October 18, 2021

PRESS RELEASE

11 RESEARCH PROPOSALS CHOSEN FOR THE THIRD CYCLE OF
THE ISRAEL PRECISION MEDICINE PARTNERSHIP (IPMP)
FEATURING UNPRECEDENTED COLLABORATIONS BETWEEN SCIENTISTS AND CLINICIANS,
ACADEMIC INSTITUTIONS AND HEALTH CARE ORGANIZATIONS

NIS 32 million in grants awarded in the current application cycle;
Total for the first three cycles: NIS 152 million

- **11 research proposals** were selected out of **99 submitted** on a wide range of topics related to human biology as it applies to medicine

- The **Israel Precision Medicine Partnership** (IPMP), launched in summer 2018, enables the expansion of personalized precision medicine research in Israel and supports promising studies that are expected to lead to major breakthroughs in this field

- The winning proposals were selected via a competitive process, based on their scientific excellence, by an international committee chaired by 2006 Nobel laureate in chemistry, **Professor Roger Kornberg**

- Grants for the projects are among the largest ever awarded to Israeli researchers by an Israeli funding body

- Research will lead to a deeper understanding of human diseases and will advance the implementation of new healthcare approaches

- The overall IPMP budget, some **NIS 210 million**, enables funding of **4** application cycles. The duration of each project is up to **4** years.

- IPMP is based on pooling budgetary resources of the Planning and Budgeting Committee (PBC) of the Council of Higher Education (CHE), the Ministry of Health, the National Digital Affairs Directorate - Ministry of Economy, and the philanthropic organizations: Yad Hanadiv and the Klarman Family Foundation (Boston)

- IPMP is operated by the Israel Science Foundation (ISF)

- In the coming months, a call for proposals for the fourth and final cycle will be issued

Professor Yuval Dor, Head of ISF's Life Sciences and Medicine Division: "In IPMP's third program cycle, we once again witnessed a wealth of outstanding research proposals that reflect the depth of science and the spirit of collaboration among researchers and physicians in Israel, and among universities, hospitals, and health funds. The winning proposals come from a variety of universities

and medical institutions, address fundamental questions in human health, and are expected to generate important scientific insights and medical applications."

_____

Research in the field of precision medicine is based on broad interdisciplinary collaborations that integrate scientific and medical knowledge, theory, in-depth analysis of medical big data, and extensive experimental work. The winning research projects utilize data from the Israeli healthcare institutions' tissue banks and unique databases, while protecting patient privacy. Israel holds a considerable relative advantage in this field, given the vast scope and high reliability of these databases.

Following a rigorous evaluation process, the international selection committee, headed by Nobel laureate in chemistry **Prof. Roger Kornberg** of Stanford University, chose the **11** winning research proposals for the third cycle of the IPMP program, awarding approximately **NIS 32 million** in grants. The first of its kind in Israel, IPMP was launched three years ago (summer 2018) with a total budget of approximately **NIS 210 million** to be distributed over the course of **4** cycles. The duration of each study will be up to **4** years.

IPMP: Background and Core Mission

IPMP focuses on achieving in-depth understanding of the mechanisms responsible for variations in disease phenotypes among individuals, and strives to advance innovative research that will lead to novel preventive, diagnostic and therapeutic approaches. Numerous studies conducted in recent years point to the fact that different people suffering from the same disease (such as diabetes, leukemia, breast cancer, Crohn's disease, and others) may have very different disease manifestations, including rate of development, severity, and response to treatment.

This substantial heterogeneity among patients has long been recognized in the medical world, but our understanding of the underlying reasons for this variability is still limited. The lack of scientifically validated data about the key factors influencing inter-individual variation has made it difficult to provide an optimal, personalized care for each and every patient.

IPMP seeks to address these challenges by utilizing a wide range of technologies, by multidisciplinary research teams, including physicians, basic researchers, theoreticians, experimentalists, computational biologists, computer scientists and data scientists, engineers, statisticians, epidemiologists, and others.

The program's funding partners are: **The Planning and Budgeting Committee** (PBC) of the Council of Higher Education (CHE), the **Ministry of Health**, the **National Digital Affairs Directorate** - Ministry of Economy, and two philanthropic organizations: **Yad Hanadiv** and the **Klarman Family Foundation** from the United States. IPMP is operated by the **Israel Science Foundation** (ISF).

The program enables Israeli researchers to advance large-scale research projects in fields of human health, which draw extensively on new collaborations between researchers in Israeli institutions of higher education and healthcare institutions, on populations of healthy and ill volunteers, and on big data repositories in hospitals and HMO databases in Israel.

