

**PRESS RELEASE**

**14 Research Proposals Chosen for Israel Precision Medicine Partnership**

**Proposals feature unprecedented collaboration between researchers**

***About NIS 60 million in grants awarded in current application cycle***

Overview

* The 14 research proposals were selected out of 111 excellent proposals submitted on a wide range of topics.
* The Israel Precision Medicine Partnership (IPMP) will drive a deeper understanding of the basis of human disease, will enable the expansion of personalized precision medicine in Israel and will facilitate breakthroughs in the field for the benefit of mankind.
* The winning proposals were selected in a competitive process based on their scientific excellence, by an international committee chaired by Prof. Roger Kornberg of Stanford University, a Nobel Prize laureate in Chemistry.
* The grants for the project are among the largest ever awarded to Israeli researchers by an Israeli body.
* The research projects will lead to a deeper understanding of human diseases and will advance the implementation of new healthcare approaches.
* The overall IPMP budget, about NIS 210 million, will allow funding of four cycles of applications. The duration of each project will be up to four years.
* The research partnership relies on pooled resources from the Planning and Budgeting Committee of the Council for Higher Education, the Digital Israel Initiative of the Ministry of Social Equality, Yad Hanadiv and the Klarman Family Foundation (Boston).
* The IPMP program is administrated and operated by the Israel Science Foundation.

**Prof. Benny Geiger, Chairman of the ISF:**

***“The Israel Precision Medicine Partnership creates new opportunities for researchers in this competitive field – research opportunities that were previously hard to imagine, even to dream of, in Israel. Furthermore, the large number of worthy applications, along with the extensive, unprecedented cooperation between university researchers and physicians in hospitals and other healthcare organizations, demonstrate the vast potential of Israeli research to contribute to global knowledge in advanced medical fields and to improve the quality of Israeli healthcare.”***

**Minister Gila Gamliel, Minister for Social Equality:**

***“As Minister for Social Equality leading the Digital Israel project, it has been an honor to lead Israel's digital revolution over the last four years. Israel is at the forefront in the world in the field of digital technology, which offers us an opportunity to ensure that nobody is left behind. The research foundation which we have established is another move in this critical revolution utilizing digital health as Israel's latest growth engine both for individual citizens and the economy at large. It is difficult to exaggerate the importance of this landmark project which integrates both the academic world and the health system in creating life-saving breakthroughs.***

***The rich clinical information that exists in the state of Israel will now be supplemented with genomic and proteomic information, which will shed light on some of the most important problems currently faced by the medical community. The IPMP foundation is the latest step forward in this historic project which will lead to a dramatic revolution in clinical research in Israel.”***

**Prof. Yaffa Zilbershats, Chair, the Planning and Budgeting Committee of the Council for Higher Education:**

**"I would like to congratulate the investigators who won the IPMP research grants.The PBC defined the promotion of big-data research, including precision medicine, as a priority field in its current  multi-annual program. The potential of this technology-rich and multi-disciplinary topic is particularly challenging, and is based on the scientific excellence of the research community in the academic higher education institutions, as well as on the existence, in Israel,  of advanced clinical-academic databases, which are essential for precision medicine. This is a unique endeavor, in its quality and high funding levels, which will position Israel in the forefront of the global research effort, and will contribute significantly to the healthcare level in Israel"**

Research in the field of precision medicine will be based on broad cooperation between various fields while integrating scientific knowledge and medical knowledge, theories, in-depth analysis of medical big data and extensive experimental work. The research projects will utilize information from the unique databases of Israeli healthcare institutions, while meticulously protecting patient privacy. Israel has an enormous relative advantage in this field due to the vast scope and high reliability of these databases.

Following a comprehensive, thorough examination, an international expert committee headed by Nobel Prize laureate **Prof. Roger Kornberg of Stanford University** selected the **14** leading research proposals for the first cycle of the IPMP program. These projects will receive research grants totaling about **NIS** **60 million**. The program is a new research partnership – the first of its kind in Israel, with a total budget of about **NIS 210 million**, to be awarded in four application cycles. The duration of each research project will be up to four years.

