emergency and disasters among Israeli nurses. Journal of Nursing Scholarship, 46, 134-42. Chosen as 'March 2014 Editor's Choice Article' of JNS.

Kagan, I., Cohen, R., Fish, M., Peri, H. (2014). Developing and implementing a computerized nursing quality control system in general medical center. Journal of Nursing Care Quality (JNCQ), 29, 83-90.

Frishman, S., Theilla, M., Singer, P., Avraham, Z., Libman, C., **Kagan, I**. (2014). JCI Accreditation and Its multiprofessional Impact on nutrition care at Rabin Medical Center, Israel. Invited (peer-reviewed) paper, published on official site of Joint Commission International (JCI): http://www.jointcommissioninternational.org/new-study-jci-accreditation-and-nutrition-care-at-rabin-medical-center/ and also in JCInsight, official newsletter of JCI, http://www.jointcommissioninternational.org/assets/3/7/jcinsightapril2014.pdf.

Kagan, I., Fish, M., Farkash-Fink, N., Barnoy, S. (2014) Computerization and its contribution to care quality and improvement: the nurses' perspective. Int J Med Inform. 83, 881-8.

Kagan, I., Biran, E., Telem., L., Steinovitz, N., Alboer, D., Ovadia, K. & Melnikov, S. (2015). Promotion or marketing of the nursing profession by nurses. *International Nursing Review*, e-published.

Kagan, I., Gaash, T., Sela, M., Cohen, S., Grigorash, S., Maximov, Y., Tabak, N. (2015). Sexual harassment by patients: the different experience of physicians, nurses and nursing aids. *Medicine & Law,* 34 (1), 5-20.

Baum, A. and **Kagan, I.** (2015). Job satisfaction and tendency to leave among psychiatric nurses. *Archives of Psychiatric Nursing,* 29, 213-216.

Kagan, I., Shachaf, S, Rapaport, S., Livni, T., Majar, B. (2016). The working conditions of Israel's public

health nurse: A case study in quality improvement. *Public Health Nursing.*

Kagan, I., Fish, M., Farkash, N. (2016). Nursing work environment before and after Joint Commission International Accreditation in tertiary medical center. *Journal of Nursing Care Quality,* published ahead of print, 21 2016.

Theilla, M., Cohen, J., Singer, P., Liebman, C., and **Kagan,** I (2016). The Assessment, Knowledge and Perceived Quality of Nutrition Care amongst Nurses. *Journal of Nutritional Medicine and Diet Care,* 2:012.

Melnikov, S., Elian Antar, T., Shor, R., Kigli-Shemesh, R., and **Kagan, I**. (2016). Nurses teaching prison officers: a workshop to reduce the stigmatization of mentally ill person inmates. *Perspectives in Psychiatric Care*, published ahead of print, 20 May 2016.

Kagan, I., Kigli-Shemesh, R., Shor, R., Melnikov, S. (2016). Between the rock and the hard place: Ethical and professional dilemmas in the management of care and functioning in a psychiatric hospital under missile attacks. *Journal of the American Psychiatric Nurses Association*, 08 2016.

Theilla, M., **Kagan, I.**, Chernov, K., Cohen, J., Kagan, I., Singer, P. (2017). Self-evaluation of quality of life in home parenteral nutrition patients; a validation study. Journal of Parenteral and *Enteral Nutrition*, doi: 10.1177/0148607117704812.

Kagan, I., Itzhaki, M., Melnikov, S. (2017). Patriotism, organizational commitment and nurses' intention to report to work in emergencies. *International Nursing Review*, e-published prior to print.

Akrish, O., Bluvstein, I., **Kagan, I.** (2017). Applicability of Tinto's "Student Integration Model" in explanation of tendency to leave among nursing students participating in accelerated (second career) program for non-nursing BA graduates. *Guf Yeda, 15*, 4-9 [Hebrew].

Warshawski, S., Barnoy, S., **Kagan, I.** (2017). Professional, generational, and gender differences in perception of organizational values among Israeli physicians and nurses: Implications for retention. *Journal of Interprofessional Care*, 1-9.

Prof. Silvia Koton, Ph.D., M.Occ.H., R.N.

Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine and
Sagol School of Neuroscience

TEL AVIV UNIVERSITY

E-mail: koton@tauex.tau.ac.il

Epidemiology of Cardiovascular Diseases & Risk Factors

Position

Associate Professor, Sackler Faculty of Medicine

Chair, Department of Nursing

Adjunct Associate Professor of Epidemiology, Johns Hopkins University

Research

Our research focuses on the epidemiology of cardiovascular diseases with a special interest in epidemiology of stroke. During the last years, our studies have covered diverse subjects including trends in stroke morbidity and mortality among different population groups in Israel and in the United States,, strategies for primary and secondary prevention of stroke, determinants of stroke outcomes and novel risk factors acting long-term and as immediate triggering factors. Taking advantage of our knowledge and skills in the environmemtal and occupational health area, we also study the health effects of pollution mainly among survivors of cardiovascular diseases.

Since the establishment of the ongoing triennial National Acute Stroke Israeli (NASIS) registry in 2004, as a member of the registry's steering committee, We carry out nationwide studies in collaboration with specialists in neurology and stroke research. These studies are aimed at characterizing management and outcomes of acute stroke patients and are an important means for providing both clinicians and health policy makers with data required for optimizing prevention strategies and care of stroke patients in Israel.

Publications

Paul NL, **Koton S**, Simoni M, Geraghty OC, Luengo-Fernandez R, Rothwell PM. Feasibility, safety and cost of outpatient management of acute minor ischaemic stroke: a population-based study. J Neurol Neurosurg Psychiatry. 2013; 84:356-61.

Koton S, Molshatzki N, Yuval, Myers V, Broday DM, Drory Y, Steinberg DM, Gerber Y. Cumulative exposure to particulate matter air pollution and long-term post-myocardial infarction outcomes. Prev Med. 2013: 57:339-44

Tanne D, **Koton S**, Bornstein NM. National stroke registries: what can we learn from them? *Neurology.* 2013; 81:1257-1259.

Koton S, Tsabari R, Molshazki N, Kushnir M, Shaien R, Eilam A, Tanne D; NASIS Investigators. Burden and outcome of prevalent ischemic brain disease in a national acute stroke registry. *Stroke*. 2013; 44:3293-3297.

Koton S, Telman G, Kimiagar I, Tanne D; NASIS Investigators. Gender differences in characteristics, management and outcome at discharge and three months after stroke in a national acute stroke registry. *Int J Cardiol.* 2013; 168:4081-4084.

Itzhaki M, **Koton S**. Knowledge, perceptions and thoughts of stroke among Arab-Muslim Israelis. Eur J Cardiovasc Nurs. 2014: 3:78-85

Cobb LK, McAdams-Demarco MA, Huxley RR, Woodward M, **Koton S**, Coresh J, Anderson CA. The association of spousal smoking status with the ability to quit smoking: the Atherosclerosis Risk in Communities study. *Am J Epidemiol.* 2014; 179:1182-1187.

Gerber Y, Myers V, Broday DM, Steinberg DM, Yuval, **Koton S**, Drory Y. Frailty status modifies the association between air pollution and post-myocardial infarction mortality: a 20-year follow-up study. *J Am Coll Cardiol.* 2014; 63:1698-1699.

Koton S, Schneider AL, Rosamond WD, Shahar E, Sang Y, Gottesman RF, Coresh J. Stroke incidence and mortality trends in US communities, 1987 to 2011. *JAMA*. 2014; 312(3):259-68.

Melnikov S, Itzhaki M, **Koton S**. Differences between new immigrants from the Former Soviet Union and veteran residents in knowledge, perception, and

risk factors of stroke. *J Cardiovasc Nurs*. 2015 Jul 1. [Epub ahead of print]

Koton S, Eizenberg Y, Tanne D, Grossman E. Trends in admission blood pressure and stroke outcome in patients with acute stroke and transient ischemic attack in a National Acute Stroke registry. *J Hypertens*. 2016; 34(2):316-22.

Eizenberg Y, **Koton S**, Tanne D, Grossman E. Association of age and admission mean arterial blood pressure in patients with stroke-data from a national stroke registry. *Hypertens Res*. 2016; 39(5):356-61.

Cobb LK, Godino JG, Selvin E, Kucharska-Newton A, Coresh J, **Koton S**. Spousal Influence on Physical Activity in Middle-Aged and Older Adults: The ARIC Study. *Am J Epidemiol*. 2016; 183(5):444-51.

Kipnis G, Tabak N, **Koton S**. Background music playback in the preoperative setting: does it reduce the level of preoperative anxiety among candidates for elective surgery? *J Perianesth Nurs*. 2016; 31:209-16.

Itzhaki M, Melnikov S, **Koton S**. Gender differences in feelings and knowledge about stroke. *J Clin Nurs.* 2016; 25:2958-66.

Kucharska-Newton A, Griswold M, Yao ZH, Foraker R, Rose K, Rosamond W, Wagenknecht L, **Koton S**, Pompeii L, Windham BG. Cardiovascular disease and patterns of change in functional status over 15 years: Findings from the Atherosclerosis Risk in Communities (ARIC) study. *J Am Heart Assoc.* 2017;6(3).

Koton S, Tanne D, Grossman E. Prestroke treatment with beta-blockers for hypertension is not associated with severity and poor outcome in patients with ischemic stroke: data from a national stroke registry. *J Hypertens.* 2017; 35:870-876.

Windham BG, Harrison KL, Lirette ST, Lutsey PL, Pompeii LA, Gabriel KP, **Koton S**, Steffen LM, Griswold ME, Mosley TH Jr. Relationship between midlife cardiovascular health and late-life physical performance: The ARIC study. *J Am Geriatr Soc*. 2017; 65:1012-1018.

Melnikov S, Itzhaki M, **Koton S**. Age-group and gender differences in stroke knowledge in an Israeli Jewish adult population. *J Cardiovasc Nurs*. 2017. doi: 10.1097/JCN.0000000000000424.

Koton S, Rexrode KM. Trends in stroke incidence in the United States: Will women overtake men? *Neurology*. 2017; 89:982-983.

Peretz S, Orion D, Last D, Mardor Y, Kimmel Y, Yehezkely S, Lotan E, Itsekson-Hayosh Z, **Koton S**, Guez D, Tanne D. Incorporation of relative cerebral blood flow into CT perfusion maps reduces false 'at risk' penumbra. *J Neurointerv Surg*. 2017 Sep 30. pii: neurintsurg-2017-013268.

Dr. Lena Lipskaya-Velikovsky, Ph.D., O.T.

Department of Occupational Therapy
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: lenalip@post.tau.ac.il

Participation in Everyday Life and Occupational Therapy Practice for People with Psychiatric Disorders

Positions

Lecturer, Sackler Faculty of Medicine

Research

Participation in meaningful activities according to personal values and choices is one of the central components of health and well-being. Moreover, it is one of the ultimate goals of health services delivery, as suggested by the WHO vision. Today, psychiatric disorders still remain one of the main reasons for disability payments all over the world due to the functional disability they cause. Our research is focused on exploring everyday functioning and participation patterns of people with psychiatric disorders that were found to be both unique and similar to those of the general population; and detecting factors affecting the everyday functioning such as functional capacity, motor abilities, sence of belonging and sensory modulation over the more conventional ones (psychiatric symptoms and cognition). In addition, we investigate efficacy of Occupational Therapy (OT) evaluation and intervention process and develop new tools and technics for practice. Since Occupational Therapy services are provided in different settings, including in mental health hospitals, one of our particular areas of interest is investigation of the OT practices in acute settings to promote successful transition to everyday life after discharge and reintegration into community.

Publications

Lipskaya, L., Kotler, M., M., Weiss, P., Kaspi, M., Gizmo-Sabag, S., Ratzon, N. (2013). Car driving in schizophrenia: Can visual memory and organization make a difference? *Disability & Rehabilitation*, *35*, 1734-1739.

Lipskaya-Velikovsky, L., Avrech- Bar, M., & Bart, O. (2014). Context and psychosocial intervention in mental health. *Scandinavian Journal of Occupational Therapy*, *21*, 136-144.

Lipskaya-Velikovsky, L., Bar-Shalita, T., Bart, O. (2015). Sensory modulation and

daily-life participation in people with schizophrenia. *Comprehensive Psychiatry, 58*, 130-137.

Lipskaya-Velikovsky, L., Jarus, T., Easterbrook, A., & Kotler, M. (2015). From hospital admission to functioning in the community: Is a prediction possible? *Psychiatry Research*, *226*, 499-506.

Lipskaya-Velikovsky, L., Kotler, M., Krupa, T. (2016) "Occupational Connections"– An intervention for in-patient psychiatry settings: description and preliminary findings. *American Journal of Occupational Therapy* 70(6):7006350010p1-7006350010p5.

Lipskaya-Velikovsky, L., Jarus, T., & Kotler, M. (2017) Factors predicting employment status following in-patient evaluation among persons with schizophrenia. *Work* 39:1300-1306.

Avrech Bar M, Margalit Pade M, Jarus T, Gat S, Kaufman Cohen Y & **Lipskaya-Velikovsky L.** (2017) Problem-Based learning in occupational therapy curriculum – Implications and challenges. DOI: 10.1080/09638288.2017.1325942

Dr. Alon Kalron, Ph.D., P.T.

Department of Physical Therapy
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: alonkalr@post.tau.ac.il

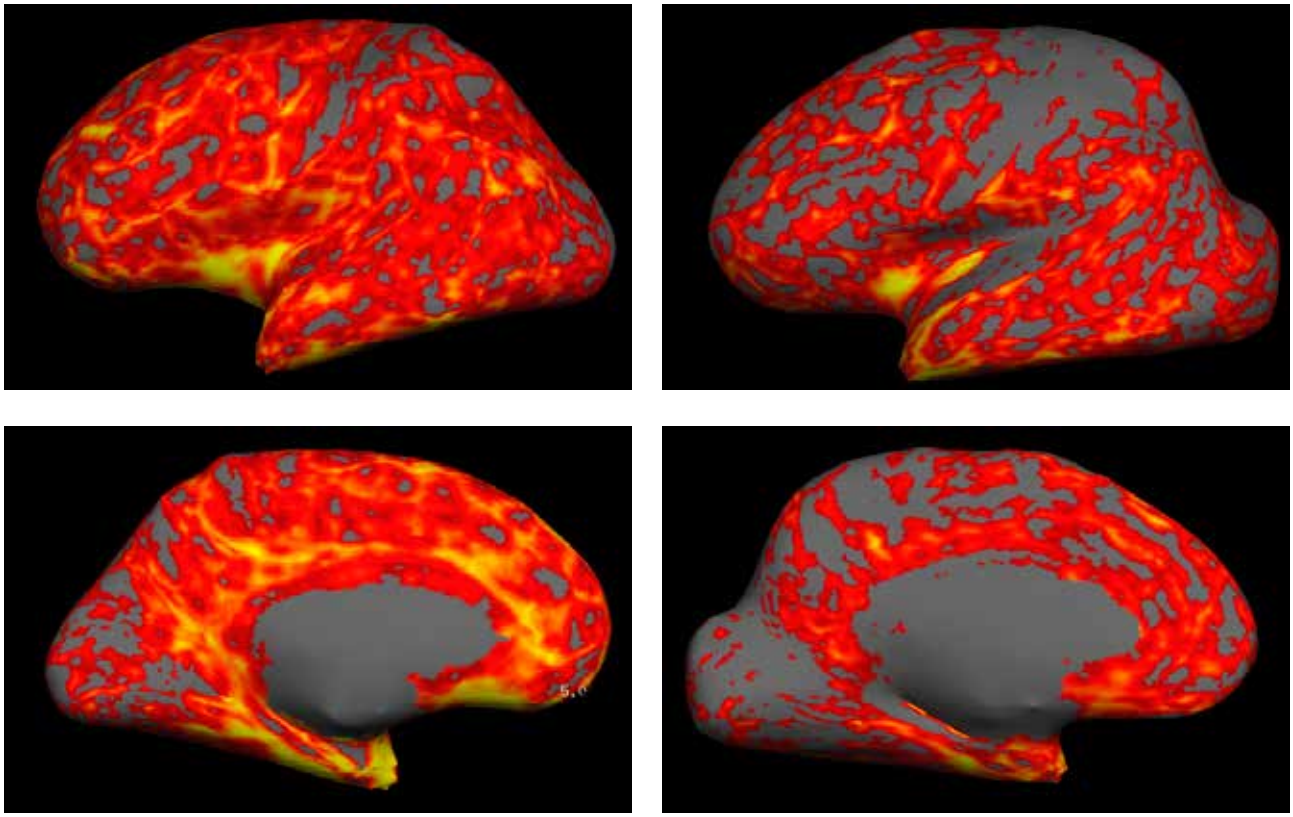
Physical Activity, Gait and Posture in People with Neurological Diseases

Position

Lecturer, Sackler Faculty of Medicine

Research

Our main research focuses on physical activity, gait and balance measurements, predictors, and outcomes in persons with neurological diseases, specifically multiple sclerosis (MS). Currently we are examining the relationship between various physical and mobility parameters with brain damage, determined by MRI methods in different neurological patient groups. Special interest is placed on aerobic function capabilities during various daily and challenging situations. We anticipate that our research will result in quantifying differences in physical activity, particularly in the rates of moderate-to-vigorous physical activity in several neurological patient groups vs. non-diseased controls. The interest in this research is based on the rationale that a better understanding of these mechanisms will facilitate the development of practical interventions, thus minimizing the negative aspects of the disease process. Overall, the research questions range from theoretical exploration to clinical application and are often multi-disciplinary in nature.



Freesurfer results showing the inflated lateral hemispheres view of two MS participants with similar age, EDSS and disease duration. Slow walker images are on the left row, normal walker images are presented on the right row. Cortical thickness is determined according to color; yellow – thick, grey- thin.

Publications

Kalron A, Dvir Z, Gurevich M, Achiron A. Do motor impairments detected on onset of multiple sclerosis suggest an early second attack? A prospective study. *NeuroRehabil*, 33:423-430; 2013.

Kalron A, Greenberg-Avrahami M, Galeb S, Achiron A. Effects of a new sensory re-education training tool on hand sensibility and manual dexterity in people with multiple sclerosis. *NeuroRehabil*, 32:943-948; 2013.

Kalron A, Dvir Z, Frid L, Achiron A. Quantifying gait impairment using an instrumented treadmill people with multiple sclerosis. *ISRN Neurology*, Article ID867575; 2013.

Kalron A, Achiron A. Postural control, falls and fear of falling in people with multiple sclerosis without mobility aids. *J Neurol Sci*, 335:186-190; 2013.

Kalron A, Bar-Sela S. A systematic review of the effectiveness of Kinesio taping® – fact or fashion? *Eur J Phys Rehabil Med*, 49:699-709; 2013.

Kalron A, Dvir Z, Givon U, Baransi H, Achiron A. Gait and jogging parameters in minimally impaired multiple sclerosis patients. *Gait Posture*, 39:297-302; 2014.

Kalron A, Achiron A. The relationship between fear of falling to spatiotemporal gait parameters measured by an instrumented treadmill in people with multiple sclerosis. *Gait Posture*, 39:739-744; 2014.

Baert I, Freeman J, Smedal T, Dalgas U, **Kalron A**, Romberg A, Conyers H, Elorriaga I, Gebara B, Gumse J, Heric A, Jensen E, Jones K, Knuts K, Maertens B, Martic A, Normann B, Rasova K, Medina CS, Truyens V, Wens I, Feys P. Responsiveness and clinically meaningful improvement, according to disability level, of walking measures after rehabilitation in multiple sclerosis: a European multi-center study. *Neurorehabil Neural Repair*, 28:621-631; 2014.

Kalron A, Frid L, Gurevich M. Concern about falling alters gait parameters in persons with multiple sclerosis. *Eur J Phys Rehabil Med*, Epub ahead of print; 2014.

Kalron A. The Relationship between specific cognitive domains, fear of falling and falls in people with multiple sclerosis. *Biomed Res Int*, Epub ahead of print; 2014.

Kalron A, Greenberg-Abrahami M, Achiron A. Validity and test-retest reliability of a measure of hand sensibility and manual dexterity in people with multiple sclerosis: the ReSense test. *Disabil Rehabil*,Epub ahead of print; 2014.

Kalron A, Pasitselskey D, Greenberg-Abrahami M, Achiron A. Do textured insoles effect postural control and spatio-temporal parameters of gait and plantar sensation in people with multiple sclerosis? *PM&R*, Epub ahead of print; 2014.

Achiron A, Givon U, Magalashvilli D, Dolev M, Liraz-Zaltsman S, **Kalron A**, Stern Y, Mazor Z, Ladkani D, Barak Y. Effect of Alfacalcidol on multiple sclerosis related fatigue: a randomized, double-blind placebo-controlled study. *Mult Scler*, Epub ahead of print; 2014.

Kalron A, Nitzani D, Givon U, Menascu S, Zeilig G, Magalashvili D, Dolev M, Stern Y, Rosenblum U, Pasitselsky D, Frid L, Barmatz C, Achiron A. A personalized, intense physical rehabilitation program improves walking in people with multiple sclerosis presenting with different levels of disability. A retrospective cohort. *BMC Neurol*, 15:21; 2015.

Kalron A. Association between perceived fatigue to gait parameters measured by an instrumented treadmill in people with multiple sclerosis: a cross sectional study. *J Neuroeng Rehabil*; 12:34; 2015.

Kalron A, Frid L. The "butterfly diagram": a gait marker for neurological and cerebellar impairment in people with multiple sclerosis. *J Neurol Sci*; 358:92-100; 2015.

Kalron A, Zeilig G. Efficacy of exercise intervention programs on cognition in people suffering from Multiple Sclerosis, Stroke and Parkinson's disease: A systematic review and meta-analysis of current evidence. *NeuroRehabil*,37:273-289; 2015.

Kalron A. Gait variability across the disability spectrum in people with multiple sclerosis. *J Neurol Sci*; 361:1-6; 2016.

Kalron A. The correlation between symptomatic fatigue to definite measures of gait in people with multiple sclerosis. *Gait Posture*; 44:178-183; 2016.

Kalron A, Fonkatz I, Frid L, Baransi H, Achiron A. The effect of balance training on postural control using the CAREN virtual reality system in people with multiple sclerosis: A pilot randomized controlled trial. *J Neuroeng Rehabil*; 13:13; 2016.

Kalron A. Construct validity of the walk ratio as a measure of gait control in people with multiple sclerosis. *Gait Posture*; 47:103-7; 2016.

Kalron A. Relationship between obesity, gait and balance in people with multiple sclerosis. *Am J Physical Med Rehabil*; 96:140-145 2016.

Kalron A. Symmetry in vertical ground reaction force is not related to walking and balance difficulties in

people with multiple sclerosis. *Gait Posture*; 47:48-50; 2016.

Kalron A. The relationship between static posturography measures and specific cognitive domains in people with multiple sclerosis. International *Journal of Rehabil Res*; 39(3):249-54; 2016.

Kalron A, Givon U. Construct validity of the Four Square Step Test in people with multiple sclerosis without mobility aids. *Arch Phys Med Rehabil*; 97(9):1496-1501; 2016.

Kalron A, Givon U. Gait characteristics according to pyramidal, sensory and cerebellar EDSS subcategories in people with multiple sclerosis. *J Neurol* 2016 263(9):1796-1801.

Kalron A, Givon U, Frid L, Dolev M, Achiron A. Static Posturography and Falls According to Pyramidal, Sensory and Cerebellar Functional Systems in People with Multiple Sclerosis. *PLoS One*; 11(10):e0164467; 2016.

Malcay O, Grinberg Y, Berkowitz S, Hershkovitz L, **Kalron A**. Cognitive-motor interference in multiple sclerosis: What happens when the gait speed is fixed? *Gait Posture*; 57:211-216; 2017.

Kalron A. The Romberg ratio in people with multiple sclerosis. *Gait and Posture*; 54:2019-213; 2017.

Kalron A, Frid L, Menascu S. Gait characteristics in adolescents with multiple sclerosis. *Pediatr Neurol*; 68:73-76; 2017.

Kalron A, Frid L, Rosenblum U, Achiron A. Pilates exercise training vs. physical therapy for improving walking and balance in people with multiple sclerosis: A randomized controlled trial. *Clinical Rehabil*; 31(3):319-328; 2017.

Kalron A. Association between gait variability, falls and mobility in people with multiple sclerosis: A specific observation on the EDSS 4.0-4.5 level. *NeuroRehabilitation*; 40(4):579-585; 2017.

Kalron A, Dolev M, Givon U. Further construct validity of the timed up and go test as a measure of ambulation in persons with multiple sclerosis. *Eur J Phys Rehabil Med*; 53:841-847; 2017

Kalron A, Allali G. Gait and cognitive impairments in multiple sclerosis: the specific contribution of falls and fear of falling. *J Neural Transm*; 124:1407-1416; 2017

Rice L, **Kalron A**, Berkowitz S, Backus D, Sosnoff J. Fall prevalence in people with multiple sclerosis who use wheelchairs and scooters. *Medicine*; 96:e7860; 2017.

Kalron A, Menascu S, Dolev M, Givon U. The walking speed reserve does not provide greater insight in detecting mobility deficits and risk of falls than preferred and fast walking speeds in peop*le with multiple sclerosis.* Mult Scler Relat *Disord*; 17:202-206; 2017.

Kalron A, Aloni R. Contrasting relationship between depression, quantitative gait characteristics and self-report walking difficulties in people with multiple sclerosis. *Mult Scler Relat Disord*;19:1-5; 2018.

Grants

2017-2018 European Network in Rehabilitation in MS

Dr. Youssef Masharawi, Ph.D., B.P.T.

Department of Physical Therapy
School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: yossefm@post.tau.ac.il

Spinal Form and Function

Position

Senior Lecturer, Sackler Faculty of Medicine

Member, Associate Board, Spine Journal

Research

Clinical, diagnostic, therapeutic, epidemiological, kinematical, and anthropometric investigations of the normal and pathological human spine.

During the last decade, we have focused our research on studying the form and function of the human spine in normal and pathological conditions. We proposed some unique models for the pathogenesis and biomechanics of several spinal pathologies. Specifically, the following research projects were investigated and categorized as clinical (diagnostic, therapeutic and clinical reasoning), kinematical and morphological:

- *Clinical/kinematic:* a. Directional and positional preference of group exercising in individuals with chronic low back pain and osteoporosis; b. Clinical reasoning and decision making; c. Kinematical evaluation of lumbar rotations in erected and fully flexed standing and sitting positions in patients with chronic low back pain.
- *Morphological/Anatomical:* a. A morphometric analysis of the normal and pathological human spine; b. Spinal shape variation and postural changes during growth.
- *Epidemiological:* An epidemiological study on spinal osteoporosis in females and sport related back injuries in children.