Collaborations between researchers in universities and healthcare institutions significantly advance research capabilities in the field in Israel, help accelerate the pace of discovery and the potential for implementing new therapeutic approaches, **and position Israel at the forefront of global precision medicine research.**

New Projects Awarded Funding

Below is a list of the 11 selected research proposals, including the researcher names and affiliations, the research topic, and the grant amount (listed alphabetically based upon the Hebrew spelling)**:**

1. **Prof. Arie Admon** (Biology) Technion-Israel Institute of Technology; **Prof. Vivian Drory** (Neurology, Sourasky Medical Center); **Prof. Eran Hornstein** (Molecular Neurobiology and Molecular Genetics, Weizmann Institute of Science); **Prof. Eran Perlson** (Physiology and Pharmacology, Tel Aviv University)

   Grant Amount: **NIS 3.6 million**

   PRIMALS - A Precision Medicine Biomarkers Study in ALS, Based on Pathology-Relevant Signals: PRIMALS is a robust precision medicine program to promote neurodegeneration patho-mechanisms and boost clinical research. PRIMALS endpoints are the discovery and substantiated validation of precision biomarkers for amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). The program builds on research in human models of disease based on stem cell and then in human patient blood samples. The researchers expect disease-specific results and conceptual breakthroughs that can be extended to other pathologies.

2. **Prof. Yonina Eldar** (Electrical Engineering, Weizmann Institute of Science); **Dr. Ahuva Grubstein** (Radiology, Rabin Medical Center)

   Grant Amount: **NIS 3.6 million**

   Improving Sonographic Diagnosis and Monitoring of Breast Cancer and Crohn's Disease Using Artificial Intelligence and Super-Resolution Algorithms: This study aims to pave the way towards a more personalized diagnosis and treatment of breast cancer and Crohn's disease. The researchers use advanced methods such as algorithms, which allow for the visualization of tiny blood vessels in ultrasound imaging, and artificial intelligence.

3. **Dr. Ronen Arbel** (Technology Marketing, Sapir College); **Prof. Martin Ellis** (Blood Bank and the Hematology Institute, Meir Medical Center); **Dr. Joseph Azuri** (Family Medicine,

Maccabi Healthcare Services); **Prof. Yuval Shahar** (Software and Information System Engineering, Ben-Gurion University)

Grant Amount: **NIS 2.8 million**

Personalized Optimization of Medical Therapy for Atrial Fibrillation Patients: This research will use artificial intelligence and data science methods to personalize and optimize treatment for atrial fibrillation, a common cardiac disorder.

4. **Prof. Ittai Ben-Porath** (Developmental Biology and Cancer Research, Institute for Medical Research Israel-Canada, Hebrew University Faculty of Medicine); **Prof. Amir Sonnenblick** (Oncology, Sourasky Medical Center); **Dr. Uri Ben-David** (Human Molecular Genetics & Biochemistry, Tel Aviv University-Faculty of Medicine)

Grant Amount: **NIS 2.2 million**

Characterization and Targeting of Cellular Senescence in Breast Tumors and their Microenvironment: During cancer development, cells often experience a variety of stresses, which can lead them to adopt a form of cell aging termed "senescence." This study dissects how the presence of senescent cells in breast cancer influences disease progression, and tests whether drugs that specifically kill cells in this state can improve disease therapy.

5. **Prof. Michal Lotem** (Oncology, Hadassah Medical Center); **Dr. Jonathan Cohen** (Sharett Institute of Oncology, and the Wohl Institute for Translational Medicine, Hadassah Medical Center and The Faculty of Medicine, Hebrew University of Jerusalem); **Dr. Leeat Keren** (Molecular Cell Biology, Weizmann Institute of Science)

Grant Amount: **NIS 2.8 million**

Unraveling Anatomically-Distinct Tumor-Immune Interactions in Melanoma Metastases by Multiplexed Imaging: Malignant melanoma is a highly lethal neoplasm, with 50% of patients succumbing to metastatic disease within five years of diagnosis. Recently, the important role of the immune system in modulating cancer progression has emerged, leading to the rapid development of cancer immunotherapies. However, biomarkers to guide therapy are lacking. This research will utilize a novel high-dimensional imaging technology (Multiplexed Ion Beam Imaging by Time of Flight) to study the tumor immune microenvironment in dozens of melanoma patients treated at Hadassah Medical Center. The goal is to generate predictive biomarkers, to guide patient-specific selection of therapies from a growing arsenal of cancer-immunotherapies.

