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.

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Graphic design: Michal Semo Kovetz, TAU Graphic Design Studio
November 2015
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 limited 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 62 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, Prof. Moshe Kotler; and Assistant to the Dean, Ms. Yael Keilin.
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The complement membrane attack complex modifies the cellular distribution of a mitochondrial chaperone – Niv Mazkereth, Zvi Fishelson
PARP Proteins in Health and Disease

Position
Associate Professor, Sackler Faculty of Medicine

Research
The general focus of our research is on signal transduction mechanisms implicating PARP (polyADP-ribose polymerase) proteins. PARPs are highly conserved proteins that are involved in a variety of processes, including epigenetic mechanisms, DNA repair, cell cycle and gene expression. PARP-1, the most abundant PARP protein, is activated by binding to single strand DNA breaks. Activated PARP-1 recruits ligases to the lesion, promoting DNA repair.

One of our contributions to this field was the discovery of alternative mechanisms activating PARP-1 in the absence of DNA breaks. This unveiled a variety of extra-nuclear signals activating PARP proteins in a variety of processes regulating gene expression.

We found that PARP-1 is a target of signal transduction mechanisms activated by intracellular Ca2+ mobilization or by the MEK-ERK phosphorylation cascade. Moreover, we found that ERK activity in the nucleus is highly up-regulated by activated PARP-1, implicating PARP-1 in ERK-dependent gene expression. Up-regulation of immediate early genes underlying long-term memory formation may underlie the pivotal role of PARP-1 in long-term memory formation during learning. Regulation of gene expression, controlling cell growth and development, may underlie the role of PARP-1 in neuronal remodeling and cardiomyocytes growth.

Recently, we found that a phenanthrene derived PARP inhibitor acts as an extra-centrosomes de-clustering agent, exclusively and efficiently eradicating human cancer cells by ‘mitotic catastrophe’ cell death, without impairing normal cells. Since many human cancer cells depend on extra-centrosomes clustering for their survival, this molecule is now used for developing a novel cancer targeting therapy.

Publications

Eradication of cancer cell treated with PJ-34 by mitotic catastrophe cell death. De-clustered extra-centrosomes and mitotic catastrophe cell death in MDA-MB-231 cells treated with PJJ-34 (20 mM) for 18 hours. Taken from Castiel et al., JoVE 2013.


**Review**


**Patents**

‘Cancer Therapy’. US 8,729,080 B2

‘Treatment of Addiction’. US 13,761,761 B1
Cancer Related Inflammation in Tumor Progression and Metastasis

Position
Senior Lecturer, Sackler Faculty of Medicine

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


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.


Reviews


Grants

2011 – 2015 European Union FP7, Marie Curie International Reintegration Grant

2012 – 2015 MOST-DKFZ (German Israeli Cooperation

2012–2016 Israel Science Foundation (ISF) Grant

2014 – 2016 Israel Cancer Association (ICA)

2014 – 2016 The Eva and Henry Frænkel Mindefond-Denmark

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
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

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).


Reviews


Grants
2011 – 2015 Functional and molecular analysis of cancer cell resistance mechanisms to complement-dependent cytotoxicity, Israel Science Foundation (ISF)
Proteomics of Breast Cancer Progression

Position
Senior Lecturer, Sackler Faculty of Medicine

Research
Our main interest is to understand the mechanisms of breast cancer progression. We are using state-of-the-art mass spectrometry-based proteomics to obtain a system-wide view of the tumor proteins. Analysis of the changes in protein levels and modifications that occur during tumor development is aimed to discover novel regulators of transformation. Combination of the proteomics technology with biochemical and genetic methods will show the significance of these candidates to cancer development and may suggest novel drug targets and tumor markers.

Publications


Pozniak, Y. and Geiger, T. Design and application of super-SILAC for proteome quantification. Meth Molec Biol. Accepted.


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).


Geiger, T., Wehner, A., Schaab, C., Cox, J. and Mann, M. Comparative proteomic analysis of eleven common cell lines reveals ubiquitous but varying expression of most proteins. Mol Cell Proteomics. 11:M111.014050 (2012)


References


Grants


2012-2016 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.
Basic and Translational and Research of Childhood Malignancies and Leukemia

Positions
Professor, Sackler Faculty of Medicine
Chair, MD-PhD program

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 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 consisting of 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


Development of Cancer Treatments Integrating Radiotherapy or Electrochemical Ablation and Immunotherapy

Prof. Yona Keisari, Ph.D.
Department of Clinical Microbiology and Immunology
Sackler Faculty of Medicine

Positions
Professor, 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 based 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


**Chapters**


**Books**

**Keisari Y.**. Tumor Ablation: effects on systemic and local anti-tumor immunity and on other tumor-microenvironment interactions. Springer, 2013.
Interaction of Nanomaterials and Electromagnetic Fields with Cells

**Positions**

Professor, 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**


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

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


Chapter


Grants

The Mechanobiology of Tissue Development
Homeostasis and Disease

Position
Senior Lecturer, Sackler Faculty of Medicine

Research
Many biological processes such as cell migration and division require mechanical forces. However, similar to chemical cues, mechanical forces also play a key regulatory role that affect many additional key biological processes. Therefore, it is not surprising that changes in the mechanical properties of tissues contribute to the development of common diseases.

Our lab uses the mouse skin epidermis as a model system to study how mechanical and geometrical cues regulate morphogenesis, affect gene expression and contribute to cell fate determination during development, homeostasis and disease. The skin is an ideal model system for these studies for the following reasons: 1) the skin is a mechanosensitive organ, capable of sensing and responding to mechanical signals. 2) Defects in the mechanical and geometrical properties of epidermal cells are among the hallmarks of common skin diseases including cancer and psoriasis 3) The epidermis can easily and rapidly be manipulated genetically in vivo, making it a tractable model system to discover novel genes and study their function.

Publications


Grants
2014–2015 Israel Cancer Research Fund (ICRF) Project Grant (co-PI Limor Broday)
2014–2018 Israeli Center for Research Excellence (I-CORE): Gene Regulation in Complex Human Disease

Left hand side: On top of classic mouse genetic tools 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.
The Wnt Signaling Pathway and Colorectal Cancer

Position
Senior Lecturer, 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.

Publications


Grants
2011 – 2015 The US-Israel Binational Scientific Foundation (BSF)
Computational Analysis of Metabolic Alterations in Cancer and Aging

Positions
Professor, Sackler Faculty of Medicine
Co-chair, TAU Bioinformatics Training Program
Joint appointment, Blavatnik School of Computer Science
Current location: University of Maryland, College Park, MD, USA

Research
Our research focuses on computational biology with an emphasis on metabolic modeling. Our lab is currently working on the development and study of large-scale models of metabolism in a variety of human tissues, in both healthy and disease states. Our efforts are focused on two main subjects: (1) We have generated the first model of cancer metabolism. This development has paved the way for the first large-scale computational search for new and selective metabolic drug targets in cancer (Nature/MSB 2011) – some which are already under various stages of further experimental testing and validation (Nature 2011). (2) We have recently developed a new approach for inferring drug target for extending life span in humans (anti-aging), which are currently under experimental investigation. Taken together, these studies and others ongoing in the lab offer new ways for harnessing computers to advance our understanding of metabolically-related human disorders, and further our ability to diagnose and treat them in a rationale-designed manner.

