Aufzien Family Center for
Prevention and Treatment
of Parkinson's Disease
Tel Aviv University

APPD

Aufzien Family Center for the Prevention and Treatment of Parkinson's Disease

FOUR-YEAR REPORT
2019-2023

Supported by the Aufzien Family, USA

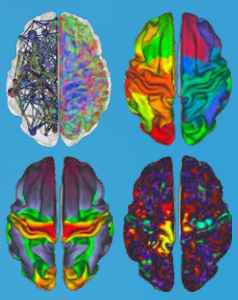

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Table of Contents.....

Letter from the Directors of the Center ....

The Aufzien Family Center for the Prevention and Treatment of Parkinson's Disease was officially inaugurated in May 2019. Together with the late Alan Aufzien, the Aufzien family helped create an unprecedented research center, which has already made a tremendous impact on Parkinson's Disease (PD). The family's generous support, along with our scientists, clinicians, trainees and staff, has accomplished so much in the last four years. We could not have anticipated a more productive period for research in PD than we have had. Over the past years, we have seen exciting growth in the number of laboratories at TAU that are moving toward PD research from 13 in 2018 to 58 today, thanks to the Aufzien Family Center activities and funding.

This progress report highlights our achievements over this period, providing updates on our initiatives, activities, programs and events, and showcases some of our noteworthy accomplishments.

Finally, because there is still so much more work to do to combat this disease, the Aufziens have generously agreed to continue their support. Therefore, the future is bright for breaking new ground in the diagnosis and treatment of PD. The Aufzien Family Center for the Prevention and Treatment of Parkinson's Disease at Tel Aviv University, in collaboration with the Brain Institute at the Tel Aviv Sourasky Medical Center, will continue to make world-level strides in the search to cure and prevent PD, reducing suffering, saving lives and bringing hope to PD patients and their families.

We look forward to working together to achieve our common goals.

Karen and Nir

Prof. Karen Avraham, PhD
Former Co-Director, Aufzien Family Center
Dean, Faculty of Medicine, Tel Aviv University
Dumont Chair for Research in Hearing Disorders

Prof. Nir Giladi, MD
Director, Aufzien Family Center
Professor, Faculty of Medicine
Tel Aviv University Sieratzki Chair in Neurology
Associate Dean, School of Medicine &
Tel Aviv Sourasky Medical Center (TASMC)
Director, Brain Institute, TASMC

Overview of APPD

Mission

The Aufzien Family Center for the Prevention and Treatment of Parkinson's Disease is an academic center at the Faculty of Medicine and Sagol School of Neuroscience at Tel Aviv University, which serves as a hub for innovative translational research in Parkinson's Disease. The Center integrates basic and clinical Parkinson's Disease research at Tel Aviv University and the hospitals affiliated to its Faculty of Medicine and builds interdepartmental collaborations. The Center has a grant program and educational activities to support cutting-edge research towards better treatment and prevention or slowing down of Parkinson's Disease progression. The Center holds monthly seminars, annual international symposiums and active student exchange programs.

Team

Founders and Co-Directors

Prof. Karen B. Avraham
Prof. Nir Giladi

Steering Committee

Prof. Sharon Hassin
Prof. Dani Offen (May 2019-September 2021)
Prof. Uri Ashery (May 2019-September 2021)
Prof Drorit Neumann (From October 2021)
Prof. Illana Gozes (From October 2021)

Global Advisory Board

Prof. Werner Poewe, Medical University Innsbruck
Prof. Susan Bressman, Icahn School of Medicine at Mount Sinai
Prof. Jeffry H. Kordower, Arizona State University

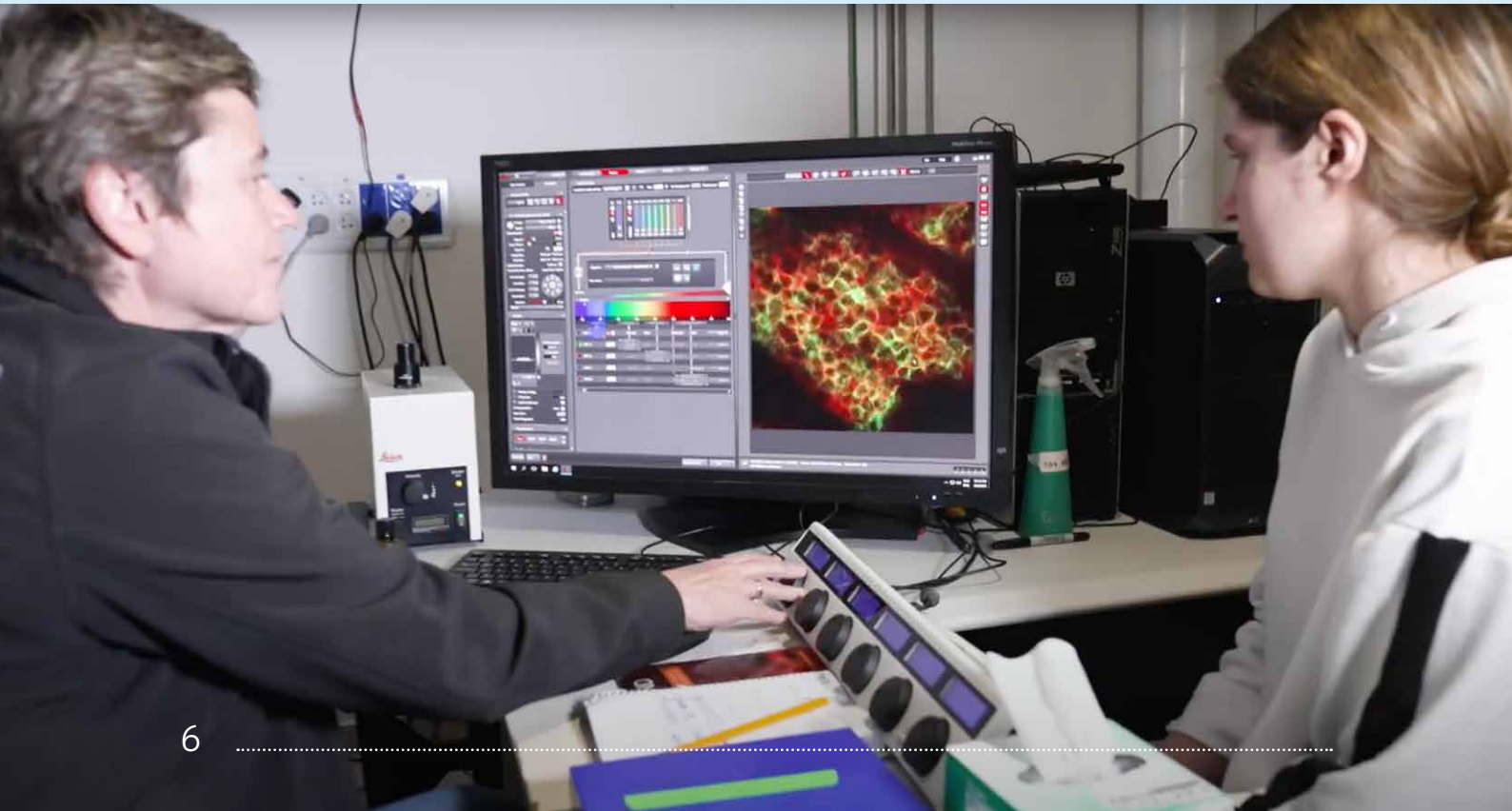
Administrative Staff

Rinat Zaslavsky, Alana Sisam, Dr. Keren Shatzman, Helen Berman

Opening of the APPD-TAU at the Board of Governor's Week, May 17, 2019

Our Research Community .....

The APPD Center established a dynamic and interconnected research community that bridges the gap between expert scientists performing basic research and clinician MDs in the field of Parkinson's disease. By recognizing the inherent value in combining diverse expertise, the Center has actively encouraged collaboration and interdisciplinary communication among scientists from various backgrounds. Through regular seminars, workshops, symposiums, and conferences the Center has provided a platform for researchers to share their findings, exchange ideas, and explore potential collaborations. Moreover, the Center facilitated joint multidisciplinary research projects, to leverage each other's insights and accelerate the translation of scientific discoveries into tangible clinical applications. This collaborative environment has nurtured a strong sense of camaraderie, breaking down traditional silos and driving collective efforts towards a common goal: unraveling the complexities of Parkinson's disease and developing transformative treatments for the benefit of patients. As a result, the APPD Center has become a world leader in Parkinson's disease research, where the synergy between basic and clinical research is not only encouraged but celebrated.