Publications

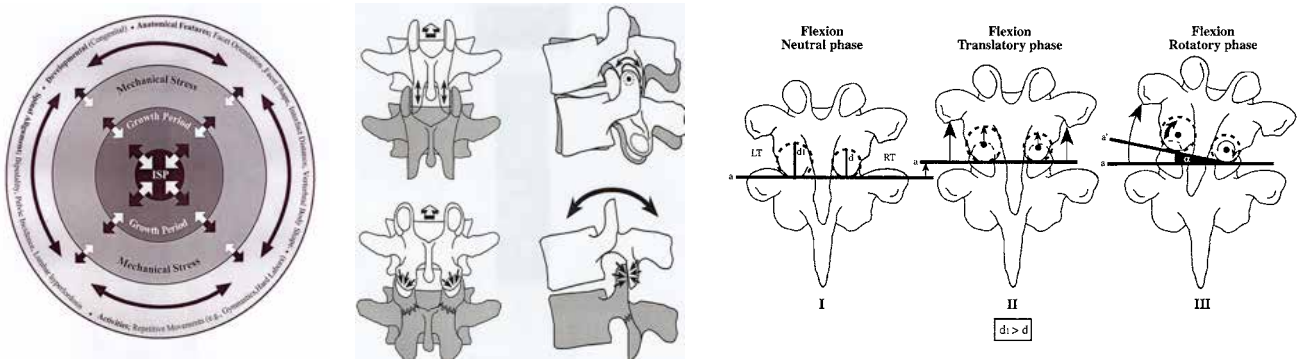
Steinberg N., Hershkovitz I., Peleg S., Dar G., **Masharawi Y**., Zeev A., Siev-Ner I. Morphological characteristics of the young scoliotic dancer. Phys Ther Sport. 14:213-220, 2013.

Masharawi Y., Nadaf N. The effect of non-weight bearing group-exercising on females with non-specific chronic low back pain: A randomized single blind controlled pilot study. J. of Back Musculo. Reh. 26:353-359, 2013.

Steinberg N., Siev-Ner I, Peleg S., Dar G., **Masharawi Y**., Zeev A., Hershkovitz I. Injuries in Female Dancers Aged 8 to 16 Years. J of Athl Train. 48:118-123, 2013.

Rothschild BM, Ho J, **Masharawi Y**. Macroscopic anatomy of the vertebral endplate: quid significat? Anthropol Anz. 71:191-217, 2014.

Segal-Snir Y, Lubetzky VA, **Masharawi Y**. Rotation exercise classes did not improve function in women with non-specific chronic low back pain: A



A B C

The suggested pathogenesis (A) and kinematics (B-C) in isthmic spondylolysis (ISP).

randomized single blind controlled study. J Back Musculoskelet Rehabil. 2015 Oct 26.

Hay O, Dar G, Abbas J, Stein D, May H, **Masharawi Y**, Peled N, Hershkovitz I. The lumbar lordosis in males and females, revisited. PLoS One. 10:e0133685, 2015.

Abu-Leil S, Floman Y, Bronstein Y, **Masharawi Y**. A morphometric analysis of all lumbar intervertebral discs and vertebral bodies in degenerative spondylolisthesis. Eur Spine J. 25:2535-2545, 2016.

Saban B, **Masharawi Y**. Pain threshold tests in patients with heel pain syndrome. Foot Ankle Int. 37:730-736, 2016.

Peleg S, Dar G, Steinberg N, **Masharawi Y**, Hershkovitz I. Sacral orientation and Scheuermann's kyphosis. Springerplus. 5:141, 2016.

Saban B, **Masharawi Y.** Three single leg standing tests for clinical assessment of chronic plantar heel pain syndrome: static stance, half-squat and heel rise. Physiotherapy. 103:237-244, 2017.

Ezra D, **Masharawi Y**, Salame K, Slon V, Alperovitch-Najenson D, Hershkovitz I. Demographic aspects in cervical vertebral bodies' size and shape (C3-C7): a skeletal study. Spine J. 17:135-142, 2017.

Reviews

Blum N, Halperin D, **Masharawi Y**. Ambulatory and hospital-based quality improvement methods in Israel. Health Serv Insights. 2014;7:25-30.

Dr. Semyon Melnikov, R.N. Ph.D.

Department of Nursing
The Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: melniko@tauex.tau.ac.il

Health Maintenance Among Immigrants from the Former USSR, Ethiopia and Arab Citizens of Israel

Position

Head, Short-day studies BA Nursing Program

Lecturer, Sackler Faculty of Medicine

Research

Health maintenance among immigrants from the former USSR, Ethiopia and among Arab citizens of Israel.

The rates of chronic illness such as ischemic heart disease and hypertension among immigrants from the former USSR (FUSSR) and among Arab citizens of Israel, and of diabetes among Ethiopian immigrants are higher than those in the general Israeli population. In my research, I focus on the study of behaviors aimed at health maintenance among immigrants from the FUSSR and Ethiopia, and Arab citizens of Israel according to Bandura's Reciprocal Determinism (1983) model. I will examine how the immigrants' and ethnic minorities members' personal characteristics, such as knowledge and attitudes toward chronic disease, together with environmental effects, are linked to behaviors aimed at maintaining health among immigrants from the FUSSR and Ethiopia, and among Arab citizens of Israel.

Publications

Kagan I, Fridman S, Shalom E, **Melnikov S**. (2017). The effect of working in an infection isolation room on hospital nurses' job satisfaction. *Journal of Nursing Management*, 00, 1-7.

Shemesh Y, Peles-Bortz A, Peled-Potashnik Y, Har-Zahav Y, Lavi J, Noimark D, **Melnikov S** (2017). Feelings of indebtedness and guilt towards donors and immunosuppressive medication adherence among heart transplant (HTx) patients, as assessed in a cross-sectional study with the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS). *Clinical Transplantation*, DOI: 10.1111/ctr.13053

Asman O, Barnoy Z, **Melnikov S**, Tabak N. (2017). Experiences, Behaviors and Perceptions of Registered Nurses Regarding Research Ethics. *Nursing Ethics*

Kagan I, Friedman S, Shalom E, **Melnikov S**. (2017). The effect of working in an infection isolation room on hospital nurses' job satisfaction. *Journal of Nursing Management*

Kagan I, Itzhaki M, **Melnikov S**. (2017). Patriotism, organizational commitment and Israeli nurses' intention to report to work in emergencies. *International Nursing Review*, DOI: 10.1111/inr.12395

Melnikov S, Itzhaki M, Koton S. (2017). Age-group and gender differences in stroke knowledge in an Israeli Jewish adult population. *Journal of Cardiovascular Nursing*, [DOI:10.1097/JCN.0000000000000424

Melnikov S, Ashkenazi T, Amra M, Peles-Bortz A. (2017). Transcendental spirituality and acquaintance with the activities of the domestic transplantation center as factors shaping attitudes toward organ donation, *Progress in Transplantation*, DOI: 10.1177/1526924817699967

Melnikov S, Elian-Antar T, Shor R, Kigli-Shemesh R, Kagan I. (2016). Nurses teaching prison officers: a workshop to reduce the stigmatization of mentally ill person inmates. *Perspectives in Psychiatric Care*.

Kagan I**,** Shor R, Kigli-Shemesh R, **Melnikov S**. (2016). Between a rock and a hard place: Ethical and professional dilemmas in the management of care and functioning in a psychiatric hospital under missile attacks. *Journal of the American Psychiatric Nurses Association*. [Epub ahead of print]

Itzhaki M, **Melnikov S**, Koton S. (2016). Gender differences in feelings and knowledge about stroke. *Journal of Clinical Nursing,* 25, 2958-2966

Peles-Bortz A, Ashkenazi T, **Melnikov S**. (2015). Spirituality as a predictive factor for signing an organ donor card. *Journal of Nursing Scholarship*, 47, 25-33

Kagan I, Biran E, Telem L, Steinovitz N, Alboer D, **Melnikov S.** (2015). Promotion and marketing of nursing profession by nurses. *International Nursing Review*, 62, 368-76

Melnikov S, Itzhaki M, Koton S. (2016). Differences between new immigrants from the Former Soviet Union and veteran residents in knowledge, perception, and risk factors of stroke. *Journal of Cardiovascular Nursing*, 31(6), 500-506

Melnikov S, Itzhaki M, Kagan I. (2014). Israeli nurses' intention to report for work in an emergency or disaster. *Journal of Nursing Scholarship*, 46, 134-142

Melnikov S, Shor R, Kigli-Shemesh R, Gun Usishkin M, Kagan I. Closing an Open Psychiatric Ward: Organizational Change and Its Effect on Staff Uncertainty, Self-Efficacy, and Professional Functioning. *Perspectives in Psychiatric Care*. 2013, 49, 103-109.

Dr. Sigal Portnoy, Ph.D.

Department of Occupational Therapy
School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: portnoys@post.tau.ac.il
URL: www.tau.ac.il/~portnoys

Computational Biomechanics in Motor Rehabilitation

Position

Lecturer, Sackler Faculty of Medicine

Research

The motor function and rehabilitation lab is dedicated to the study of motor mechanisms and rehabilitation strategies. The major research themes of the laboratory are:

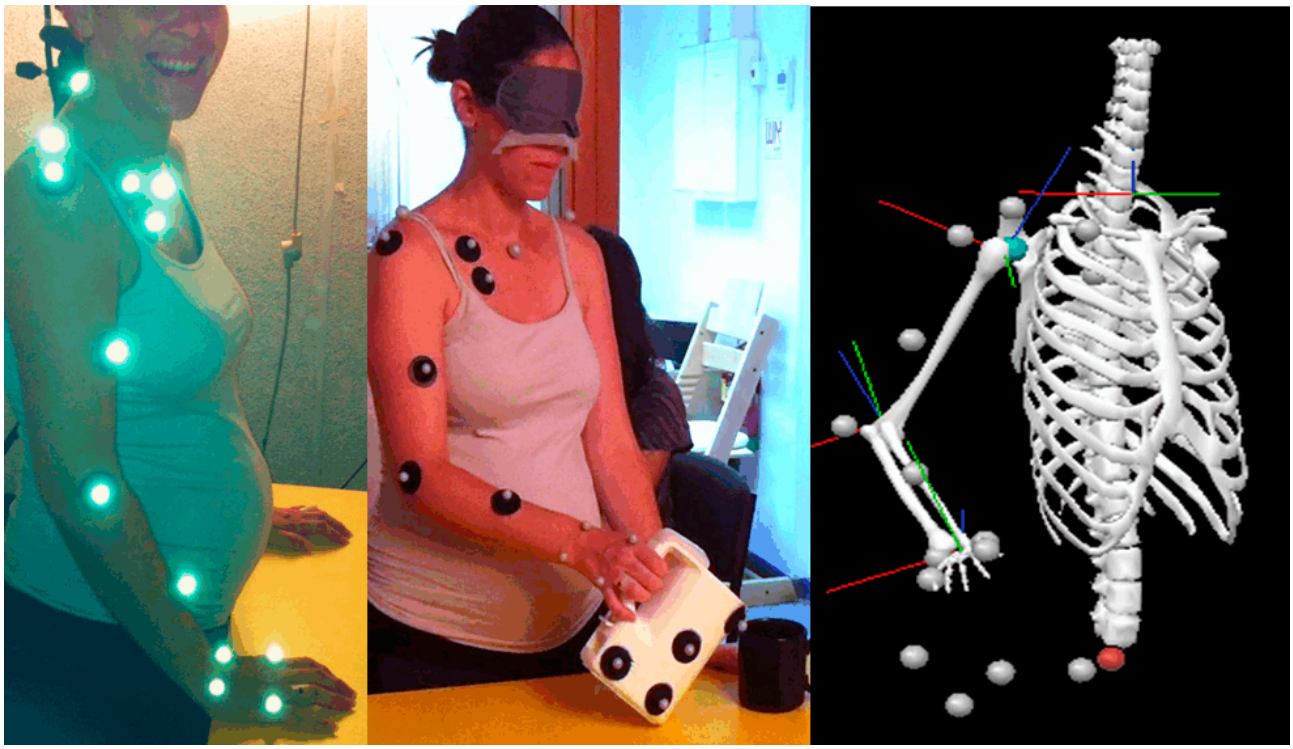
1. Design of new evaluation and treatment tools for clinicians, based on state-of-the-art technologies.
2. Quantification, evaluation and feedback, provided to the motor-impaired patient by utilizing real-time data of the kinematics, kinetics and muscular activity patterns.
3. Development of innovative assistive technology and out-of-clinic rehabilitation solutions.

The work in the laboratory is highly interdisciplinary, combining aspects of biomedical engineering, rehabilitation medicine, physiotherapy, and occupational therapy.

Publications

Portnoy S, Schwartz I. Gait characteristics of post-poliomyelitis patients: standardization of quantitative data report, *Annals of Physical and Rehabilitation Medicine*. S1877-0657(13)00103-6. 2013.

Portnoy S, Rosenberg L, Alazraki T, Elyakim E, Friedman J. Differences in muscle activity patterns, visuomotor abilities, and graphical product quality in children drawing activities on horizontal or vertical surfaces, *Journal of Electromyography and Kinesiology,* 25: 540-547, 2015.



3D kinematics of daily activities acquired using a passive-marker-based motion capture system

Portnoy S, Halaby O, Dekel-Chen D, Dierick F. Effect of an auditory feedback substitution, tactilo-kinesthetic, or visual feedback on kinematics of pouring water from kettle into cup, *Applied Ergonomics,* 51: 44-49, 2015.

Simana E, Simian SR, **Portnoy S,** Jaffe A, Dekel BC, Feasibility study – Vitamin D loading determination by Ftir-Atr, *Information and Control Systems*, 3: 107-111, 2015.

Portnoy S, Frechtel A, Raveh E, Schwartz I. Prevention of genu recurvatum in post stroke patients using a new orthosis, *Physical Medicine and Rehabilitation*, 7:1042-1051, 2015.

Levanon Y, Gefen A, Lerman Y, **Portnoy S,** Ratzon NZ. Key Strike forces and high level of musculoskeletal symptoms, *Safety and Health at Work*, 2016.

Rabin A, **Portnoy S,** Kozol Z. The association between visual assessment of quality of movement and 3-dimensional analysis of pelvis, hip, and knee kinematics during a lateral step down test, *Journal of Strength and Conditioning Research*, 2016.

S. Portnoy, A. Hersch, T. Sofer, S. Tresser. Comparison of reaction time and center of pressure movement between paired-play and solo-play of a virtual reality game, *Games for Health Journal,* 6(3), 147-151, 2017.

D. Rand, K. Ben-Chaim, R. Malka, **S. Portnoy**. Development of Internet-based Tasks for the Executive Function Performance Test, *American Journal of Occupational Therapy*, Accepted for Publication, 2016.

S. Portnoy, S. Reif, T. Mendelboim, D. Rand. Comparing postural control of individuals with chronic stroke to healthy participants: clinical tools and center of pressure movement. *European Journal of Physical Rehabilitation Medicine*, Accepted for Publication, 2017.

E. Raveh, J. Friedman, **S. Portnoy**. Visuomotor behaviours and performance in a dual-task paradigm with and without vibrotactile feedback when using a myoelectric controlled hand, *Assistive Technology*, 19, 1-7, 2017.

Y. Kaufman-Cohen, J. Friedman, Y. Levanon, G Yaacobi, N. Doron, **S. Portnoy**. Wrist plane of motion and ranges of the dominant and non-dominant hand during daily activities, *American Journal of Occupation Therapy*, Accepted, 2017.

F. Dierick, M. Dehas, JL. Isambert, S. Injeyan, AF. Bouché, Y. Bleyenheuft, **S. Portnoy**. Does subtype of stroke influence gait and posture outcomes after a neurorehabilitation intervention combining robotic-assisted treadmill and neurofacilitory therapy?, *Plos One*, Accepted for Publication, 2017.

S. Portnoy, A. Mimouni-Bloch, L. Rosenberg, H. Offek, T. Berman, M. Kochavi, G. Orman, J. Friedman. Graphical product quality and muscle activity in children with mild disabilities drawing on horizontal or vertical oriented tablet, *American Journal of Occupation Therapy*, Accepted for Publication, 2017.

D. Shoseyov, T. Cohen-Kaufman, I. Schwartz, **S. Portnoy**. Comparison of activity and fatigue of the respiratory muscles and pulmonary characteristics between post-polio patients and controls: a pilot study. *Plos One*, 12:e0182036. 2017.

Portnoy S, Hersch A, Sofer T, Tresser S. Comparison of path length and ranges of movement of the center of pressure and reaction time and between paired-play and solo-play of a virtual reality game. *Games Health* J. 6:147-151, 2017.

Chapter

Portnoy S, Gefen A. Patient-specific modeling of subjects with a lower limb amputation, Patient-Specific Modeling in Tomorrow's Medicine, Studies in Mechanobiology, Tissue Engineering and Biomaterials Volume 09, 2012, pp 441-459.

Dr. Debbie Rand, Ph.D., O.T.

Department of Occupational Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: drand@post.tau.ac.il

Gaming for Rehabilitation of Neurological and Geriatric Populations

Position

Senior Lecturer, Sackler Faculty of Medicine

Chair, Department of Occupational Therapy

Research

Our research focuses on achieving a better understanding of the factors hindering and facilitating recovery post-stroke. We have developed interventions aimed to improve the motor recovery and executive functions deficits of these individuals, in order to enhance function in daily living. The effectiveness of these novel interventions is assessed by conducting randomized clinical trials, the highest level of clinical research. We have researched the effectiveness of a 'Community' and a 'Home' based intervention using video-games compared to traditional therapy for enhancing daily function and participation of individuals with chronic stroke. We are currently collaborating to investigate the use of touchscreen tablets for self-training of the weaker upper extremity to improve dexterity of individuals with acquired brain injury and to improve cognitive abilities of older adults with Mild Cognitive Impairments.

Publications

Rand D, Ben-Chaim KL, Malka R, Portnoy S. Development of internet-based tasks for the executive function performance test. Am J Occ Ther, in press.

Rand D, Givon N, Averch Bar M. A video-game group intervention; experiences and perceptions of adults with chronic stroke and their therapists. Can J Occ Ther, in Press.

Yacoby A, Zeilig G, Weingarden H, Weiss R, **Rand D**. Feasibility, adherence and satisfaction of video-games versus traditional self-training of the upper extremity in chronic stroke; a pilot randomized controlled trial. Am J Occ Ther, in press.

Rand D, Weingarden H, Weiss R, Yacoby A, Reif S, Malka R, Shiller DA, Zeilig G. (2017). Self-training to improve UE function at the chronic stage post-stroke: a pilot randomized controlled trial. Dis Rehab, 39, 15, 1541-1548.

Levin C, Gur-Yaish N, Agmon M, Gil E, **Rand D**, King B, Zisberg A. (2017). Development and psychometric testing of a measure of older adult patients' attitudes towards mobility during hospitalization (ATM-H) Geriatric Nursing. Ger Nurs 38:119-123

Agmon M, Zisberg A, Gil E, **Rand D**, Gur-Yaish N, Azriel M. (2017). association between 900 steps a day and functional decline in older hospitalized patients. *JAMA Int Med*, 1;177:272-274.

Portnoy S, Reif S, Mendelboim T, **Rand D**. (2017). Postural control of individuals with chronic stroke compared to healthy participants: TUG, FRT and center of pressure movement. European J Phys Rehab Med, 8. doi: 10.23736/S1973-9087.17.04522-1.

Rozental-Iluz C, Zeilig G, Weingarden H, **Rand D**. Improving executive function deficits by playing interactive video-games; a secondary analysis of a randomized controlled trial for individuals with chronic stroke. Eur J Phys Rehabil Med. 2016.

Kizony R, Zeilig G, Dudkiewicz I, Schejter-Margalit T, **Rand D**. (2016). Tablet Apps and dexterity: Comparison between 3 age groups and proof of concept for stroke rehabilitation. J Neurol Phys Ther. 2016, 40:31-9.

Givon N, Zeilig G, Weingarden H, **Rand D**. Video-games used in a group setting is feasible and effective to improve indicators of physical activity in individuals with chronic stroke: A randomized controlled trial. Clin Rehabil. 2016, 30:383-92.

Rand D, Zeilig G, Kizony R. Rehab-let: touchscreen tablet for self-training impaired dexterity post stroke: study protocol for a pilot randomized controlled trial. Trials. 2015, 16:277.

Frost Y, Weingarden H, Zeilig G, Nota A, **Rand D.** Self-care self-efficacy correlates with independence in basic activities of daily living in individuals with chronic stroke. J Stroke Cerebrovasc Dis. 2015, 24:1649-55.

Ratzon NZ, Friedman S, Zamir S, Amit Y, **Rand D.** Functional capacity evaluation; does it change the determination of the degree of work disability? Disabil Health J. 2015, 8:80-85.

Rand D, Eng JJ. Predicting daily-use of the affected upper extremity one year poststroke. J Stroke Cerebrovasc Dis. 2015, 24:274-283.

Givon N, **Rand D**. Group therapy using video games for individuals with chronic stroke. Isr J Occup Ther. 2014, 23:H94-H104.

Rand D, Givon N, Weingarden H, Nota, A., & Zeilig, G. Eliciting upper extremity purposeful movements using video games a comparison with traditional therapy for stroke rehabilitation. Neurorehabil Neural Repair, 2014, 28:733-739. [Epub ahead of print]

Erez N, Weiss PL, Kizony R, **Rand D**. Comparing performance within a virtual supermarket of children with traumatic brain injury to typically developing children: a pilot study. OTJR. 2013, 33:218-227.

Book Chapters

Weiss PL, Kizony R, Feintuch U, **Rand D**, Katz N. Textbook of Neural Repair and Rehabilitation Section: Technology of Rehabilitation. Chapter # 47: Virtual Reality Applications in, iNeurorehabilitation. In press.

Grants

2017–2019	Maccabi Healthcare Services Research Fund
2017–2019	Israel National Institute for Health Policy Research

Prof. Navah Z. Ratzon, Ph.D., O.T.

Department of Occupational Therapy
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: navah@post.tau.ac.il

Investigating the Ergonomics of Occupational Tasks and Driving Rehabilitation

Position

Associate Professor, Sackler Faculty of Medicine

Research

Our research focuses on the ergonomics of occupational tasks such as typing and playing musical instruments. Our current research integrates the usage of 3-dimensional advanced technologies to evaluate the movement of hands, specific devices to evaluate force, computerized technologies to evaluate sitting which enable to refer to dynamic situations and the change in risk factors while performing different tasks. These studies have provided essential information concerning risk factors for musculoskeletal disorders and have led to more recent investigations of the determinants of postural patterns amongst children that may contribute to risks in adolescence and adulthood. The anticipated outcomes of these programs of research are to develop training programs and/or contribute to workspace design to minimize these risks.

Driving rehabilitation is another major area of research. Research explores the impact of disease and disorder on driving with the aim of developing appropriate rehabilitation programs, reflecting the importance of 'driving' as a factor in independence as well as a marker of function for variety of populations.

Publications

Ratzon, N., Ben Ari (Shevil), E., Froom, P., Friedman, S., Amit, Y. (2013). Functional capacity evaluation of work performance among individuals with pelvic injuries following motor vehicle accidents. *Work: A Journal of Prevention, Assessment & Rehabilitation*, 45, 191-200.

Lipskaya-Velikovsky, L., Kotler, M., Weiss, P., Kaspi, M., Gamzo, S.,**Ratzon, N.** (2013). Car Driving in Schizophrenia: Can Visual Memory and Organization Make a Difference? *Disability and Rehabilitation,* 35, 1734-1739.

Liberman, L., **Ratzon, N.**, Bart, O. (2013). The profile of performance skills and emotional factors in the context of participation among young children with Developmental Coordination Disorder. *Research in Developmental Disabilities,* 34, 87-94.

Lahav, O., Apter, A., **Ratzon, N.** (2013). Psychological adjustment and levels of self-esteem in children with visual-motor integration difficulties influences the results of a randomized intervention trial. *Research in Developmental Disabilities*, 34, 56-64.

Rosenberg, L., Bart, O., **Ratzon, N. Z.**, & Jarus, T. (2013). Complementary contribution of parents and therapists in the assessment process of children. *Australia Occupational Therapy Journal*, *60*, 410-415.

Gat, S., & **Ratzon, N. Z**. (2014). Comparison of occupational therapy students' perceived skills after traditional and nontraditional fieldwork. *The American Journal of Occupational Therapy*, *68* , e47-e54.

Shichror, R., Sarid, A., **Ratzon, N.** (2014) Determining the Sampling Time Frame for In-Vehicle Data Recorder Measurement in Assessing Drivers. *Transportation Research Part C*, *42C*, 99-106.

Karni, S., Bentur, N., & **Ratzon, N.** (2014) Participation and Quality of Life of Cognitively Impaired Older Women in Israel Following Hip Fractures. *Occupational Therapy International.* 21, 91-97.

Naveh, Y., Weiss, P., **Ratzon, N.Z**. (2014). Affordable driving simulation for use in a rehabilitation setting: preliminary findings. *The Israeli Journal of Occupational Therapy, 23,* E-115-E130.

Levanon, Y., Gefen, A., Lerman, Y., **Ratzon, N**. (2014). Validity of the modified RULA for computer workers and reliability of one observation compared to six. *Ergonomics, 57,* 1856-1863**.**

Ratzon, N.Z., Amit, Y., Friedman, S., Zamir, S., Rand, D. (2014). Functional capacity evaluation; does it change the determination of the degree of work disability? *Disability and Health Journal,* 8, 80-85.

Golebowicz, M., Levanon, Y., Palti, R., **Ratzon, N.Z**. (2015). Efficacy of a telerehabilitation intervention program using biofeedback among computer operators. *Ergonomics,* 58*,* 791-802.

Naveh, Y., Shapira, A., **Ratzon, N.Z**. (2015). Using a driving simulator during vehicle adaptation. *British Journal of Occupational Therapy*, 78, 377-382.

Rottenberg, Y., **Ratzon, N**., Jacobs, J. M., Cohen, M., Peretz, T, de Boer, A.G.E. (2016). Unemployment risk and income change after testicular cancer diagnosis: a population based study. *Urologic Oncology: Seminars and Original Investigations*, 34, 5-27.

Ratzon, N.Z., Abraham Bar-Niv, N., Froom, P. (2016). The effect of a structured personalized ergonomic intervention program for hospital nurses with reported musculoskeletal pain: an assigned randomized control trial. *Work*, 54*,* 367-377.

Levanon, Y., Gefen, A., Lerman, Y., Portnoy, S., **Ratzon, N**. (2016). Key strike forces and high level of musculoskeletal symptoms safety and health at work. *Safety and Health at Work*. (ahead of print).

Marom, B, Carel, R.S., Sharabi, M. **Ratzon, N.Z**. (2016). Cross-cultural adaption of the 12-item version of the world health organization disability assessment schedule 2.0 (WHODAS 2.0) for Hebrew-speaking subjects. *Disability and Rehabilitation*. (ahead of print)

Ratzon, Z.N., Uziely, B., de Boer, A.G.E.M, Rottenberg, Y. (2016). Unemployment risk and decreased income 2 and 4 years after thyroid cancer diagnosis: a population based study. *Thyroid*. (ahead of print)

Avrech-Bar, M., **Ratzon, N.Z.** (2016). Enhancing new students' knowledge, competence, awareness and interest in accessibility. *Hong Kong Journal of Occupational Therapy.* In press.