Background and the core mission of the IPMP program:

The IPMP program focuses on achieving in-depth understanding of the mechanisms responsible for variable features of the same disease in different patients, and strives to advance innovative, groundbreaking research that will lead to in-depth understanding of human biology and the mechanisms underlying the patient-to-patient variability of human diseases. Many studies conducted in recent years point to the fact that different people suffering from the same disease (for example: diabetes, various kinds of leukemia, breast cancer, Crohn's disease, etc.) may have different disease manifestations, including the disease’s rate of development, different severities and variability in response to treatment.

The medical field has recognized for a long time the existence of heterogeneity between patients, but the underlying *reasons* are still largely unknown. Without substantiated information on the factors influencing this heterogeneity, it is not possible to provide an optimal, personalized care to each and every patient.

**The IPMP program will face these challenges, utilizing a wide range of technologies, based on close collaboration between multi-disciplinary groups, including physicians, basic researchers, theoreticians, experimentalists, bioinformaticians, computer scientists and big-data specialists, engineers, statisticians, epidemiologists and others.**

The program was initiated about six months ago when a call request for proposals was issued, inviting Israeli researchers to apply for grants. The call for applications followed commitment for funding by program partners: the Planning and Budgeting Committee of the Council for Higher Education, the Digital Israel Initiative of the Ministry of Social Equality and two philanthropic foundations: the Yad Hanadiv Foundation in Israel and the Klarman Family Foundation in the U.S. The partnership is operated and administrated by the Israel Science Foundation.

The program will allow Israeli researchers to conduct comprehensive and large-scale research projects in fields of human health that rely on extensive cooperation between researchers in Israeli institutions of higher education and healthcare organizations, communities of both sick and healthy volunteers and big data stored on Israeli hospital and HMO databases.

It should be noted that the cooperation between researchers in universities and healthcare institutions will significantly advance Israeli research capabilities in the field, will help accelerate the rate of discoveries and the potential for implementing new healthcare approaches, **while situating Israel as a trailblazer at the forefront of global science in the field of precision medicine.**

In December **2018**, a first request for proposals was sent to researchers in the field. In response, **111** research proposals were submitted. These proposals were based on an unprecedented level of cooperation and touched on a wide range of topics in the fields of human medicine. The proposals underwent a comprehensive judging process by international experts and **14** were selected for funding.

In September **2019**, the next call for proposals will be issued for the second of four planned submission cycles.

Projects that received funding

**The following is a list of the 14 selected research proposals, including researcher names and specialization, the research topic and the grant amount:**

**1. Prof. Karen Avraham,** Tel Aviv University, Human Molecular Genetics and Biochemistry

 Grant Amount: **NIS 5.0 million**

**Big Data to Therapy: Personalized Medicine for the Deaf in the Diverse Jewish Population**

The overall goal of Prof. Avraham’s research is to define the genetic pathways governing the function of the mammalian inner ear and how variants in these pathways lead to deafness. Through the discovery of genes involved in deafness, Prof. Avraham is establishing genotype-phenotype correlations to set criteria for treatment and rehabilitation of the hearing-impaired population in Israel. In this project, the basis for hearing loss will be determined using genetic analysis of samples from thousands of patients, identified through a collaboration with the Maccabi Tipa biobank. Audiology and genetics clinics will be informed of new findings, establishing a guideline for precision medicine for hearing loss in Israel

**2. Prof. Tamar Geiger**, Tel Aviv University, Human Molecular Genetics & Biochemistry

 **Prof. Neta Erez**, Tel Aviv University, Department of Pathology

 **Prof. Gal Markel**, Chaim Sheba Medical Center, Ella Lemelbaum Institute for Immuno-Oncology

 Grant Amount: **NIS 5.2 million**

**Advancing Immunotherapy with Metabolic Drugs: Towards Improved Melanoma Treatment**

Immunotherapy revolutionized cancer treatment, leading to durable responses even in the most aggressive cancer types, such as melanoma. Despite this success, more than 50% of melanoma patients do not respond to treatment. Our previous work showed an association between the metabolic state of the melanoma cells with immunotherapy response. In the current project we aim to increase treatment efficacy by combining immunotherapy with metabolic drugs *in-vitro*, *in-vivo* and in patients. We will then examine the effects on all cell populations in the tumor microenvironment. Through development of single cell proteomics approaches and integration with single cell RNA-seq, we aim to obtain a comprehensive functional view of melanoma response.