Publications

Metabolic drug targets (x-axis) that are predicted to selectively kill cancer cells of different types (y-axis).


Translation efficiency is determined by both codon bias and folding energy. (T. Tuller, Y. Waldman, M. Kupiec, **E. Ruppin**), *Proc Nati Acad Sci USA*, 17: 3645–3650 (2010)


**Review**


**Grants**

2011-2015 US-Israeli Binational Science Foundation (BSF) for studying human host-pathogen metabolic interactions in the gut
Angiogenic Switch Using Rationally-Designed Theranostic Nanomedicines

Positions
Associate 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
Editorial board member, Advanced Drug Delivery Reviews
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, NMR, HPLC, in situ hybridization, bioinformatics, polymer chemistry, molecular imaging, angiogenesis assays, animal models of cancer (human xenografts in mice, syngeneic and transgenic mice models), pharmacokinetics and pharmacodynamics.

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.
Publications


Reviews


Chapters


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”.

Sackler Faculty of Medicine Research 2015

Cancer and Molecular Therapies 32
The ATM-Mediated DNA Damage Response

Positions

Professor, 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 alluded “protein kinase”.

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


Reviews


Book Chapter

Grants
2011-2015
Israel Science Foundation: The ATM and WRN Proteins at the Crossroads of Genomic Stability, Cancer and Aging

2011-2015
German-Israel Foundation for Scientific Research and Development: UBE4B: A New Player in the Interface between the Ubiquitin Arena and the DNA Damage response
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.
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 orthotopically 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 its 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


Review


Grants

2010 – 2015 Sackler Foundation, Establishment of the Tel Aviv University Sackler Cellular and Molecular Imaging Center (SCMIC)
Significant 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.
Normal and Diseased Potassium Channels in Human Brain and Heart

**Position**
Professor, Sackler Faculty of Medicine

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

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.
Publications

Manuscripts


Reviews


Grants


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

**Position**
Professor of Physiology, Sackler Faculty of Medicine

**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**


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**
GIRK1

**B**
excitation 514 nm

**C**
normalized FL intensity %

**D**
Ratio

**E**
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, G\(_{\alpha}\) and G\(_{bg}\) synergistically alter the conformation of GIRK1 subunit.


**Grants**

2013-2016 Mechanisms of isoform-specific regulation of L-type Ca²⁺ channels by protein kinases. German-Israel Foundation (GIF), With S. Weiss and E. Klussmann.
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


Research

Shnayderman I, Katz-Leurer M. An aerobic walking programme versus muscle strengthening programme


Mechanisms, Regulation and Pharmacology of Calcium Transporting NCX Proteins

Positions
Associate Professor, Sackler Faculty of Medicine

Research
Calcium (Ca²⁺) is a major regulator in the living cell. In many cell-types the Na⁺/Ca²⁺ exchanger proteins (NCX) represent a major Ca²⁺ extruding system and thus, play a key role in regulating the Ca²⁺-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 Ca²⁺ reabsorption, mitochondrial bioenergetics, etc. Altered expression and regulation of NCX proteins is a chief contributor to Ca²⁺-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-threatening arrhythmias and contractile malfunction. Selective pharmacological targeting of NCX variants is expected to recover Ca²⁺ 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 Ca²⁺ sensor located on CBD1. These findings may allow the identification of drug candidates targeting the disease-related NCX variants.

Publications


Reviews


Grants

2013-2017 Fields Center of Molecular Cardiology

2010-2015 USA-Israel Binational Science Foundation

2014-2018 Israeli Science Foundation
Epidemiology of Cardiovascular Diseases

Position
Senior Lecturer, Sackler Faculty of Medicine
Chair, Post Basic B.A. Program for Registered Nurses

Research
Our research focuses on the epidemiology of cardiovascular diseases with especial 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, 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 environmental 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, I carry out nationwide studies in collaboration with specialists in neurology and stroke research. Theses 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


Itzhaki M, Koton S. Primary prevention of stroke: knowledge and attitudes among healthy adult population. JINA 2011;6:26-7. (Hebrew)


Reviews
Koton S. Risk factors for ischemic stroke and intracerebral hemorrhage: Updated review based on the INTERSTROKE study. JINA 2010;4:24-5. (Hebrew)


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**

**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**


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.


**Grants**

2012-2015 MRI imaging of infarct macrophage subset, Binational Science Foundation (BSF)

2012-2015 Israeli National Nanotechnology Initiative and Helmsley Charitable Trust for a focal technology area (FTA) on Nanomedicines for Personalized Theranostics

2014-2019 Israel Science Foundations, Role of macrophages in myocardial regeneration
### Dental Health and Medicine

![Image of various smiles]

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Sackler Faculty of Medicine Research 2015  
51  
Dental Health and Medicine
Biochemical Aspects of Dental Restorations and Orthodontic Tooth Movement

Positions
Associate 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


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


**Grants**

2013-2016 The use of peptide nanostructures for the reinforcement of dental materials, Kamin Fund
Behavioral Sciences in Dentistry

Positions
Professor, Sackler Faculty of Medicine
Head, School of Dental 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


Chapters


A Novel Primitive Stem Cell Population in Adult and Elderly Oral Mucosa – Basic Research and Clinical Translation

Position
Professor of Oral Biology, School of Dental Medicine

Research
Our research focuses on the biology of a new stem cell population recently discovered in our laboratory. We found, that in contrast to other tissues, the oral mucosa of the adult and elderly organism harbors a primitive neural crest-like stem cell population, which is capable of expressing embryonic associated markers and of differentiating into cell lineages of the 3 germ layers – ectoderm, mesoderm and endoderm. We term this population “oral mucosa derived stem cells – OMSC”. Using cutting edge technologies, we are investigating the genetic and epigenetic mechanisms that maintain such a fetal-like stem cell population in the adult and aging oral mucosa, and study how these mechanisms and OMSC are affected by chronic and neurodegenerative diseases as diabetes and Parkinson’s Disease. By elucidating these mechanisms, we aim to develop new therapeutic approaches for treating chronic diseases associated with ageing.

Based on OMSC plasticity and stemness we are currently testing their therapeutic potential for the treatment of diabetic chronic wounds, Parkinson’s disease, skeletal defects, inflammatory bowel disorders, retinal disorders and periodontal diseases.

We have developed unique fibrin-based matrices for OMSC delivery and tissue engineering purposes.

Publications
Friedmann A, Gissel K, Soudan M, Kleber BM, Pitaru S, Dietrich T. Randomized controlled

Human OMSC co-expressing neural crest markers – p75 (red) and pluripotency associated markers – Oct4 (green) are located in specific niches within the lamina the lamina propria of the adult human oral mucosa.


**Grants**

2012 – 2016 Oral mucosa stem cells for the generation of a primordial periodontium - The effect of aging and diabetes type 2. US-Israel Binational Science Foundation
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


J. Abbas, K. Hamoud, H. May, N. Peled, R. Sarig, D. Stein, D. Alperovitch-Najenson, I. Hershkovitz. Socioeconomic and physical characteristics of

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).