Ratzon, N.Z., Kadury Lunievsky, E., Ashkenasi, A., Laks, J., Cohen, H.A. (2016). Simulated driving skills evaluation with pre-driving lesson ADHD teenagers. *American Journal of Occupational Therapy*. In press.

Shefer Eini, D., Ratzon, N.Z., Rizzo, A. A., Yeh, S.C., Lange, B.,, Yaffe, B., Daich, A., Weiss. P. L., Kizony, R. (2016). Camera-tracking gaming control device for evaluation of wrist range of motion. *Journal of Hand Therapy*. In press.

Rottenberg, Y., Jacobs, J.M., **Ratzon, N.Z.**, Grinshpun, A., Cohen, M., Uziely, B. de Boer, A.G.E.M. (2016) Unemployment risk 2 years and 4 years following gastric cancer diagnosis: a population based study. *Journal of Cancer Survivorship*. 11, 119-125.

Rottenberg, Y., **Ratzon, N.Z.**, Cohen, M., Hubert, A., Uziely, B., de Boer, A.G.E.M. (2016) Unemployment risk at 2 and 4 years following colorectal cancer diagnosis: a population based study. *European Journal of Cancer*. 69, 70-76.

Grants

2016-2019 Insurance Research Fund, The Israeli Association of Insurance Company

Dr. Angela Ruban, Ph.D.

Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: angellruban@post.tau.ac.il
URL: https://angellruban71.wixsite.com/angellruban

The Role of Glutamate Excitotoxicity in Neurodegenerative and Malignant Diseases

Position

Lecturer, Sackler Faculty of Medicine

Research

Glutamate (Glu) has been shown to play a role not only in neural processes, such as learning and memory, but in bioenergetics, biosynthetic and metabolic oncogenic pathways as well. High extracellular Glu concentrations, such as those found in numerous CNS pathological conditions, ultimately cause the excitotoxic death of the exposed neurons and entail irreversible neurological deficits. Our research focuses on the mechanisms that maintain the Glu homeostasis in brain extracellular fluids and their role in the pathogenesis of neurodegenerative and malignant diseases. Our aim is to determine the impact of excess extracellular Glu levels and the various antiglutamatergic therapeutic strategies on the progression of the malignant and neurodegenerative diseases. We believe that a profound understanding of the glutamate signaling pathways may provide novel therapeutic opportunities for various CNS diseases.

Publications

Pérez-Mato M, Ramos-Cabrer P, Sobrino T, Blanco M, **Ruban A**, Mirelman D, Menendez P, Castillo J, Campos F.: Human recombinant glutamate oxaloacetate transaminase 1 (GOT1) supplemented with oxaloacetate induces a protective effect after cerebral ischemia. *Cell Death Dis.* Vol. 9; 5:e992, 2014.

Ruban A, Mohar B, Jona G, Teichberg VI. Blood glutamate scavenging as a novel neuroprotective treatment for paraoxon intoxication. *J Cereb Blood Flow Metab*. 34; 221-7, 2014.

Schwartz-Arad D, Ofec R, Eliyahu G, **Ruban A**, Sterer N. Long term follow-up of dental implants placed in autologous onlay bone graft. *Clin Implant Dent Rel Res*. 2014.

Ruban A, Biton, I, Markovich, A. and Mirelman, D. MRS of brain metabolite levels demonstrates the ability of scavenging of excess brain glutamate to protect against nerve agent induced seizures. *Int J Mol Sci*. Vol. 16; 3226-36, 2015.

Ruban A, Cohen-Kashi Malina K, Cooper I, Graubardt N, Babakin L, Jona G, and Teichberg V. Combined treatment of an ALS rat model with recombinant GOT1 and oxaloacetic acid: a novel neuroprotective treatment. *Neurodegen Dis.* Vol. 15: 233-42, 2015.

Grants

2016 – 2019 Israel Science Foundation (ISF)

2016 – 2018 Cancer League, University of California (UCSF)

Dr. Miriam Theilla, Ph.D.

Department of Nursing
Steyer School of Health Professions
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: miriamt@post.tau.ac.il

The Effect of Fish Oil Enriched Diet on Wound Healing Processes in ICU Patients

Positions

Lecturer, Sackler Faculty of Medicine

Research

Wound healing is the complex, multi-stage response to tissue injury. This physiologic repair response requires a dynamic temporal and spatial interplay of several cell types, including local parenchymal and mesenchymal cells as well as resident and recruited inflammatory cells. N-3 Fatty acids are recognized as influencing both wound healing and immunity .Our group studies the impact and the specific role of fish oil- and micronutrient enriched formulae on the healing of pressure ulcers and on immune function mediated through a modulation of expression of adhesion molecules in critically ill patients

Our results show a reduction in inflammation levels of C – reactive protein concentrations and increasing levels of adhesion molecules preceding the subsequent reduction in ulcer severity of critically ill patients.

The formulae may ameliorate the inflammatory response, both in magnitude and duration, probably mediated by an effect on adhesion molecule expression. by promoting the transition from an inflammatory to reparative stage of wound healing.

Publications

Anbar R, Beloosesky Y, Cohen J, Madar Z, Weiss A, **Theilla M**, Koren Hakim T, Frishman S, Singer P. Tight Calorie Control in geriatric patients following hip fracture decreases complications: a randomized, controlled study. Clinical Nutrition 33:23-8, 2014

Frishman, S, **Theilla M**, Singer P, Avraham Z, Libman C, Kagan I. JCI Accreditation and its multiprofessional impact on nutrition care at Rabin Medical Center, Israel. Invited (peer-reviewed) paper, published 01 April 2014 on official site of Joint Commission International (JCI): http://www.jointcommissioninternational.org/new-study-jci-accreditation-and-nutrition-care-at-rabin-medical-center/

Green P, **Theilla M**, Singer P. Lipid metabolism in critical illness. Curr Opin Clin Nutr Metab Care. 2016;19:111-5.

Theilla M, Ławiński M, Cohen J, Hadar E, Kagan I, Perkewick M, Singer P. Safety of home parenteral nutrition during pregnancy. Clin Nutr. 2015 Dec 12. [Epub ahead of print]

Kagan I, Cohen J, Stein M, Bendavid I, Pinsker D, Silva V, **Theilla M**, Anbar R, Lev S, Grinev M, Singer P. Preemptive enteral nutrition enriched with eicosapentaenoic acid, gamma-linolenic acid and antioxidants in severe multiple trauma: a prospective, randomized, double-blind study. Intensive Care Med. 2015;41:460-9.

Lupinsky L, Singer P, **Theilla M**, Grinev M, Hirsh R, Lev S, Kagan I, Attal-Singer J. Comparison between two metabolic monitors in the measurement of resting energy expenditure and oxygen consumption in diabetic and non-diabetic ambulatory and hospitalized patients. Nutrition. 2015;31:176-9.

Theilla M, Grinev M., Kosak S.Hiesmayr M., Singer P. Clinical Nutrition ESPEN. Fight against malnutrition: The results of a 2006–2012 prospective national and global nutrition day survey. E-SPEN Journal, 2015.

Theilla M, Grunev M, Kosak S, Hiesmayr M, Singer P. The Nutrition Day Israel working group. Fight against malnutrition: The results of a 2006-2012 prospective national and global NutritionDay survey. Clinical Nutrition ESPEN, 2015.

Theilla M, Cohen J, Singer P, Liebman C, Kagan I. The assessment, knowledge and perceived quality of nutrition care amongst nurses. Nutri Med Diet Care 2016

Ben-David I, Singer P, **Theilla M**, Themessl-Huber M, Sulz I, Mouhieddine M, Schuh C, Mora B., Hiesmayr

M. NutritionDay ICU: A 7 year worldwide prevalence study of nutrition practice in intensive care. Clinical Nutrition, 2016.

Zusman O, **Theilla M**, Cohen J, Kagan I, Ben-David I, Singer P. Resting energy expenditure, calorie and protein consumption in critically ill patients: A retrospective cohort study. Crit Care 2016; 20: 367.

Chapters and Reviews

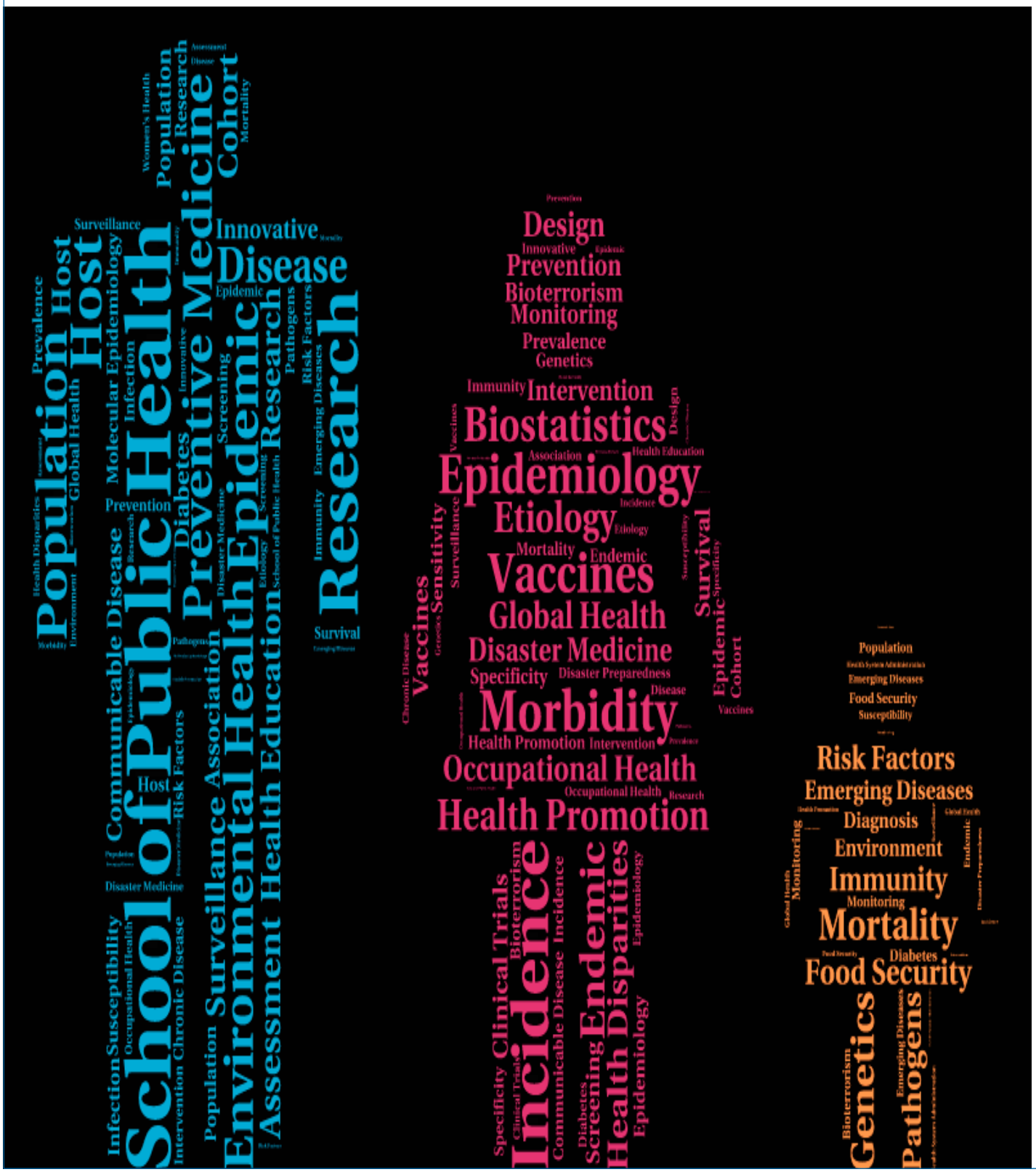
Singer P, **Theilla M**, Cohen J. Use of intravenous lipids: what do the guidelines say? World Rev Nutr Diet. 2015;112:163-71.

Singer P, **Theilla M**, Cohen J. Intravenous lipids: what do the guidelines say. Institute for Nutrition Research and Critical Care Department. *In press*.

Green P, **Theilla M**, Singer P. Lipid metabolism in critical illness. Current Opinion in Clinical Nutrition & Metabolism Care, 2016.

Kagan I, **Theilla M**, Singer P. Is total parenteral nutrition (TPN) an evil in trauma patients? Curr Trauma, 2016.

Public Health



Prof. Daniel I. Cohen, Ph.D.

Department of Epidemiology and Preventive Medicine
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: dancohen@post.tau.ac.il

Epidemiology of Infectious Diseases

Positions

Professor of Epidemiology and Preventive Medicine

Head, School of Public Health, Sackler Faculty of Medicine

Incumbent of Diana & Stanley Steyer Chair of Cancer Prevention and Control

Director, Stanley Steyer Institute for Cancer Epidemiology and Research

Director, Tel Aviv University Center for the Study of Bioterrorism

Research

Emerging Infectious Diseases, Vaccinology

(1) The study of risk and protective host factors against enteric diseases; identification of correlates of protection related to the immune response and host microbiota; development of enteric vaccines (2) Development of laboratory-based surveillance methods for enteric diseases (3) Seroepidemiology of vaccine-preventable diseases to monitor the immune status of the Israeli population (4) The study of the association between selected infectious agents (e.g. Helicobacter pylori, Human Papilloma Virus) and cancer.

Publications

Di giovine P, Kafatos G, Nardone A, Andrews N, Olander, Alfarone G, Broughton K, **Cohen D**, Kriz B, Mikova I, O'flanagan D, Schneider F, Selga I, Valinsky I, Velicko I, Karacs I, Pebody R, Von hunolstein C. Comparative seroepidemiology of diphtheria in six European countries and Israel. *Epidemiol Infect*. 2013, 141:132-42.

Eriksen J, Davidkin I, Kafatos G, Andrews N, Barbara C, **Cohen D**, Duks A, Griskevicius A, Johansen K, Bartha K, Kriz B, Mitis G, Mossong J, Nardone A, O'Flanagan D13, DE Ory F, Pistol A, Theeten H, Prosenc K, Slacikova M, Pebody R: Seroepidemiology of mumps in Europe (1996-2008): why do outbreaks occur in highly vaccinated populations? *Epidemiol Infect* 2013, 141:651-666.

Feldman N, Adler A, Molshatzki N, Navon-Venezia S, Khabra E, **Cohen D**, Carmeli Y: Gastrointestinal colonization by KPC-producing Klebsiella pneumoniae following hospital discharge: duration of carriage and risk factors for persistent carriage. *Clin Microbiol Infec* 2013, 19:E190-E196.

Levine H, Balicer RD, Zarka S, Sela T, Rozhavski V, **Cohen D**, Kayouf R, Ambar R, Porat N, Dagan R: Dynamics of Pneumococcal Acquisition and Carriage in Young Adults during Training in Confined Settings in Israel. *Plos One* 2012, 7: e46491.

Leventhal A, Ramlawi A, Belbiesi A, Sheikh S, Haddadin A, Husseini S, Abdeen Z, **Cohen D**: Enhanced surveillance for detection and management of infectious diseases: regional collaboration in the Middle East. *Emerging Health Threats J* 2013, 6.

Muhsen K, Kassem E, Rubinstein U, Schachter Y, Kremer A, Goren S, Zilberstein I, Ephros M, **Cohen D**, Shulman LM: Incidence and characteristics of sporadic *Norovirus Gastroenteritis* associated with hospitalization of children less than 5 years of age in Israel. *Pediatr Infect Dis J* 2013, 32:688-90

Weil M, Shohat T, Bromberg M, Bassal R, Dichtiar R, Mandelboim M, Sofer D, **Cohen D**, Mendelson E. The dynamics of infection and the persistence of immunity to A(H1N1)pdm09 virus in Israel. *Influenza Other Respir Viruses.* 2013, 7:838-46 .

Farag T, Faruque AS, Yukun Wu, Das SK, Hossain A, Ahmed S, Ahmed D, Dilruba N, Kotloff K, Panchilangam S, Nataro J, **Cohen D,** Blackwelder WC, Levine MM. Housefly population density correlates with shigellosis among children in Mirzapur, Bangladesh: A Time Series Analysis. *PLoS Negl Trop Dis* 2013, 7: e2280.

Markovich MP, Shohat T, Riklis I, Avni R, Yujelevski-Rozenblit D, Bassal R, **Cohen D,**_Rorman E:

Seroepidemiology of Toxoplasma gondii infection in the Israeli population. *Epidemiol Infect*: 2014, 142:149-55.

Bassal R, Schejter E, Bachar R, Shapira H, Sandbank J, Supino Rosin L, Schvimer M, **Cohen D**, Keinan-Boker L: Cervical Pap screening among Israeli women, 2005-2010. Archives of Gynecology and *Obstetrics* 2014, 289:615-22.

Cohen D, Bassal R, Goren S, Rouach T, Taran D, Schemberg B, Peled N, Kenes Y, Ken-Dror S, Vasilev V, Nissan I, Agmon V, Shohat T. Recent trends in the epidemiology of shigellosis in Israel*. Epidemiol Infect*. 2014, 142:2583-94.

Muhsen K, Kassem E, Efraim S, Goren S, **Cohen D**, Ephros M. Incidence and risk factors for intussusception among children in northern Israel from 1992 to 2009: a retrospective study. BMC Pediatr. 2014;14(1):218.

Tobias J, Kassem E, Rubinstein U, Bialik A, Vutukuru S, Navaro A, Rokney A, Valinsky L, Ephros M, **Cohen D**, Muhsen K. Involvement of main diarrheagenic Escherichia coli, with emphasis on enteroaggregative E. coli, in severe non-epidemic pediatric diarrhea in a high-income country. BMC Infect Dis. 2015;15(1):79

Muhsen K, Goren S. **Cohen D**. Helicobacter pylori Infection in Early Childhood and Growth at School Age. Helicobacter. 2015 ;20(6):410-7.

Muhsen K, Rubenstein U, Kassem E, Goren S, Schachter Y, Kremer A, Shulman L.M, Ephros M, **Cohen D**. A significant and consistent reduction in rotavirus gastroenteritis hospitalization of children under five years of age, following the introduction of universal rotavirus immunization in Israel. Hum Vaccin Immunother. 2015;11(10):2475-82

Muhsen K, Chodick G, Goren S, Anis E, Ziv-Baran T, Shalev V, **Cohen D.** Change in incidence of clinic visits for all-cause and rotavirus gastroenteritis in young children following the introduction of universal rotavirus vaccination in Israel. *Euro Surveill*. 2015;20(42).

Mor O, Bassal R, Michaeli, M, Wax M, Ram D, Cohen-Ezra O, **Cohen D**, Mendelson E, Ben-Ari Z, Shohat T. Prevalence of Hepatitis E virus antibodies in Israel. *Emerg Infect Dis*. 2015; 21: 692-694.

Behar A, Fookes MC, Goren S, Thomson NR, **Cohen D**. Whole genome analysis to detect potential vaccine-induced changes on Shigella sonnei genome. *Vaccine.* 2015;33:2978-83.

Mor O, Ofir I, Pavel R, Bassal R, Kra-Oz K, **Cohen D**, Shohat T, Mendelson E. Parvovirus B19V infection in Israel: Prevalence and occurrence of acute infection between 2008 and 2013. *Epidemiol Infect*. 2016;144:207-14.

Bassal R, Schejter E, Bachar R, Perri T, Korach J, Jakobson-Setton A, Ben-David LH, **Cohen D**, Keinan-Boker L. Risk factors for cervical cancer and cin3 in Jewish women in israel - two case control studies. *Asian Pac J Cancer Prev*. 2016;17:2067-73.

Bassal R, Lerner L, Valinsky L, Agmon V, Peled N, Block C, Keller N, Keness Y, Taran D, Shainberg B, Ken-Dror S, Treygerman O, Rouach T, Lowenthal S, Shohat T, **Cohen D**. Trends in the epidemiology of *Campylobacteriosis* in Israel (1999-2012). *Foodborne Pathog Dis*. 2016;13:448-55.

Baker KS, Dallman TJ, Behar A, Weill FX, Gouali M, Sobel J, Fookes M, Valinsky L, Gal-Mor O, Connor TR, Nissan I, Bertrand S, Parkhill J, Jenkins C, **Cohen D**, Thomson NR. Travel- and community-based transmission of multidrug-resistant shigella sonnei lineage among international orthodox Jewish communities. *Emerg Infect Dis*. 2016;22:1545-53.

Glatman-Freedman A, Kaufman Z, Kopel E, Bassal R, Taran D, Valinsky L, Agmon V, Shpriz M, **Cohen D**, Anis E, Shohat T. Near real-time space-time cluster analysis for detection of enteric disease outbreaks in a community setting. *J Infect*. 2016;73:99-106.

Muhsen K, Kassem E, Rubenstein U, Goren S, Ephros M, **Cohen D,** Shulman LM. Incidence of rotavirus gastroenteritis hospitalizations and genotypes, before and five years after introducing universal immunization in Israel. *Vaccine*. 2016; 34:5916-5922.

Miller-Roll T, Na'amnih W, **Cohen D**, Carmeli Y, Adler A. Molecular types and antimicrobial susceptibility patterns of Clostridium difficile isolates in different epidemiological settings in a tertiary care center in Israel. *Diagn Microbiol Infect Dis*. 2016; 86:450-454.

Bassal R, Weil M, **Cohen D**, Mendelson E, Shohat T. Seroprevalence of Hepatitis A 12-years following the implementation of toddlers' vaccination: A population based study in Israel. *Pediatr Infect Dis J.* 2017 May 11. (in press).

Na'amnih W, Adler A, Miller-Roll T, **Cohen D**, Carmeli Y. Incidence and Risk Factors for Community and Hospital acquisition of Clostridium Difficile Infection in Tel Aviv Sourasky Medical Center. *Infect Cont Hosp Epidemiol* 2017.

Muhsen M, Anis E, Rubinstein U, Kassem E, Goren S, Shulman L, Ephros M, **Cohen D**. Effectiveness of rotavirus pentavalent vaccine under a universal immunization program in Israel, 2011-2015: a case-control study. *Clin Microbiol Infect* 2017 (in press).

Launay O, Lewis DJM, Anemona A, Loulergue P, Leahy J, Sciré AS, Maugard A, Marchetti E, Zancan S, Huo Z, Rondini S, Marhaba R, Finco O, Martin LB, Auerbach J, **Cohen D**, Saul A, Gerke C, Podda A. Safety profile and immunologic responses of a novel vaccine against shigella sonnei administered intramuscularly, intradermally and intranasally: results from two parallel randomized phase 1 clinical studies in healthy adult volunteers in Europe. *EBioMedicine.* 2017.

Bassal R, Shohat T, Kaufman Z, Mannasse B, Shinar E, Amichay D, Barak M, Ben-Dor A, Bar Haim A, **Cohen D**, Mendelson E, Lustig Y. The seroprevalence of West Nile Virus in Israel: A nationwide cross sectional study. *PLoS One.* 2017.

Reviews

Ashkenazi S, **Cohen D**. An update on vaccines against Shigella. Therapeutic advances in vaccines. *Ther Adv Vaccines*. 2013;1:113-23.

Muhsen K, **Cohen D**. Rotavirus vaccines in Israel: uptake and impact. *Hum Vacc Immunotherap*. 2017; 13 (7).

Grants

2011-2017	European Union: "Development of vaccines against Shigella and enterotoxigenc E. coli enteric diseases" (Leader 2 WPs)
2017-2019	Ministry of Agriculture, Development of a New vaccine Against Brucellosis
2017	Nuclear Threat Initiative, Advanced Training in Epidemiology of Israeli, Palestinian and Jordanian Students and Health Professionals

Prof. Jiska Cohen-Mansfield, Ph.D.

Department of Health Promotion
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: jiska@post.tau.ac.il

Aging and End of Life

Positions

Professor, Department of Health Promotion, Sackler Faculty of Medicine

Director, Minerva Center for the Interdisciplinary Study of End of Life

Dr Igor Orshtein Chair for Research in Aging

Research

Health and Mental Health Promotion in older persons:

- Preventing loneliness and social isolation in older persons
- Promoting physical activity in old age
- Age segregation and integration in society
- Methodologies for alleviating memory difficulties

End of Life

- Delineating end of life as a life stage
- Encountering the gap between the good death and the usual death
- Dementia
  - Understanding symptoms and behaviors in dementia
  - Improving dementia care
- Promoting dignity at the end of life

Publications

Cohen-Mansfield J, Juravel-Jaffe A, Cohen A, Rasooly I, Golander H. (2013) Physicians' practice and familiarity with treatment for agitation associated with dementia in Israeli nursing homes. *Int Psychogeriatr,* 25:236-44.

Cohen-Mansfield J. (2013) Smoking and mortality among persons aged 75-94. *Prev Med*, 56:185-9.

Cohen-Mansfield, J., Shmotkin, D., Malkinson, R, Bartur, L., Hazan, H. (2013) Parental bereavement increases mortality in older persons. *Psychological Trauma: Theory, Research, Practice, and Policy*. 5:84-92.

Husebo BS, Ballard C, Cohen-Mansfield J, Seifert R, Aarsland D. (2013) The response of agitated behavior to pain management in persons with dementia. *Am J Geriatr Psychiatry*, 22:708-17.

Cohen-Mansfield J. (2013) Even with regular use of an observational scale to assess pain among nursing home residents with dementia, pain-relieving interventions are not frequently used. *Evid Based Nurs*. 17:24-5

Cohen-Mansfield J, Thein K, Marx MS, Dakheel-Ali M, Jensen B. (2013) Sources of discomfort in persons with dementia. *JAMA Intern Med*, 173:1378-9.

Cohen-Mansfield J, Shmotkin D, Blumstein Z, Shorek A, Eyal N, Hazan H. (2013) CALAS Team. The old, old-old, and the oldest old: continuation or distinct categories? An examination of the relationship between age and changes in health, function,and wellbeing. Int J Aging Hum Dev. 77:37-57.

Cohen-Mansfield J. (2013) Nonpharmacologic treatment of behavioral disorders in dementia. Curr Treat Options Neurol. 15:765-85.

Cohen-Mansfield J, Garms-Homolová V, Bentwich M. (2013) Migrant home attendants: regulation and practice in 7 countries. Am J Public Health. 103:e30-9.

Cohen-Mansfield J, Golander H, Heinik J. (2013) Delusions and hallucinations in persons with dementia: a comparison of the perceptions of formal and informal caregivers. J Geriatr Psychiatry Neurol. 26:251-8.

Cohen-Mansfield, J., Dakheel-Ali, M., Jensen, B. (2013) Predicting Service Use and Intent to Use Services of Older Adult Residents of Two Naturally Occurring Retirement Communities. *Social Work Research* 37:313-326.