**3. Prof. Michael Danilenko**, Ben-Gurion University, Clinical Biochemistry & Pharmacology – Health

 Sciences

 **Dr. Eitan Rubin**, Ben-Gurion University, Shraga Segal Dept. of Microbiology, Immunology & Genetics

 **Dr. Michael Milyavsky**, Tel Aviv University, Department of Pathology, Sackler School of Medicine

 **Prof. Mordechai Deutsch**, Bar-Ilan University, Physics

 Grant Amount: **NIS 4.2 million**

**The Israel Leukemia Registry: Integration of an AML Clinical Database with Personalized Ex Vivo and In Vivo Validated Single-Cell Characteristics to Improve Prognosis**

This project will advance the understanding of the molecular basis of Acute Myeloid Leukemia (AML), one of the most aggressive blood cancers. The project will establish a national registry of Israeli AML patients, including clinical data as well as genetic and molecular characteristics, and drug responsiveness of patient-derived AML cells. The resulting unique integrated database will be available to attending physicians for the purpose of optimizing AML treatment in a personalized manner.

**4. Prof. Asaf Hellman**, Hebrew University, Department of Developmental Biology and Cancer Research
 **Prof. Benjamin Glaser**, Hadassah Medical Center, Ein Kerem, Endocrinology and Metabolism
 **Prof. Gilad Twig**, Hebrew University, Military Medicine

 Grant Amount: **NIS 5.1 million**

**Evaluating the Risk of Developing Type-2 Diabetes Based on DNA Methylation Signatures at Key Regulatory Elements in Peripheral Whole Blood**

This project will develop an effective, practical protocol for predicting the risk of an individual to develop type 2 diabetes, years before the onset of disease, using novel analysis of DNA modifications in blood cells, developed by Prof. Hellman. The project will make use of a unique cohort of young Israeli adults, made available through collaboration with the Israel Defense Forces Biobank, which includes blood samples that were collected for over three decades, and can now be linked to current medical records, allowing for prospective analyses.

The extensive database and molecular insights generated by this project will be made available to the research community, while strictly protecting donor privacy. It is expected to illuminate mechanisms of disease, to pave the way for improving precision medicine protocols, and to revolutionize the approach to diabetes prevention among young adults.

**5. Prof. Itay Chowers**, Hadassah Medical Center, Ein Kerem, Ophthalmology
 **Prof. Haime Levy**, Hadassah Medical Center, Ein Kerem, Department of Ophthalmology
 **Prof. Amit Meller**, Technion, Biomedical Engineering

 Grant Amount: **NIS 4.7 million**

**Combined Omics and Electronic Medical Records: Big Data for Prediction of Phenotype Sub-Types, Progression, and Treatment Outcome in Age-Related Macular Degeneration**

The research will focus on age-related macular degeneration (AMD), the most common cause of blindness in the developed world. In this research we will utilize comprehensive clinical information from electronic medical charts of thousands of patients, combined with analysis of retinal images, and extensive characterization of the genome and the expression of protein of patients in order to obtain insights to AMD. The research will hopefully enable the identification of factors that are associated with specific phenotypes of AMD, as well as with the response to treatment in the neovascular stage of the disease. Such findings may hopefully significantly improve the understanding and the treatment of AMD.