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 (accepted for publication) 2014.
Bone Regeneration in the Jaws

Positions
Professor
Chair, Department of Periodontology and Oral Implantology
Gerald Niznick Chair of Implantology

Research
Current research is focused on modification of techniques of bone regeneration, investigating the biological qualities of various bone substitute used to augment atrophic sites in the jaws and stabilizing collagen membrane used in guided bone regeneration procedures.

- Implant stability – histologic study.
- Use of synthetic materials in periodontal defects.
- Evaluation of novel implants – histologic study
- Grafting extraction sockets
- Stabilization of resorbable collagen membranes

Publications


Stabilizing collagen membrane used in guided bone regeneration procedures.

a. Histological view (x40) of a native collagen membranes 21 days after implantation with phosphate buffered saline (0 mg/mL TTC); versus b. similar membrane after treatment with 50 mg/mL TTC. Collagen stained in red/brown with Avi-din-Biotin-HRP reaction.


Chapters

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.)
Cell Replacement Therapy for Diabetes

**Position**

Professor, Sackler Faculty of Medicine
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**


**Reviews**


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.


### Grants

- **2012-2017** Stem cells for biological assays of novel drugs and predictive toxicology, Innovative Medicines Initiative (IMI)
- **2013-2017** Generation of human insulin-producing cells by redifferentiation of cells expanded from pancreatic islet beta cells through inhibition of the NOTCH pathway, Israel Science Foundation (ISF)
Pathobiology of Secretory Granule Packaging and Growth

Positions
Professor, Sackler Faculty of Medicine
Chair, Department of Pathology
Academic Advisory Committee, ISEF Foundation
Academic Advisory Committee, Gazit-Globe Foundation

Research topics
Unit Granule formation: The classical model of secretory granule formation holds that proteins are transported from the RER to the Golgi zone where they can undergo post-transitional modification. They are then packaged for secretion by concentration within membrane-bound condensing vacuoles. The transportation of secretory proteins occurs in a vectorial way. The newly synthesized proteins in the RER are moved, probably via a vesicular transport, to the proximal side of the Golgi cisternae, the cis Golgi side. While moving through the Golgi cisternae the proteins undergo many modifications; most of the steps of which have not yet been resolved. The processed proteins are packed into vesicles that bud off the Golgi cisternae. The elucidation of this sequence of protein synthesis, packaging and secretion constitutes a major contribution to cell biology. It is well documented that granules in various cellular systems increase in size as time passes. For example, after degranulation is induced in either mast cells or mouse pancreatic acinar cells, granules start to accumulate. If the cell is not re-sensitized, the granule size distribution becomes broader and the mean granule size is increased. We have demonstrated that the unit granule volume is conserved; indicating that the granule size increase is probably due to homotypic fusion. The mechanism of polymerization is theoretically and experimentally investigated by us. It is found that two major mechanisms may lead to polymerization. The first one is defined as unit addition mechanism, while the second one is defined as a random addition process. We have demonstrated that the pancreatic acinar cell and mast cell granule size distribution is better fitted to the unit addition model rather than the random addition model. The Chediak-Higashi syndrome is an example of a random mechanism of granule growth.
Publications


Reviews


Chapters


Invited editorials


Grants

2014-2017 Binational Science Foundation (Co-PI, Ronit Sagi-Eisenberg)
Dr. Koret Hirschberg, Ph.D.
Department of Pathology
Sackler Faculty of Medicine

Intracellular Membrane Trafficking

Position
Senior Lecturer, 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 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


Benjamin S, Weidberg H, Rapaport D, Pekar O, Nudelman M, Segal D, Hirschberg K, Katzav S, Ehrlich M, Horowitz M. EHD2 mediates trafficking...


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

**Grants**

2012-2015 German Israel Foundation (GIF)
2012-2016 Israel Science Foundation (ISF) Grant, Surface expression of proteins is regulated by sorting and selection in endoplasmic reticulum exit sites and in the Golgi apparatus
Pancreas Development and Function: 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 another pancreatic cell population, the mesenchymal cells. Our results indicate the pivotal role of mesenchymal cells in the regulation of insulin secretion, and blood glucose levels. Using transgenic mouse models, we study how mesenchymal cells and insulin-producing cells communicate with one another, 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 mesenchymal and other pancreatic cell types in both healthy and diseased mouse models.

Publications


**Grants**

2012–2016 Marie Curie Career Integration grant (CIG)

Cellular composition of the pancreas: elucidating the role of mesenchymal signaling pathways

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
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.

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, immunohistochemistry, 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


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

Positions
Professor, Sackler Faculty of Medicine
Chair, M.Sc. Studies, 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 we made a novel, original discovery, together with Prof. Mittelman from the Sourasky Medical Center, 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. The studies are based on a variety of in-vitro and murine experimental models, and include also an avenue of elucidating the relevance and possible clinical application of the results.

Publications
Katz O., M. Stuible, N. Golishevski, L. Lifshitz, M. L. Tremblay, M. Gassmann, M. Mittelman and D. Neumann. Erythropoietin treatment leads to reduced...


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

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 (991 citations); the development of the first cell-free system of ROS production; the discovery of the cytosolic oxidase components (673 citations); the discovery of the role of the small GTPase Rac in oxidase activation (832 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 p67phox. 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 p67phox. This finding is based on a novel methodology, designed by us, in which we measure the binding of recombinant p67phox 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 p67phox. “Mutating” either C369 or C371 to R resulted in stabilization of binding of “activated” p67phox to Nox2 by the establishment of disulfide bonds between cysteines 369 and 371 in Nox2 and yet unidentified cysteines in p67phox.
in loss of p67\textsubscript{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\textsubscript{phox} to the catalytic component of the NADPH oxidase complex is redox regulated and involves the establishment of disulfide bonds between p67\textsubscript{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\textsubscript{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 \textit{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**


Mizrahi, A., Berdichevsky, Y., Casey, P. J., and Pick, E. A prenylated p47\textsubscript{phox}-p67\textsubscript{phox}-Rac1 chimera is a quintessential NADPH oxidase activator. Membrane association and functional capacity. \textit{J. Biol. Chem.} 285, 25485–25499, 2010


Pick, E., and Dahan, I. Strategies for identifying synthetic peptides to act as inhibitors of NADPH oxidases, or “All that you did and did not want to know about Nox inhibitory peptides”. \textit{Cell. Mol. Life Sci.}, 69:2283–305, 2011


Dahan, I., and Pick, E. Strategies for identifying synthetic peptides to act as inhibitors of NADPH oxidases, or “All that you did and did not want to know about Nox inhibitory peptides”. \textit{Cell. Mol. Life Sci.} 69, 2283–2305, 2012


Chapter/Review


**Grants**

2013-2017 Assembly of the phagocyte NADPH oxidase complex, Israel Science Foundation
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
Chair, Department of Human Molecular Genetics and 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


Reviews


Grants

2014-2015 “Identification of a metabolic gene associated with protection of Laron syndrome patients from malignant transformation”. Carl and Leonora Fingerhut Fund for Cancer Research, Sackler School of Medicine, Tel Aviv University

2014-2016 “Intracellular αvβ3 integrin and nuclear IGF1R as chronic lymphocytic leukemia markers”. Varda and Boaz Dotan Research Center in Hemato-Oncology, Tel Aviv University.