Shmotkin, D., Eyal, N., Hazan, H., Shkolnik, T., Shorek, A., & Cohen-Mansfield, J. (2013). Between

the Subjective and the Objective: How Informative Is Subjective Evaluation of Memory Among the Old-Old? *Clinical Gerontologist*, *36*, 294-315.

Cohen-Mansfield J, Marx MS, Thein K. (2014) What is discomfort in persons with dementia who are agitated?-Reply. JAMA Intern Med. 174:292-3.

Cohen-Mansfield J, Golander H, Arnheim G, Cohen R. Reactions and interventions for delusions in nursing home residents with dementia. Am J Alzheimers Dis Other Demen. 2014. 29:386-394

Cohen-Mansfield J, Buckwalter K, Beattie E, Rose K, Neville C, Kolanowski A. (2014) Expanded review criteria: The case of nonpharmacological interventions in dementia. J Alzheimers Dis. 41:15-28.

Cohen-Mansfield J, Perach R. (2015) Interventions for alleviating loneliness among older persons: a critical review. Am J Health Promot. 29:e109-25.

Cohen-Mansfield J, Ray CA. Whose responsibility is it to make life worth

Cohen-Mansfield J, Cohen R, Buettner L, Eyal N, Jakobovits H, Rebok G, Rotenberg-Shpigelman S, Sternberg S. Interventions for older persons reporting memory difficulties: a randomized controlled pilot study. Int J Geriatr Psychiatry. 2015;30(5):478-86.

Cohen-Mansfield J, Marx MS, Dakheel-Ali M, Thein K. The use and utility of specific nonpharmacological interventions for behavioral symptoms in dementia: an exploratory study. Am J Geriatr Psychiatry. 2015;23(2):160-70.

Cohen-Mansfield J, Thein K, Marx MS. Predictors of the impact of nonpharmacologic interventions for agitation in nursing home residents with advanced dementia. J Clin Psychiatry. 2014;75(7):e666-e671.

Landau C, Lev-Ari S, **Cohen-Mansfield J**, Tillinger E, Geva R, Tarrasch R, Mitnik I, Friedman E. Randomized controlled trial of Inquiry-Based Stress Reduction (IBSR) technique for BRCA1/2 mutation carriers. Psychooncology. 2014;24:726-731.

Kenigsberg PA, Aquino JP, Bérard A, Gzil F, Andrieu S, Banerjee S, Brémond F, Buée L, **Cohen-Mansfield J**, Mangialasche F, Platel H, Salmon E, Robert P. Dementia beyond 2025: Knowledge and uncertainties. Dementia (London). 2016;15:6-21.

Cohen-Mansfield J, Jensen B. Intergenerational programs in schools: Prevalence and perceptions of impact. J Appl Gerontol. 2015 Feb 19. pii: 0733464815570663

Cohen-Mansfield J, Dakheel-Ali M, Marx MS, Thein K, Regier NG. Which unmet needs contribute to behavior problems in persons with advanced dementia? Psychiatry Res. 2015;228(1):59-64.

Cohen-Mansfield J, Thein K, Marx MS, Dakheel-Ali M, Jensen B. Sources of discomfort in persons with dementia: Scale and initial results. Behavioural Neurology, 2015, Article ID 732832.

Ray CA, Ingram V, **Cohen-Mansfield J**. Systematic review of planned care transitions for persons with dementia. Neurodegener Dis Manag. 2015;5(4):317-31.

Cohen-Mansfield J, Hazan H, Lerman Y, Shalom V. Correlates and predictors of loneliness in older-adults: a review of quantitative results informed by qualitative insights. Int Psychogeriatr. 2016 Apr;28(4):557-76. doi: 10.1017/S1041610215001532. Epub 2015 Oct 1. PubMed PMID: 26424033.

Cohen-Mansfield J. Non-pharmacological interventions for agitation in dementia: various strategies demonstrate effectiveness for care home residents; further research in home settings is needed. Evid Based Nurs. 2016;19(1):31.

Cohen-Mansfield J. Predictors of smoking cessation in old-old age. Nicotine Tob Res. 2016 Jan 17.

Cohen-Mansfield J, Cohen R, Golander H, Heinik J. The impact of psychotic symptoms on the persons with dementia experiencing them. Am J Geriatr Psychiatry. 2016;24(3):213-20.

Cohen-Mansfield J, Shmotkin D, Hazan H. Changes in religiosity in old age: an exploratory study. Int J Aging Hum Dev. 2016

Cohen-Mansfield, J, and Regev, I. Retirement preparation programs: An examination of retirement perceptions, self-mastery, and well-being. Research on Social Work Practice. 2016,

Cohen-Mansfield, J., Perach, R. Kadmon Stern, T., Albeck, S., Rotem, D., Arnow, TL, Lerma, Y. Telephone hotline for aging: Information needs, quality of service, and insights *International Social Work* 2016

Cohen-Mansfield J, Gavendo R, Blackburn E. Activity preferences of persons with dementia: An examination of reports by formal and informal caregivers. Dementia (London). 2017;1471301217740716.

Cohen-Mansfield J, Sela AH, Iecovich E, Golander H. Quality of care for frail older persons in a homecare setting: what is it and how can it be measured? Int Psychogeriatr. 2017;2:1-9.

Lanctôt KL, Amatniek J, Ancoli-Israel S, Arnold SE, Ballard C, **Cohen-Mansfield J**, Ismail Z, Lyketsos C, Miller DS, Musiek E, Osorio RS, Rosenberg PB,

Satlin A, Steffens D, Tariot P, Bain LJ, Carrillo MC, Hendrix JA, Jurgens H, Boot B. Neuropsychiatric signs and symptoms of Alzheimer's disease: New treatment paradigms. Alzheimers Dement (N Y). 2017;3:440-449.

Cohen-Mansfield J, Cohen R, Skornick-Bouchbinder M, Brill S. What is the End of Life period? Trajectories and characterization based on primary caregiver reports. J Gerontol A Biol Sci Med Sci. 2017 Oct 12.

Cohen-Mansfield J. Activity groups for persons with dementia: Personal predictors of participation, engagement and mood. Psychiatry Res. 2017;257:375-380.

Cohen-Mansfield J, Skornick-Bouchbinder M, Hoshen M, Brill S. The relationship between health services standardized costs and mortality is non-linear: Results from a large HMO population. Health Policy. 2017;121:1008-1014.

Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, Ballard C, Banerjee S, Burns A, **Cohen-Mansfield J**, Cooper C, Fox N, Gitlin LN, Howard R, Kales HC, Larson EB, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L, Mukadam N. Dementia prevention, intervention, and care. Lancet. 2017;pii: S0140-6736(17)31363-6.

Cohen-Mansfield J, Skornick-Bouchbinder M, Cohen R, Brill S. Treatment and communication-that is what matters: an analysis of complaints regarding end-of-life care. J Palliat Med. 2017;20:1359-1365.

Cohen-Mansfield J, Ray CA, Hai T, Marcu C, Callahan BL, Freedman M. The ultimate outlier: transitional care for persons with dementia and BPSD. Curr Alzheimer Res. 2017;14:969-977.

Cohen-Mansfield J, Golander H, Iecovich E, Jensen B. Social engagement care for frail older persons: desire for it and provision by live-in migrant caregivers. J Gerontol B Psychol Sci Soc Sci. 2017;doi: 10.1093/geronb/gbx052.

Cohen-Mansfield J, Golander H, Cohen R. Rethinking psychosis in dementia: an analysis of antecedents and explanations. Am J Alzheimers Dis Other Demen. 2017;32:265-271.

Cohen-Mansfield J, Hai T, Comishen M. Group engagement in persons with dementia: The concept and its measurement. Psychiatry Res. 2017;251:237-243

Berenbaum R, Tziraki C, **Cohen-Mansfield J**. The right to mourn in dementia: To tell or not to tell when someone dies in dementia day care. Death Stud. 2017;41:353-359.

Chapters

Cohen-Mansfield J Advances in Alzheimer's Disease Research: Implications for Family Caregiving In: Zarit, S. H., and Talley, R. C. (Eds.) (2013). Caregiving for Alzheimer's Disease and Related Disorders. New York: Springer. Chapter 12, pp. 181-202.

Cohen-Mansfield, J. 2014. "Understanding Behaviour" in Excellence in Dementia Care, Research into Practice. Edited by Murna Downs and Barbara Bowsers. Chapter 16. Open University Press. McGraw Hill. 2nd edition. P220-239.

Cohen-Mansfield, J. (2015). Behavioral and Psychological Symptoms of Dementia In: P.A. Lichtenberg, B.T. Mast (Eds.) APA Handbook of Clinical Geropsychology. Vol 2. Chapter 11, pp. 271-317. American Psychological Association.

Cohen-Mansfield J, Skornick-Bouchbinder M, Brill S. Trajectories of end of life: a systematic review. J Gerontol B Psychol Sci Soc Sci. 2017;doi: 10.1093/geronb/gbx093

Grants

2016-2019 Israel Ministry of Science. Enhancing quality of care at the end of life.

Prof. Yariv Gerber, Ph.D.

Department of Epidemiology and Preventive Medicine
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: yarivg@post.tau.ac.il

Cardiovascular Disease Epidemiology

Positions

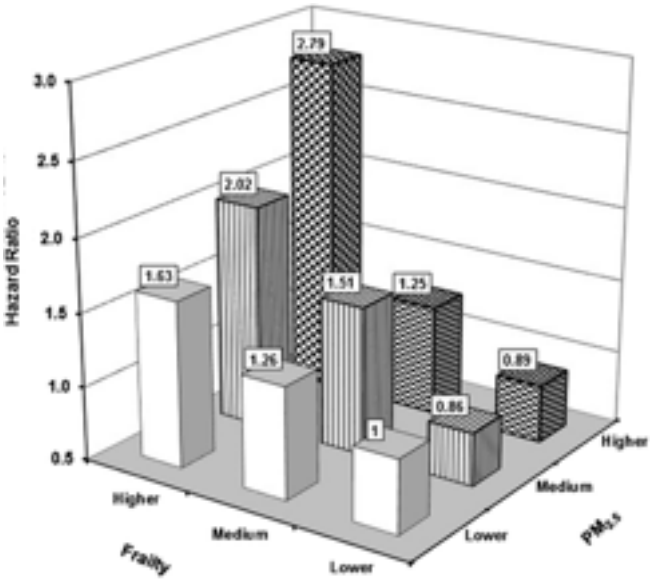
Professor, Sackler Faculty of Medicine

Adjunct Faculty, Health Sciences Research, College of Medicine, Mayo Clinic, Minnesota

Chair, Dept. of Epidemiology and Preventive Medicine, Sackler Faculty of Medicine

Research

Our research covers a wide array of topics related to the epidemiology of cardiovascular diseases. These include risk factor and biomarker evaluation, secular trend analysis, and outcomes research. We have a particular interest in assessing long-term prognosis after acute myocardial infarction. This type of investigation usually combines data from multiple sources, including interviews and questionnaires, laboratory measurements involving blood specimens, GIS-derived environmental data, interviews and questionnaires. We are also interested in methodological aspects involved in conducting and interpreting observational studies.



Effect modification of the association between chronic exposure to PM2.5 and post-myocardial infarction mortality by frailty status. A positive dose-response relationship between chronic exposure to PM2.5 and mortality is evident among frailer participants only. PM2.5, particulate matter ≤2.5 μm in diameter. Figure created by authors from data in Gerber et al. *J Am Coll Cardiol*. 2014;63:1698–99.

Publications

Gerber Y, Melton LJ 3rd, McNallan SM, Jiang R, Weston SA, Roger VL. Cardiovascular and non-cardiovascular disease associations with hip fractures. Am J Med 2013; 126:169.e19-26.

Gerber Y, Weston SA, Berardi C, McNallan SM, Jiang R, Redfield MM, Roger VL. Contemporary trends in heart failure with reduced and preserved ejection fraction after myocardial infarction: a community study. Am J Epidemiol 2013; 178:1272-80.

Myers V, Broday DM, Steinberg DM, Yuval, Drory Y, **Gerber Y**. Exposure to particulate air pollution and long-term incidence of frailty after myocardial infarction. Ann Epidemiol 2013;2:395-400.

Koton S, Molshatzki N, Yuval, Myers V, Broday DM, Drory Y, Steinberg DM, **Gerber Y**. Cumulative exposure to particulate matter air pollution and long-term post-myocardial infarction outcomes. Prev Med 2013; 57:339-44.

Myers V, Drory Y, **Gerber Y**. Clinical relevance of frailty trajectory post myocardial infarction. Eur J Prev Cardiol 2014: 21:758-766.

Gerber Y, Myers V, Broday DM, Steinberg DM, Yuval, Koton S, Drory Y. Frailty status modifies the association between air pollution and post-myocardial infarction mortality: a 20-year follow-up study. J Am Coll Cardiol. 2014; 63:1698-9.

Hasin T, **Gerber Y**, McNallan SM, Weston SA, Kushwaha SS, Nelson TJ, Cerhan JR, Roger VL. Patients with heart failure have an increased risk of cancer. *J Am Coll Cardiol* 2013;62:881-6.

Benyamini Y, Roziner I, Goldbourt U, Drory Y, **Gerber Y.** Depression and anxiety following myocardial infarction and their inverse associations with future health behaviors and quality of life. *Ann Behav Med* 2013;46:310-21.

Lurie I, Myers V, Goldbourt U, **Gerber Y.** Perceived social support following myocardial infarction and long-term development of frailty. *Eur J Prev Cardiol* 2015;22:1346-53.

Gerber Y, Weston SA, Jiang R, Roger VL. The changing epidemiology of myocardial infarction in Olmsted County, Minnesota, 1995-2012. *Am J Med* 2015;128:144-51.

Gerber Y, Weston SA, Redfield MM, Chamberlain AM, McNallan SM, Jiang R, Killian JM, Roger VL. Contemporary appraisal of the heart failure epidemic, 2000-2010. *JAMA Intern Med* 2015;175:996-1004.

Manemann SM, **Gerber Y**, Chamberlain AM, Dunlay SM, Bell MR, Jaffe AS, Weston SA, Killian JM, Kors J, Roger VL. Acute coronary syndromes in the community. *Mayo Clin Proc* 2015;90:597-605.

Gerber Y, Weston SA, Enriquez-Sarano M, Berardi C, Chamberlain AM, Manemann SM, Jiang R, Dunlay SM, Roger VL. Mortality associated with heart failure after myocardial infarction: a contemporary community perspective. *Circ Heart Fail* 2015;9:e002460.

Gerber Y, Weston SA, Enriquez-Sarano M, Manemann SM, Chamberlain AM, Jiang R, Roger VL. Atherosclerotic burden and heart failure after myocardial infarction. *JAMA Card* 2016; in press.

Weiss-Faratci N, Lurie I, Neumark Y, Malowany M, Cohen G, Benyamini Y, Goldbourt U, **Gerber Y.** Perceived social support at different times after myocardial infarction and long-term mortality risk: a prospective cohort study. *Ann Epidemiol* 2016: in press.

Reviews & chapters

Myers V, **Gerber Y.** *Socioeconomic Aspects of Cardiovascular Health*. In "Interdisciplinary Concepts of Cardiovascular Health: Epidemiology, Pathophysiology and Molecular Mechanisms"; Wakabayashi I and Groschner K (Editors). Publisher: Springer-Verlag New York, LLC (2013).

Myers V, Rosen LJ, **Gerber Y.** *Primary Risk Factors: Tobacco.* In "Interdisciplinary Concepts of Cardiovascular Health: Epidemiology, Pathophysiology and Molecular Mechanisms"; Wakabayashi I and Groschner K (Editors). Publisher: Springer-Verlag New York, LLC (2013).

Roger VL, **Gerber Y.** Coronary disease deaths: From birth cohorts to prevention. *Rev Esp Cardiol* (Engl Ed) 2015;68(5):361-2.

Myers V, **Gerber Y.** *Physical Activity and Recovery from Cardiovascular Disease: A Psychological Perspective.* In "Handbook of Psychocardiology"; Alvarenga M and Byrne D (Editors). Publisher: Springer Reference Ltd (2016).

Cohen G, **Gerber Y.** Air pollution and successful aging: recent evidence and new perspectives. *Curr Environ Health Rep* 2017;4(1):1-11.

Grants

2016-2017 The Israel Cancer Association (ICA), Chronic residential exposure to outdoor air pollution and cancer incidence in a high-risk population: A cohort study.

2016-2018 Bircher-Benner Foundation: Development of a frailty evaluation tool in a high-risk Israeli population.

2017-2020 Chief Scientist Office, Ministry of Health: A prospective study of dietary patterns in relation to healthy aging.

Prof. Uri Goldbourt, Ph.D.

Department of Epidemiology and Preventive Medicine
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: goldbu1@post.tau.ac.il
https://med.tau.ac.il/profile/goldbu1

Investigating Cardiovascular Risk Factors and Outcomes, Predictors of Frailty and Declining Cognitive Function

Positions

Professor Emeritus, Sackler Faculty of Medicine

Honorary Member, Israeli Heart Society

Founding Chairman, Israel Heart Society Working Group on Epidemiology and Prevention

Research

The pioneering large scale epidemiological study named “The Israeli Ischemic Heart Disease project” (IIHD project) was initiated in the Jerusalem, Tel Aviv and Haifa areas in 1963. Over the years three stages of extended mortality follow up, in 1978, 1986 and 2011, as well as a "dementia phase" among survivors in 2000, Charlson morbidity index as of 2002 and cancer follow up though 2011 were added. Results of IIHD laid the foundation for the teaching of epidemiology of CVD in Israel. BIP (Bezafibrate Infarction Prevention) was the most extensive locally planned and executed in Israeli Cardiology, involving over 15,000 screened patients and 3090 original participants with coronary heart disease (CHD)

Current involvement:

Dementia and multiple morbidity, over the last years of life, in the above mentioned cohort (IIHD) and several research groups.

Epidemiology of stroke.

Epidemiology of cognitive decline and frailty among the BIP survivors (two recurrent examinations)

Cancer incidence in the IIHD.

Vegan health profile, associated putative risk lowering and cost-benefit factors.

Diverse multinational meta-analytic collaborations (Oxford, Cambridge, Sydney, Harvard)

Publications

Benderly M, Haim M, Boyko V, **Goldbourt U.** Socioeconomic status indicators and incidence of heart failure among men and women with coronary heart disease. J Card Fail. 2013;19(2):117-24

Dunsky A, Zach S, Zeev A, **Goldbourt U**, Shimony T, Goldsmith R, Netz Y Prediction of standing height among Israeli older adults: results from a national survey. Ann Hum Biol. 2012;39(6):499-504

Netz Y, Dunsky A, Zach S, Goldsmith R, Shimony T, **Goldbourt U**, Zeev. A Psychological functioning and adherence to the recommended dose of physical activity in later life: results from a national health survey. Int Psychogeriatr. 2012;24(12):2027-36.

Zach S, Zeev A, Dunsky A, **Goldbourt U**, Shimony T, Goldsmith R, Netz Y. Adolescents' physical activity habits--results from a national health survey. Child Care Health Dev. 2013;39(1):103-8.

Zach S, Zeev A, Dunsky A, **Goldbourt U**, Shimony T, Goldsmith R, Netz Y. Perceived body size versus healthy body size and physical activity among adolescents - Results of a national survey. Eur J Sport Sci. 2013;13(6):723-31.

Ravona-Springer R, Beeri MS, **Goldbourt U**. Satisfaction with current status at work and lack of motivation to improve it during midlife is associated with increased risk for dementia in subjects who survived thirty-seven years later. J Alzheimers Dis. 2013;36(4):769-80.

Ravona-Springer R, Schnaider-Beeri M, **Goldbourt U**. Body weight variability in midlife and risk for dementia in old age. Neurology. 2013:30;80(18):1677-83.

Weinstein G, **Goldbourt U**, Tanne D. Body height and late-life cognition among patients with atherothrombotic disease. Alzheimer Dis Assoc Disord. 2013;27(2):145-52

Kliper E, Bashat DB, Bornstein NM, Shenhar-Tsarfaty S, Hallevi H, Auriel E, Shopin L, Bloch S, Berliner

S, Giladi N, **Goldbourt U**, Shapira I, Korczyn AD, Assayag EB. Cognitive decline after stroke: relation to inflammatory biomarkers and hippocampal volume. Stroke. 2013;44(5):1433-5.

Lawrence YR, Morag O, Benderly M, Boyko V, Novikov I, Dicker AP, **Goldbourt U**, Behar S, Barchana M, Wolf I. Association between metabolic syndrome, diabetes mellitus and prostate cancer risk. Prostate Cancer Prostatic Dis. 2013;16(2):181-6

Molshatzki N, **Goldbourt U**, Tanne D. Perceived hardships at midlife: prediction of long-term stroke mortality. Int J Cardiol. 2013;168(3):2278-81.

Benyamini Y, Roziner I, **Goldbourt U**, Drory Y, Gerber Y. Depression and anxiety following myocardial infarction and their inverse associations with future health behaviors and quality of life. Ann Behav Med 2013;46:310-21.

Emerging Risk Factors Collaboration., Di Angelantonio E, Gao P, Khan H, Butterworth AS, Wormser D, Kaptoge S, Kondapally Seshasai SR, Thompson A, Sarwar N, Willeit P, Ridker PM, Barr EL, Khaw KT, Psaty BM, Brenner H, Balkau B, Dekker JM, Lawlor DA, Daimon M, Willeit J, Njølstad I, Nissinen A, Brunner EJ, Kuller LH, Price JF, Sundström J, Knuiman MW, Feskens EJ, Verschuren WM, Wald N, Bakker SJ, Whincup PH, Ford I, **Goldbourt U**, et al. Glycated hemoglobin measurement and prediction of cardiovascular disease. JAMA. 2014;311(12):1225-33.

Tolstrup JS, Hvidtfeldt UA, Flachs EM, Spiegelman D, Heitmann BL, Bälter K, **Goldbourt U**, Hallmans G, Knekt P, Liu S, Pereira M, Stevens J, Virtamo J, Feskanich D. Smoking and risk of coronary heart disease in younger, middle-aged, and older adults. Am J Public Health. 2014;104(1):96-102.

Lurie I, Myers V, **Goldbourt U,** Gerber Y. Perceived social support following myocardial infarction and long-term development of frailty. Eur J Prev Cardiol 2015;22:1346-53

Molshatzki N, Weinstein G, Streifler JY, **Goldbourt U**, Tanne D. Serum uric acid and subsequent cognitive performance in patients with pre-existing cardiovascular disease. PLoS One. 2015 ;10(3)

Orlev Y, Yahalom G, Cohen OS, Elincx-Benizri S, Kozlova E, Inzelberg R, **Goldbourt U**, Hassin-Baer S. Exploring determinants of progression in Parkinson's disease. Is there a difference among Jewish ethnic groups? Parkinsonism Relat Disord. 2015: 21(3):184-8.

Weinstein G, **Goldbourt U**, Tanne D. Angina pectoris severity among coronary heart disease patients is associated with subsequent cognitive impairment. Alzheimer Dis Assoc Disord. 2015;29(1):6-11

Haratz S, Weinstein G, Molshazki N, Beeri MS, Ravona-Springer R, Marzeliak O, **Goldbourt U**, Tanne D. Impaired Cerebral hemodynamics and cognitive performance in patients with Atherothrombotic Disease. J Alzheimers Dis. 2015;46(1):137-44.

Eisen A, Benderly M, Behar S, **Goldbourt U**, Haim M. Inflammation and future risk of symptomatic heart failure in patients with stable coronary artery disease. Am Heart J. 2014;167(5):707-14

Dankner R, Drory Y, Geulayov G, Ziv A, Novikov I, Zlotnick AY, Moshkovitz Y, Elami A, Schwammenthal E, **Goldbourt U**. A Controlled intervention to increase participation in cardiac rehabilitation. Eur J Prev Cardiol. 2015;22(9):1121-8.

White IR, Rapsomaniki E; Emerging Risk Factors Collaboration. Covariate-adjusted measures of discrimination for survival data. Biom J. 2015;57(4):592-613

Cholesterol Treatment Trialists' (CTT) Collaboration., Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, Simes J, Collins R, Kirby A, Colhoun H, Braunwald E, La Rosa J, Pedersen TR, Tonkin A, Davis B, Sleight P, Franzosi MG, Baigent C, Keech A. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. Lancet. 2015;385:1397-405

Keinan-Boker L, **Goldbourt U**. Cancer incidence in Holocaust male survivors - An Israeli cohort study. Int J Cancer. 2016;139(11):2426-35.

Weiss-Faratci N, Lurie I, Neumark Y, Malowany M, Cohen G, Benyamini Y, **Goldbourt U**, Gerber Y. Perceived social support at different times after myocardial infarction and long-term mortality risk: a prospective cohort study. Ann Epidemiol. 2016;26(6):424-8

Weinstein G, Lutski M, **Goldbourt U**, Tanne D. C-reactive protein is related to future cognitive impairment and decline in elderly individuals with cardiovascular disease. Arch Gerontol Geriatr. 2017;69:31-37

Weiss-Faratci N, Lurie I, Benyamini Y, Cohen G, **Goldbourt U**, Gerber Y. Optimism during hospitalization for first acute myocardial infarction and long-term mortality risk: a prospective cohort study. Mayo Clin Proc. 2017;92(1):49-56.

Lutski M, Tanne D, **Goldbourt U**. Tall stature in coronary heart disease patients is associated with

decreased risk of frailty in late life. Geriatr Gerontol Int. 2017;17:1270-1277.

Paige E, Barrett J, Pennells L, Sweeting M, Willeit P, Di Angelantonio E, Gudnason V, Nordestgaard BG, Psaty BM, **Goldbourt U**, et al. Repeated Measurements of blood pressure and cholesterol improves cardiovacular disease prediction: An indibidual participant-data meta-analysis. Am J Epidemiol. 2017; 186:899-907.

Lotan K, **Goldbourt U**, Gerber Y. Smoking status and incidence of cancer after myocardial infarction: a follow-up study of over 20 years. Am J Med. 2017; 130:1084-1091.

Weinstein G, Lutski M, **Goldbourt U**, Tanne D C-reactive protein is related to future cognitive impairment and decline in elderly individuals with cardiovascular disease. Arch Gerontol Geriatr 2017.;69:31-37

Benderly M, Chetrit A, Murad H, Abu-Saad K, Gillon-Keren M, Rogowski O, Sela BA, Kanety H, Harats D, Atamna A, Alpert G, **Goldbourt U**, Kalter-Leibovici O. Cardiovascular health among two ethnic groups living in the same region: A population-based study. Int J Cardiol. 2017;228:23-30.

Lutski M, Weinstein G, **Goldbourt U**, Tanne D. Insulin resistance and future cognitive performance and cognitive decline in elderly patients with cardiovascular disease. J Alzheimers Dis. 2017;57(2):633-643.

Ravona-Springer R, Schnaider-Beeri M, **Goldbourt U**. Triceps and subscapular skinfold in men aged 40-65 and dementia prevalence 36 years later. J Alzheimers Dis. 2017;57(3):873-883.