Around the Board of Governor's: Presentation of the Aufzien Family Center for the Prevention and Treatment of PD, May 2023

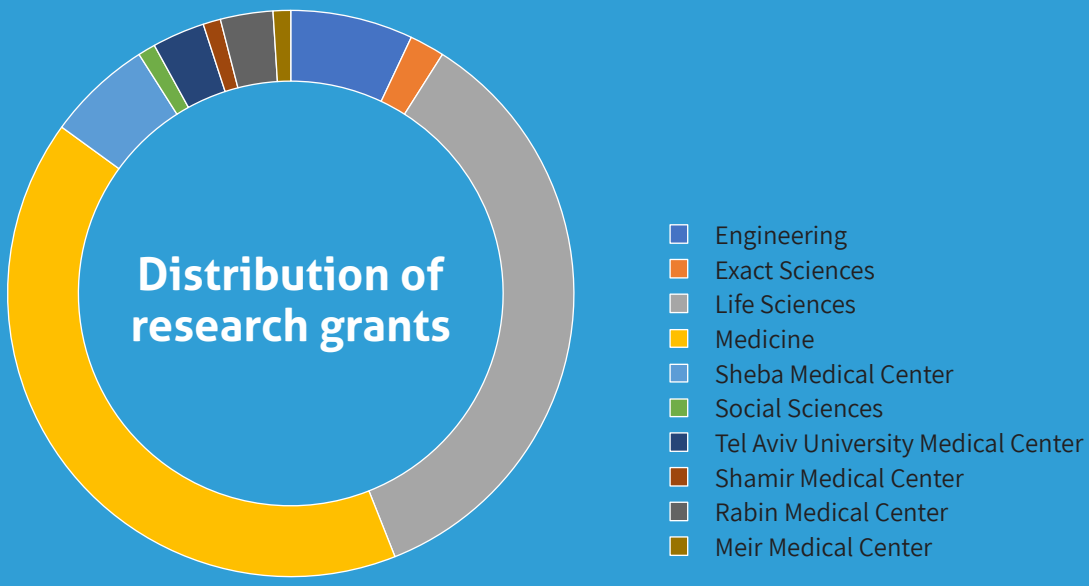
More than 500 faculty members and their graduate students participated in APPD events.

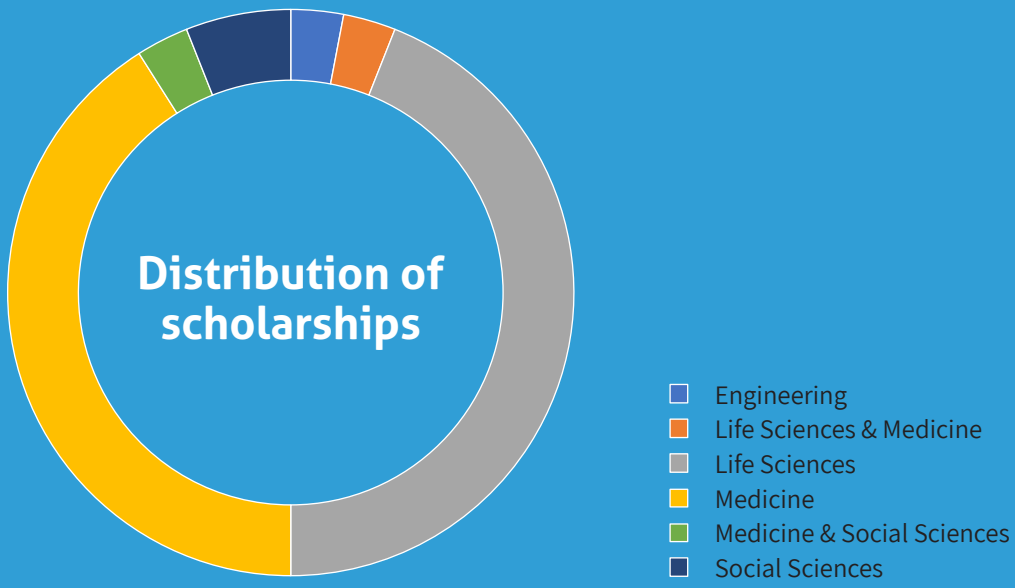
We thank the faculty members and staff who helped in planning and organizing the activities:

- From the Faculty of Medicine: Prof. Daniel Offen, Dr. Avraham Ashkenazi, Prof. Sharon Hassin, Prof. Noam Shomron
- From the Faculty of Life Sciences: Prof. Uri Ashery, Prof. Mia Horowitz
- From Tel Aviv Medical Center: Dr. Yael Manor, Prof. Roy Alcalay

Distribution of Funding

APPD is proud to have funded **33** research projects during its first five years, thereby providing support of more than **2 million** USD to **41** faculty members. The Center promotes innovative research and supports individual as well as collaborative grants. Many of the grants awarded supported new collaborations between faculty members.





Grant programs

APPD 1st Grant Program, 2019

$100,000 Awards

Studying the link between increased levels of insulin degrading enzyme to PD progression: Evaluation of antibodies for early diagnosis and treatment of PD
Researcher: **Prof. Itai Benhar** (Life Sciences)

Inhibition of exosome synthesis as a novel therapeutic target for Parkinson's disease
Researchers: **Prof. Dani Offen** (Medicine), **Prof. Ruth Djaldetti** (Medicine & Rabin Medical Center)

LRRK2-mediated phosphorylation of the Rab GTPase Rab12 as regulator of Rab12 connectivity and axonal transport; Exploring a novel link underlying Parkinson's disease
Researcher: **Prof. Ronit Sagi-Eisenberg** (Medicine)

$25,000 Awards

The mitochondrial unfolded protein response and SUMO in the C. elegans model for Parkinson's disease
Researcher: **Prof. Limor Broday** (Medicine)

Parkinson's imbalance: Its origins and treatment
Researchers: **Prof. Matti Mintz** (Social Sciences), **Dr. Nirit Lev** (Medicine & Meir Medical Center), **Prof. Carlos Gordon** (Medicine & Meir Medical Center)

Is there a connection between AD and PD? Exploring the possibility that ApoE4 affects PD hallmarks
Researcher: **Prof. Ronit Pinkas-Kramarski** (Life Sciences)

Tracking dopaminergic integrity in Parkinson's disease without PET
Researchers: **Dr. Ido Tavor** (Medicine), **Dr. Dan Stein** (Medicine & Sheba Medical Center), **Dr. David Groashar** (Medicine & Rabin Medical Center)

APPD 2nd Grant Program, 2020

$100,000 Awards

Exploring the role of APOE4 expression in the pathology of Parkinson's disease
Researcher: **Prof. Ronit Pinkas-Kramarski** (Life Sciences)

Establishing a human relevant Brain-On-a-Chip platform for elucidating pathways and cellular dysfunction in Parkinson's disease
Researcher: **Dr. Ben Maoz** (Biomedical Engineering)

Accumulation of the quinolinic acid neurometabolite and cross-seeding of α-synuclein as a novel mechanism and potential treatment target in Parkinson's disease
Researcher: **Prof. Ehud Gazit** (Life Sciences)

$25,000 Award

Identification of a novel secretion mechanism of α-synuclein in Parkinson's disease
Researcher: **Dr. Avraham Ashkenazi (**Medicine)

Developing a novel platform for alpha-synuclein aggregates detection using super-resolution microscopy
Researcher: **Prof. Uri Ashery** (Life Sciences)

Targeting the role of insulin resistance on inflammatory process in Parkinson's disease
Researcher: **Prof. Dan Frenkel** (Life Sciences)

APPD 3rd Grant Program, 2021

$100,000 Awards

Revealing mechanisms of the lipid scramblase ANO6/TMEM16F in α-synuclein pathological behavior
Researcher: **Dr. Avraham Ashkenazi (**Medicine)

Studies on the interplay between mutant GBA1 and mutant LRRK2 alleles in development of Parkinson disease using Drosophila models
Researchers: **Dr. Moshe Parnas** (Medicine), **Prof. Mia Horowitz** (Life Sciences)

The molecular mechanism of GDNF transport in Parkinson Disease
Researchers: **Prof. Eran Perlson** (Medicine), **Prof. Sharon Hassin** (Medicine & Sheba Medical Center), **Dr. Amir Dori** (Medicine & Sheba Medical Center)

Beyond RBD: covert REM sleep abnormalities in Parkinson disease
Researcher: **Prof. Yuval Nir** (Medicine)

$25,000 Award

Implementing a novel platform for alpha-synuclein aggregates detection using super-resolution microscopy and artificial intelligence
Researcher: **Prof. Uri Ashery** (Life Sciences)

APPD 4th Grant Program, 2022

$100,000 Awards

Patient-derived high-risk mutations as a tool for deciphering cellular Parkinson's Disease-associated processes
Researchers: **Prof. Uri Ashery** (Life Sciences), **Dr. Ben Maoz (**Biomedical Engineering), **Prof. Roded Sharan** (Exact Sciences)

Bio-engineering functional, implantable human dopaminergic networks to treat Parkinson's Disease
Researcher: **Prof. Tal Dvir** (Life Sciences)

$50,000 Awards

Personalized cannabis therapy based on objective measurements to reduce adverse reactions in Parkinson's Disease patients
Researchers: **Prof. Mordechai Lorberboym (**Medicine & Shamir Medical Center), **Prof. Yankel Gabet** (Medicine)