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

Alternative Splicing Generates Transcriptomic Diversity in Genetic Disorders & Cancer

Positions
Professor, Sackler Faculty of Medicine

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


Gelfman S, Cohen N, Yearim A, Ast G. DNA-methylation effect on cotranscriptional splicing is

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.


Reviews


Grants

2012-2015 ISF – Morasha for Neurodegenerative Diseases, Tissue-specific alternative splicing disease


2013-2018 Israel Science Foundation, Identification of novel determinants of splicing regulation

2014-2015 Israel Cancer Research Fund (ICRF) Project Grant
Genomic Analysis of Hereditary Hearing Loss

Positions
Professor, Sackler Faculty of Medicine
Vice Dean for Preclinical Affairs, Sackler Faculty of Medicine
Scientific Board Member, I-CORE for Gene Regulation in Complex Human Disease
President, Federation of the Israel Societies for Experimental Biology (ILANIT)
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 encompassed the prevalence of connexin 26 mutations in these populations, the most common form of deafness, 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. Most recently, 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.

Publications
Manuscripts


**Grants**

2011 – 2015 Gene Expression and microRNA Regulation in Hair and Supporting Cells of Mouse, Israel Science Foundation

2011 – 2016 Gene Discovery for Hearing Loss in Middle East by Massively Parallel Sequencing, National Institutes of Health, Co-PI: Moien Kanaan


Genomic-scale Bioinformatics 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 bioinformatics 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


Reviews


Genomic Biomarkers for CNS Drug Response

Positions

Director, National Laboratory for the Genetics of Israeli Populations

Adjunct Professor, University of Florida, Gainesville, FL, USA

Senior Editor, Pharmacogenomics

Editorial Board: Trends in Molecular Medicine, Genome Medicine, CNS Drugs, Biopreservation and Biobanking, Drug Development Research, Pharmaceutical Biology

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 Antidepressant 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. Pharmacogenetics education: 10 years of experience at Tel Aviv University. Pharmacogenomics. 11:647-649 (2010).

Gurwitz D, Pirmohamed M. Pharmacogenomics: the importance of accurate phenotypes. Pharmacogenomics. 11:469-470 (2010).


Pharmacogenomics
SSRI antidepressants response biomarkers. Cell lines identifies several microRNAs as tentative wide expression profiling of human lymphoblastoid

decision making: economic evaluations of


**Grants**


**2014 – 2018** Deciphering beta-amyloid and tau neurotoxicity: Genome-wide expression profiling for sensitivity biomarkers, Israel Science Foundation. Jointly with Illana Gozes

microRNA and DICER in Differentiation and Malignant Transformation of Melanocytes

Position
Senior Lecturer, 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

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.


Reviews


Grants

2012-2015 Fritz Thyssen Stiftung
2012-2016 Israeli Center for Research Excellence (I-CORE): Gene Regulation in Complex Human Disease
Genetic and Metabolic Research of Age-Dependent Chronic Degenerative Disease

**Positions**
Professor, Sackler Faculty of Medicine  
Chair, Department of Anatomy and Anthropology  
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 in 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.

**Publications**

Sergey Ermakov, Mohammad R. Toliat, Zvi Cohen, Ida Malkin, Peter Nürnberg, **Gregory Livshits**. Association study of polymorphisms in the *ALPL* and *ENPP1* loci, related to bone mineralization and diverse skeletal traits. *Bone* 2010; 46: 1244-50.


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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 Livshits et al 2011, Ann Rheumat Dis.
Yulia Vistoropsky, Sergey Ermakov, Mohammed Toliat, Svetlana Trofimov, Janine Altmüller, Ida Malkin, Peter Nürnberg, Gregory Livshits. Genetic determinants of circulating levels of Tumor Necrosis Factor Receptor II and their association with TNFRII gene variants. *Cytokine* 2010; 51: 28-34.


Anna Leonov, Svetlana Trofimov, Sergey Ermakov, **Gregory Livshits.** Quantitative genetic study of amphiregulin and fractalkine circulating levels – potential markers of arthropathies. *Osteoarthritis & Cartilage*, 2011; 19:737-742

**Gregory Livshits.** Maria Popham, Ida Malkin, Philip N Sambrook, Alex J MacGregor, Timothy Spector, Frances MK Williams. Degenerative disc disease and genetic predisposition are the main risk factors for low back pain in women: The UK Twin Spine Study (TUTSS). *Ann Rheumat Dis* 2011; 70:1740-1745


Sergey Ermakov, Trofimov S, Malkin I, **Livshits G.** A significant association exists between receptor tyrosine kinase-like orphan receptor 2 gene variants and the OPG/RANKL ratio in human plasma. *Osteoporos Int*, 2011; 23:1899-1907


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.


Ida Malkin, Frances MK Williams, Genevieve LaChance, Timothy Spector, Alex J MacGregor,


### Reviews


### 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

Genomics and Gene Regulation by Small RNAs

Positions
Senior Lecturer, Sackler Faculty of Medicine
Academic Director, BioAbroad
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


Rokah OH, Granot G, Ovcharenko A, Modai S, Pasmanik-Chor M, Toren A, Shomron N, Shlipberg O. Downregulation of miR-31, miR-155, and miR-


**Grants**

2011-2015 I-CORE Program of the Planning and Budgeting Committee, The Israel

Genomics & Personalized Medicine
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<td>2013-2016</td>
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<td>Chemical, Biological, Radiological and Nuclear (CBRN) Defence</td>
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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 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 emotion and music.

Publications


Voice, Speaking Rate, Stuttering and Fluency Disorders

Positions
Senior Lecturer, 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 characteristics, 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 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, perceptual 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


Correct gender identification rates for boys and girls in the six age groups for (A) sentences and (B) vowels.


Chapters


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 implications:
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


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 –binaural 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.

**Publications**


‘Bottom-Up’ and ‘Top-Down’ Processes in Human Auditory Perception and Recognition

Position
Associate Professor, Sackler Faculty of Medicine
Committee Member, Israel Auditory Society of Research
Chairperson, Committee of Head of Communication Disorders Depts in Israel (CHE)

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, multitalker, 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 learning in infants and in older children. We utilize 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


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.


**Chapters in Books**


Hearing Science and Clinical Audiology

Position
Associate Professor, Sackler Faculty of Medicine and School of Education

Research
- Speech perception and production by the hearing impaired
- The implications of hearing loss on communication, cognitive and socio-emotional functioning 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
Most, T. & Kozlovski, L. (2010). Academic and social functioning of adolescents with hearing loss who are included individually in regular classrooms. DASH-Dibur, Safa & Shmia, 29, 103-122 (Hebrew)


**Chapter**

Hearing Science and Clinical Audiology

Position
Professor, Sackler Faculty of Medicine
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


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. 2012. Linguistic processing in Hebrew-speaking children from low and high SES backgrounds. Reading & Writing, 25, 1427-1448.