Dr. Khitam Muhsen, Ph.D.

Department of Epidemiology and Preventive Medicine
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: kmuhsen@post.tau.ac.il

Helicobacter pylori, Enteric Infections and Their Role in Health and Disease

Positions

Senior Lecturer, Sackler Faculty of Medicine

Research

Helicobacter pylori infection is acquired during early childhood. It causes chronic gastritis, which mostly remains asymptomatic; however in a small portion of the infected people *H. pylori* causes peptic ulcers and gastric cancer. Our research focuses on the role of *H. pylori* in extragastric diseases such as iron deficiency anemia, cognitive function, and diabetes mellitus. Epidemiology of enteric infections in various populations consists an additional main research area in our group.

Our research involves population-based studies in which we integrate various epidemiological and biostatistical methods, as well as biological markers assessed by immunological and microbiological tools.

Publications

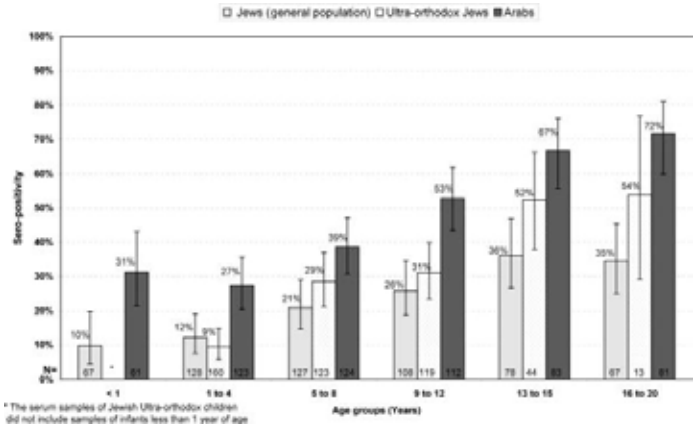
Muhsen K, Kassem E, Rubinstein U, Schachter Y, Kremer A, Goren S, Zilberstein I, Ephros M, Cohen D, Shulman ML. Incidence and characteristics of sporadic norovirus gastroenteritis associated with hospitalizations of children < 5 years of age in Israel. Pediatr Infect Dis J. 2013 32:688-90.

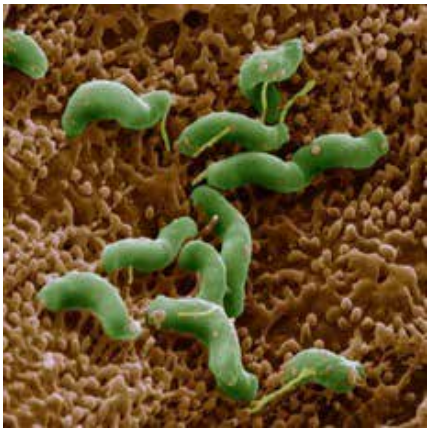
Muhsen K, Levine MM. A systematic review and meta-analysis of the association between *Giardia lamblia* and endemic pediatric diarrhea in developing countries. Clin Infect Dis. 2012; 55 Suppl 4:S271-93.

Levine MM, Kotloff KL, Nataro JP, **Muhsen K**. The Global Enteric Multicenter Study (GEMS); Impetus, Rationale and Genesis. Clin Infect Dis. 2012; 55 Suppl 4:S215-24.

Farag TH, Nasrin D, Wu Y, **Muhsen K**, Blackwelder W, Sommerfelt H, Panchalingan S, Nataro JP, Kotloff KL, Levine MM. Some epidemiological, clinical, microbiological and organizational assumptions that influenced the design and performance of GEMS-1. Clin Infect Dis. 2012; 55 Suppl 4:S225-31.

Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, Wu Y, Sow SO, Sur D, Breiman RF, Faruque AS, Zaidi AK, Saha D, Alonso PL, Tamboura B, Sanogo D, Onwuchekwa U, Manna B, Ramamurthy T, Kanungo S, Ochieng JB, Omore R, Oundo JO, Hossain A, Das SK, Ahmed S, Qureshi S, Quadri F, Adegbola RA, Antonio M, Hossain MJ, Akinsola A, Mandomando I, Nhampossa T, Acácio S, Biswas K, O'Reilly CE, Mintz ED, Berkeley LY, **Muhsen K**, Sommerfelt H, Robins-Browne RM,





Levine MM. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. Lancet. 2013; 382:209-22

Muhsen K, Cohen D, Levine MM. Can *Giardia lamblia* infection lower the risk of acute diarrhea among pre-school children? J Trop Pediatr. 2014, 60:99-103

Muhsen K, Lagos R, Reymann M, Graham DY, Pasetti MF, Levine MM. Age-dependent association among *Helicobacter pylori* infection, serum pepsinogen levels and immune response of children to live oral cholera vaccine CVD 103-HgR PLoS One. 2014, 15; 9:e83999.

Muhsen K, Pasetti MF, Reymann MK, Graham DY, Levine MM. *Helicobacter pylori* infection affects immune responses following vaccination of typhoid-naïve U.S. adults with attenuated *Salmonella* Typhi oral vaccine CVD 908-*htrA*. J Infect Dis. 2014, 209:1452-8

Boyd MA, Tennant SM, Saague VA, Simon R, **Muhsen K**, Ramachandran G, Cross AS, Galen JE, Pasetti MF, Levine MM. Serum bactericidal assays to evaluate typhoidal and nontyphoidal salmonella vaccines. *Clin Vaccine Immunol*. 2014;21:712-21.

Muhsen K, Kassem E, Efraim S, Goren S, Cohen D, Ephros M. Incidence and risk factors for intussusception among children in northern Israel from 1992 to 2009: a retrospective study. *BMC Pediatr*. 2014;14(1):218.

Tobias J, Kassem E, Rubinstein U, Bialik A, Vutukuru S, Navaro A, Rokney A, Valinsky L, Ephros M, Cohen D, **Muhsen K**. Involvement of main diarrheagenic Escherichia coli, with emphasis on enteroaggregative E. coli, in severe non-epidemic pediatric diarrhea in a high-income country. *BMC Infect Dis*. 2015;15(1):79

Muhsen K, Goren S. Cohen D. Helicobacter pylori Infection in Early Childhood and Growth at School Age. *Helicobacter*. 2015 ;20(6):410-7.

Muhsen K, Rubenstein U, Kassem E, Goren S, Schachter Y, Kremer A, Shulman L.M, Ephros M, Cohen D. A significant and consistent reduction in rotavirus gastroenteritis hospitalization of children under five years of age, following the introduction of universal rotavirus immunization in Israel. *Hum Vaccin Immunother.* 2015;11(10):2475-82

Muhsen K, Chodick G, Goren S, Anis E, Ziv-Baran T, Shalev V, Cohen D. Change in incidence of clinic visits for all-cause and rotavirus gastroenteritis in young children following the introduction of universal rotavirus vaccination in Israel. *Euro Surveill.* 2015;20(42).

Shindler-Itskovitch T, Ravona-Springer R, Leibovitz A, **Muhsen K**. A systematic review and meta-analysis of the association between Helicobacter pylori infection and dementia. *J Alzheimers Dis*. 2016;52(4):1431-42.

Sow SO, **Muhsen K**, Nasrin D, Blackwelder WC, Wu Y, Farag T, Panchalingham S, Sur S, Zaidi AKM, Faruque ASG, Saha D, Adegbola R, Alonso PL, Breiman RF, Q, Tamboura B, Sanogo D, Onwuchekwa U,Manna B , Ramamurthy T, Kanungo S, Ahmed S, Qureshi S , Quadri F, Hossain A, Das SK, Antonio M, Hossain MJ, Mandomando I, Nhampossa T, Acácio S, Omore R, Ochieng JB, Oundo JO, Mintz ED, O'Reilly CE, Berkeley LY, Livio S, Tennant SM, Sommerfelt H, Nataro JP, Ziv-Baran T, Robins-Browne RM, Liu J, Houpt E, Kotloff KL, Levine MM. The burden of Cryptosporidium diarrhea disease among children <24 months of age in moderate/high mortality regions of sub-Saharan Africa and South Asia, utilizing data from the Global Enteric Multicenter Study (GEMS). *PLoS Negl Trop Dis*. 2016;10(5):e0004729.

Muhsen K, Kassem E, Rubenstein U, Goren S, Ephros M, Cohen D, Shulman L.M. Incidence of rotavirus gastroenteritis hospitalizations and genotypes, before and five years after introducing universal immunization in Israel. Vaccine. 2016;34:5916-5922.

Hudak L, Jaraisy A, Haj S, **Muhsen K**. An updated systematic review and meta-analysis of observational studies on the association between *Helicobacter pylori* infection and iron deficiency anemia. Helicobacter. 2017;22.

Muhsen K, Anis E, Rubinstein U, Kassem E, Goren S, Shulman LM, Ephros M, Cohen D. Effectiveness of rotavirus pentavalent vaccine under a universal immunization program in Israel, 2011-2015: a case-control study. Clin Microbiol Infect. 2017. pii: S1198-743X(17)30229-X.

Muhsen K, Green MS, Soskolne V, Neumark Y. Inequalities in non-communicable diseases between the major population groups in Israel: achievements and challenges. Lancet. pii: S0140-6736(17)30574-3.

Kassem E, Naamna M, Mawassy K, Beer-Davidson G, **Muhsen K.** Helicobacter pylori infection, serum pepsinogens, and pediatric abdominal pain. Eur J Pediatr. 2017. doi: 10.1007/s00431-017-2955-3.

Chapters and Reviews

Tennant SM, **Muhsen K**, Pasetti MF. Gut immunology and oral vaccination. In "Molecular Vaccines- From Prophylaxis to Therapy". 2013. Editor Matthias Giese

M. Springer Vienna. ISBN: 978-3-7091-1418-6 (Print) 978-3-7091-1419-3 (Online)

Dror G. **Muhsen K.** *Helicobacter pylori* infection and children's growth- an overview. J Pediatr Gastroenterol Nutr. 2016;62:e48-59.

Tennant SM, **Muhsen K**, Pasetti MF. Gut immunology and oral vaccination. In "Molecular Vaccines- From Prophylaxis to Therapy". 2013. Editor Matthias Giese M. Springer Vienna.

Haj S, Raviv M, **Muhsen K.** *Helicobacter pylori* infection and diabetes mellitus. In "Extradigestive Manifestations of *Helicobacter pylori* Infection - An Overview". 2016 Editor Bruna Maria Roesler.

Grants

2015-2017	Israel National Institute for Health Policy and Health Services Research (PI)
2016-2018	Israel Ministry of Health (PI)
2016-2018	BSF (PI with Prof. MM Levine, USA)
2018-2021	Israel National Institute for Health Policy and Health Services Research

Dr. Chava Peretz, Ph.D.

Department of Epidemiology
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: cperetz@post.tau.ac.il

Epidemiology of Parkinson's Disease and Environmental Epidemiology

Positions

Senior Lecturer, Sackler Faculty of Medicine

Chair, School of Public Health Seminars

Research

Our research focuses on two main fields: 1. Neuro-epidemiology, and 2. Environmental epidemiology, with a special interest in methodological issues.

In neuro-epidemiology, we study the epidemiology of neuro-generative diseases. Specifically, we follow up and investigate a large cohort of patients with Parkinson's disease on disease burden, etiology, early-markers and co-morbidity. The cohort was derived through a drugs-purchased dataset that was linked to clinical and administrative databases.

In the area of environmental epidemiology, we study the short term effects of air pollution on adverse health outcomes such as birth-defects, emergency-room visits and mortality. We also evaluate vulnerability to air pollution hazards of specific sub-groups such as subjects with diabetes. In light of global climate changes, we study the short-term effects of ambient temperature on mortality and on the occurrence of food-borne diseases. These studies involve a temporal/spatial analysis.

Publications

Agay-Shay K, Amitai Y, **Peretz C,** Linn S, Friger M, Peled A. Exploratory spatial data analysis of congenital malformations in Israel, 2000-2006. *ISPRS Int J Geo-Inf.* 2013; *2*:237-255

Agay-Shay K, Friger M, Linn S, Peled A, Amitai Y, **Peretz C.** Ambient temperature and congenital heart defects. *Hum Reprod.* 2013; 28:2289-97.

Leone M, D'Ippoliti D, De Sario M, Analitis A, Menne B, Katsouyanni K, De'donato FK, Basagana X, Salah AB, Casimiro E, Dörtbudak Z, Iñiguez C, **Peretz C,** Wolf T, Michelozzi P. A time series study on the effects of heat on mortality and evaluation of heterogeneity into European and Eastern-Southern Mediterranean cities: results of EU CIRCE project. *Environ Health*. 2013; 12:55.

Weinberger M, Lerner L, Valinsky L, Moran-Gilad J, Nissan I, Agmon V, **Peretz C.** Increased incidence of *Campylobacter* spp. infection and high rates among children, Israel. *Emerg Infect Dis J* 2013. 2013.

Gurevich T, Machmid H, Klepikov D, Ezra A, Giladi N, **Peretz C**. Head-up tilt testing for detecting orthostatic hypotension: how long do we need to wait? *Neuroepidemiology*. 2014;43(3-4):239-43.

Agay-Shay K, Peled A, Crespo AV, **Peretz C**, Amitai Y, Linn S, Friger M, Nieuwenhuijsen MJ.Green spaces and adverse pregnancy outcomes. *Occup Environ Med*. 2014;71(8):562-9.

Gurevich T, Balash Y, Merims D, **Peretz C**, Herman T, Hausdorff JM, Giladi N. Effect of rivastigmine on mobility of patients with higher-level gait disorder: a pilot exploratory study. *Drugs R D.* 2014;14(2):57-62.

Zuk L, Tlumek H, Katz-Leurer M, **Peretz C**, Carmeli E. A new tool for identifying children with motor problems: reliability and validity study. *J Child Neurol*. 2014;29(5):592-8.

Sade M, Zlotnik Y, Kloog I, Novack V, **Peretz C**, Ifergane G. Parkinson's Disease Prevalence and Proximity to Agricultural Cultivated Fields. Yitshak. *Parkinsons Dis*. 2015;2015:576564.

Khamis S, Dar G, **Peretz C**, Yizhar Z. The Relationship Between Foot and Pelvic Alignment While Standing. *J Hum Kinet*. 2015;46:85-97.

Peretz C, Gurel R, Rozani V, Gurevich T, El-Ad B, Tsamir J, Giladi N. Cancer incidence among Parkinson's disease patients in a 10-yrs time-window around disease onset: A large-scale cohort study. *Parkinsonism Relat Disord*. 2016;28:68-72.

Levcovich A, Lazarovitch T, Moran-Gilad J, **Peretz C**, Yakunin E, Valinsky L, Weinberger M. Complex clinical and microbiological effects on Legionnaires' disease outcone; A retrospective cohort study. *BMC Infect Dis*. 2016;16:75.

Peretz C, Segev H, Rozani V, Gurevich T, El-Ad B, Tsamir J, Giladi N. Comparison of Selegiline and Rasagiline Therapies in Parkinson Disease: A Real-life Study. *Clin Neuropharmaco*l. 2016

Zitser J, **Peretz C**, Ber David A, Shabtai H, Ezra A, Kestenbaum M, Brozgol M, Rosenberg A, Herman T, Balash Y, Gadoth A, Thaler A, Stebbins GT, Goetz CG, Tilley BC, Luo ST, Liu Y, Giladi N, Gurevich T. Validation of the Hebrew version of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale. *Parkinsonism Relat Disor*d. 2017;pii: S1353-8020(17)30341-3.

Zitser J, Thaler A, Inbar N, Gad A, Faust-Socher A, Paleacu D, Anca-Herschkovitch M, Balash Y, Shabtai H, Ash EL, Merkin L, Manor Y, Kestenbaum M, Bar David A, **Peretz C**, Naiman T, Bar-Shira A, Orr-Urtreger A, Dangoor N, Giladi N, Gurevich T. Two ethnic clusters with Huntington Disease in Israel: The case of Mountain Jews and Karaites. *Neurodegener Dis*. 2017;17:281-285.

Rozani V, Giladi N, El-Ad B, Gurevich T, Tsamir J, Hemo B, **Peretz C**. Statin adherence and the risk of Parkinson's disease: A population-based cohort study. *PLoS One*. 2017;12:e0175054.

Dr. Laura (Leah) J. Rosen, Ph.D.

Department of Health Promotion
School of Public Health
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: rosenl@post.tau.ac.il

Improving Public Health, and Control Tobacco Use and Exposure

Positions

Senior Lecturer, Sackler Faculty of Medicine

Chair, Dept. of Health Promotion, School of Public Health

Affiliated Faculty, Harvard Global Center for Tobacco Control

Appointed Member, Israel Public Committee for Reduction of Tobacco Use and Damage

Temporary Adviser, European Advisory Council on Health Research (EACHr), World Health Organization

External Steering Committee Member, World Health Organization EvipNet

Research

Our primary goal is to contribute to public health, at the national and global levels, through conducting research, advancing public health research methods and evidence-based health policy, and teaching and mentoring students. We focus on methodological issues of public health and health promotion research, including understanding and improving the evidence base for public health policy, systematic reviews, and rigorous evaluation of health promotion interventions.

Our main substantive research interest is tobacco, one of the major public health problems of our time. This includes the epidemiology of tobacco use, exposure, and harm, with a focus on the Israeli context; and development and evaluation of intervention programs and strategies to reduce tobacco use and exposure at the individual, local, and national levels. Specific research projects include: monitoring and evaluation of the recent governmentally-approved National Tobacco Control Plan; development of an intervention to protect young children from tobacco smoke exposure; understanding tobacco use initiation among youth; research on changes in tobacco use during Israeli military service, the study of smoking cessation among adults, research on the exposure of the Israeli public to tobacco smoke, and understanding public and policy-maker attitudes towards governmental intervention for tobacco control.

Publications

Rosen L, Rier D, Connolly G, Oren A, Landau C, Schwartz R. Do health policy advisors know what the public wants? An empirical comparison of how health policy advisors assess public preferences regarding smoke-free air, and what the public actually prefers. Israel Journal of Health Policy Research 2013, 2:20.

Rosen L. An intuitive approach to understanding the attributable fraction of disease due to a risk factor: the case of smoking. Int. J. Environ. Res. Public Health 2013, 10, 2932-2943.

Ioscovich A, Davidson E, Orbach-Zinger S, Rudich Z, Ivry S, Rosen L, Avidan A Ginosar Y. Performance of aseptic technique during neuraxial analgesia for labor before and after the publication of international guidelines on aseptic technique. IJHPR 2014 3:9.

Rosen L, Rozhavski V, Levine H, Sela T, Bar-Ze'ev Y, Molina-Hazan V, Zarka S. Smoking initiation among Israeli adolescents: A 24-year time-to-event analysis. Prev Med (In Press)

Rosen LJ, Myers V, Hovell M, Zucker D, Ben Noach M. Meta-analysis of parental protection of children from tobacco smoke exposure. Pediatrics. 2014;133(4):698-714.

Rosen LJ, Tillinger E, Guttman N, Rosenblat S, Zucker DM, Stillman F, Myers V. Parental receptivity to child biomarker testing for tobacco smoke exposure: A qualitative study. Patient Educ Couns. 2015;98(11):1439-45.

Rosen LJ, Myers V, Winickoff JP, Kott J. Effectiveness of interventions to reduce tobacco smoke pollution in homes: a systematic review and meta-analysis. Int J Environ Res Public Health. 2015;12:16043-59.

Rosen L, Kostjukovsky I. Parental risk perceptions of child exposure to tobacco smoke. BMC Public Health 2015;15:90.

Rosen L, Zucker D, Hovell M, Brown N, Ram A, Myers V. Feasibility of measuring tobacco smoke air pollution in homes: report from a pilot study. Int. J. Environ. Res. Public Health 2015; 12:15129-15142.

Rosen L, Suhami R. The art and science of study identification: A comparative analysis of two systematic reviews. BMC Med. Res. Methodol. 2016;16:24

Levy D, Abrams D, Levy J, **Rosen L**. Complying with the framework convention for tobacco control: an application of the abridged SimSmoke model to Israel. Israel J Health Policy Res. In press.

Rosen LJ, Lev E, Guttman N, Tillinger E, Rosenblat S, Zucker DM, Myers V. Parental perceptions and misconceptions of child tobacco smoke exposure. Nicotine Tob Res. 2017;doi: 10.1093/ntr/ntx169

Zarka S, Levine H, Rozhavski V, Sela T, Bar-Ze'ev Y, Molina-Hazan V, **Rosen LJ.** Smoking behavior change during compulsory military service in Israel, 1987-2011. Nicotine Tob Res. 2017;19:1322-1329.

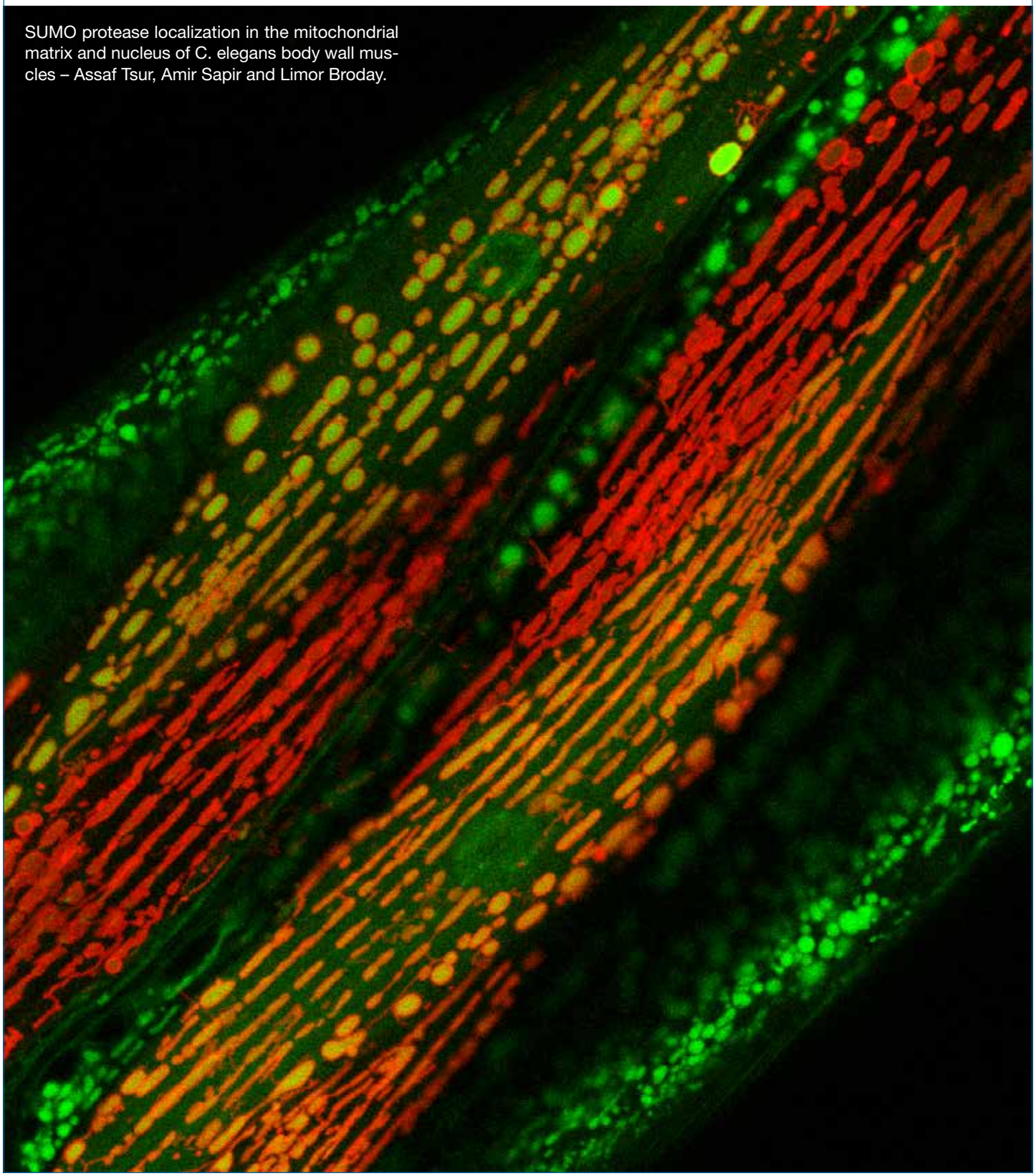
Reviews and Chapters

Rosen LJ, Peled-Raz M. Tobacco policy in Israel: 1948-2014 and beyond. Isr J Health Policy Res. 2015;4:12.

Grants

2012-2017 Flight Attendant Medical Research Institute (FAMRI).

Reproduction, Development and Evolution



SUMO protease localization in the mitochondrial matrix and nucleus of C. elegans body wall muscles – Assaf Tsur, Amir Sapir and Limor Broday.

Dr. Limor Broday, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: broday@post.tau.ac.il

Molecular Analysis of Ubiquitin and SUMO Pathways in the *C. Elegans* Model

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

Protein modifications by ubiquitin and ubiquitin-like proteins are essential for many cellular regulatory mechanisms. De-regulation of such processes is a cause for many human diseases. The main objective of our research is to understand, at a mechanistic and molecular level, how these processes are regulated. We use the nematode *C. elegans* as a model system to analyze various elements of the ubiquitin and ubiquitin-like system

Current lab projects:

Regulation of morphogenetic processes by SUMO (small ubiquitin-like modifier)

The role of E3 ubiquitin ligases in normal development and under cellular stress conditions

Publications

Linhart, E Halperin, Y. Darom, A. Kidron, S. **Broday, L**. and Shamir. R. 2012. A novel cis-regulatory motif pair in the promoters of germline and oogenesis genes in *C. elegans. Genome Res*. 22:76-83.

Kuang E, Okumura CY, Sheffy-Levin S, Varsano T, Shu VC, Qi J, Niesman IR, Yang HJ, López-Otín C, Yang WY, Reed JC, **Broday L**, Nizet V, Ronai ZA. 2012. Regulation of ATG4B stability by RNF5 limits basal levels of autophagy and influences susceptibility to bacterial infection. *PLoS Genet*. 8:e1003007.

Sapir, A., Tsur, A., Koorman, T., Ching, K., Mishra, P., Bardenheier, A., Podolsky, L., Bening-Abu-Shach, U., Boxem, M., Chou, TF., **Broday, L**., Sternberg, P.W. 2014. Controlled sumoylation of the mevalonate pathway enzyme HMGS-1 regulates metabolism during aging. *Proc Natl Acad Sci USA* 111:E3880-E3889.

Tsur, A., Bening Ab-Shach, U., and **Broday, L.** 2015. ULP-2 SUMO protease regulates E-cadherin recruitment to adherens junctions. *Developmental Cell.* 35:1-15, 2015. *Preview:* Adhesion with a SUMO. Developmental Cell. 35, 2015. *Featured in Research Highlight:* SUMO controls a tug of war at junctions. Nature Rev. Mol. Cell. Biol. 16:641, 2015.