Mesenchymal stem cells extracellular vesicles loaded with therapeutic proteins for the treatment of Parkinson's Disease
Researcher: **Prof. Dani Offen (**Medicine)

$25,000 Awards

Psychedelics in Parkinson's disease: Treatment and mechanisms
Researcher: **Prof. Hagit Eldar-Finkelman (**Medicine)

Playing with my ears: Audiomotor skill learning across ears and hands in PD patients
Researchers: **Prof. Roy Mukamel** (Social Sciences), **Dr. Neomi Singer** (Tel Aviv Sourasky Medical Center)

The role of the lipid transporter ABCA7 as potential treatment in Parkinson's disease
Researcher: **Prof. Dan Frenkel** (Life Sciences)

APPD 5th Grant Program, 2023

$100,000 Award

REM sleep microstructure as a window for understanding the neurobiology of depression in Parkinson's disease
Researchers: **Dr. Noham Wolpe** (Medicine), **Prof. Riva Tauman** (Tel Aviv Sourasky Medical Center)

$75,000 Award

Unraveling personalized profiles of cognitive-motor interactions using naturalistic, virtual reality-based behaviors in people with Parkinson's Disease
Researchers: **Prof. Jason Friedman** (Medicine), **Prof. Meir Plotnik** (Medicine & Sheba Medical Center), **Dr. Benedetta Heimler** (Sheba Medical Center)

$50,000 Awards

Exploring the role of Rab12, the enigmatic player in Parkinson's disease, and its regulation by the newly identified crosstalk between LRRK2 and protein kinase Cb.
Researcher: **Prof. Ronit Sagi-Eisenberg** (Medicine)

Studies on the modifying effect of mutant LRRK2 on mutant GBA1 that controls severity of Parkinson disease in Drosophila models.
Researchers: **Dr. Moshe Parnas** (Medicine), **Prof. Mia Horowitz** (Life Sciences)

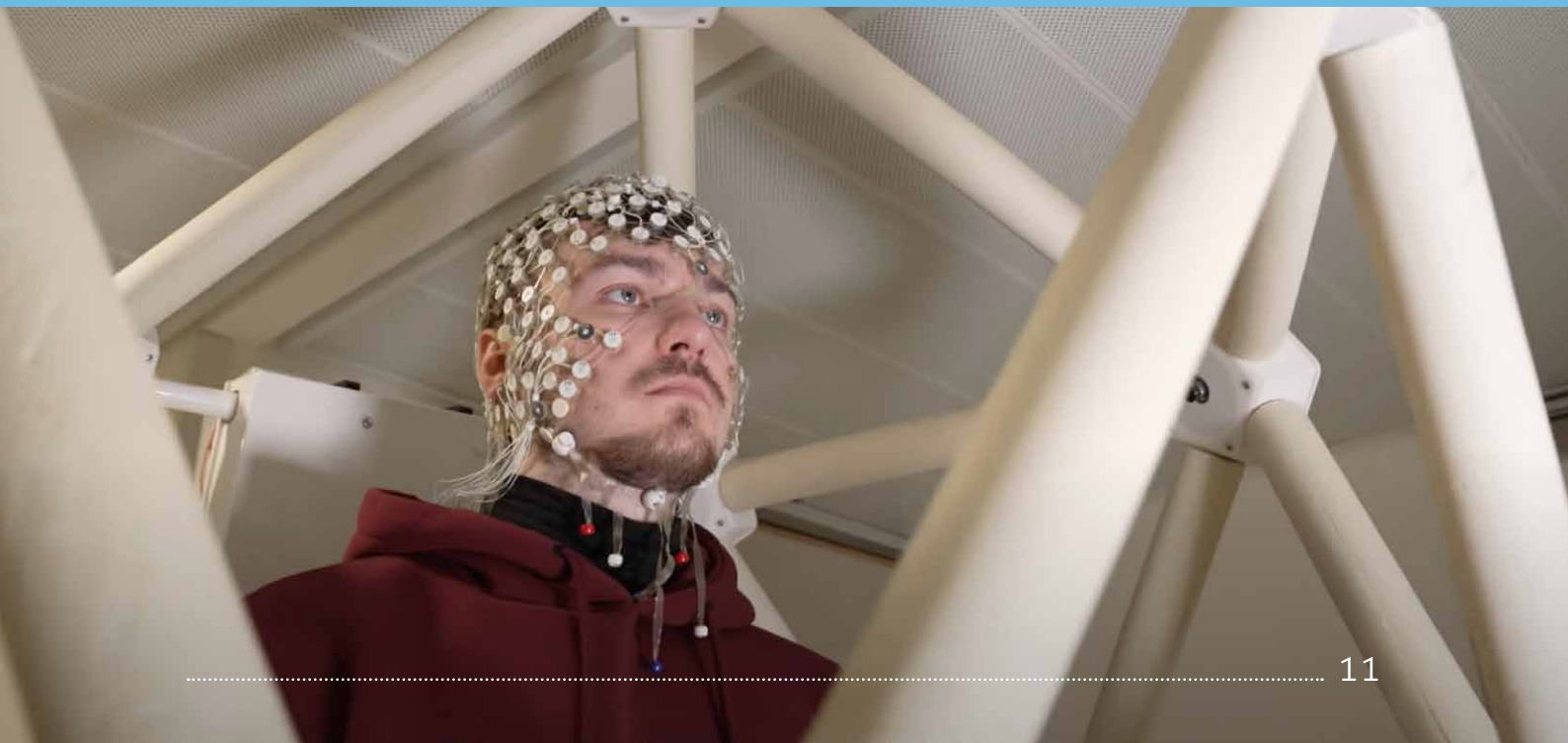
$25,000 Awards

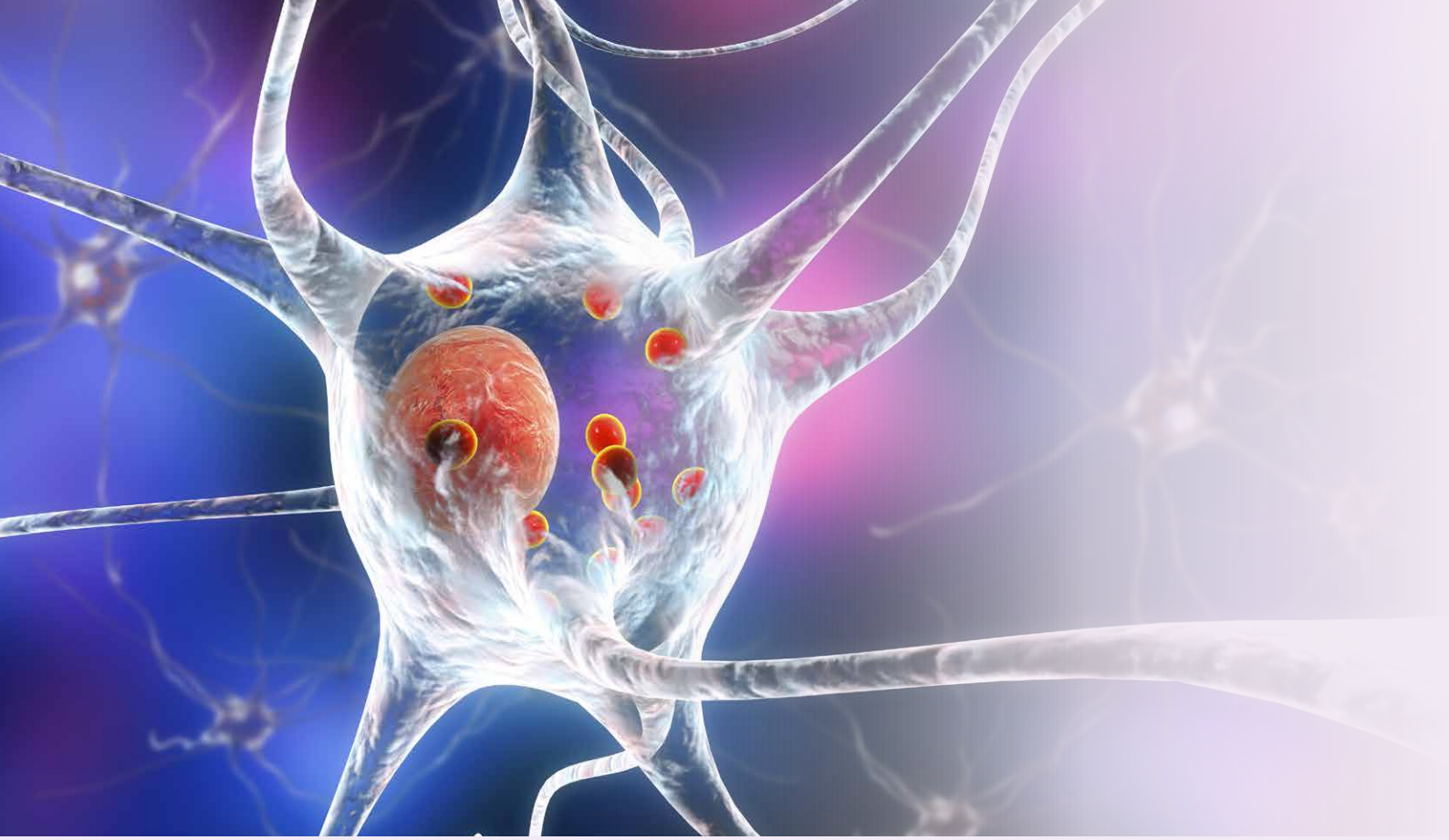
Characterization of the role in Parkinson's disease of the Rab1 GTPase, a master regulator of the endomembrane system.
Researcher: **Prof. Koret Hirschberg** (Medicine)