Chapters and books


Grants


2013-2017 Verb structure and Semantics in Development. Israel Science Foundation.
Infectious Diseases

Three colors pseudorabies virus plaque – Oren Kobiler.
Genetic Bases of Host Response to Infections and Chronic Diseases

Position
Associate Professor, Sackler Faculty of Medicine

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 involve 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 Pneumonia.

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


Review and editorials


Grants

2012-2015 European Sequence and Genotyping Institutes (ESGI), Understanding genetic susceptibility to fungal infection using naïve collaborative cross mice (Collaborators: Ron Shamir and Irit Gat-Viks (TAU), Richard Mott (University of Oxford)

2013-2016 EU-FP7-Infrafrontier, European Mouse Mutant and Archiving (EMMA) (co-PI*, collaborators: 23 Members from European countries)

2014-2015 Bela and Zeigmond Altar and Semha Torkeltov Fund for Cancer Research, APC gene in intestinal cancer development in Collaborative Cross mice

2014-2015 Israel Cancer Research Fund (ICRF) Project Grant
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


Reviews


A. Spread of three alpha herpesvirus (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.
Human Mold Infections

Positions
Associate Professor, Sackler Faculty of Medicine
Chair, Department of Human Microbiology and Immunology
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


Arnusch CJ, Ulm H, Josten M, Shadkchan Y, Osherov N, Sahl HG, Shai Y. Ultrashort peptide bioconjugates are exclusively antifungal agents and synergize with

The pathogenic mold Aspergillus fumigatus


Levdansky E, Kashi O, Sharon H, Shadkchan Y, Osherov N. The Aspergillus fumigatus cspA gene encoding a repeat-rich cell wall protein is important for normal conidial cell wall architecture and interaction with host cells. Eukaryot Cell. 2010, 1403-15


Reviews


Grants
2012–2016 Binational Science Foundation
2014–2016 Israel-Italy Cooperation Grant-
2014–2017 Infect-ERA Net Joint European Grant
Host-Virus Interactions in Bacterial Systems

Position
Associate 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


Goren MG, Yosef I, Edgar R, and Qimron U. The bacterial CRISPR/Cas system as analog of the


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.


**Grants**

2014-2017 Israeli Ministry of Health Grant
2013-2018 ERC Starting Grant
2014-2019 Israel Science Foundation Grant
Viral Host Interactions of Positive Strand 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 Hepatitis C virus (HCV) and Dengue virus.

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 HCV assembly.

**Publications**


**Grants**

2012-2016 Israel Science Foundation (ISF) Grant
A mast cell showing the microtubule network (green), actin (red) and secretory granules (blue) – Ofir Klein, Ronit Sagi-Eisenberg.
Regulatory Mechanisms in Mucosal Inflammation

**Position**
Senior Lecturer, 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**


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 gastrointestinal epithelial in conditions such as inflammatory bowel disease (IBD).


Reviews and Chapters


Stein M, Munitz, A. Targeting interleukin 5 in asthma and hypereosinophilic syndromes. *Recent Pat Inflamm Allergy Drug Discov*. 2010;4;201-209.


Grants

2013-2016 Fritz Thyssen Stiftung, The role of IL-13Rα1 in pulmonary fibrosis

2012-2016 US-Israel Binational Scientific Foundation (BSF), The expression and function of paired immunoglobulin-like receptor B in eosinophils

2011-2015 The Israel Science Foundation (ISF), Expression and function of CLM-1 in eosinophils

2014-2017 Israel Ministry of Health

2014-2015 Israeli Cancer Association

2014-2015 ICRF Research Career Development Award
Cell Death and Immune Response: the Role of Necroptosis and Pyroptosis in Inflammation

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

NLRP3 inflammasome and interleukin-1 activation in the absence of MLKL. Nature Comm, 6, 6282, 2015.


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.


Reviews


Molecular Basis of Allergic Diseases: Genomic and Functional Analyses

Positions
Professor, Sackler Faculty of Medicine
Chair, Scholarship Committee, Graduate School of Medicine

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. Exploring the genetic connections between the size of the mast cell secretory granules and mastocytosis.
2. Mast cells and cancer – the good, the bad and the ugly.
3. Decoding the Rab networks that control mast cell function.

Publications
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

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.


**Review**


**Grants**

2012-2015 The Israel Science Foundation, Dissecting the molecular mechanisms underlying mast cell exocytosis; new insights provided by the small GTPase Rab5
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 excursion 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 psychomoral 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. Jewish bioethics: rabbinic law and theology in their social and historical contexts. Cambridge University Press. In press.

Publications
Barilan YM. From hope in palliative care to hope as a virtue and a life skill. (An original keynote article with a response to commentators) Philosophy, Psychiatry and Psychology. 2012; 19:165-181.
Barilan YM, Brusa M, Halperin P. Triage in disaster medicine: ethical strategies in various scenarios. In:


Barilan YM, Brusa M. Deliberation at the hub of medical education: beyond virtue ethics and code of practice. Medicine, Health Care and Philosophy 2012 (Published online first)


Barilan YM. Informed consent: between waiver and excellence in responsible deliberation. Medicine, Health Care and Philosophy 2010; 13:89-95.

Brusa M, Barilan YM. Cultural circumcision in EU public hospitals: an ethical discussion.

Grants
2012-2015 COST (EU join collaborative grant), Ethics in Disaster Medicine.
Studying Doctor-Patient Relationships, Communication and Medical Professionalism

Positions
Senior Lecturer, Sackler Faculty of Medicine
Adjunct Assistant Research Professor of Medicine, Department of Internal Medicine, Indiana University, Indianapolis, USA

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


Reviews


Grants

2012-2014 The Magi Foundation, A different beginning: Foundation blocks for combining humor and creativity in constructing doctor-patient relationship, PI

2014-2015 Israel Cancer Association, Using narrative writing on breaking bad news encounters to improve the communication skills of medical professionals in cancer care, PI

2014-2015 The Israel National Institute for Health Policy Research, Organizational and inter-organizational dimensions of health information exchanges in Israel, Co-PI

2014-2016 The Magi Foundation, Identifying best practices for communication challenges of medical clowns with patients parents, adolescent patients and medical teams, PI
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.
Investigating the Molecular Basis of Visual System Development

Positions
Associate 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


Review

Grants
2012-2015 Roles for microRNA in RPE differentiation, Morasha, Israel Science Foundation
2012-2015 Roles for Pax6 in neurons of the olfactory bulb, midbrain and retina, German Israeli Foundation (Co-PI with Magdalena Goetz).
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 and endocytosis. Research methods combine cell biology, molecular biology and biochemistry disciplines together with bioinformatics and computational biology.

Publications

Sackler Faculty of Medicine Research 2015  142  Nervous System and Behavioral Disorders


Reviews


Neuronal Plasticity and Nerve Cell Protection in Disease

Positions
Professor of Clinical Biochemistry, Sackler Faculty of Medicine
Lily and Avraham Gildor Chair for the Investigation of Growth Factors
Director, Levie-Edershein-Gitter Institute for Functional Brain Imaging
Director, Dr. Diana and Zelman Elton Laboratory for Molecular Neuroendocrinology
Editor-in-Chief, Journal of Molecular Neuroscience

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 neuroprotective 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).