Sagi D, Rak R, Gingold H, Adir I, Maayan G, Dahan O, **Broday L**, Pilpel Y, Rechavi O. 2016. Tissue- and time-specific expression of otherwise identical tRNA genes. *PLoS Genet.* 25;12(8):e1006264.

Surana, P., Gowda, C., Tripathi, V., **Broday, L.**, and Das, R. Structural and functional analysis of SMO-1, the SUMO homolog in *Caenorhabditis elegans. PLoS One*. 2017

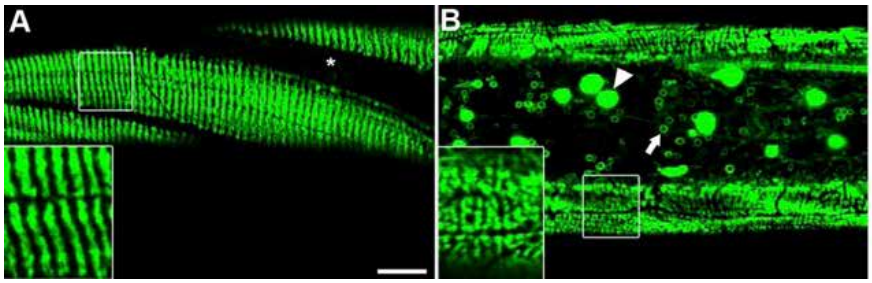
Reviews

Broday L. 2017. The SUMO system in *Caenorhabditis elegans development. Int J Dev Biol*. 6:159-164.

Grants

2015-2018 Israel Science Foundation (ISF)

2017-2018 Ministry of Defense, IDF



(A) Organization of the *C. elegans* epidermal intermediate filament protein IFB-1 in circumferential bands in wild-type animal. (B) Abnormal filaments and formation of inclusions in *smo-1* deleted worms.

Dr. Yankel Gabet, D.M.D., Ph.D.

Department of Anatomy & Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: yankel@post.tau.ac.il

Genetic and Hormonal Regulation of Bone Metabolism

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

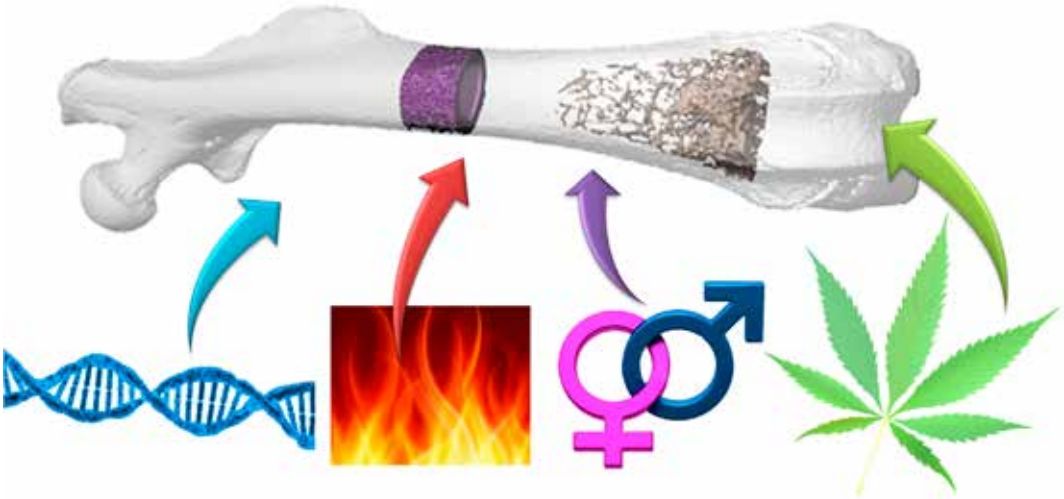
Genetics: Our laboratory focuses on the genetic and hormonal regulation of bone remodeling, microarchitecture and strength. These traits have a high degree of heritability, and one aspect of our research is to characterize new genetic determinants of bone remodeling as well as elucidate the mechanism of action of selected genes. Our GWAS confirmed the role of AVP (vasopressin) and OXT (precursor of oxytocin) in bone and identified for the first time Rhbdf2 as a significant determinant of bone structure.

Sex hormones: We investigate the actions of sex hormones with an emphasis on the skeletal dimorphism between males and females, and their interaction with other genes and transcription factors.

Erythropoietin: Epo is the main hormone that regulates blood cells production. We are investigating the role of Epo in bone remodeling in general and on the bone cells in particular.

Inflammation-induced osteolysis: Today, most dental implants undergo surface roughening to enhance osseointegration. However, ultrasonic scaling performed routinely for oral hygiene releases particles from titanium implants. We found that these particles stimulate the secretion of inflammatory cytokines and induce osteoclastogenesis in vitro and in vivo.

Cannabinoids: Cannabis-derived and endogenous cannabinoids are important regulators of bone cells. We investigate the beneficial actions of cannabinoids in bone fracture healing, osteoporosis, Osteogenesis Imperfecta, and inflammation-induced bone destruction.



Regulation of bone turnover and microstructure by genetic determinants, inflammation, sex hormones and cannabis/endocannabinoids.

Publications

Artsi A, Cohen-Kfir E, Gurt I, Shahar R, Bajayo A, Kalish N, Bellido T, **Gabet Y**, Dresner-Pollak R. (2014) The Sirtuin1 activator SRT3025 down-regulates sclerostin and rescues ovariectomy-induced bone loss and biomechanical deterioration in female mice. *Endocrinology* 155:3508-15.

Dolkart O, Liron T, Chechik O, Somjen D, Brosh T, Maman E, **Gabet Y**. (2014) Statins enhance Rotator Cuff healing by stimulating the COX2/PGE2/EP4 pathway in a rat model: an in vivo and in vitro study. *Am J Sports Med*. 42:2869-76.

Hiram-Bab S, Liron L, Deshet-Unger N, Mittelman M, Gassmann M, Rauner M, Franke K, Wielockx B, Neumann D, **Gabet Y**. (2015) Erythropoietin directly stimulates osteoclast precursors and induces bone loss. *FASEB J*. 29:1890-900.

Martin A, Xiong J, Koromila T, Chang S, Song YS, Krum SA, **Gabet Y**, Frenkel B. (2015) Estrogens antagonize RUNX2-mediated osteoblast-driven osteoclastogenesis through regulating RANKL membrane association. *Bone* 75:96-104

Kogan NM, Bajayo A, Wasserman E, Raphael B, Breuer A, Stok KS, Villarreal Escudero AV, Sondergaard R, Attar-Namdar M, Friedlander-Barenboim S, Mechoulam R, Müller R, Melamed E, **Gabet Y***, Bab I. (2015) Cannabidiol, a major non-psychotrophic cannabis constituent enhances fracture healing and stimulates lysil hydroxylase activity in osteoblasts. *J Bone Min Res*. 30:1905-1913. *corresponding author.

Elsner JJ, Shemesh M, Shefy-Peleg A, **Gabet Y**, Zylberberg E, Linder-Ganz E. (2015) Quantification of in vitro wear of a synthetic meniscus implant using gravimetric and micro-CT measurements. *J Mech Behav Biomed Mater.*, 49:310-320.

Barak S, Iezzi G, Neuman M, Piattelli A, Perrotti V, **Gabet Y**. (2015) A new device for improving dental implants anchorage: a histological and microcomputed tomography study in the rabbit. *Clinical Oral Implants Research*, Epub.

Garfinkel BP, Arad S, Le PT, Bustin M, Rosen CJ, **Gabet Y***, Orly J*. (2015) Proportionate dwarfism in mice lacking heterochromatin protein 1 binding protein 3 (HP1BP3) is associated with alterations in the endocrine IGF-1 pathway. *Endocrinology*. Accepted, ePub.

Hershkovitz I, Weber GW, Fornai C, Gopher A, Barkai R, Slon V, Quam R, **Gabet Y** and Sarig R. New Middle Pleistocene dental remains from Qesem Cave (Israel). *Quaternary International*, accepted ePub.

Barak S, Iezzi G, Neuman M, Piattelli A, Perrotti V, **Gabet Y**. (2015) A new device for improving dental implants anchorage: a histological and microcomputed tomography study in the rabbit. *Clinical Oral Implants Research*, Epub.

Raphael B, **Gabet Y**. (2015) The skeletal endocannabinoid system: clinical and experimental insights. *J Basic Clin Physiol Pharmacol*. ePub; Accepted.

Levy R, Mott RF, Iraqi FA, **Gabet Y**. Collaborative cross mice in a genetic association study reveal new candidate genes for bone microarchitecture. (2015) *BMC Genomics*; 16:1013.

Bell RE, Golan T, Sheinboim D, Malcov H, Amar D, Salamon A, Liron T, Gelfman S, **Gabet Y**, Shamir R, Levy C. (2016) Enhancer methylation dynamics contribute to cancer plasticity and patient mortality. *Genome Research*; 26:601-11.

Masarwi M, **Gabet Y,** Dolkart O, Brosh T, Shamir R, Phillip M, Gat-Yablonski G. (2016) Skeletal effect of casein and whey protein intake during catch-up growth in young male Sprague-Dawley rats. *Br J Nutr*. 116:59-69.

Raygorodskaya M, **Gabet Y,** Shochat C, Kobyliansky E, Torchinsky A, Karasik D. (2016) Intrauterine stress induces bone loss in adult offspring of C3H/HeJ mice having high bone mass phenotype but not C57BL/6J mice with low bone mass phenotype. *Bone*; 87, 114-119.

Hiram-Bab S, Neumann N, **Gabet Y**. (2016) Erythropoietin in bone - Controversies and consensus. *Cytokine*. Accepted Jan 2016.

Rauner M, Franke K, Murray M, Singh RP, Hiram-Bab S, Platzbecker U, Gassmann M, Socolovsky M, Neumann D, **Gabet Y**, Chavakis T, Hofbauer LC, Wielockx B. (2016) Increased EPO Levels Are Associated with Bone Loss in Mice Lacking PHD2 in EPO-Producing Cells. *J Bone Miner Res*; Accepted Apr 2016.

Gabet Y, Bab I. A validated method for titanium implant anchorage analysis using microct and biomechanical testing biological sciences. *Adv Tech Biol Med*. Accepted June 6, 2016.

Deshet-Unger N, Hiram-Bab S, Haim-Ohana Y, Mittelman M, Gabet Y, Neumann D. Erythropoietin treatment in murine multiple myeloma: immune gain and bone loss. Scientific Reports, Accepted July 2016

Gilboa D, Haim-Ohana Y, Deshet-Unger N, Ben-Califa N, Hiram-Bab S, Reuveni D, Zigmond E, Gassmann M, Gabet Y, Varol C, Neumann D. (2017)

Erythropoietin enhances Kupffer cell number and activity in the challenged liver. *Sci Rep.* 7:10379.

Bar-Maisels M, Gabet Y, Shamir R, Hiram-Bab S, Pasmanik-Chor M, Phillip M, Bar-Yoseph F, Gat-Yablonski G. (2017) Beta palmitate improves bone length and quality during catch-up growth in young rats. *Nutrients*. 9(7).

Hiram-Bab S, Neumann D, Gabet Y. (2017) Context-dependent skeletal effects of erythropoietin. *Vitam Horm.* 105:161-179.

Martin A, Yu J, Xiong J, Khalid AB, Katzenellenbogen B, Kim SH, Katzenellenbogen JA, Malaivijitnond S, Gabet Y, Krum SA, Frenkel B. ((2017) Estrogens and androgens inhibit association of RANKL with the pre-osteoblast membrane through post-translational mechanisms. *J Cell Physiol.* 232:3798-3807.

Eger M, Sterer N, Liron T, Kohavi D, Gabet Y. (2017) Scaling of titanium implants entrains inflammation-induced osteolysis. *Sci Rep.* 7:39612.

Liron T, Raphael B, Hiram-Bab S, Bab IA, Gabet Y. (2018) Bone loss in C57BL/6J-OlaHsd mice, a substrain of C57BL/6J carrying mutated alpha-synuclein and multimerin-1 genes. *J Cell Physiol.* 233:371-377.

Grants

2012-2017 Israel Science Foundation (ISF) Grant

2015-2017 American Society for Bone and Mineral Research GAP Award

2015-2017 Kalytera Therapeutics Ltd

2016-2017 Israel Cancer Association (co-PI)

2018-2021 German-Israeli Foundation (GIF)

Prof. Israel Hershkovitz, Ph.D.

Department of Anatomy and Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email:anatom2@post.tau.ac.il

Evolutionary Medicine, Paleopathology and Bio-history

Position

Professor, Sackler Faculty of Medicine

Head, Dan David Laboratory for the Search and Study of Modern Humans

Director, Tassia and Joseph Meychan Chair for the History and Philosophy of Medicine

Research

Biohistory: The social and biological impact the transition from foraging and hunting to farming had on human populations. Although a rapid event in human evolution, the 'agriculuture revolution' was the most significant cultural process in human history, something that forever changed the face of humanity (culturally and biologically). Unlike many other paleoanthropological studies, we adopt an 'osteobiographic' approach, i.e., life history as recorded in bones. The study is based on several hundreds of Natufian and Neolithic skeletons (large portion of them were excavated by the team), housed at Tel Aviv University. The study, besides traditional methods, applies new methods and technologies as CT, Micro-CT, SEM, Histochemistry, aDNA, Isotope analyses.

Human evolution: Searching for the origin of anatomically modern humans. The origin of anatomically modern *Homo sapiens* and the fate of the Neanderthals have been fundamental questions in human evolutionary studies for over a century. New fossils excavated at Qesem, Misliya and Manot caves, may shed light on the above questions.

Evolutionary medicine: This section is divided into three topics: 1) Establishing valid methods for identifying diseases in ancient bones, 2) Identifying diseases in the fossil record, 3) Evolutionary perspective of current diseases.

Publications

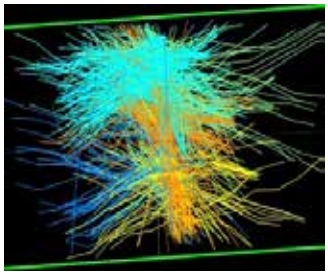
R. Sarig, Lianopoulos NV, **Hershkovitz I**, Vardimon AD. The arrangement of the interproximal interfaces in the human permanent dentition. *Clin Oral Investig*. 2013, 17:731-8

N. Steinberg, **Hershkovitz I**, Peleg S, Dar G, Masharawi Y, Zeev A, Siev-Ner I. Morphological characteristics of the young scoliotic dancer. *Phys Ther Sport*. 2013, 14:213-20.

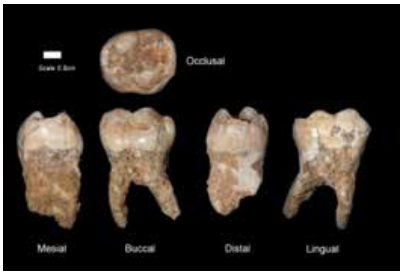
V. Slon, **Hershkovitz I**, May H. The value of cadaver CT scans in gross anatomy laboratory. *Anat Sci Educ*. 2014, 7:80-2.

N. Steinberg, Siev-Ner I, Peleg S, Dar G, Masharawi Y, Zeev A, **Hershkovitz I**. Injuries in female dancers aged 8 to 16 years. *J Athletic Training*, 2013, 48:118-123.

H. Cohen, V. Sloan, H. May, **I. Hershkovitz**, E. Peled, D. Norman. Musculoskeletal wounds characteristic



3D reconstruction of the annulus fibrosus, MRI study. Disc herniation project.



Teeth from Qesem cave 300,000 years. Modern human origin project.

Hyperostosis frontalis interna (HFI) identified via CT and direct observation (skeletal).

of the second Lebanon war. *Forensic Med Anat Res*. 2013, 1:14-17.

H. May, Cohen H, Medlej B, Kornreich L, Peled N, **Hershkovitz I**. Computed tomography-enhanced anatomy course using enterprise visualization. *Anat Sci Educ*. 2013, 6:332-41.

H. Valladas, Mercier N, **Hershkovitz I**, Zaidner Y, Tsatskin A, Yeshurun R, Vialettes L, Joron J-L, Reyss J-L, Weinstein-Evron M. Dating the Lower to Middle Paleolithic transition in the Levant: A view from Misliya Cave, Mount Carmel, Israel. *J Hum Evol*. 2013, X: 1-9.

J. Abbas, Hamoud K, May H, Peled N, Sarig R, Stein D, Alperovitch-Najenson D, **Hershkovitz I**. Socioeconomic and physical characteristics of degenerative lumbar spinal stenosis individuals. *Spine (Phila Pa 1976).* 2013 Feb 1. [Epub ahead of print]

R. Sarig, Slon V, Abbas J, May H, Shpack N, Vardimon AD, **Hershkovitz I**. Malocclusion in early anatomically modern human: a reflection on the etiology of modern dental misalignment. *PLoS One*. 2013;8:e80771

Slon V, Sarig R, **Hershkovitz I**, Khalaily H, Milevski I. The plastered skulls from the Pre-Pottery Neolithic B site of Yiftahel (Israel)--a computed tomography-based analysis. *PLoS One*. 2014 9:e89242.

Hershkovitz I, Marder O, Ayalon A, Bar-Matthews M, Yasur G, Boaretto E, Caracuta V, Alex B, Frumkin A, Goder-Goldberger M, Gunz P, Holloway RL, Latimer B, Lavi R, Matthews A, Slon V, Mayer DB, Berna F, Bar-Oz G, Yeshurun R, May H, Hans MG, Weber GW, Barzilai O. Levantine cranium from Manot Cave (Israel) foreshadows the first European modern humans. *Nature*. 520(7546):216-9, 2015.

Hershkovitz I, Donoghue HD, Minnikin DE, May H, Lee OY, Feldman M, Galili E, Spigelman M, Rothschild BM, Bar-Gal GK. Tuberculosis origin: The Neolithic scenario. *Tuberculosis (Edinb).* 95 Suppl 1:S122-6, 2015.

Slon V, Stein D, Cohen H, Sella-Tunis T, May H, **Hershkovitz I**. Vertebral hemangiomas: their demographical characteristics, location along the spine and position within the vertebral body. *Eur Spine J*. 24(10):2189-95, 2015.

Sarig R, **Hershkovitz I**, Shpack N, May H, Vardimon AD. Rate and pattern of interproximal dental attrition. *Eur J Oral Sci*. 123(4):276-81, 2015.

Hay O, Dar G, Abbas J, Stein D, May H, Masharawi Y, Peled N, **Hershkovitz I**. The lumbar lordosis in males and females, revisited. *PLoS One*. 10(8):e0133685, 2015.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, **Hershkovitz I**, Brosh T. The impact velocity and bone fracture pattern: Forensic perspective. *Forensic Sci Int*. 7;266:54-62, 2016.

Abbas J, Slon V, May H, Peled N, **Hershkovitz I**, Hamoud K. Paraspinal muscles density: a marker for degenerative lumbar spinal stenosis? *BMC Musculoskelet Disord.* 17:422, 2016.

Alex B, Barzilai O, **Hershkovitz I**, Marder O, Berna F, Caracuta V, Abulafia T, Davis L, Goder-Goldberger M, Lavi R, Mintz E, Regev L, Bar-Yosef Mayer D, Tejero JM, Yeshurun R, Ayalon A, Bar-Matthews M, Yasur G, Frumkin A, Latimer B, Hans MG, Boaretto E. Radiocarbon chronology of Manot Cave, Israel and Upper Paleolithic dispersals. *Sci Adv.* 3:e1701450, 2017.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, **Hershkovitz I**. The influence of impact direction and axial loading on the bone fracture pattern. *Forensic Sci Int.* 277:197-206, 2017.

Abbas J, Slon V, Stein D, Peled N, **Hershkovitz I**, Hamoud K. In the quest for degenerative lumbar spinal stenosis etiology: the Schmorl's nodes model. *BMC Musculoskelet Disord.* 18:164, 2017.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, **Hershkovitz I**. The effect of impact tool geometry and soft material covering on long bone fracture patterns in children. *Int J Legal Med*. 131:1011-1021, 2017.

Steinberg N, Tenenbaum S, **Hershkovitz I**, Zeev A, Siev-Ner I. Lower extremity and spine characteristics in young dancers with and without patellofemoral pain. *Res Sports Med.* 25:166-180, 2017.

Ezra D, Masharawi Y, Salame K, Slon V, Alperovitch-Najenson D, **Hershkovitz I**. Demographic aspects in cervical vertebral bodies' size and shape (C3-C7): a skeletal study. *Spine J.* 17:135-142, 2017.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, **Hershkovitz I**. The influence of impact direction and axial loading on the bone *fracture pattern. Forensic Sci Int.* 277:197-206, 2017.

Prof. Michael M. Kozlov, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: michk@post.tau.ac.il

Theoretical Biophysics of Membranes and Cytoskeleton

Position

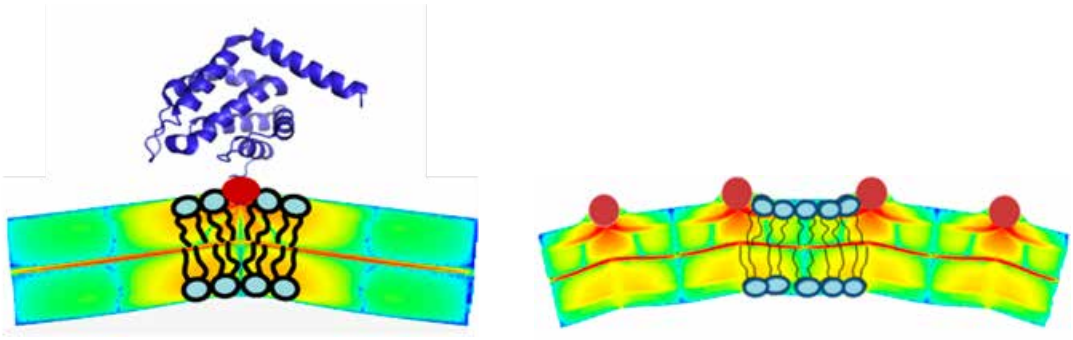
Professor, Sackler Faculty of Medicine

Joseph Klafter Chair in Biophysics

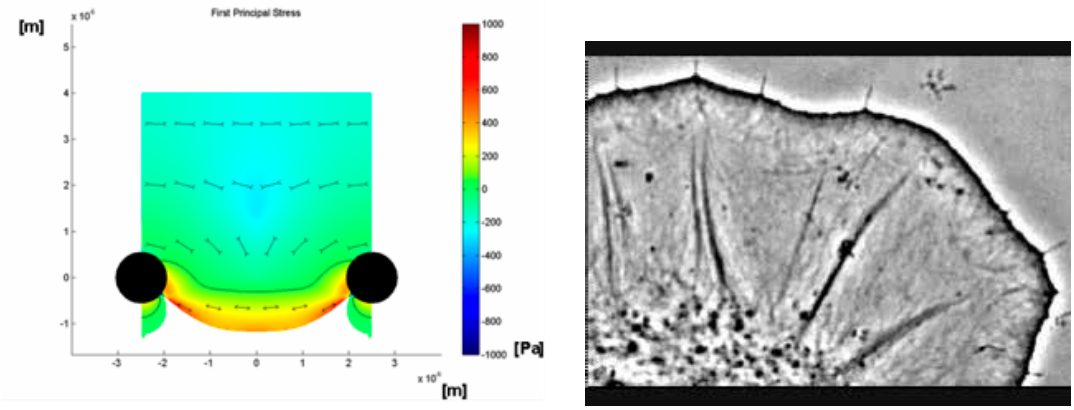
Research

We model the mechanisms of shaping and remodeling of intracellular membranes by specialized proteins that includes generation of large membrane curvatures, membrane fission and fusion. Our goal is to reveal the common mechanistic themes in the function of membrane shaping proteins acting in different intracellular systems. In this way, we hope to be able to understand whether every stage of membrane shaping needs a special protein or the same protein machinery can enable both membrane curvature generation and fission and/or fusion. Specifically, we model the action of BAR domain proteins, Epsins and Dynamins in endocytosis, Reticulons and their partners in shaping the Endoplasmaic Reticulum, and ESCRT-III complexes in fission of cytokinetic tubes.

We model the mechanisms underlying the dynamic organization of the actin cytoskeleton and the system of cell adhesion in polarizing and moving cells. Our major goal is to understand the mechanosensitivity of the cytoskeletal systems and its role in the system temporal rearrangements and steady-state structures.



Computational results for membrane curvature generation by amphipathic N-terminal helices of N-BAR domains, ENTH domains and small G-proteins.



Computational modeling of lamellipodium boundary formation resulting from actin-focal adhesion interaction (left), the phenomenon observed in moving fibroblasts (right, courtesy of A. Verkhovsky).

Publications

Leikina E., Melikov K., Sanyal S., Verma S.K., Eun B., Gebert C., Pfeifer K., Lizunov V.A., **Kozlov M.M.**, Chernomordik L.V. Extracellular annexins and dynamin are important for sequential steps in myoblast fusion. *J Cell Biol*. 2013. 200:109-23.

Schweitzer Y, **Kozlov M.M.** Cell motion mediated by friction forces: understanding the major principles. *Soft Matter*. 2013. 9:5186-5195

Terasaki M., Shemesh T., Kasthuri N., Klemm R.W., Schalek R., Hayworth K.J., Hand A.R., Yankova M., Huber G., Lichtman J.W., Rapoport T.A., **Kozlov M.M**. Stacked endoplasmic reticulum sheets are connected by helicoidal membrane motifs. *Cell*. 2013;154:285-96.

G. Fabrikant, S. Gupta, G.V. Shivashankar, **M.M. Kozlov**. Model of T-cell nuclear deformation by the cortical actin layer. *Biophys J*. 105:1316-23, 2013

F. Campelo, **M.M. Kozlov**. Sensing membrane stresses by protein insertions. *PLoS Comp Biol*. 10: e1003556, 2014.

Y. Schweitzer, A.D. Lieber, K. Keren, **M.M. Kozlov**. Theoretical analysis of membrane tension in moving cells. *Biophys J*.106:84-92, 2014.

Y. Schweitzer, T. Shemesh, **M.M. Kozlov**. A model for shaping membrane sheets by protein scaffolds. *Biophys. J*. 109:564-573, 2015.

A.D. Lieber, Y. Schweitzer, **M.M. Kozlov,** K. Keren. Front-to-rear membrane tension gradient in rapidly moving cells. *Biophys. J*. 108:1599-1603, 2015.

Y.H. Tee, T. Shemesh, V. Thiagarajan, R.F. Hariadi, K.L. Anderson, C. Page, N. Volkmann, D. Hanein, S. Sivaramakrishnan, **M.M. Kozlov**, A.D. Bershadsky. Cellular chirality arising from the self-organization of the actin cytoskeleton. *Nature Cell Biol*. 17:445-457, 2015.