The effect of circadian disruption on dopaminergic neurons function and parkinsonism.
Researcher: **Prof. Yoav Gothilf** (Life Sciences)

A friend or a foe: the role of cholesterol and its metabolite in α-synuclein cell-to-cell transmission.
Researcher: **Dr. Avraham Ashkenazi (**Medicine)

Amyloid cross-seeding by metabolite assemblies: A new paradigm for Parkinson's disease.
Researcher: **Prof. Ehud Gazit** (Life Sciences)





Infrastructure Support

Human Stem Cell Differentiation Core for Precision Medicine (HSPM)

The mission of the HSPM is to develop differentiation protocols and functional assays for iPSC-derived material to model diseases and provide support for TAU researchers to promote their academic innovations (drugs, biological tools, nanomaterials, etc.) aimed for translational precision medicine for Parkinson's Disease.
Researcher: **Dr. Ben Maoz** (Biomedical Engineering)

MALDI Equipment

Matrix-assisted laser desorption/ionization (MALDI) mass spectrometry imaging (MSI) is emerging as a powerful tool for investigating the distribution of molecules within biological systems through direct analysis of thin tissue sections. The MALDI will be used in part to analyze elucidate region-specific distribution profiles of neuropeptides in animal models of Parkinson's Disease, including in response to drug therapy.
Researcher: **Dr. Lior Mayo** (Life Sciences)

Consortiums

The interplay between stress and Parkinson's disease manifestations and neurodegeneration

Researchers: **Prof. Talma Hendler** (Medicine & Tel Aviv Sourasky Medical Center), **Dr. Anat Mirelman** (Medicine & Tel Aviv Sourasky Medical Center), **Dr. Jeffrey Hausdorff** (Medicine & Tel Aviv Sourasky Medical Center), **Dr. Yuval Nir** (Medicine), **Dr. Gal Raz** (Arts & Tel Aviv Sourasky Medical Center), **Dr. Dan Frenkel** (Life Sciences)

Elucidating mutation-perturbed signaling-regulatory pathways and cellular dysfunction in Parkinson's Disease

Researchers: **Dr. Ben Maoz** (Biomedical Engineering), **Prof. Nir Giladi** (Medicine & Tel Aviv Sourasky Medical Center), **Prof. Uri Ashery** (Life Sciences), **Prof. Avi Orr-Urtreger** (Medicine & Tel Aviv Sourasky Medical Center), **Prof. Anat Mirelman** (Medicine & Tel Aviv Sourasky Medical Center), **Prof. Dani Offen** (Medicine), **Dr. Avraham Ashkenazi** (Medicine), **Prof. Roded Sharan** (Exact Sciences)

Our grant funding provided breakthroughs in understanding of the molecular basis and biological mechanisms of PD, biomarkers, association with other diseases and in advancing treatments and technologies and drug candidates for pre-clinical and clinical evaluation.

Molecular basis and biological mechanisms of PD

Prof. Uri Ashery has developed a unique digital visual system to identify and study the generation of synuclein aggregates in skin biopsies of PD patients and subjects at risk. His groundbreaking work has been recognized by the Michael J. Fox Foundation as a true breakthrough and is now supported by a generous grant to take it toward clinical use.

Dr. Ben Maoz, together with his collaborators, has developed a first ever Brain-on-a-Chip system using neurons that were developed from skin cells of PD patients who carry the Ashkenazi mutation that causes PD (GBA and LRRK2), as well as from their first-degree relatives. This PD brain model is now in use to better understand the way these Ashkenazi mutations are causing PD, as well as to test new drugs that hopefully will decrease the risk to develop PD in subjects at risk (children of PD patients).

Prof. Ronit Sagi-Eisenberg studies the Rab12 enzyme, which is a key regulator of intracellular membrane trafficking, with close correlations with the LRRK2 gene – the most common cause of familial PD. Her studies have unraveled the interactions of Rab12 in its different states with different proteins, and indicate that restoring the balance of Rab12 connectivity may be able to reestablish cellular homeostasis and relieve PD pathogenesis.

Prof. Limor Broday examined the mitochondrial unfolded protein response and SUMO in the C. *elegans* model for PD.

Prof. Mia Horowitz and **Dr. Moshe Parnas** studied the interplay between mutant GBA1 and mutant LRRK2 alleles in the development of PD using Drosophila models

Prof. Eran Perlson, **Prof. Sharon Hassin** and **Dr. Amir Dori** studied the molecular mechanism of GDNF transport in PD.

Association with symptoms and disease

Prof. Matti Mintz, **Dr. Nirit Lev**, and **Prof. Carlos Gordon** examined both the origins and treatment options for imbalance in PD.

Prof. Ronit Pinkas-Kramarski studied the potential connection between Alzheimer's disease and PD, by exploring the possibility that ApoE4 affects PD hallmarks

Prof. Roy Mukamel and **Dr. Neomi Singer** examined audiomotor skill learning across ears and hands in PD patients.

Identification of PD biomarkers

Prof. Yuval Nir has been focusing his work on understanding the role of sleep, specifically the REM sleep phase (when one dreams), on PD pathogenesis, hypothesizing that disturbed REM sleep is provoking neurodegeneration and Parkinson's.

Dr. Avraham Ashkenazi and his team studied the mechanisms involved in the pathological behavior of α-synuclein in PD, and focused on identifying biomarkers of pre-motor PD and metabolic

intervention points useful in the development of candidate treatments. Dr. Ashkenazi has been awarded a DOD grant for this research.

Prof. Anat Mirelman has demonstrated that early changes in turns in bed during sleep is a very sensitive marker of early PD and is detecting motor disturbances in the prodromal stages.

Prof. Roy Alcalay has been involved in the development of new blood and CSF biomarkers that can detect PD as well as reflect brain pathology (synuclein) and mitochondrial DNA changes.

Prof. Itai Benhar studied the link between increased levels of insulin degrading enzyme to PD progression, and evaluated antibodies for early diagnosis and treatment of PD.

Testing of advanced new treatments

Prof. Giladi and the TASMC team have been involved in – and are leading – many groundbreaking **phase 1,2 and 3 clinical trials** with exciting new treatments aiming to slow down or cure PD. The TASMC team has led, with Sanofi from Boston, the world's first ever clinical trial targeting the GBA - PD patients using Venglustat. In addition, they have collaborated with Biogen in Boston to test mononoclonal antibodies against synuclein in recently diagnosed PD patients, bringing these technologies to patients. Furthermore, the TASMC team is involved in several phase 1 and 2 clinical trials with gene therapy, stem cell therapy, small molecule therapy and brain stimulation technologies such as TMS, TDcS and DBS. These remarkable and groundbreaking new technologies are coming to TASMC to be tested because of the expertise the TASMC team has developed and their worldwide reputation.

Implementation of national genetics program for early prevention

Prof. Giladi, in collaboration with **Prof. Orr-Urtreger** and **Prof. Roy Alcalay**, has developed and studied a cohort of more than 3,000 PD patients from Ashkenazi Jewish origins, an ethnic group with a unique genetic conserved substrate, using a whole-genome approach as well as expression studies to identify PD biomarkers. With the Aufzien Center's tremendous support in the last four years, this cohort has been expanded into the **Israel Prodromal Parkinson Initiative (IPPI)** program, facilitating sequencing of thousands of PD patients and their families toward laying the groundwork for early diagnosis and treatment before the onset of symptoms.

Development of technologies & drug candidates for pre-clinical and clinical evaluation

Prof. Dani Offen is developing a unique and very promising system to deliver drugs to the brain through a nasal spray and particles called exosomes that bring the drugs directly to the brain from the nose. His research has demonstrated that next generation anti-Parkinson's drugs can be given with this technology.

Prof. Ehud Gazit has been developing a new line of drugs targeting the amyloid changes responsible for neurodegeneration. This original direction for future treatment of PD can be used to prevent or protect from Parkinson's onset.

Prof. Ronit Pinkas-Kramarski and her teams are working on finding ways to protect neurons. They discovered that mutations of the microglia – immune cells of the brain – may play a crucial role in the development of Parkinson's. Modifying the activity of microglia to reduce their neurotoxic properties and enhance their neuroprotective effects may pave the way for new drugs and therapies.

Dr. Ido Tavor, Dr. Dan Stein and **Dr. David Groashar** tracked dopaminergic integrity in PD without PET.