**6. Dr. Dan Yamin**, Tel Aviv University, Industrial Engineering
 **Dr. Erez Shmueli**, Tel Aviv University, Industrial Engineering

 Grant Amount: **NIS 5 million**

**Big Data Integration for Personalized Diagnosis of Infectious Diseases: Group A Streptococcus Pharyngitis and Influenza**

We will develop a pioneering methodology to substantially improve the diagnosis of two highly common infectious diseases: group A Streptococcal pharyngitis and influenza virus. Our methodology integrates big and rich data from mobile devices and medical records about three critical layers: the individual patient, the general population and the disease dynamics. Outcomes of our study can lead to a breakthrough in the guidelines for detection of the two diseases, and to the establishment of a general framework for computerized decision-support systems for primary care physicians worldwide.

**7. Prof. Yael Mandel-Gutfreund**, Technion-Israel Institute of Technology, Biology

 **Prof. Dana Wolf**, Hadassah Medical Center, Ein Kerem, Clinical Microbiology & Infectious Diseases

 Grant Amount: **NIS 1.5 million**

**A Single-Cell Based Approach to Study Transcriptomic Heterogeneity in Prenatal Clinical Samples from Congenital Human Cytomegalovirus (HCMV) Infections**

Human cytomegalovirus (HCMV) is the most common cause of congenital infection and neurodevelopmental disease worldwide, yet no reliable prenatal markers for disease have been identified. In this research project we will develop and employ a novel single-cell based approach to uncover the unique responses of maternal and fetal cells to HCMV infection, within the authentic tissue complexity of the placenta and in clinical samples from natural congenital infections. We will correlate the observed patterns with congenital HCMV disease outcome, paving the way for prenatal prediction of the risk for congenital HCMV-induced defects in newborns.

**8. Prof. Yael Mardor**, Sheba Medical Center, Advanced Technology Center

 **Prof. Miri Sklar-Levy**, Sheba Medical Center,

 Grant Amount: **NIS 1.5 million**

**Development and Application of Advanced Analysis Platform for MRI-Based Blood Vessel Characterization in Tumor/Benign Breast Tissues for Personalized Patient Management**

During the proposed study we will collect clinical, histological and radiological data, including delayed contrast MRI, from 400 women with breast lesions, to develop an advanced analysis platform for MRI-based blood vessel characterization in abnormal breast tissues. The resulting platform is expected to enable: 1. personalized diagnosis – differentiation between benign and malignant tissues for deciding whether to perform biopsy and to plan biopsies; 2. personalized malignant lesion characterization, such as cancer type and grade; and 3. personalized assessment of response – differentiation of active tumor from treatment-induced effects. In addition, a large, rapidly-growing database of clinical, histological and MRI data of women with breast lesions will be created.

**9.** **Prof. Eran Segal**, Weizmann Institute of Science, Computer Science & Applied Mathematics
 **Prof. Ran Kornowski**, Rabin Medical Center, Department of Cardiology

 Grant Amount: **NIS 6.2 million**

**Predicting Cardiovascular Disease Risk from Personalized Multi-Omic Data**

Prediction of future cardiovascular disease by developing algorithms, based on personalized multi-omic data (microbiome, immune, metabolome), diet and lifestyle using longitudinal follow-up data of participants with high cardiovascular risk.

**10. Prof. Raz Somech, Chaim Sheba Medical Center, Edmond and Lily Safra Children's Hospital,**

 **Pediatric** Department and Pediatric Immunology
 **Dr. Ayal Hendel**, Bar-Ilan University, Mina & Everard Goodman Faculty of Life Sciences
 **Dr. Yu Nee Lee**, Chaim Sheba Medical Center, Immunology

 Grant Amount: **NIS 6.2 million**

**Primary Immunodeficiencies: From Early Diagnosis and Gene Discovery to Personalized Therapy**

Biology and medicine are undergoing a tremendous revolution where the use of advanced technologies, sophisticated bioinformatics and big data, revealing immediate impact on translation to medicine including disease diagnosis, treatment and outcome. Thus, the main objective of this project, that combines clinical and basic scientific skills is to extend our knowledge on pathways controlling human immunity in early life, to increase the number of primary immunodeficiency diseases to be diagnosed early in life, understand new disease patho-mechanisms and to develop a novel and personalized gene-based treatment.