Publications
Dresner E, Agam G, Gozes I. Activity-dependent neuroprotective protein (ADNP) expression level is correlated with the expression of the sister protein ADNP2: deregulation in schizophrenia. Eur Neuropsychopharmacol 21:355-361.

The NAP-motif of activity-dependent neuroprotective protein (ADNP) regulates dendritic spines through Microtubule End Binding (EB) proteins.


Reviews


Gozes I. The cytoskeleton as a drug target for neuroprotection: the case of the autism-mutated ADNP. Biol Chem. 2015


Grants

2012-2015  Israeli Ministry of Science and Technology – New Models for ALS (with Rivka Ofir)

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)
The Molecular Basis of the Regulation of Immune 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**


**Reviews**


**Grants**

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, Tel Aviv University
Director, Functional Brain Center, Cooperation of Wohl Institute for Advanced Imaging, Tel Aviv Sourasky Medical Center and Levi-Edersheim-Gitter Institute for Human Neuroimaging, TAU
Steering Committee, I-CORE in Advanced Cognitive Science

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.

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).
Publications


Chapters and Reviews
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.

Publications


Reviews


Grants

2014 – 2018 EU Marie Curie Career Integration Grant (CIG)
2013 – 2018 I-CORE Cognitive Neuroscience
Dr. Moshe Parnas, Ph.D.
Department of Physiology and Pharmacology
Sackler Faculty of Medicine
Sagol School of Neuroscience

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


Review

Drosophila as a model system for systems neuroscience. A. Using the genetic tools available for Drosophila 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 manipulation of the activity of neural circuits in behaving animals.
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 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


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.

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.


Reviews and chapters


Grants

2011-2015 ISF (Israel Science Foundation), The Dual Role of Dynein in GDNF Signaling

2011-2015 Marie Curie International Reintegration Grants (IRG), Retrogade Signaling.

2013-2016 Small Molecule Screen for Neuromuscular Junction Maintenance, Rosetrees Trust

2013-2016 E-Rare-2, European Research Projects on Rare Diseases driven by Young Investigators. Project Coordinator. The Molecular Basis of Neurodegeneration and Muscle Atrophy in ALS. (Co-PIs: Roded Sharan, TAU; Edgar Gomes, U of Paris; Marcus Kruger, Max Planck; Del Bene Fillippo, Ins Curie; Alberto Rodendo, 12th Oct Uni Hospital Madrid).

2013-2018 Molecular Communication Mechanism of Motor Neuron Survival and Synapse Maintenance, European Research Council (ERC) Starter Grant
Brain Injuries: Cognitive, Behavioral and Cellular Outcome

Position
Professor, Sackler Faculty of Medicine

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


Molecular Mechanisms of Drugs for Neuropsychiatric Disorders

Positions
Professor, Sackler Faculty of Medicine
Dr. Miriam and Sheldon G. Adelson Chair in Biology of Addictive Diseases
Head, Varda and Shalom Yoram Institute for Human Genome Research

Research
Main projects in the lab include:
1. Presynaptic monoamine transportes and the vesicular monoamine transporter as targets for neuropsychiatric drugs.
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

(A) Six representative coronal slices of T₂-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 T₂ maps, demonstrating the damaged thiamine-deficient areas on day 14.


Grants
2011-2015 Novel herbal treatment for anxiety disorder, Israel Science Foundation
Novel Antioxidant and Stem Cells for Treatment of Degenerative Diseases

Positions
Professor, 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-acetylcystein (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. Locally applied leptin induces regional aortic wall degeneration in apeo deficient


Grants
2013 – 2014 Baharv Fund for Glaucoma Research, Sackler Faculty of Medicine.
Regulation of Hippocampal Plasticity: Single Synapses to Alzheimer’s Disease

Positions
Senior Lecturer, Sackler Faculty of Medicine
Committee Member, IBRO
Scientific Advisory Council Member, American Federation for Aging Research (AFAR)
Organizing Committee Member, Israel Society for Physiology and Pharmacology
Committee Member, Sagol School of Neuroscience, TAU
Committee Member, Center for Nanoscience and Nanotechnology, TAU

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


Grants
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

Grants
2012 – 2015 European Union FP7
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


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-sensitive 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.


Reviews


Grants

2016-2021 ERC Starting Grant
Dr. Tami Bar-Shalita, Ph.D., O.T.
Department of Occupational Therapy
School of Health Professions
Sackler Faculty of Medicine

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 13% of otherwise healthy individuals. Our research is aiming to better understand and expand the therapeutic modalities by identifying biomarkers that would specify this health condition, applying psychophysical and neurophysiological methodologies (see below) to characterize children and adults with SMD, suggesting a unique perspective associating SMD with pain.

Moreover in trying to understand the potential role of SMD in neurodevelopmental trajectory, we study this disorder in other health conditions such as chronic pain, mental health, substance abuse, and neurodevelopmental disorders.

Another area of research is embedded in occupational science: Leisure activities are usually perceived as promoting health and well-being. In recent years we’re witness to such activities that are harmful, specifically substance abuse activities. This research is exploring substance abuse activities in Israeli adolescents applying an occupational perspective.

Publications

Manuscripts


EEG of resting state (5 min) in controls and SMD adults recorded from frontal and central cortical sites demonstrated lower power cortical oscillations at δ (orange), β (yellow) and α (green)
Positions
Associate Professor, Sackler Faculty of Medicine
Chair, Department of Nursing, Stanley Steyer School of Health Professions

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
of different sites of different credibility. Nursing and Health Sciences, 13, 366-370.


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


Investigating Pain Perception and Mechanisms of Chronic Pain

Position
Associate Professor, Sackler Faculty of Medicine

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 events 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


R. Defrin, A. Sheraizin, L. Malichi, O. Shachen. Spatial summation and spatial discrimination of...


Chapter

Models and Rehabilitation of Grasping

Positions
Senior Lecturer, Sackler Faculty of Medicine
Associate Investigator, ARC Centre of Excellence in Cognition and Its Disorders, Australia

Research
We study human movement in typical and clinical populations, with a focus on grasping and finger movements. Our approach is to construct mathematical models that describe movement and force generation by the hand, 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
Friedman, J., & Korman, M. (2012). Kinematic strategies underlying improvement in the acquisition

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).