Prof. Tal Dvir is developing a bio-engineering functional, implantable human dopaminergic networks to treat PD.

Prof. Mordechai Lorberboym and **Prof. Yankel Gabet** worked on a personalized cannabis therapy based on objective measurements to reduce adverse reactions in PD patients.

Prof. Hagit Eldar-Finkelman examined psychedelics mechanisms for treatment of PD.

Prof. Dan Frenkel studied the role of the lipid transporter ABCA7 as potential treatment in PD.

Transformation into a world-renowned hub of R&D in the field

TAU and TASMC, with the support of the Aufzien family, have become a world leader in Parkinson's research, as reflected, for example, by our key role in the **Parkinson's Progression Markers Initiative (PPMI)** run by the Michel J. Fox Foundation. We are taking part in the most exciting phase 1 and 2 clinical trials with groundbreaking new technologies by recruiting trial subjects, and also by taking a prominent role in global advisory boards and steering committees. We also guide global initiatives regarding the introduction of digital health in PD diagnosis and follow up by leading and contributing to international consortia established by the Michel J. Fox Foundation, the National Institutes of Health (NIH), the American Parkinson Foundation and the European Union by Profs. Giladi, Hausdorff, Alcalay and Mirelman. Furthermore, our basic research in PD pathogenesis is garnering increasing attention and worldwide recognition through grants from the American Department of Defense (DOD), the European Union, the MJF Foundation, as well as the NIH and the Israel Science Foundation (ISF). In addition, we are regularly approached by top Parkinson's research centers for collaboration. One such example is a European research center in northern Italy called EURAC, which is focusing on PD pathogenesis and natural history. We are establishing a large-scale collaboration with five different laboratories at TAU and EURAC partners.

The Aufzien Center has been promoting, supporting and accelerating research at the Israeli HMOs since recognizing the unique opportunities created by the Israel medical system through its national health plans. We utilize two decades' worth of electronic medical records (EMRs) available on all Israeli citizens to learn about the natural history of PD at the prodromal stage, as well as about risk and protective factors. Furthermore, we study potential new treatments using repurposed existing drugs. For example, we assess the potential use of anti-diabetic drugs (GLP1-agonists) as a protective treatment in PD and the role of cholesterol and statins in PD risk, as well as the anti-leukemia drug Maravirok to protect from Parkinson's dementia. We believe that this approach can bring groundbreaking treatments to patients much more swiftly than the traditional approach to drug development.

Scholarship Programs

Excellence Fellowships

Post-doctoral fellows

Paul Ashim
Amyloid-like aggregates of a Gaucher disease metabolite seed aggregation of α-Synuclein: Mechanism and development of novel therapeutics for Parkinson's disease
Advisor: Prof. Daniel Segal

Noa Barak
Developing a super-resolution microscopy platform for early detection of alpha synuclein aggregation in human body fluids
Advisor: Prof. Uri Ashery

Vijay Kumar
Glucosylceramide, a major substrate in Gaucher disease forms amyloid-like fibrils that induce α-Synuclein aggregation.
Advisor: Prof. Daniel Segal

Luba Farberov
The molecular mechanism of GDNF transport in Parkinson disease
Advisor: Prof. Eran Perlson

Yanina Ivashko-Pachima
Rotenone toxicity cellular model to test SKIP as a disease-modifying intervention in PD
Advisors: Prof. Illana Gozes, Prof. Yehonatan Sharabi

Kumar Sourav
Intracellular seeding of α-synuclein aggregation by self-assemblies
Advisor: Prof. Daniel Segal

Hila Tamir Ostrover
A novel machine learning system for manual dexterity training in patients with PD
Advisor: Prof. Jason Friedman

Pushpendra Mani Mishra
Amyloid-like fibrils of lipids – novel cause of Parkinson's in sphingolipidoses
Advisor: Prof. Daniel Segal

Lea Peko
Enhanced drug delivery to the brain in Parkinson's disease using ultrasound-mediated blood brain barrier opening
Advisor: Dr. Tali Ilovitsh

PhD students

Stav Cohen Adi
Characterization of α-synuclein secretion mechanisms in Parkinson's disease
Advisor: Dr. Avraham Ashkenazi

Andrew Dagay
The mechanism of action of spinal cord stimulation to treat parkinsonian gait and balance problem
Advisors: Prof. Anat Mirelman

Netta Dunsky-Moran
Neurofeedback to stop parkinsonian tremor
Advisors: Prof. Nir Giladi, Prof. Thalma Hendler

Shay Herman
The role of extracellular vesicles in the progression and pathology of PD
Advisor: Prof. Dani Offen

Saar Lanir
Effect of cannabis on sleep and memory consolidation in PD patients
Advisor: Prof. Nir Giladi

Lior Nechushtai
The involvement of APOE4 in Parkinson's disease
Advisor: Prof. Ronit Pinkas-Kramarski

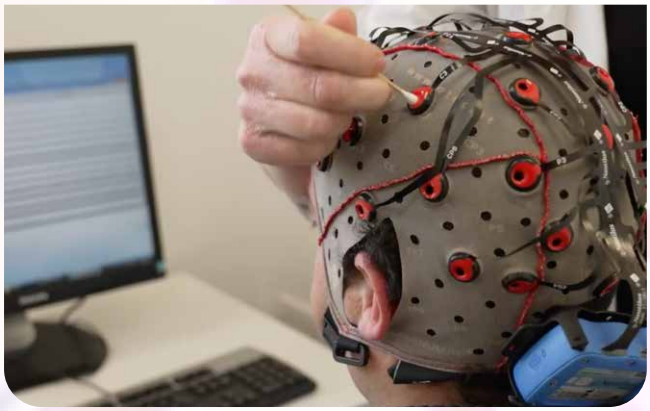
Jana Omar
Elucidating the role and underlying mechanisms of Rab12 functions
Advisor: Prof. Ronit Sagi Eisenberg

Rotem Orad
Brain imaging changes in neurodegenerative diseases: An advanced MRI study
Advisor: Prof. Dafna Ben-Bashat

Roy Rabinowitz
Treatment of LRRK2-related Parkinson's patients through immunotherapy
Advisor: Prof. Dani Offen

Dorin Sade Yazdi
Seeding of amyloids in Parkinson's disease: The involvement of neurometabolites assemblies in the initiation of pathological processes
Advisor: Prof. Ehud Gazit

Ilana Sogolovsky-Bard
Metabolite self-assembly in Parkinson's
Advisors: Prof. Ehud Gazit, Prof. Limor Broday



Adi Tessler
Targeting CD157+ Myeloid cells during Parkinson's disease
Advisor: Dr. Lior Mayo

Guy Shapira
The transcriptomic basis of THC micro-dose induced neuroprotection
Advisor: Prof. Noam Shomron

Omer Glixman
Audiomotor skill learning across ears and hands in PD patients
Advisor: Prof. Roy Mukamel

Adi Cohen
Regulating molecular aging by the engineering of a bispecific CTLA4-VISTA for a tunable immune response
Advisor: Dr. Maayan Gal

Master's students

Margarita Galves
Mechanisms of post-transcriptional modifications in the regulation of mammalian macroautophagy
Advisor: Dr. Avraham Ashkenazi

Vera Serebryany
Possible interaction between GBA1 and LRRK2 genes, involved in the development of Parkinson's disease, using a Drosophila model
Advisor: Prof. Mia Horowitz

Yifat Weiss
Establishing an in vitro platform for studying a-Syn aggregates propagation
Advisor: Prof. Uri Ashery

Yael Yaakov
Motor imbalance in Parkinson patients: Its relation to multi-sensory integration
Advisors: Prof. Matti Mintz & Prof. Sigal Portnoy

Sapir Fajerzstein
Quantitative analysis of blood-brain barrier dysfunction in Parkinson's disease using dynamic contrast-enhanced MRI
Advisor: Prof. Dafna Ben Bashat

Rachel Levy
Structure-based optimization of the IDE inhibitor to increase its physicochemical propoerties for PD therapy
Advisors: Prof. Dan Frenkel & Dr. Rotem Rubinstein

Events

Events are an integral part of APPD's work and mission to bring together the PD communities to promote discussions and research collaborations. APPD hosted conferences, seminars and meetings between 2019-2023. These events support the productive exchange of ideas among the academy, hospitals, physicians, paramedical teams, HMOs and industry.

The Aufzien Center has become a facilitator of better and more direct **communication between PD researchers and established Israeli clinicians** taking care of PD patients in Israel, by supporting an annual, two-day brainstorming meeting in which both clinicians and scientists discuss unmet needs in Parkinson's research and treatment. In addition, we have encouraged PD patients and their families to take an active role in the Israeli Parkinson's community by establishing an annual Israel Parkinson's Conference that brings together patients and family members with scientists, clinicians and industry representatives to share and explore directions for improving patient care.