Y. Schweitzer, **M.M. Kozlov**. Membrane-mediated interaction between strongly anisotropic protein scaffolds. *PLoS Comp. Biol*. 11:2 e1004054, 2015.

U. Manor, S. Bartholomew, G. Golani, E. Christenson, **M. Kozlov**, H. Higgs, J. Spudich, J. Lippincott-Schwartz. A mitochondria-anchored isoform of the actin-nucleating spire protein regulates mitochondrial division. *eLife*: doi: 10.7554/eLife.08828, 2015.

Yu M, Yuan X, Lu C, Le S, Kawamura R, Efremov AK, Zhao Z, **Kozlov MM**, Sheetz M, Bershadsky A, Yan J. mDia1 senses both force and torque during F-actin filament polymerization. *Nat Commun*. 8:1650, 2017.

Hirama T, Lu SM, Kay JG, Maekawa M, **Kozlov MM**, Grinstein S, Fairn GD. Membrane curvature induced by proximity of anionic phospholipids can initiate endocytosis. *Nat Commun*. 8:1393, 2017.

Campelo F, van Galen J, Turacchio G, Parashuraman S, **Kozlov MM**, García-Parajo MF, Malhotra V. Sphingomyelin metabolism controls the shape and function of the Golgi cisternae.

Reviews

M.M. Kozlov, F. Campelo, N. Liska, L.V. Chernomordik, S.J. Marrink, H.T. McMahon. *Curr Opin Cell Biol*. Mechanisms shaping cell membranes. 29:53–60, 2014

F. Campelo, C. Arnarez, S.J. Marrink, **M.M. Kozlov**. Helfrich model of membrane bending: From Gibbs theory of liquid interfaces to membranes as thick anisotropic elastic layers. *Adv Colloid Interface Sci*. 208: 25–33, 2014

M.M. Kozlov, L.V. Chernomordik. Membrane tension and membrane fusion. *Curr. Opin. Struct. Biol.* 33:61-67, 2015.

L.V. Chernomordik, **M.M. Kozlov**. Myoblast fusion: playing hard to get. *Dev. Cell*. 32(5): 529-530, 2015.

M.M. Kozlov, W. Weissenhorn, P. Bassereau. Membrane remodeling: theoretical principles, structures of protein scaffolds and forces involved. Ecole de Physique des Houches, E. Pebay-Peyroula, H. Nury, F. Parcy, R.W.H. Ruigrok, C.Ziegler, L.F. Cuglindolo eds., Oxford University Press, pp. 287-331, 2016.

Grants

2017	EU-ITM
2015-2018	Israel Science Foundation

Dr. Hila May, Ph.D.

Department of Anatomy and Anthropology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

mayhila@post.tau.ac.il

Laboratory for Bio-History and Evolutionary Medicine

Position

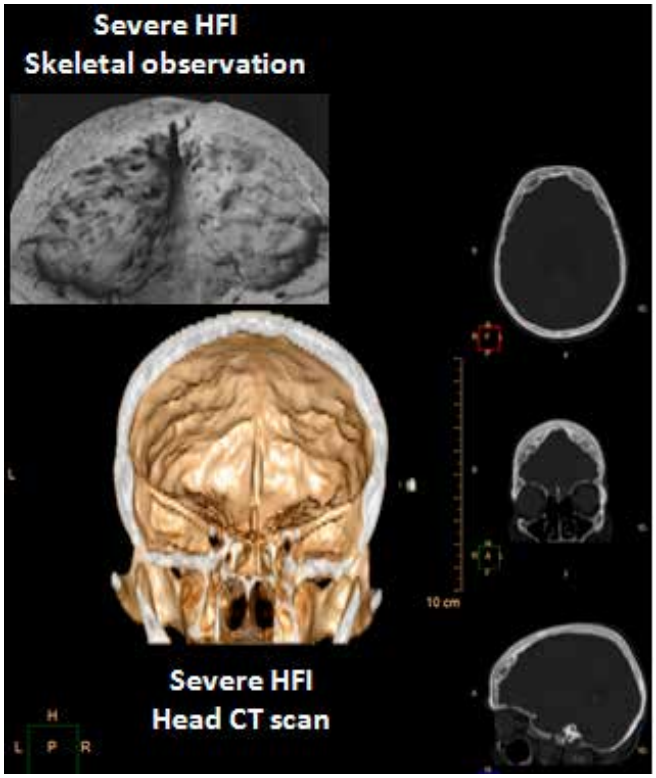
Lecturer

Research

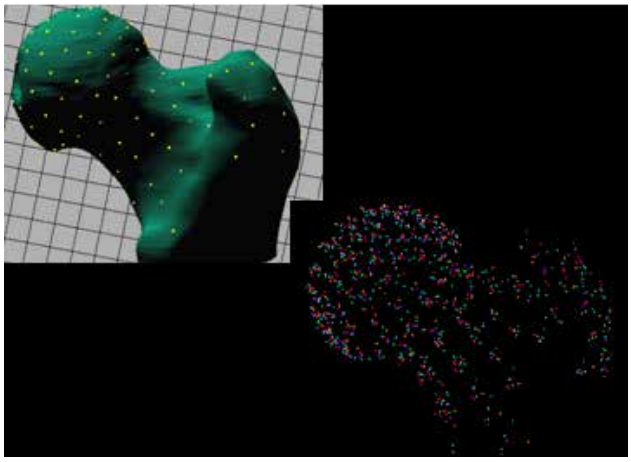
Inter-disciplinary laboratory focusing on two major topics: evolutionary history of anatomical systems and their impact on current population health, and reconstruction of ancient populations' daily life, based on their skeletal remains, with emphasis on the interaction between genetic and socio-cultural factors.

The bio-history study of ancient populations is based on both morphological and molecular (aDNA) methods.

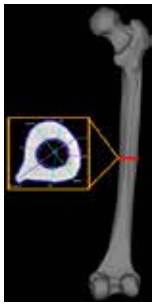
Reconstructing past population daily life: revealing daily activities of prehistoric and historic populations is a challenging task considering the evidence at hand (bones). Nevertheless, bones may furnish us with information otherwise not available, e.g., division of labor, social stratification, intensity of physical activities, health and nutrition, demography (sex ratio, mortality, family size, etc.). Beside traditional methods, the studies are being carried out utilizing advanced 3D analysis methods based on CT, micro-CT and 3D surface scans. The accompanied genetic studies, in addition to supporting and confirming observed pathologies in the bones, i.e., identifying pathogens suspected to cause diseases such as TB, leprosy, etc., also contribute to questions related to populations' migration from and to the Southern



Hyperostosis frontalis interna (HFI) identified via CT and direct observation (skeletal).



Geometric-morphometrics analysis of the proximal femur.



Femoral mid-shaft cross-sectional analysis of hunter-gatherer (Natufian), dated to ~15,000 years ago.

Levant, and questions related to population structure (e.g., extended family) and biological relationships between the local populations.

The evolutionary medicine studies focus on the quest for evolutionary explanations for common diseases found in modern human populations. We estimate the benefits and costs behind anatomical changes through evolution in order to better understand how compromised designs are being developed, and their outcomes (i.e., diseases).

Publications

J Abbas, K Hamoud, **H May**, N Peled, R Sarig, D Stein, D Alperovitch-Najenson, I Hershkovitz. Socioeconomic and physical characteristics of individuals with degenerative lumbar spinal stenosis. *Spine (Phila Pa 1976)*, 38, E554-E561, 2013.

H May, H Cohen, B Medlej, L Kornreich, N Peled, I Hershkovitz. Computed tomography-enhanced anatomy course using enterprise visualization. *Anat Sci Educ*, 6, 332-334, 2013.

H Cohen, V Slon, **H May**, I Hershkovitz, E Peled, D Norman. Musculoskeletal wounds characteristics of the Second Lebanon War. *Forensic Med Anar Res*, 1, 14-17, 2013.

R Sarig, V Slon, J Abbas, **H May**, N Shpack, AD Vardimon, I Hershkovitz. Malocclusion in early anatomically modern human: a reflection on the etiology of modern dental misalignment. *PLoS One*, 8, e80771, 2013.

V Slon, I Hershkovitz, **H May**. The value of cadaver CT scans in gross anatomy laboratory. *Anat Sci Educ*, 7, 80-82, 2014.

I Hershkovitz, M Spigelman, R Sarig, DS Lim, IS Lee, CS Oh, **H May**, E Boaretto, YS Kim, SD Lee, N Peled, MJ Kim, T Toledano, GK Bar-Gal, DH Shin. A possible case of cherubism in a 17th-century Korean mummy. *PLoS One*, 9, e1024412014, 2014.

R Sarig, I Hershkovitz, N Shvalb, T Sella-Tunis, **H May**, AD Vardimon. Proximal attrition facets: morphometric, demographic, and aging characteristics. *Eur J Oral Sci*, 122, 271-8, 2014.

Hershkovitz I, Marder O, Ayalon A, Bar-Matthews M, Yasur G, Boaretto E, Caracuta V, Alex B, Frumkin A, Goder-Goldberger M, Gunz P, Holloway RL, Latimer B, Lavi R, Matthews A, Slon V, Mayer DB, Berna F, Bar-Oz G, Yeshurun R, **May H**, Hans MG, Weber GW, Barzilai O. Levantine cranium from Manot Cave (Israel) foreshadows the first European modern humans. *Nature*. 520(7546):216-9, 2015.

Hershkovitz I, Donoghue HD, Minnikin DE, **May H**, Lee OY, Feldman M, Galili E, Spigelman M, Rothschild BM, Bar-Gal GK. Tuberculosis origin: The Neolithic scenario. *Tuberculosis (Edinb).* 95 Suppl 1:S122-6, 2015.

Slon V, Stein D, Cohen H, Sella-Tunis T, **May H**, Hershkovitz I. Vertebral hemangiomas: their demographical characteristics, location along the spine and position within the vertebral body. *Eur Spine J*. 24(10):2189-95, 2015.

Sarig R, Hershkovitz I, Shpack N, **May H**, Vardimon AD. Rate and pattern of interproximal dental attrition. *Eur J Oral Sci*. 123(4):276-81, 2015.

Hay O, Dar G, Abbas J, Stein D, **May H**, Masharawi Y, Peled N, Hershkovitz I. The lumbar lordosis in males and females, revisited. *PLoS One*. 10(8):e0133685, 2015.

May H, Ruff C. Physical burden and lower limb bone structure at the origin of agriculture in the levant. *Am J Phys Anthropol*. doi: 10.1002/ajpa.23003, 2016

Cohen H, Kugel C, **May H**, Medlej B, Stein D, Slon V, Hershkovitz I, Brosh T. The impact velocity and bone fracture pattern: Forensic perspective. *Forensic Sci Int*. 7;266:54-62, 2016.

Abbas J, Slon V, May H, Peled N, Hershkovitz I, Hamoud K. Paraspinal muscles density: a marker for degenerative lumbar spinal stenosis? BMC Musculoskelet Disord. 17:422, 2016.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, Hershkovitz I. The influence of impact direction and axial loading on the bone fracture pattern. Forensic Sci Int. 277:197-206, 2017.

Cohen H, Kugel C, May H, Medlej B, Stein D, Slon V, Brosh T, Hershkovitz I. The effect of impact tool geometry and soft material covering on long bone fracture patterns in children. Int J Legal Med. 131:1011-1021, 2017.

Tunis TS, Sarig R, Cohen H, Medlej B, Peled N, May H. Sex estimation using computed tomography of the mandible. Int J Legal Med. 131:1691-1700, 2017.

Grants

2016-2017 Israel Science Foundation (Equipment).

2016-2019 Israel Science Foundation: From Hunting to Farming: Exploring Micro-Evolutionary Trends in the Human Masticatory System and their Implications at the Terminal Pleistocene Levant

Prof. Ruth Shalgi, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: shalgir@post.tau.ac.il
URL: www2.tau.ac.il/Person/medicine/researcher.asp?id=abfdfkcgh

Reproduction in Animal Models and in Humans

Positions

Professor Emeritus, Sackler Faculty of Medicine

Research

Our research focuses on Reproductive Physiology in animal models and in humans. The current research directions investigated in the laboratory are:

- The role of Fyn kinase, member of the Src family kinases, during meiosis and early events of oocyte activation, as well as in cancer cells (Figure-left panel).
- Fertility preservation – the signaling pathway leading to apoptosis in aging oocytes and in oocytes exposed to chemotherapeutic treatments and potential protectants (Figure -right panel).
- Regulation of angiogenesis in reproductive organs by Pigment epithelium derived factor (PEDF) and treatment of reproductive angiogenic-related pathologies.

Various research methods are routinely used in the laboratory, ranging from *in vivo* animal studies and cells cultures to an array of protein methodologies such as western blotting, immunohistochemistry, molecular biology techniques as well as cellular and molecular imaging.

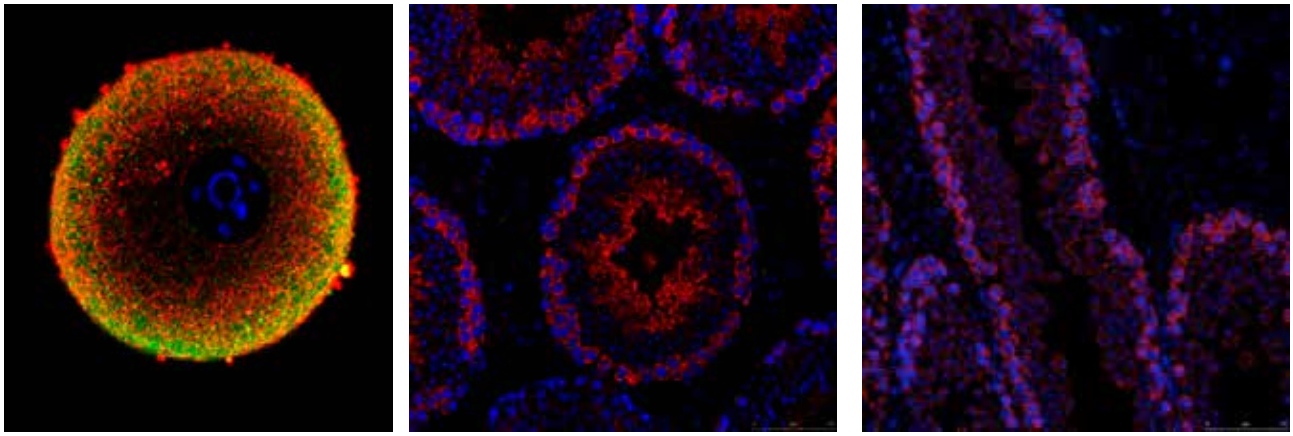
Publications

Chuderland*, D., Ben-Ami* I., Ronel, R., Kraicer-Kaplan, R., Grossman, H., Satchi-Fainaro, R., Eldar-Boock, A. and, **Shalgi, R**. Hormonal regulation of pigment epithelium derived factor (PEDF) in granulosa cells. *Mol Hum Reprod*. 19:72-81 2013

Chuderland*, D., Ben-Ami* R., Kraicer-Kaplan, R., Grossman, H., Ronel, R. and **Shalgi, R.** The role of pigment epithelium-derived factor in the pathophysiology and treatment of ovarian hyperstimulation syndrome in mice. *J Clin Endocr Metab*. 98:E258-66, 2013.

Chuderland, D.*, Hasky, N.*, Ben-Ami, I., Kaplan-Kraicer, R., Grossman, H. and **Shalgi R.** A physiological approach for treating endometriosis by recombinant pigment epithelial derived factor (PEDF). *Hum Reprod*. 28:1626-34, 2013.

Ninio-Many, L., Grossman, H., Chuderland D., Shomron, N. and **Shalgi, R.** microRNA-125a-3p



Left panel- Human oocyte stained for DNA (blue); cytoskeleton (tubulin; red); protein (Fyn kinase; green). Arrow – Germinal vesicle (genetic material); C- Cytoplasm. Confocal microscopy. Right panels -Section of sperm producing tubules in mouse testis before (left) and after treatment with chemotherapy (right). The drug led to loss of sperm (S) production. DNA (blue); protein (DAZL; red). Immunofluorescent microscopy.

reduces proliferation and migration of HEK 293T cells by targeting Fyn. *J Cell Sci*, 126:2867-2876, 2013.

Levi M, Ghetler Y, Shulman A and **Shalgi, R**. Morphologic and molecular markers indicate maturation-competence of human oocytes. *Hum Reprod*. 28:2482-9. 2013.

Ben Aharon, I., Bar Joseph, H., Tzabari, M., Shekman, B., Farzam, N., Levi, M., **Shalgi, R.,** Stemmer, SM. and Savion, N. Doxorubicin-induced vascular toxicity – Targeting potential pathways may reduce procoagulant activity. *PLoS One*, 8, e75157, 2013.

Chuderland D., Ben-Ami, I., Fridler, S., Hasky, N., Ninio-Many, L., Goldberg, K., Bar-Josef, H., Grossman, H., and **Shalgi, R.** Hormonal regulation of Pigment epithelium-derived factor (PEDF) expression in the endometrium. *Mol Cell Endocr*. 390, 85-92, 2014.

Ninio-Many, L., Grossman, H., Levi, M., Zilber, S., Tsarfaty, I., Shomron, N., Tuvar, A., Chuderland D., Stemmer, S.M., Ben-Aharon, I.* and **Shalgi R.*** MicroRNA miR-125a-3p modulates molecular pathway of motility and migration in prostate cancer cells. *Oncoscience*. 1, 250-261, 2014._

Bar-Joseph, H., Ido Ben-Ami, I., Ron-El, R., **Shalgi, R*.** and Chuderland, D*. Pigment epithelium-derived factor (PEDF) exerts anti oxidative effects in granulosa cells. *Feril Steril* 102:891-898.e3. 2014.

Uri-Belapolsky, S., Shaish, A., Eliyahu, E., Grossman, H., Levi, M., Chuderland, D., Ninio-Many, L., Hasky, N., Shashar, D., Almog, T., Kandel-Kfir, M., Harats, D., **Shalgi, R.*** and Kamari, Y*. Interleukin-1 deficiency prolongs ovarian lifespan in mice. *Proc Natl Acad Sci USA*. 111:12492-7. 2014.

*Highlighted by World of Reproductive Biology: Overcoming Age in the Ovary Biol Reprod biolreprod.114.124776; published ahead of print August 27, 2014,

*Recommended by F1000Prime Interleukin-1 deficiency prolongs ovarian lifespan in mice. Rep. 2014; 6. Published online Sep 10, 2014.

Yesilaltay, A., Dokshin, G., Busso, D., Galiani, D., Chavarria, T.E., Vasile, E., Quilaqueo, L., **Shalgi, R.,** Dekel, N., Albertini, D., Rigotti, A., Page, D.C., Krieger, D.C. Excess cholesterol induces mouse oocyte activation and may cause infertility. *Proc Natl Acad Sci USA*. 111:E4972-80. 2014.

Bar-Joseph, H., Stemmer, S.M., Tsarfaty, I., **Shalgi, R.** and Ben Aharon, I. Chemotherapy -induced vascular toxicity – Real-time in vivo imaging of vessel impairment. *J Vis Exp*. e51650, http://www.jove.com/video/51650, 2015.

Hasky, N., Uri-Belapolsky S., Goldberg, K., Miller, I., Grossman, H., Stemmer, S.M. Ben-Aharon, I*. and **Shalgi, R*.** Gonadotropin-releasing hormone agonists for fertility preservation – unraveling the enigma? *Hum Reprod*. 30:1089–1101, 2015.

Grossman, H., Chuderland, D., Ninio-Many, L., Hasky, N., Kaplan-Kraicer, R. and **Shalgi, R**. A novel regulatory pathway in granulosa cells, the LH/human chorionic gonadotropin-microRNA-125a-3p-Fyn pathway, is required for ovulation. *FASEB J*. 29:3206-16, 2015.

Levi, M., Tzabari M., Savion, N., Stemmer, S.M., **Shalgi, R.*** and Ben-Aharon, I.* Dexrazoxane exacerbates doxorubicin-induced testicular toxicity. *Reproduction* 150: 357–366, 2015.

Levi, M., Hasky, N., Stemmer, S.M., **Shalgi, R.*** and Ben-Aharon, I.*. Anti-Müllerian hormone is a marker for chemotherapy-induced testicular toxicity. *Endocrinology* en20151310; 2015 [Epub ahead of print]

Miller-Zmora, I., Chuderland, D., Ron-El R., **Shalgi, R.*** and Ben-Ami, I.* GnRH agonist modulates PEDF/VEGF ratio inversely to hCG in granulosa cells. *J Clin Endocrinol Metab*. jc20152312. 2015 [Epub ahead of print]

Levi, M., **Shalgi, R.**, Brenner, B., Perl, G., Purim, O., Amit, L., Stemmer, S.M. and Ben-Aharon, I. The impact of oxaliplatin on the gonads – from bedside to the bench. *Mol Hum Reprod* 21(12):885-93 2015

Goldberg, K., Bar Joseph, H., Grossman, H., Hasky, N., Uri-Belapolsky, S., Stemmer, S.M., Chuderland, D*., **Shalgi, R.*** and Ben-Aharon, I.* Pigment epithelium-derived factor alleviates tamoxifen-induced endometrial hyperplasia. *Mol Cancer Ther.* 14(12):2840-9 2015

Bar-Joseph, H., Ben-Ami, I., Ron-El, R., **Shalgi, R.*** and Chuderland, D*. Pigment epithelium-derived factor (PEDF) regulation by hCG in granulosa cells. *Reproduction* 151 (2) 179-185, 2016.

Levi, M., Popovtzer, A., Tzabari, M., Mizrachi, A., Savion, N., Stemmer, S.M., **Shalgi, R.** and Ben-Aharon, I. Cetuximab intensifies cisplatin-induced testicular toxicity. *Reprod Biomed Online.* Apr 20. pii: S1472-6483(16)30067-0; 2016

Miller, I., Chuderland, D., Grossman, H., Ron-El R., Ben-Ami, I.* and **Shalgi, R*.** The dual role of pigment PEDF in the pathogenesis of OHSS: negating both angiogenic and inflammatory pathways. *J Clin Endocrinol Metab*. 101:4699-4709. 2016.

Uri-Belapolsky, S., Ninio-Many, L., Shaish, A., Levi, M., Harats, D., Kamari, Y*. and **Shalgi, R*.** Interleukin

1-alpha deficiency increases the expression of follicle-stimulating hormone receptors in granulosa cells. *Mol. Reprod. Dev*. 84: 460–467. 2017.

Grossman, H., Har-Paz, E., Gindi N., Irit, M., Levi, M., Nevo, N., Galiani, D., Dekel, N. and **Shalgi R.** Regulation of GVBD in mouse oocytes by miR-125a-3p and Fyn kinase through modulation of actin filaments. *Sci Rep.* 7:2238. 2017.

Reviews

Levi, M., Kraicer-Kaplan, R. and **Shalgi, R.** Regulation of division in mammalian oocytes: Implications for polar body formation. *Mol. Hum. Reprod*. 324-338, 2011.

Levi, M., Ninio-Mani, L. and **Shalgi R.** Src protein Kinases in oocytes and embryos. Chapter 4 submitted to the book: "Mouse Development: From Oocyte to Stem Cells", Results and Problems in Cell Differentiation (RPCD) Series, Springer Publishing. 55:93-106. 2012.

Ben-Aharon, I. and **Shalgi, R.** What lies beyond chemotherapy induced ovarian toxicity. *Reproduction*, 144:153-163, 2012.

Chuderland, D., Ben-Ami, I., Bar-Joseph, H. and **Shalgi, R**. Pigment epithelium-derived factor (PEDF) in the reproductive system. *Reproduction*. 148:R53-R61. 2014

Ninio-Many, L., **Shalgi, R.** and Ben-Aharon, I. miR-125a – Does the difference lie in the isoform? *Cell Cycle*.14:785-6. 2015.

Grossman, H. and **Shalgi, R.** A Role of microRNAs in cell differentiation during gonad development. Results Probl Cell Differ.;58:309-36;2016

Grants

2014-2018	Israel Science Foundation (ISF) – Post transcription regulation of Fyn kinase by miR-125a-3p in the ovary – potential relevance to ovarian function
2016-2017	Israel Cancer Association – miR-125a-induced cellular switch elicits a response to anti-HER2 targeted therapy in cancer cells
2016-2017	The Colton Foundation. PEDF for the treatment for uterine fibroids.

Prof. Ronen Zaidel Bar, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: zaidelbar@gmail.com
URL: http://celladhesionlab.com/

Cellular Mechanics and Tissue Morphogenesis

Positions

Associate Professor, Sackler Faculty of Medicine

Visiting Professor, Mechanobiology Institute, Singapore

Research

Our main interest is in understanding how mechanical forces are generated by cells and how cells use these forces to change shape and move, as happens during cell division, cell migration and tissue morphogenesis. We focus on distinct cellular structures that mediate cell adhesion and contractility: cell-matrix and cell-cell junctions and the actomyosin cytoskeleton. Together, these structures are responsible for the dynamic control of cell and tissue shape during development and homeostasis and their mis-regulation is associated with various diseases.

We take a multi-scale approach in our investigations, from single proteins to an entire organism, and employ a variety of tools, including genetic engineering, proteomics, biochemistry and bioinformatics, but primarily relying on live imaging with fluorescence microscopy.

Our findings, both in mammalian cells and in the nematode *C. elegans*, are defining the protein network regulating cell adhesion and contractility in vivo and elucidating molecular mechanisms of mechanosensing and mechanotransduction.

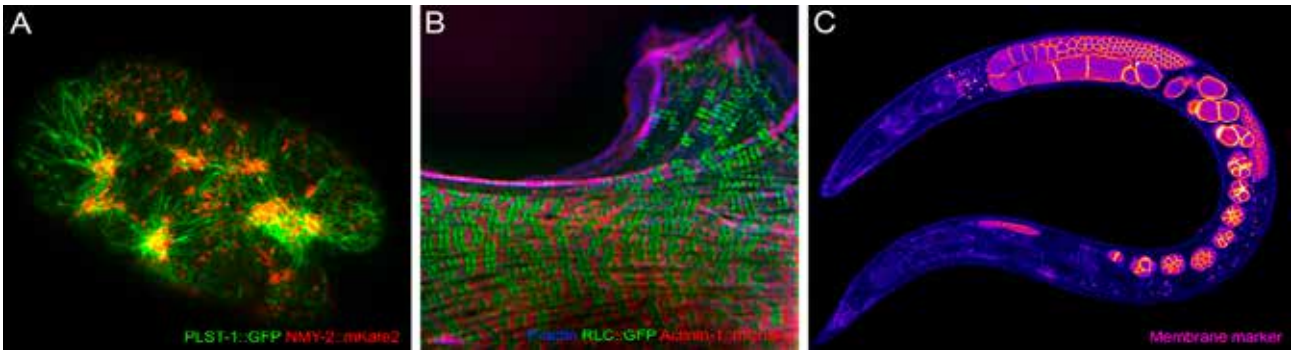
Publications

Ding W-Y, Ong H-T, Hara Y, Wongsantichon J, Toyama Y, Robinson R, Nédélec F, **Zaidel-Bar R.** Plastin increases cortical connectivity to facilitate robust polarization and timely cytokinesis. Journal of Cell Biology 216(5): 1371-1386. 2017.