**11. Prof. Roy Kishony**, Technion-Israel Institute of Technology, Faculty of Biology, Faculty of Computer

 Science, Director of the Lorry I. Lokey Interdisciplinary Center for Life Sciences & Engineering

 Grant Amount: **NIS 4 million**

**Personalized Treatment of urinary tract infections with Antibiotics**

The use and misuse of antibiotics, promotes the spread of antibiotic resistance. This issue is of particular importance in urinary tract infections (UTIs) which are among the most common bacterial infections worldwide. While the pathogens causing UTIs are commonly resistant to different antibiotics, treatment is often chosen empirically, in absence of antibiotic susceptibility testing, risking ineffective treatments and adverse outcomes. Using a combined computational-experimental approach we are currently developing algorithms which, based on demographics and clinical data, predict infection-specific profile of resistance, and suggest an optimized personally-tailored treatment accordingly. These algorithms have the potential to reduce mismatched antibiotic treatment, both improving healthcare and helping in the global effort to impede the antibiotic resistance epidemic.

**12. Prof. Hermona Soreq**, Hebrew University, Biological Chemistry
 **Prof. Shahar Arzy**, Hebrew University & Hadassah Medical Center, Ein Kerem, Neurology
 **Prof. Yonatan Loewenstein**, Hebrew University, Neurobiology, Cognitive Sciences and ELSC

 Grant Amount: **NIS 1.5 million**

**Neuronal Hyperactivity in Prodromal Alzheimer’s Disease: Combining Comprehensive Digital Health, Imaging and Biochemical/Molecular Analyses Towards Personalized Diagnosis**

Recent developments in neuroscience and the wish to develop personalized medicine approaches for Alzheimer’s disease (AD) led us to define an alternative approach to AD: instead of memory decline as the major symptom, AD would be described as damaging one’s orientation in space (navigation), time (memory) and social links (personal recognition). This induces over-activation of memory to compensate for the damage, and the symptoms worsen when the compensation system fails. We found supportive evidence for this hypothesis at several complementary levels: brain imaging, brain tissues gene expression analyses and machine learning processing of patients’ data, all at several disease stages. In the planned multi-disciplinary project, we hope to develop novel diagnostic means and deduce better therapeutics by (1) A construction of a personal ‘world’ for each patient; (2) building a digital test for each patient; and (3) deriving therapeutic conclusions at the level of each man and woman patient.

**13. Prof. Tomer Shlomi**, Technion, Computer Science and Biology
 **Prof. Gilad Amiel**, Rambam Health Care Campus, Urology
 **Dr. Itay Maza**, Rambam Health Care Campus, Gastroenterology

 Grant Amount: **NIS 3 million**

 **Towards Population-Wide Cancer Early Diagnosis Via Cost-Effective Metabolomics of Serum Samples**

This project will take advantage of a novel technology for rapid, high-throughput and cheap analysis of multiple metabolite and lipids in serum, towards developing a cancer diagnostic method for the 5 most frequent cancers in Israel: breast, lung, colon, prostate, and bladder cancer. Through a collaboration between researchers and clinicians at the Technion, Rambam Hospital, the Israeli Midgam BioBank, and Clalit Health Services, thousands of samples from healthy controls and cancer patients will be assessed, towards two clinical applications: stratification of patients prior to biopsy, and population-level cancer screening.

**14. Dr. Liran Shlush**, Weizmann Institute of Science, Immunology
 **Prof. Yinon Ben-Neriah**, Hebrew University, Lautenberg Center for Immunology
 **Prof. Amos Tanay**, Weizmann Institute of Science, Computer Science and Applied Mathematics
 **Prof. Ron Shamir**, Tel Aviv University, School of Computer Science

 Grant Amount: **NIS 6.2 million**

**Multi-Dimensional Analysis and the Human Aging Blood System**

The ageing of the blood system is a complex process with overarching implications on the pathogenesis of several age-related diseases. In the current study we aim at improving dramatically our understanding of the aging blood using sensitive molecular techniques to analyze the dynamics of single blood cells among aging individuals. We will combine multidimensional analytical models to process clinical and molecular data and to develop preventive blood aging therapies.