The Aufzien Center has played a pivotal role in the creation of the Israeli Parkinson's community. We have established, supported and organized the Israel Parkinson's Congress that brings together researchers, clinicians, industry, patients and families annually to meet and share insights and experiences. Last year the congress focused on technology and Parkinson's, while this year's meeting focused on hope.

APPD hosted conferences, seminars and meetings between 2019-2023.

Conferences

June 13, 2019
International Conference at TAU

March 30-31, 2020
Second Parkinson Conference, Online, Tel Aviv. Co-organizers: Prof. Karen Avraham, Prof. Nir Giladi

Oct 13-14, 2020
Healthy Ageing Webinar Conference. Organizer: Prof. Karen Avraham, Funding provided by BIRAX UK-Israel Fund

Dec 17-18, 2020
Parkinson's School of Industry, TAU & Tel-Aviv Medical Center. Organizer: Prof. Nir Giladi

Feb 18, 2021
The Road to Preventing Parkinson's Disease Webinar Prof. Nir Giladi & Prof. Karen Avraham

April 29, 2021
The Israeli Parkinson's Virtual Conference Organizers: Prof. Sharon Hassin, Prof. Nir Giladi, Prof. Karen Avraham (with Israeli Parkinson's Association)

May 27-28, 2021
Brainstorming for Parkinson's Disease. Organizers: Prof. Karen Avraham, Prof. Nir Giladi. Key opinion leaders in PD in Israel: Researchers and clinicians

April 11, 2022
World PD Day Conference, Smolarz Auditorium, Tel Aviv University

June 9-10, 2022
Brainstorming for PD Workshop, Herzliya

March 13-15, 2023
4th International Freezing of Gait Workshop, Jerusalem

April 19, 2023
World PD Day Conference, Expo Tel Aviv

May 15, 2023
Around the Board of Governor's: Presentation of the Aufzien Family Center for the Prevention and Treatment of PD

Monthly lecture series

Nov 7, 2019
Prof. Nir Giladi, TASMC & School of Medicine, Tel Aviv University
The path to cure Parkinson's disease

Dec 19, 2019
Prof. Hagai Bergman, The Hebrew University of Jerusalem
PD as a network disorder

April 23, 2020
Prof. Serge Przedborski, Columbia University
Mitochondria and the two-century journey of Parkinson's disease

May 26, 2020
Prof. Hui Yang, Chinese Academy of Sciences, Shanghai
Glia-to-neuron conversion via gene editing alleviates symptoms in Parkinson's disease and retinal disease mouse models

July 16, 2020
Prof. Brit Mollenhauer, University of Goettingen
Biological markers in PD

July 21, 2020
Prof. Ted M. Dawson, M.D., Ph.D., John Hopkins University School of Medicine
A deep molecular understanding of Parkinson's disease reveals innovative disease modifying therapies

August 11, 2020
Prof. Valina Dawson, John Hopkins University School of Medicine
Modeling sporadic Parkinson's disease

Oct 29, 2020
Prof. Ronald Postuma, McGill University
REM sleep behavior disorder: A window into early neurodegeneration

Jan 14, 2021
Prof. Dafna Ben-Bashat, Sagol Brain Institute, TASMC & School of Medicine, Tel Aviv University
Quantitative magnetic resonance imaging for the diagnosis of Parkinson's disease

March 18, 2021
Aufzien Family Center Fellowship Awardees Lectures, Tel Aviv University

April 19, 2021
Dr. Michael Lazarou, Monash University, Australia
Maintaining mitochondrial health in Parkinson's disease: The role of PINK1 and Parkin mitophagy

April 22, 2021
Prof. Alice Nieuwboer, KU Leuven
Moving forward in understanding freezing of gait in Parkinson's disease

May 20, 2021
Prof. Andrew B. Singleton, NIH
Collaborative progress in neurodegenerative disease

Oct. 28, 2021
Prof. Sebastian Kadener, Brandeis University
A role for circRNAs in aging, Parkinson's disease and other neurodegenerative disorders

Nov. 25, 2021
Prof. Roy Alcalay, TASMC and Coulmbia University
Towards precision medicine in Parkinson's disease

Dec. 30, 2021
Prof. Hermona Soreq, The Hebrew University of Jerusalem
The role of stress in neurodegeneration

Feb. 24, 2022
Aufzien Family Center Fellowship Awardees Lectures, Tel Aviv University

March 31, 2022
Prof. Yehonatan Sharabi, Sheba Medical Center & Tel Aviv University
Autonomic nervous system and Parkinson's disease: insights on mechanisms and treatment

May 26, 2022
Prof. Moussa B.H. Youdim, Technion
The Future of Parkinson's Disease: Why Multi-Target Drugs

October 27, 2022
Dr. Ariadna Laguna Tuset, Neuroscience Institute of the Autonomous University of Barcelona
The gut microbiota and PD

November 24, 2022
Prof. Leonidas Stefanis, Biomedical Research Foundation of the Academy of Athens
Chaperone-medicated autophagy in neurodegenerative proteinpathies

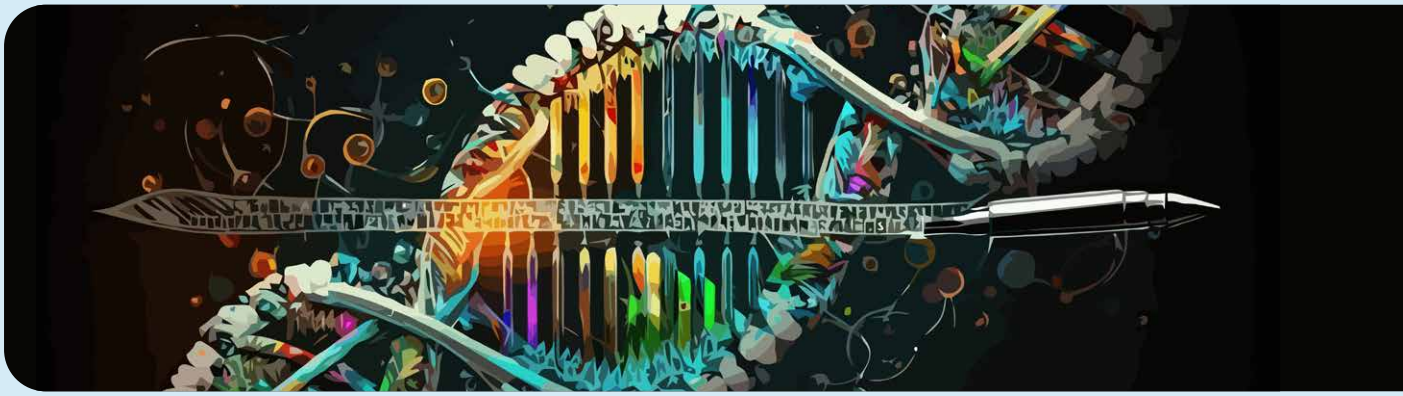
December 29, 2022
Dr. Rick Helmich, Donders Institute for Brain, Cognition and Behaviour & Radboud University Medical Centre, Nijmegen, Netherlands
Tremor: Generators, modulators and mechanism-based interventions

March 30, 2023
Aufzien Family Center Grant Awardees Lectures, Tel Aviv University

April 27, 2023
Dr. Mark R. Cookson, NIH
The role(s) of Leucine-rich repeat kinase 2 in inherited and sporadic Parkinson's disease

May 18, 2023
Prof. Jeffrey M. Hausdorff, TASMC & School of Medicine, Tel Aviv University
Freezing of Gait: overview, update, and open questions

June 29, 2023
Prof. Ming Guo, MIT
Mitochondrial dynamics in Parkinson's Disease pathogenesis



Educational activities

Nov 24-26, 2020
Aufzien Virtual Course: Parkinson's Disease for the Biotech and Pharmaceutical Industry

Scientific Prizes.....