Hearing Science and Clinical Audiology

Position
Professor, 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


Dr. Michal Itzhaki, R.N., Ph.D.
Department of Nursing
Stanley Steyer School of Health Professions
Sackler Faculty of Medicine

Email: itzhakim@post.tau.ac.il

Knowledge and Perceptions of Patients and Caregivers on Health and Illness Situations

Position
Lecturer, Sackler Faculty of Medicine

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


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


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)


Harpaz I, Mozes V, Mintz L, Zilberman N, Itzhaki M. Self fulfillment as a motive to change. From Hi


**Chapter**

Position
Lecturer, Sackler Faculty of Medicine
Head, Nursing Continuous Education Unit
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


**Grants**

2013-2015 PI, study “Patient’s and health caregivers’ perception on quality, safety culture and patient involvement in medical care in general hospitals in Israel”

Research Board, The Israel National Institute for Health Policy and Health Services Research (NIHP), Israel
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, sense 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-Velikovsky, L.**, Jarus, T., & Kotler, M. Factors predicting employment status following in-patient evaluation among persons with schizophrenia. *Work (in press)*
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**


**Grants**

2014 – National Multiple Sclerosis Society Pilot Grant.
Computational Motor Control and Clinical Applications to Upper-Limb Rehabilitation

Position
Senior Lecturer, Sackler Faculty of Medicine
Chair, Department of Physical Therapy
Associate Editor, Rehabilitation, 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

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.


Krasovsky T., Berman S., Liebermann D.G., Kinematic features of continuous hand reaching movements under simple and complex rhythmical constraints. J. Electromyography & Kinesiology 2010, 20, 636-641


Chapters


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., Siev-Ner I., Peleg S., Dar G., Masharawi Y., Hershkovitz I. Injury pattern in young non-

The suggested pathogenesis (A) and kinematics (B-C) in isthmic spondylolysis (ISP).


Attitudes Toward Organ/Tissues Donation and Transplantation

Position
Lecturer, Sackler Faculty of Medicine

Research
Patients on organ transplant waiting lists continue to far exceed donor rates. Our research seeks to understand the barriers preventing people in Israel from donating organs/tissues for transplantation. The study tries to elucidate attitudes and perceptions regarding different sides of organ/tissues donation and transplantation. The research attempts to expound the understanding of emotional and ethical issues to which the transplant patients, organ donors and their family and health care professionals are exposed.

Publications


Dr. Sigal Portnoy, Ph.D.
Department of Occupational Therapy
School of Health Professions
Sackler Faculty of Medicine

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.

Publications


The work in the laboratory is highly interdisciplinary, combining aspects of biomedical engineering, rehabilitation medicine, physiotherapy, and occupational therapy.

Computational Biomechanics in Motor Rehabilitation

3D kinematics of daily activities acquired using a passive-marker-based motion capture system


Chapter

Gaming as a Means of Rehabilitation of Neurological and Geriatric Populations

Position
Senior Lecturer, Sackler Faculty of Medicine
Head of M.Sc. Program, Department of Occupational Therapy

Research
Our research focuses on achieving a better understanding of the factors hindering and facilitating recovery posts-stroke. We have developed interventions aimed to improve the motor recovery and executive functions deficits that these individuals experience, in order to enhance function in daily living. The effectiveness of these novel interventions is assessed by conducting clinical trials.

Our current research project aims to assess the effectiveness of a ‘Community’ and ‘Home’ based VR therapy (using video games) as opposed to traditional therapy for enhancing daily function and participation of individuals with chronic stroke living in the community. The daily physical activity (daily walking and arm use) of these individuals is quantified by an innovative form of instrumentation technology (accelerometers). We are also investigating the use of Apps that run on Tablets for self-training of the impaired hand during rehabilitation of individuals following acquired brain injury.

Publications


Rand D, Eng JJ. Disparity between functional recovery and daily use of the upper and lower extremities during subacute stroke rehabilitation. Neurorehabil Neural Repair, 2012, 26:76-84.


Book Chapters
Tools, Methodologies & Analysis, S. Cobb and B. Lange (Eds). In press.


Grants
2011-2015 EU, Marie Curie International Reintegration Grant (FP7-PEOPLE-2010-IRG) –
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


**Grants**

2009-2013 National Road Safety Authority Grant
2012-2014 Office of Senior Citizens Grant
2013-2014 National Insurance Institute Grant
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**


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


Chapter
Prof. Daniel I. Cohen, Ph.D.
Department of Epidemiology and Preventive Medicine
School of Public Health
Sackler Faculty of Medicine

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


Leventhal A, Ramlawi A, Belbiesi A, Sheikh S, Haddadin A, Husseini S, Abdeen Z, Cohen D: Enhanced surveillance for detection and management...


**Reviews**


**Cohen D**, Muhsen K. Association between Helicobacter pylori colonization and glycated hemoglobin levels: Is this another reason to eradicate Helicobacter pylori in adulthood? J Inf Dis; 2012;205:1183-5 (editorial)

**Grants**

2011-2015 European Union, Development of vaccines against Shigella and enterotoxigenic *E. coli* enteric diseases. Leader of 2 WPs.

2013-2016 Israel National Institute for Health Policy and Health Services Research “Evaluation of the impact of the introduction of universal immunization with the rotavirus vaccine on the burden of severe childhood diarrhea associated with rotavirus in Israel”
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

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


persons with dementia. *Journal of Nervous and Mental Disease*, 198:586-92


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


**Chapters**


Positions
Associate Professor, Sackler Faculty of Medicine
Adjunct Associate Professor of Epidemiology, College of Medicine, Mayo Clinic, Minnesota

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, and clinical details obtained through medical records and examinations. We are also interested in methodological aspects involved in conducting and interpreting observational studies.

Publications

Osteoporotic fracture-free survival curves by time period adjusted for age, sex, and prior fracture among Olmsted County, Minnesota, residents with incident myocardial infarction in 1979–1989 (A), 1990–1999 (B), and 2000–2006 (C) versus community control subjects.


Dr. Khitam Muhsen, Ph.D.
Department of Epidemiology and Preventive Medicine
School of Public Health
Sackler Faculty of Medicine

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

Helicobacter pylori, Enteric Infections and Their Role in Health and Disease


Muhsen K, Jurban M, Goren S, Cohen D. Incidence, age of acquisition and risk factors of Helicobacter


Human OMSC co-expressing neural crest markers – p75 (red) and pluripotency associated markers – Oct4 (green) are located in specific niches within the lamina the lamina propria of the adult human oral mucosa.


Chapter

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)

Grants

2013-2016 MAOF award, Higher Council for Education- Israel

2013-2016 Israel National Institute for Health Policy and Health Services Research (Co-PI with Prof. D. Cohen)

2014-2015 Bill and Melinda Gates Foundation, Multicenter study with University of MD

2014-2015 Israel Cancer Association

2014-2016 Israel National Health Policy Research Institute
Dr. Chava Peretz, Ph.D.
Department of Epidemiology
School of Public Health
Sackler Faculty of Medicine

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


Dr. Laura (Leah) J. Rosen, Ph. D.
Department of Health Promotion
School of Public Health
Sackler Faculty of Medicine

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

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, Ben Noach M, Rosenberg E. Missing the forest (plot) for the trees? A critique of the systematic review in tobacco control. BMC Medical Research Methodology 2010, 10:34.


Grants

SUMO protease localization in the mitochondrial matrix and nucleus of C. elegans body wall muscles – Assaf Tsur, Amir Sapir and Limor Broday.
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


Grants
2011–2015 The role of SUMO in the assembly of cytoskeletal intermediate filaments, The Israel Science Foundation (ISF).
2014–2015 Israel Cancer Research Fund (ICRF) Project Grant (co-PI Chen Luxenburg)
2014–2016 ICRF Project Grant

(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.
Genetic and Hormonal Regulation of Bone Metabolism

Position
Senior Lecturer, Sackler Faculty of Medicine

Research
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.