6. **Prof. Ephrat Levy-Lahad** (Medical Genetics, Shaare Zedek Medical Center); **Dr. Yuval Tabach** (Developmental Biology and Cancer Research, Hebrew University-Faculty of Medicine); **Dr. Paul Renbaum** (Medical Genetics, Shaare Zedek Medical Center)

Grant Amount: **NIS 2.2 million**

Solving the Unsolved: Integrated Computational and Functional Framework for Optimized Gene Identification and Therapy in Rare Hereditary Diseases: The genetic basis of rare hereditary diseases is often not identified despite significant advances in genomic sequencing and analysis, and there are few specific treatments. This research aims to address these challenges by developing a comprehensive platform, utilizing new methods based on principles of gene co-evolution. This platform will lead to discovery of new disease genes, and facilitate new treatments for rare diseases, using existing drugs approved for other indications (drug repurposing).

7. **Prof. Eran Meshorer** (Genetics, Hebrew University-Edmond J. Safra Campus); **Prof. Nissim Benvenisty** (Genetics, Hebrew University-Edmond J. Safra Campus); **Prof. Shulamit Levenberg** (Biomedical Engineering, Technion); **Prof. Ohad Birk** (Genetics, Ben-Gurion University)

   Grant Amount: **NIS 2.8 million**

   Modeling and Defining Personalized Therapies of Neurological Disorders Using Human Pluripotent Stem Cells: The researchers are developing two-dimensional (neuronal differentiation) and three-dimensional (generation of mini-brain organoids) models for neurological diseases using human pluripotent stem cells. These models will be used for genetic screens and for identifying relevant drugs.

8. **Prof. Nir Friedman** (School of Computer Science and Engineering, Hebrew University-Edmond J. Safra Campus); **Prof. Eithan Galun (**Gene Therapy Institute, Hadassah Medical Center)

   Grant Amount: **NIS 3.6 million**

   Liver Liquid Biopsy: This project takes the team's recently developed minimally-invasive "liquid biopsy" and extends it to address clinical needs, focusing on two liver diseases: Nonalcoholic fatty liver disease (NAFLD) and acute post-transplantation liver rejection. The researchers will recruit patient cohorts and perform detailed molecular analysis of repeated samples of plasma and liver biopsies. They will analyze them using advanced AI methods to determine how information from patients can impact the diagnosis and treatment in these patients.

9. **Prof. Aaron Ciechanover** (Faculty of Medicine, Technion Integrated Cancer Center); **Prof. Michael Elad** (Computer Science, Technion); **Prof. Tsila Zuckerman** (Hematology, Rambam Health Care Campus); **Dr. Yaniv Zohar** (Institute of Pathology Rambam Health Care Campus)

   Grant Amount: **NIS 3.6 million**

Metabolic Nuclear Sequestration of the Proteasome as the Achilles' Heel of Tumor Growth: A Platform for Development of Patient-Specific Management and Treatment Modalities: Cells of all organisms are equipped with a system for degradation of proteins, the ubiquitin-proteasome system (2004 Nobel Prize in Chemistry). One of its numerous functions is to degrade dispensable cellular proteins and provide building blocks for the generation of essential proteins. The researchers found a way to mislead the cells and to inhibit activation of the proteolytic system during starvation stress, which resulted in their death. The effect is selective to malignant cells which have high metabolic rate and are therefore more sensitive for deficiency in essential building blocks compared with their healthy counterparts. As the inhibitory compounds are non-toxic natural dietary components, they can be developed into potential novel cancer therapeutic modalities.

10. **Prof. Ron Kimmel** (Computer Science, Technion)

Grant Amount: **NIS 1.4 million**

Prognosis, Response to Therapy, and Molecular Profiling of Cancer by Computerized Analysis of Digital Cytology and Histology Images: The researcher will explore the use of advanced machine learning image analysis techniques for the exploration of information hidden in histopathology in order to classify the type of hormonal receptors from hematoxilin and eosin staining of the specific type of cancer. The team's early results on tissue micro arrays demonstrate the feasibility to estimate estrogen and progesterone receptors without the need for immunohistochemistry in breast cancer. If successful, the results of the study will allow for personalized optimized treatment, efficiently and accurately.

11. **Dr. Dror Shouval** (Institute of Gastroenterology, Hepatology and Liver Diseases, Schneider Children's Medical Center of Israel); **Dr. Shalev Itzkovitz** (Molecular Cell Biology Weizmann Institute of Science); **Dr. Ruth Scherz-Shouval** (Biomolecular Sciences, Weizmann Institute of Science); **Dr. Henit Yanai** (Gastroenterology, Rabin Medical Center)

Grant Amount: **NIS 2.8 million**

Associating Stromal Cell Signatures with Structural Damage and Clinical Outcomes in Patients with Ulcerative Colitis: Ulcerative colitis is a chronic inflammatory disease of the large intestine that affects millions of people worldwide. The goal of this study is to explore how fibroblasts, the cells which build the connective tissue that provides structure to each organ, contribute to this inflammatory condition and to healing. This study will define signatures of tissue damage at the time of diagnosis of ulcerative colitis, and use these to predict disease complications over time.