2022

Prof. Hagai Bergman, Hebrew University of Jerusalem (Established)

Dr. Avner Thaler, TASMC & Faculty of Medicine, Tel Aviv University (Junior)

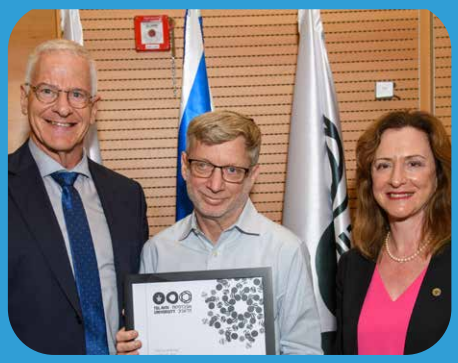
Special award to **Prof. Rafi Eldor** for his significant contribution to Parkinson's rehabilitation through dance

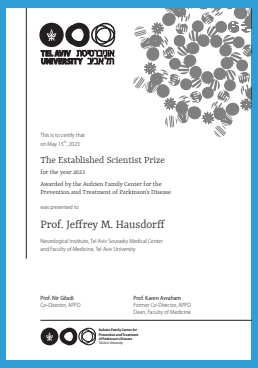
2023

Prof. Jeffrey M. Hausdorff, TASMC & Faculty of Medicine, Tel Aviv University (Established)

Prof. Aviv Mezer, Hebrew University of Jerusalem (Junior)

Karen Avraham, Nir Giladi, Hagai Bergman





Karen Avraham, Nir Giladi, Jeff Hausdorff

Karen Avraham, Nir Giladi, Avner Thaler

Karen Avraham, Nir Giladi, Aviv Metzer

Travel Awards

Lior Ankor
Neuroscience 2022 San Diego
Mir-126 5p in iPSC-derived dopaminergic neurons of PD patients
Advisor: Prof. Eran Perlson

Stav Cohen Adiv
Neuroscience 2022 San Diego
Influence of membrane phospholipids scramblase on α-synuclein pathological behavior in Parkinson's disease
Advisor: Dr. Avraham Ashkenazi

Andrew Dagay
Israel Society for Neuroscience Conference
Overnight distribution of rapid eye movement sleep without atonia (RSWA) in people with Parkinson's disease and healthy participants
Advisor: Prof. Anat Mirelman

Lihi Eisenberg
International Parkinson & Movement Disorder Society Conference
Exploring the association between Helicobacter pylori & PD
Advisor: Prof. Chava Peretz, Prof. Nir Giladi

Yael Ezra
Israel Society for Neuroscience Conference
Mapping the changes in brain connectivity using EEG in patients with Parkinson's disease
Advisor: Dr. Inbal Maiden

Saar Lanir
Sleep Europe Congress
The relationship between sleep and Parkinson's disease
Advisor: Prof. Nir Giladi

Sarah Leviashvili
Israel Society for Neuroscience Conference
Mapping the changes in brain connectivity using EEG in patients with Parkinson's disease
Advisor: Dr. Inbal Maiden

Stav Cohen Adiv
Israel Society for Neuroscience Conference
Influence of membrane phospholipids on α-synuclein pathological behavior in Parkinson's disease
Advisor: Dr. Avi Ashkenazi

Lihi Eisenberg
International Parkinson & Movement Disorder Society Conference
Exploring the association between helicobacter & PD
Advisors: Prof. Chava Peretz, Prof. Nir Giladi

Ofir Sade
Research Collaboration at Würzburg University
Early detection of Parkinson's disease through analysis of α-Synuclein aggregates in skin biopsies using super resolution microscopy
Advisor: Prof. Uri Ashery

Netta Dunsky-Moran
Organization for Human Brain Mapping (OHBM) Montréal 2023 Annual Meeting
Neural response to tempo in music unveils multidomain processing abnormality in Parkinson's disease
Advisor: Prof. Nir Giladi

Collaborations

Industry Advisory Board

Company	Member
NeuroDerm	Sheila Oren
Medtronic	Orit Spiegelmann
Pharma2B	Hadas Friedman
Elminda	Ronen Gadot
Intel	Chen Admati
Prilenia	Michal Geva
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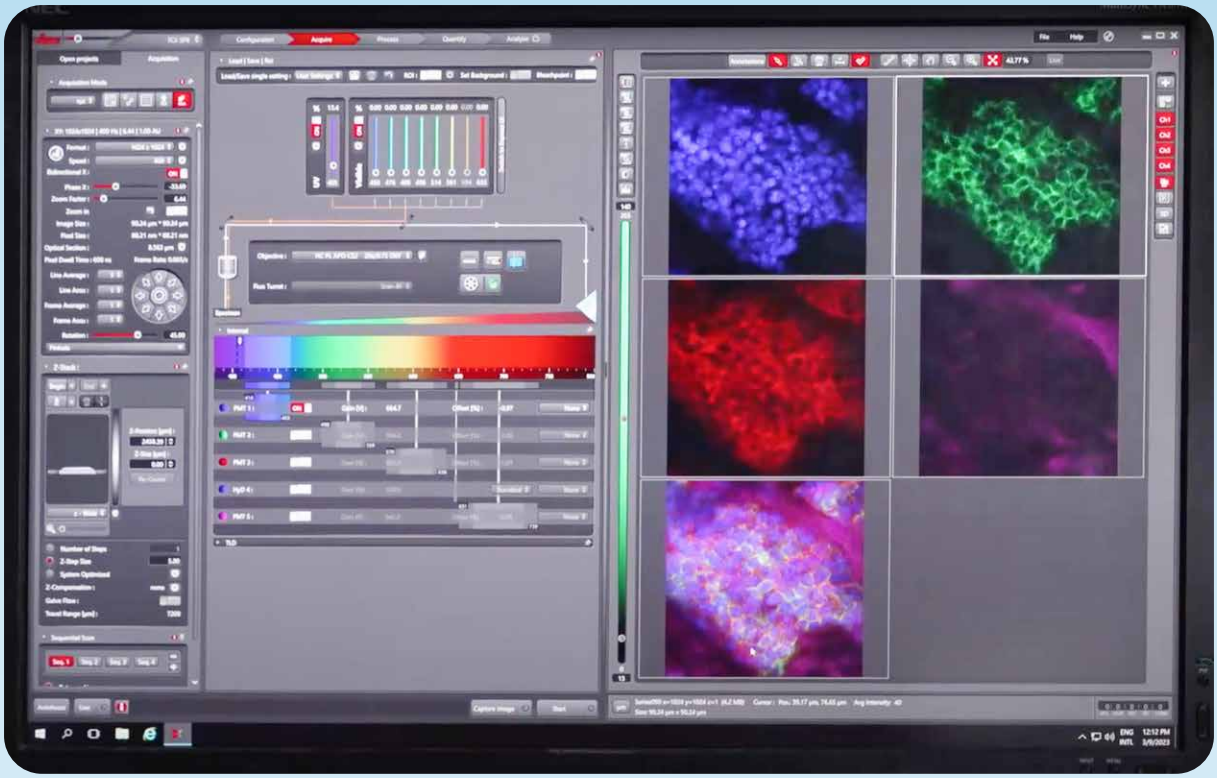

Affiliated Researchers .....

Prof. Roy Alcalay
Prof. Uri Ashery
Dr. Avraham Ashkenazi
Prof. Dafna Ben-Bashat
Prof. Itai Benhar
Prof. Limor Broday
Prof. Ruth Djaldetti
Dr. Amir Dori
Prof. Tal Dvir
Prof. Hagit Eldar-Finkelman
Prof. Dan Frenkel
Prof. Jason Friedman
Prof. Yankel Gabet
Dr. Maayan Gal
Prof. Ehud Gazit
Prof. Nir Giladi
Prof. Carlos Gordon
Prof. Yoav Gothilf
Prof. Illana Gozes
Dr. David Groshar
Prof. Sharon Hassin
Prof. Jeffrey Hausdorff
Dr. Benedetta Heimler
Prof. Talma Hendler
Prof. Koret Hirschberg
Prof. Mia Horowitz
Dr. Tali Ilovitsh
Dr. Nirit Lev
Prof. Mordechai Lorberboym
Dr. Inbal Maiden
Dr. Ben Maoz
Dr. Lior Mayo
Prof. Matti Mintz
Prof. Anat Mirelman
Prof. Roy Mukamel
Prof. Drorit Neumann
Prof. Yuval Nir
Prof. Daniel Offen
Dr. Sheila Oren
Prof. Avi Orr-Urtreger (Incumbent of the Norma and Alan Aufzien Chair for Parkinson's Disease and Neurological Disorders of the Brain)
Dr. Moshe Parnas
Prof. Chava Peretz
Prof. Eran Perlson
Prof. Ronit Pinkas-Kramarski
Prof. Meir Plotnik
Prof. Sigal Portnoy
Dr. Gal Raz
Dr. Rotem Rubinstein
Prof. Ronit Sagi-Eisenberg
Prof. Daniel Segal
Prof. Yehonatan Sharabi
Prof. Roded Sharan
Prof. Noam Shomron
Dr. Neomi Singer
Dr. Dan Stein
Prof. Riva Tauman
Dr. Ido Tavor
Dr. Avner Thaler
Dr. Noham Wolpe

Selected List of Publications .....

2019-present

KrishnaKumar VG, Paul A, Gazit E, Segal D (2019) Naphthoquinone Tryptophan hybrids: A promising small molecule scaffold for mitigating aggregation of amyloidogenic proteins and peptides. Frontiers in Cell and Developmental Biology 7, 242.

Herman T, Dagan M, Shema-Shiratzky S, Reches T, Brozgol M, Giladi N, ... & Hausdorff JM (2020) Advantages of timing the duration of a freezing of gait-provoking test in individuals with Parkinson's disease. *Journal of Neurology*, 267, 2582-2588.

Reches T, Dagan M, Herman T, Gazit E, Gouskova NA, Giladi N, ... & Hausdorff JM (2020) Using wearable sensors and machine learning to automatically detect freezing of gait during a FOG-provoking test. *Sensors* 20, 4474.