Hu S, Dasbiswas K, Guo Z, Tee Y-H, Thiagarajan V, Hersen P, Chew L, Safran S, **Zaidel-Bar R*** and Bershadsky AD*. Long range self-organization of cytoskeletal myosin-II filament stacks. Nature Cell Biology 19(2):133-141. 2017. *corresponding author

Bertocchi C, Wang Y, Ravasio A, Wu Y, Sailov T, Baird MA, Davidson MW, **Zaidel-Bar R**, Ladoux B, Mege RM, and Kanchanawong P. Nanoscale architecture of cadherin-based adhesions. Nature Cell Biology 19(1):28-37. 2017.

Padmanabhan A, Ong H-T and **Zaidel-Bar R**. Non-junctional E-Cadherin Clusters Regulate the Actomyosin Cortex in the C. elegans Zygote. Current Biology 27:1-10. 2017.



Actomyosin-generated forces shape cells and tissues: (A) A contractile actomyosin network at the cortex of a *C. elegans* early embryo. It is essential for cell polarization and division. **(B)** Actin and myosin self-organize into arrays of parallel stress fibers in a REF52 fibroblast. They are required for cell spreading and adhesion. **(C)** The germline of *C. elegans*, highlighted by a membrane marker, is like an assembly line for embryos. Actomyosin contractility is essential for maintaining germline architecture and for moving oocytes and embryos along.

Vaman Rao M and **Zaidel-Bar R**. Formin-mediated actin polymerization at cell-cell junctions stabilizes E-cadherin and maintains monolayer integrity during wound repair. Molecular Biology of the Cell 27(18):2844-56. 2016.

Biswas KH, Hartman KL, **Zaidel-Bar R*** and Groves JT*. Sustained α-catenin conformational activation at E-cadherin junctions in the absence of mechanical force. Biophysical Journal 111(5):1044-52. 2016. *corresponding author

Budirahardja Y, Tan PY, Doan T, Weisdepp P, **Zaidel-Bar R**. The AP-2 transcription factor APTF-2 is required for neuroblast and epidermal morphogenesis in Caenorhabditis elegans embryogenesis. PLoS Genetics 12(5):e1006048. 2016.

Biswas KH, Hartman KL, Yu C-H, Harrison OJ, Song H, Smith AW, Huang WYC, Lin W-C, Guo Z, Padmanabhan A, Troyanovsky SM, Dustin ML, Shapiro L, Honig B, **Zaidel-Bar R** and Groves JT E-cadherin junction formation involves an active kinetic nucleation process. PNAS 112(35):10932-7. 2015.

Erami Z, Anannya O, Schwarz JP, Timpson P, Yao W, **Zaidel-Bar R**, and Anderson KI. There are four dynamically and functionally distinct populations of E-cadherin in cell junctions. Biology Open 4(11):1481-9. 2015.

Hu S, Tee YH, Kabla A, **Zaidel-Bar R**, Bershadsky A, Hersen P. Structured illumination microscopy reveals focal adhesions are composed of linear subunits. Cytoskeleton 72(5):235-45. 2015.

Budirahardja Y, Doan T, and **Zaidel-Bar R**. Glycosyl phosphatidylinositol anchor biosynthesis is essential for maintaining epithelial integrity during Caenorhabditis elegans embryogenesis. PLoS Genetics 11(3):e1005082. 2015.

Wu Y, Kanchanawong P, and **Zaidel-Bar R**. Actin-delimited adhesion-independent clustering of E-cadherin forms the nanoscale building blocks of adherens junctions. Developmental Cell 32(2):139-54. 2015.

Tan P-Y and **Zaidel-Bar R**. Transient membrane localization of SPV-1 drives cyclical actomyosin contractions in the C. elegans spermatheca. Current Biology 25(2):141-51. 2015.

Guo Z, Neilson LJ, Hang Z, Murray P, Zanivan S, and **Zaidel-Bar R**. E-cadherin adhesome complexity and robustness resolved by quantitative proteomics. Science Signaling 7(354), rs7. 2014.

Murray P, and **Zaidel-Bar R**. Premetazoan origins and evolution of the cadherin adhesome. Biology Open 3:1183-1195. 2014.

Vaman Rao M. Chu P-H, Hahn KM, and **Zaidel-Bar R**. A novel tool for the activation of endogenous diaphanous-related formins by light reveals thickening of stress fibers without an apparent increase in tension. Cytoskeleton (Hoboken) 70(7):394-407. 2013.

Reviews

Sethi K, Cram EJ, **Zaidel-Bar R**. Stretch-induced actomyosin contraction in epithelial tubes: Mechanotransduction pathways for tubular homeostasis. Semin Cell Dev Biol. 2017 pii: S1084-9521(17)30176-3. 2017.

Biswas KH, **Zaidel-Bar R**. Early events in the assembly of E-cadherin adhesions. Experimental Cell Research. pii: S0014-4827(17)30090-3. 2017.

Padmanabhan A, Vaman Rao M, Yao W, and **Zaidel-Bar R**. Jack of all trades: functional modularity in adherens junctions. Current Opinion in Cell Biology 36:32-40. 2015.

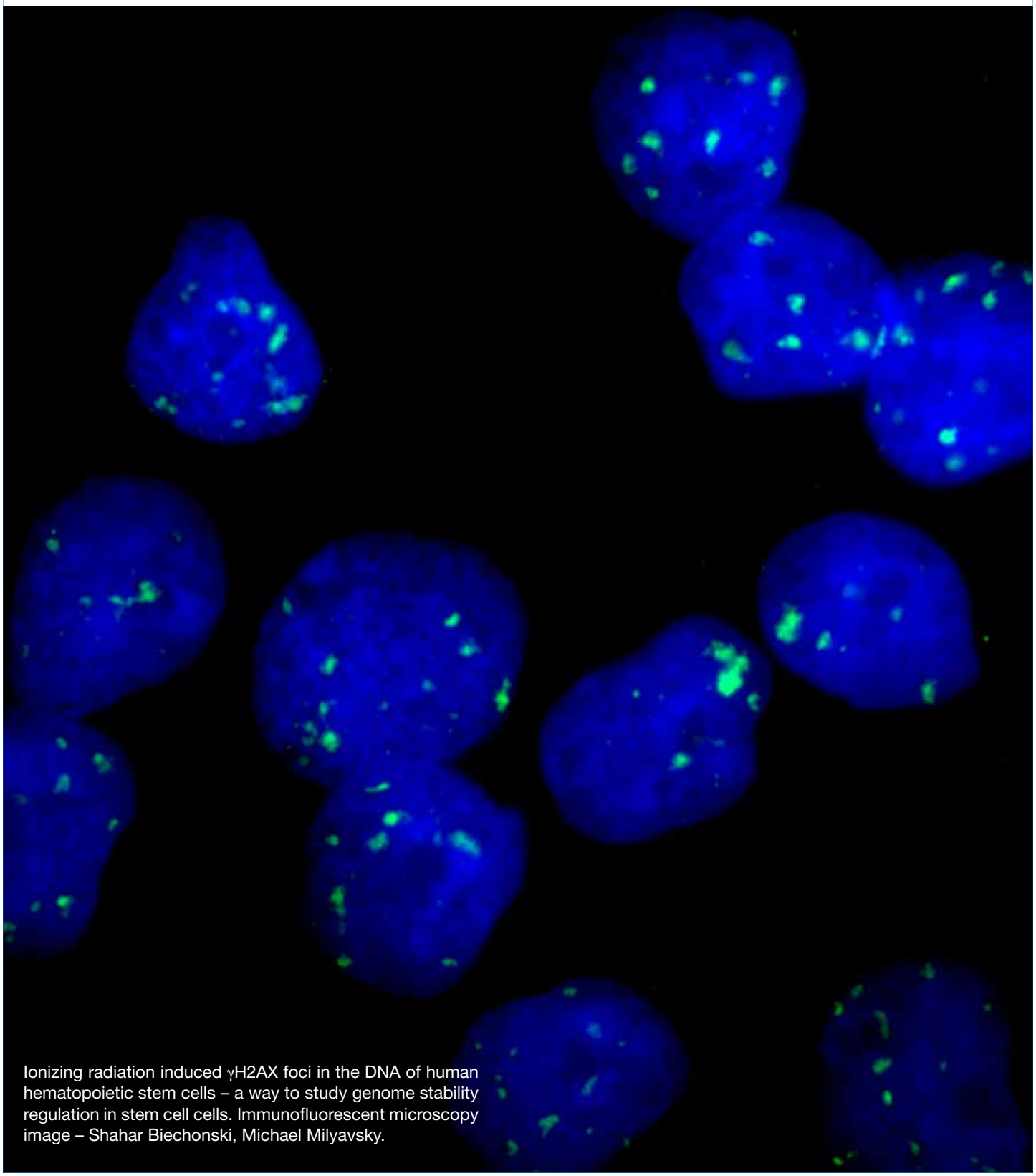
Zaidel-Bar R, Gou Z, and Luxenburg C. The contractome - a systems view of actomyosin contractility in non-muscle cells. Journal of Cell Science 128(12):2209-17. 2015.

Zaidel-Bar R. Cadherin adhesome components and interactions at a glance. Journal of Cell Science 126:373-378. 2013.

Grants

2014 –2018	National Research Foundation Singapore: Controlling cell-cell signaling using synthetic biometric interfaces
2015 –2017	Mechanobiolgy Institute Singapore: Unraveling the coupling between cell-cell and cell-matrix adhesions.
2016 –2018	Ministry of Education Tier2: Regulation of actomyosin cortex force generation by non-junctional E-cadherin.
2017 –2020	Israel Science Foundation Research grant: Mechanotransduction in contractile tubes: using the *C. elegans* spermatheca as a model to study the regulation of RHO-1- and Ca2+-dependent actomyosin contractility in response to stretching.
2017 –2020	Israel Science Foundation Equipment Grant

Stem Cells and Regenerative Medicine



Ionizing radiation induced γH2AX foci in the DNA of human hematopoietic stem cells – a way to study genome stability regulation in stem cell cells. Immunofluorescent microscopy image – Shahar Biechonski, Michael Milyavsky.

Prof. Dafna Benayahu, Ph.D.

Department of Cell and Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

Email: dafnab@post.tau.ac.il

Musculoskeletal – Stem cells and Nanotechnology

Position

Professor, Sackler Faculty of Medicine

Research

Our interest is to follow the differentiation of skeletal stem cells and their lineage fate. The balance between skeletal stem cells and the adipose lineage is studied at the cellular and molecular biology levels. In sillico characterization using bioinformatics of genes profiling and identification of biomarkers networks to identify markers for stem cells. Recent projects we gave shown that biomechanics play a role in the stem cells activation and function under normal physiology and along aging. The ultimate goal of the research is to study how to improve the stem cells functionality. Such knowledge will provide novel approaches to combat skeletal changes due to aging or metabolic disease. The use of stem cell is also developed towards tissue regeneration along with development of novel collagen-based-scaffold.

Research methods used include bioinformatics, gene cloning, qRT-PCR, cell biology analysis including immunofluorescence, scanning electron microscopy and biochemistry. Nanotechnology combines the cell fate differentiation with multidisciplinary approaches for the development of new platforms for cell analysis.

Publications

Marcus Y, Shefer G, Sasson K, Kohen F, Limor R, Pappo O, Nevo N, Biton I, Bach M, Berkutzki T, Fridkin M, **Benayahu D**, Shechter Y, Stern N. 2013. Angiotensin 1-7 as a novel means to prevent the metabolic syndrome: lessons from the fructose-fed rat model. Diabetic 62(4):1121-1130.

Shefer G, Rauner G, Stuelsatz P, **Benayahu D**, Yablonka-Reuveni Z. 2013 Moderate-intensity treadmill running promotes expansion of the satellite cell pool in young and old mice. FEBS J. 280(17): 4063-4073.

Shoham N, Sasson A, Lin FH, **Benayahu D,** HAj-Ali R, Gefen A. 2013. Mechanics of hyaluronic acid/adipic acid dihydrazide hydrogel: towards developing a vessel for delivery of preadipocytes to native tissues Journal of the Mechanical Behavior of Biomedical Materials. J Mech Behav Biomed Mater. 22; 28C:320-331.

Shoham N, Girshovitz P, Katzengold R, Shaked NT, **Benayahu D**, Gefen A. 2014. Adipocyte Stiffness Increases with Accumulation of Lipid Droplets. Biophysical J 106: 1-11.

Ben-Or Frank M, Shoham N, **Benayahu D**, Gefen A. 2014 Effects of accumulation of Lipid Droplets on load transfer between and within Adipocytes. Biomechanics and Modeling in Mechanobiology (Accepted).

Sharabi M, Mandelberg Y, **Benayahu D**, Benayahu Y, Azem A, Haj-Ali R. A new class of bio-composite materials of unique collagen fibers. 2014. Journal of the Mechanical Behavior of Biomedical Materials 36:71-81.

Shkolyar A, Gefen A, **Benayahu D**, Greenspan H. Automatic detection of cell divisions (mitosis) in live-imaging microscopy images using Convolutional Neural Networks. Conf Proc IEEE Eng Med Biol Soc. 2015;2015:743-6.

Salomon-Kent R, Marom R, John S, Dundr M, Schiltz LR, Gutierrez J, Workman J, **Benayahu D**, Hager GL. New face for chromatin-related mesenchymal modulator: n-chd9 localizes to nucleoli and interacts with ribosomal genes. J Cell Physiol. 2015;230(9):2270-80.

Shoham N, Mor-Yossef Moldovan L, **Benayahu D**, Gefen A.Multiscale modeling of tissue-engineered fat: is there a deformation-driven positive feedback loop in adipogenesis? Tissue Eng Part A. 2015;21(7-8):1354-63.

Katzengold R, Shoham N, **Benayahu D**, Gefen A. Simulating single cell experiments in mechanical

testing of adipocytes. Biomech Model Mechanobiol. 2015;14(3):537-47.

Katzengold R, **Benayahu D**, Gefen A. 2015 Simulating single cell experiments in mechanical testing of adipocytes. Biomechanics and Modeling in Mechanobiology 14: 537-547.

Yildirima C, **Benayahu D**, Adamovskia M, Wollenberger U. 2015. An electrochemical assay for differentiation of the osteoblastic cell line (MBA-15) on the sensor chip. Electroanalysis 27:1350-1358.

Sharabi M, **Benayahu D,** Benayahu Y, Issacs J, Haj-Ali R, 2015. Laminated Collagen-based biocomposites for tailor designed soft tissue mimetics. Composites Science and Technology 117:268-275.

Shoham N, Levy A, Shabshin N, **Benayahu D**, Gefen A. A multiscale modeling framework for studying the mechanobiology of sarcopenic obesity. 2016;16:275-295.

Mandelberg Y, **Benayahu D**, Benayahu Y. Octocoral Sarcophyton auritum Verseveldt & Benayahu, 1978: Microanatomy and Presence of Collagen Fibers. Biol Bull. 2016;230(1):68-77.

Yang X, Li Y, Liu X, Huang Q, He W, Zhang R, Feng Q, **Benayahu D.** The stimulatory effect of silica nanoparticles on osteogenic differentiation of human mesenchymal stem cells. Biomed Mater. 2016;12:015001.

Shemesh S, Sidon E, Kaisler E, Sheinis D, Velkes S, Ohana N, **Benayahu D.** Diabetes mellitus is associated with increased elastin fiber loss in ligamentum flavum of patients with lumbar spinal canal stenosis: results of a pilot histological study. Eur Spine J. 2017;doi: 10.1007/s00586-017-5315-0.

Yang X, Liu X, Li Y, Huang Q, He W, Zhang R, Feng Q, **Benayahu D.** The negative effect of silica nanoparticles on adipogenic differentiation of human mesenchymal stem cells. Mater Sci Eng C Mater Biol Appl. 2017;81:341-348.

Grants

2015-2017 Ministry of Science Cooperation , Israel-china

2016-2019 Ministry of Science Cooperation, Jointly with Prof. R. Haj-Ali

2016-2020 Israel Science Foundation, Jointly with Prof. A. Gefen

Dr. Chen Luxenburg, Ph.D.

Department of Cell & Developmental Biology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: lux@post.tau.ac.il
www.luxenburglab.com

Cytoskeletal Regulation of Epidermal Stem Cells

Position

Senior Lecturer, Sackler Faculty of Medicine

Research

Our laboratory studies how cytoskeleton-derived signals control stem cell's ability to give rise to a functional tissue during development, to maintain it throughout life and repair it upon wounding.

The actomyosin cytoskeleton is a complex cellular structure that plays a role in many biological processes. Classic studies established its role in cell structural organization. However, new studies demonstrate that the cytoskeleton plays a major role in regulatory processes that control signal transduction, gene expression and stem cell lineage specification.

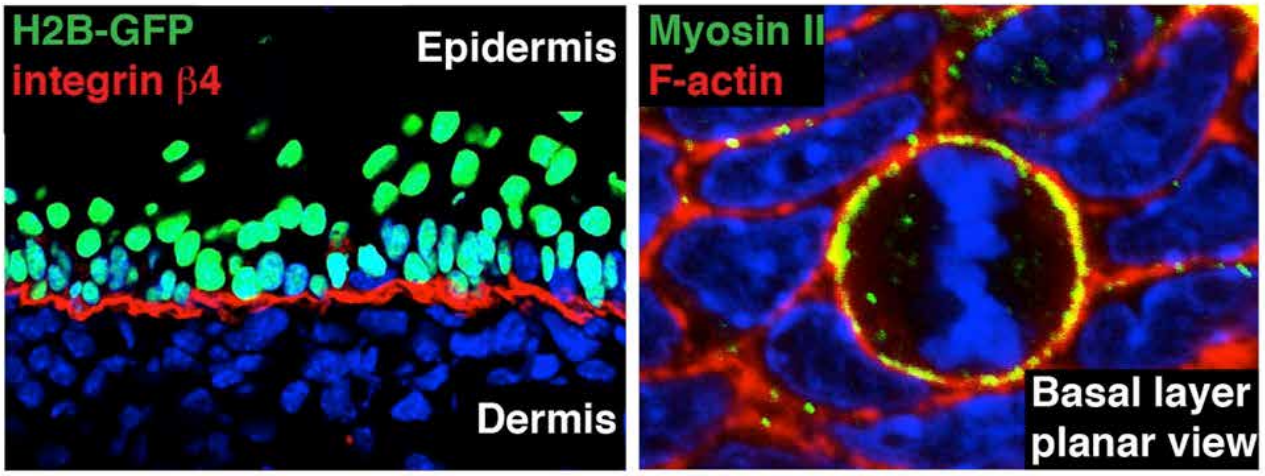
Our laboratory uses the skin epidermis as its main model system. Projects in the lab explore both skin development and skin common diseases such as cancer and psoriasis. In addition to classic genetic tools and in vivo models we also use state of the art technology to manipulate stem cells in utero. Genome wide analysis of gene expression, quantitative digital microscopy and a variety of molecular and cellular methods are all commonly used in our lab.

Publications

Luxenburg C, Heller E, Pasolli HA, Chai S, Nikolova M, Stokes N, Fuchs E. Wdr1-mediated cell shape dynamics and cortical tension are essential for epidermal planar cell polarity. *Nat Cell Biol*. 2015;17:592-604.

Zaidel-Bar R, Zhenhuan G, **Luxenburg C**. The contractome--a systems view of actomyosin contractility in non-muscle cells. *J Cell Sci.* 2015;128:2209-17.

Peled A, Sarig O, Samuelov L, Bertolini M, Ziv L, Weissglas-Volkov D, Eskin-Schwartz M, Adase



Left hand side**:** We use state of the art *in utero* injections of lentivirus (H2B-GFP+ cells in the epidermis) to manipulate gene expression in epidermal stem cells/progenitors early in embryonic development, before cell fate specification.
Right hand side**:** Whole mount image of embryonic epidermis showing an early mitotic cell and its interphase neighbors in planar view. Note the dramatic differences in cell shape. We demonstrated that mitotic rounding is important for cells ability to orient their spindle and undergo asymmetric cell division.

CA, Malchin N, Bochner R, Fainberg G, Goldberg I, Sugawara K, Baniel A, Tsuruta D, **Luxenburg C,** Adir N, Duverger O, Morasso M, Shalev S, Gallo RL, Shomron N, Paus R, Sprecher E. (2016) Mutations in TSPEAR, encoding a regulator of Notch signaling, affect tooth and hair follicle morphogenesis. *PLoS Genet* 13;12:e1006369.

Dor-On E, Raviv S, Cohen Y, Adir O, Padmanabhan K, **Luxenburg C**. (2017) T-plastin is essential for basement membrane assembly and epidermal morphogenesis. *Sci Signal*. 2017;10(481).

Reviews

Luxenburg C, Geiger B. (2017) Multiscale view of cytoskeletal mechanoregulation of cell and tissue polarity. *Handb Exp Pharmacol.* 235:263-284

Grants

2014–2018	Israeli Center for Research Excellence (I-CORE): Gene Regulation in Complex Human Disease
2015-2020	Israel Science Foundation (ISF) Grant

Dr. Michael Milyavsky, Ph.D.

Department of Pathology
Sackler Faculty of Medicine

TEL AVIV UNIVERSITY

E-mail: mmilyavsky@post.tau.ac.il

DNA Damage Response in Normal and Leukemia Hematopoietic Stem Cells

Position

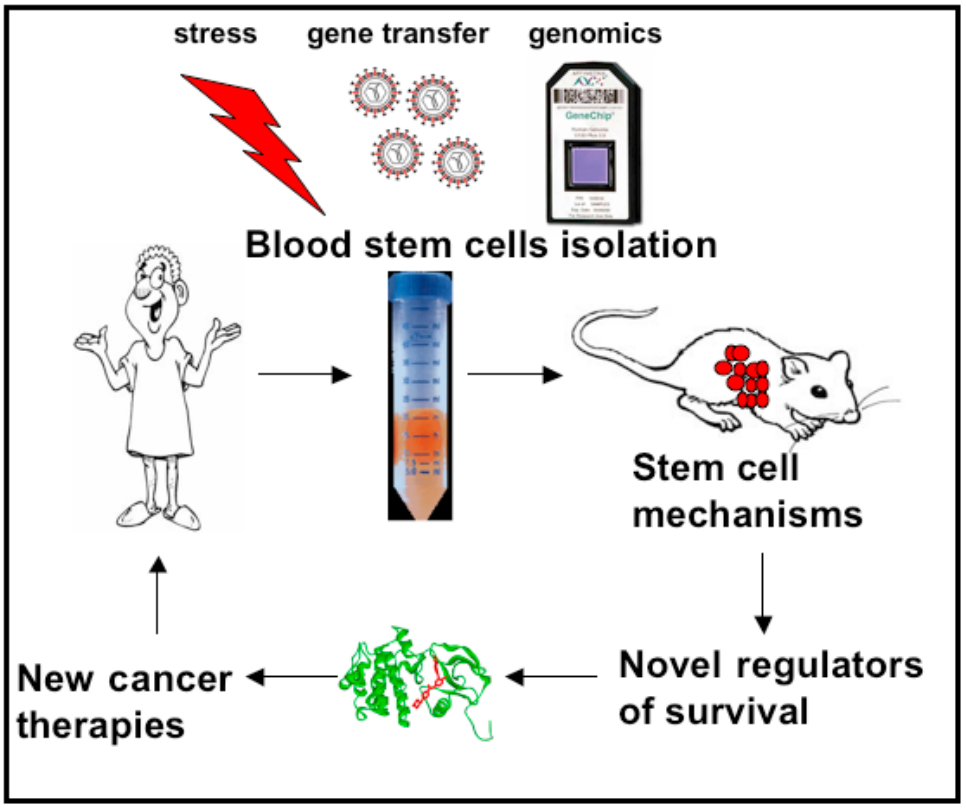
Senior Lecturer, Sackler Faculty of Medicine

Research

Accumulation of unrepaired DNA damage in hematopoietic stem cells (HSC) is associated with bone marrow failure and accelerated leukemogenesis. Our laboratory aims to understand how HSC cope with DNA damage to preserve normal blood regeneration and to limit the risk of leukemogenesis. In addition, we strive to discover how leukemia stem cells escape therapy and try to devise strategies to prevent this from happening. To address these questions we study DNA damage signaling and its outcomes in highly purified human normal and leukemia cell subsets. We employ flow cytometry, immunofluorescent and biochemical analyses, lentiviral gene transfer-mediated functional screens, expression/microRNA profiling, clonal *in vitro* assays and, most importantly, *in vivo* repopulation mouse assays of human normal HSC and leukemia-initiating cells.

Publications

Louria-Hayon I., Ruston J.C.F., , Gish G, Jin J, Kofler M. M., Lambert J-P., Adissu H. A., **Milyavsky M**, Herrington R., Minden M. D., Dick J. E., Gingras A-C., Iscove N. N., and T. Pawson. 2013. The Lnk adaptor suppresses radiation resistance and radiation-induced B-cell malignancies by inhibiting IL-11 signaling. *Proc Natl Acad Sci USA* 110: 20599-604.



Milyavsky M, Gole B, Wiesmüller L. Replication stress in MLL-rearrangements.*Oncoscience*. 2015;2:938-9.

Biechonski, S., Gourevich, D., Rall, M., Aqaqe, N., Yassin, M., Zipin-Roitman, A., Trakhtenbrot, L., Olender, L., Raz, Y., Wiesmuller, L., Jaffa, A. J., Grisaru, D., Elad, D., and **Milyavsky, M**. 2017. Quercetin alters DNA damage response in human hematopoietic cells via TopoII- and PI3K- dependent mechanisms that contribute to MLL rearrangements. *Int J Cancer*, 15; 140(4):864-876.

Zipin-Roitman, A., Aqaqe, N., Yassin, M., Biechonski, S., Amar, M., van Delft, M.F., Gan, O.I., McDermott, S.P., Buzina, A., Ketela, T., Shlush, L., Xie, S., Voisin, V., Moffat, J., Minden, M., Dick, J.E., **Milyavsky, M**. 2017. SMYD2 Lysine methyltransferase regulates leukemia cell growth and regeneration after genotoxic stress. *Oncotarget,* 8:16712-16727

Review

Biechonski, S., and M. Milyavsky. 2013. Differences between human and rodent dna-damage response in hematopoietic stem cells: at the crossroads of self-renewal, aging and leukemogenesis. *Transl Cancer Res* 2:372-383.

Grants

2014-2017 Israel Cancer Research Fund (ICRF)

2016-2018 German Israeli Foundation for Scientific Research and Development (GIF)

2014-2019 Israel Science Foundation (ISF) Grant: Elucidation of DNA damage response mechanisms in human normal and malignant hematopoietic stem cells.