Hormones also play critical roles in the regulation of bone mass and structure. We investigate the actions of sex hormones with emphasize on the skeletal dimorphism between males and females, and their interaction with other genes and transcription factors. We also study the effect of erythropoietin, the main hormone that regulate blood cells production in the bone tissue in general and on the bone cells in particular. Lastly, we examine the impact of titanium particles on the secretion of inflammatory cytokines and on bone resorption.

Genetic regulation of bone microarchitecture: µCT images from diaphyseal cortical (A,B) and metaphyseal trabecular bone (C,D). Note the structural differences due solely to genetic diversity between the animals.

Erythropoietin (EPO)-induced bone loss: µCT images from EPO-treated mice versus controls (left) showing dramatic bone loss due to increased osteoclastogenesis (right).
Publications


Chapter


Grants

2012-2017 Israel Science Foundation (ISF) Grant
2013-2015 Rothstein Foundation
2015-2016 American Society for Bone and Mineral Research GAP Award
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 ‘agriculture 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


Wasser DE, Hershkovitz I. The question of ethnic variability and the Darwinian significance of 3D reconstruction of the anulus 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).


Reviews

Prof. Michael M. Kozlov, Ph.D.
Department of Physiology and Pharmacology
Sackler Faculty of Medicine
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 Endoplasmic 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


Reviews


Grants

2011-2015 The Israel Science Foundation (ISF), Membrane Shaping by Proteins
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

Severe HFI Skeletal observation

Geometric-morphometrics analysis of the proximal femur.

Femoral mid-shaft cross-sectional analysis of hunter-gatherer (Natufian), dated to ~15,000 years ago.

Hyperostosis frontalis interna (HFI) identified via CT and direct observation (skeletal).
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


Investigating Normal and Deficient Visual Functions

Position
Associate Professor, Sackler Faculty of Medicine

Research
Our research focuses on function, development and plasticity of perceptual interactions in normal and abnormal visual cortex. In our research, we have revealed a unique pattern of neural interactions, both excitatory and inhibitory, underlying global behavior involved in contour integration and texture segmentation. Specifically, a network of long-range intra-cortical connections supporting integration of collinear elements of the visual input is characterized beyond its spatial properties, especially emphasizing the temporal dynamics. Using of training protocols based on spatial and temporal masking paradigms is another area of interest. Studies on the effects of perceptual learning on visual function are conducted, including cases of abnormal visual development, considered as untreatable, such as amblyopia.

The laboratory combines techniques such as psychophysics, visual evoked potentials (VEP), event-related potentials (ERP) and eye movement recording. Computational modeling of neural networks of long-range interactions provides theoretical framework for our empirical findings.

Ongoing studies:

Clinical: Amblyopia, Major depression, ADHD, Pharmacological effects on vision, Vision in eye diseases

Development: Visual acuity, Contrast sensitivity, Lateral interactions, Visual crowding, Contour integration, Visual grouping

Learning: Learning to see faster, Improvement of normal vision, Improvement of impaired vision, Adaptation vs. learning, Visual rehabilitation, Refraction plasticity, Visual Performance


Publications


Reproduction in Animal Models and in Humans

**Positions**
Professor, Sackler Faculty of Medicine
Gabriel Pinkas Chair for the Prevention and Diagnosis of Congenital Anomalies
Executive Committee, Open University, Member

**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.

- The role of Interleukin-1alpha in reproductive aging and in chemotherapy-induced exhaustion of ovarian follicular pool.

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**


Bar-Joseph, H., Ben-Aharon, I., Rizel, S., Stemmer, S.M., Tzabari, M. and **Shalgi, R**. Doxorubicin-induced

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.


*Recommended by Cell Cycle; 9:8, 1460-1461; April 15, 2010


oocyte activation and may cause infertility. *Proc Natl Acad Sci USA.* 111:E4972-80. 2014.


**Reviews**


**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

2015-2016 Lau Mintz Foundation, Sackler School of Medicine, TAU – The role of miR-125a-3p and Fyn in oocytes' meiosis
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 Blechonski, Michael Milyavsky.
Musculoskeletal – Stem cells and Nanotechnology

**Position**
Professor, Sackler Faculty of Medicine
Chair, Department of Cell and Developmental Biology

**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 silico 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 new platform for cell analysis.

**Publications**


Shefer G, Rauner G., Yablonka-Reuveni, Z, Benayahu D, 2010. Reduced satellite cell numbers and myogenic capacity in aging can be alleviated by endurance exercise. PloS One 5:e13307

Shefer G and Benayahu D. 2010. SVEP1 is a novel marker of activated pre-determined skeletal muscle satellite cells. Stem Cell Rev. 6:42-49


Glaït-Santar C, Benayahu D. 2012. Regulation of SVEP1 gene expression by 17beta-estradiol and TNFalpha in pre-osteoblastic and mammary
adenocarcinoma cells. Journal of Steroid Biochemistry and Molecular Biology 130:36-44.


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)


Grants

2012 -2016 Israel Science Foundation Jointly with A. Gefen
Modeling the Nervous System in Development and Disease Using Pluripotent Stem Cells

Position
Lecturer, Sackler Faculty of Medicine

Research
Our lab makes use of human embryonic stem cells in order to elucidate developmental programs in the human nervous system, with particular interest in neural stem cells (NSCs).

The NSC ontogeny dogma predicts that early developing NSCs are highly potent and can yield all nervous system cell types, but they rapidly lose this potential as development proceeds. Because NSCs behave similarly in culture, they are almost useless for studying differentiation to most neuronal cell types – a major impediment for understanding basic development and application to regenerative medicine.

Our main goal is to learn the biology of early neural stem cells in the lab in order to develop strategies for standardizing their growth in culture without loss of differentiation potential. Such continuously self renewing cells will serve as a gold standard NSCs for studying nervous system development and disease, making cells for therapy and discovering novel drugs.

We use a variety of techniques in mouse and human embryonic stem cells and NSCs cells including transgenics (genetic labeling), viral expression of coding genes and microRNAs, classic stem cell assays, FACS-sorting and stem cell differentiation, and two-photon/confocal live cell imaging.

Publications


**Grants**

2010-2015 ISF, Self-renewal of ES cell-derived neural stem cells
2012-2015 IRG, Modeling neural diseases with neural rosettes
2013-2015 BrightFocus, Roles for RPE-specific microRNAs in retinal diseases
2013-2016 Morasha, Modeling pathogenesis of cerebral disorders
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**


**Review**


**Grants**

- 2013-2015 FP7-PEOPLE-2012- Marie Curie Career Integration Grants (CIG)
- 2014-2015 ICRF Research Career Development Award
- 2014-2019 Israel Science Foundation (ISF) Grant: Elucidation of DNA damage response mechanisms in human normal and malignant hematopoietic stem cells.
- 2014-2016 Varda and Boaz Dotan Center for Hematological Malignancies: Chromatin Structures Governing Therapy Resistance In Myeloid Leukemia