Thaler A, Shenhar-Tsarfaty S, Shaked Y, Gurevich T, Omer N, Bar-Shira A, Gana-Weisz M, Goldstein O, Kestenbaum M, Cedarbaum JM, Orr-Urtreger A, Giladi N, Mirelman A (2020) Metabolic syndrome does not influence the phenotype of LRRK2 and GBA related Parkinson's disease. *Scientific Reports* 10, 9329.

Ivashko-Pachima Y, Seroogy KB, Sharabi Y, Gozes I (2021) Parkinson disease-modification encompassing rotenone and 6-hydroxydopamine neurotoxicity by the microtubule-protecting drug candidate SKIP. *Journal of Molecular Neuroscience* 71,1515–1524.

Sade Yazdi D, Laor Bar-Yosef D, Adsi H, Kreisera T, Shahaf S, Beraa S, Zaguria D, Shaham-Nivd S, Oluwatobae DS, Levy D, Gartnera M, Doe TD, Frenkel D, Gazit E (2021) Homocysteine fibrillar assemblies display cross-talk with Alzheimer's disease β-amyloid polypeptide. *Proceedings of the National Academy of Sciences USA* 118, e2017575118.

Dagan M*, Manor B*, Herman T, Gouskova N, Vanderhorst V, Giladi N,... & Hausdorff JM (2021) Multi-target transcranial electrical stimulation for freezing of gait: a randomized controlled trial. *Movement Disorders* 36, 2693-2698. *equal authors

Dagan M, Herman T, Bernad-Elazari H, Gazit E, Maidan I, Giladi N, ... & Hausdorff JM (2021) Dopaminergic therapy and prefrontal activation during walking in individuals with Parkinson's disease: does the levodopa overdose hypothesis extend to gait? *Journal of Neurology* 268, 658-668.

Schneider N, Dagan M, Katz R, Thumm PC, Brozgol M, Giladi N, ... & Hausdorff JM (2021) Combining transcranial direct current stimulation with a motor-cognitive task: the impact on dual-task walking costs in older adults. *Journal of NeuroEngineering and Rehabilitation* 18, 1-13.

Omar J, Rosenbaum E, Efergan A, Sneineh BA, Yeheskel A, Maruta Y, Fukuda M, Sagi-Eisenberg R (2021) Biochemical and structural insights into Rab12 interactions with RILP and its family members. *Scientific Reports* 11, 10317.

Paul A, Jacoby G, Laor Bar-Yosef D, Beck R, Gazit E, Segal D (2021) Glucosylceramide associated with Gaucher disease forms amyloid-like twisted ribbon fibrils that induce α-Synuclein aggregation. *ACS Nano* 15, 11854-11868.

Paul A, Segal D, Zacco E (2021) Glycans to improve efficacy and solubility of protein aggregation inhibitors. *Neural Regeneration Research* 16, 2215-2216.

Sharabi Y, Vatine GD, Ashkenazi A (2021) Parkinson's disease outside the brain: targeting the autonomic nervous system. *Lancet Neurology* 20, 868-876.

Maoz BM, Asplund M, Maggio N, Vlachos A (2021) Technology-based approaches toward a better understanding of neurocoagulation in brain homeostasis. *Cell and Tissue Research* 387, 1-6.

Paul A, KrishnaKumar VG, Huber A, Arad E, Engel H, Jelinek R, Gazit E, Segal D (2021) Inhibition of tau amyloid formation and disruption of its preformed fibrils by Naphthoquinone-Dopamine hybrid. *FEBS Journal* 288, 4267-4290.

Maoz BM (2021) Brain-on-a-Chip: Characterizing the next generation of advanced in vitro platforms

for modeling the central nervous system. *APL Bioengineering* 5, 030902.

Gottfried I, Schottlender N, Ashery U (2021) Hyperbaric oxygen treatment—from mechanisms to cognitive improvement. *Biomolecules* 11, 1520.

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Cohen-Adiv S, Ashkenazi A (2022) Fatty acid balance regulates alpha-synuclein pathology. *Trends in Neurosciences* 45, 417-418.

Leviashvili S, Ezra Y, Droby A, Ding H, Groppa S, Mirelman A, Muthuraman M, Maidan I (2022) EEG-based mapping of resting-state functional brain networks in patients with Parkinson's disease. *Biomimetics* 7, 231.

Lang AE, Siderowf AD, Macklin EA, Poewe W, Brooks DJ, Fernandez HH, Rascol O, Giladi N, Stocchi F, Tanner CM, Dam T, et al. for the SPARK Investigators (2022) Trial of Cinpanemab in Early Parkinson's disease. *New England Journal of Medicine* 387, 408–420.

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Galves M, Sperber M, Amer-Sarsour F, Elkon R, Ashkenazi A (2023) Transcriptional profiling of the response to starvation and fattening reveals differential regulation of autophagy genes in mammals. *Proceedings. Biological Sciences* 290, 20230407.

Nir Y, de Lecea (2023) Sleep and vigilance states: Embracing spatiotemporal dynamics. *Neuron* 111, 1998-2011.

Giladi N, Alcalay RN, Cutter G, Gasser T, Gurevich T, Höglinger GU, Marek K, Pacchetti C, Schapira AHV, Scherzer CR, Simuni T, Minini P, Sardi SP, Peterschmitt MJ (2023). Safety and efficacy of venglustat in GBA1-associated Parkinson's disease: an international, multicentre, double-blind, randomised, placebo-controlled, phase 2 trial. *The Lancet. Neurology*, 22, 661–671.

Sela M, Poley M, Mora-Raimundo P, Kaduri M, Avital A, Adir O, Kagan S, Rozencweig A, Weiss Y, Sade O, Leichtmann-Bardoogo Y, Shklover J, Shainsky-Roitman J, Ashery U, Maoz BM, Schroeder A (2023) Brain-targeted liposomes loaded with monoclonal antibodies reduce alpha-synuclein aggregation and improve behavioral symptoms in Parkinson's disease. *Advanced Materials* 27:e2304654.

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of co-cultures and 3D systems. *Biomedical Optics Express* 14, 5223-5237.

Nechushtai L, Frenkel D, Pinkas-Kramarski R (2023) Autophagy in Parkinson's disease. *Biomolecules* 13, 01435.

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Droby A, Thaler A, Mirelman A (2023) Imaging markers in genetic forms of Parkinson's disease. *Brain Sciences* 13, 1212.

Bar-On M, Baharav S, Katzir Z, Mirelman A, Sosnik R, Maidan I (2023) Task-related reorganization of cognitive network in Parkinson's disease using electrophysiology. *Movement Disorders* 38, 2031-2040.

Cohen M, Herman T, Ganz N, Badichi I, Gurevich T, Hausdorff JM (2023) Multidisciplinary intensive rehabilitation program for people with Parkinson's disease: gaps between the clinic and real-world mobility. *International Journal of Environmental Research and Public Health*. 20, 3806.

Saleh MA, Amer-Sarsour F, Berant A, Pasmanik-Chor M, Kobo H, Sharabi Y, Ashkenazi A (2024) Chronic and acute exposure to rotenone reveals distinct Parkinson's disease-related phenotypes in human iPSC-derived peripheral neurons. *Free Radical Biology and Medicine*. Online Jan 19.

Publicity

EMBO COMMUNITY

Tel Aviv hosts new centre for Parkinson's disease research

Karen Avraham at the opening of the Tel Aviv University Aufzien Center

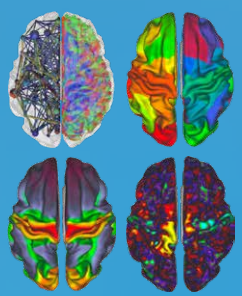
The Aufzien Family Center for the Prevention and Treatment of Parkinson's Disease (APPD) is a new academic research center at the Faculty of Medicine and Sagol School of Neuroscience at Tel Aviv University, Israel. Established with a generous donation from the Aufzien family, and co-directed by EMBO Member Karen B. Avraham and Nir Giladi, the APPD will serve as a hub for innovative translational research in Parkinson's disease.

The centre supports cutting-edge research towards better treatment and prevention, or slowing down, of Parkinson's disease (PD) progression through a grant programme and activities such as regular seminars, annual international symposia and student exchange programmes.

The research at the APPD will encompass the entire drug development cycle from basic research through commercialization with a focus on expanding the understanding of the molecular basis and biological mechanisms of PD, the identification of PD biomarkers, and the development of technologies and drug candidates for pre-clinical and clinical evaluation. In addition, the aim is to promote the exchange of ideas among researchers, clinical staff, physicians and those working in industry.

TV channel 13 (Hebrew) clip

Dr. Avner Thaler (a movement disorders fellow at the TASMC; https://www.cbf-tlv.com/avner-thaler), Prof. Nir Giladi, Prof. Avi Orr-Urtreger (Tel Aviv University Professor and incumbent of the Norma and Alan Aufzien Chair for Parkinson's Disease and Neurological Disorders of the Brain), and Prof. Anat Mirelman (Director, Laboratory for Early Markers of Neurodegeneration (LEMON), TASMC and Tel Aviv University Professor)



Thank you
for your interest in APPD

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