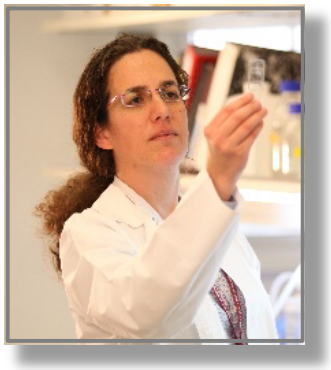
Israel Cancer Research Fund

ICRF Research Grants Newly Awarded in 2021

Newly funded awards as of September 1, 2021.
The 2021-2022 fundraising cycle is in process, and this information will be updated periodically.

Israel Cancer Research Fund

BEVERLEY LIBRACH ABSHEZ INITIATIVE FOR OVARIAN AND FEMALE REPRODUCTIVE SYSTEM CANCERS - awarded $100,000/year for 3 years



Ruth Perets, MD, PhD, Rambam Health Care Campus

A novel, highly-specific mouse model for studying high-grade serous ovarian cancer pathogenesis and prevention

About the Investigator:

Dr. Perets is a physician-scientist and medical oncologist whose work is focused on patients with gynecological malignancies. She received her B. Med., M. Sc., M.D. and Ph.D. degrees from the Hebrew University of Jerusalem and she was a postdoctoral fellow at the Dana-Farber Cancer Institute in Boston, Massachusetts. Dr. Perets is currently a Senior Medical Oncologist and Member of the Clinical Research Institute at Rambam Medical Center and a faculty member at the Technion, the Israel Institute of Technology, in Haifa.

About the Research:

High-grade serous ovarian cancer (HGSC) is the most common subtype of ovarian cancer and one of the most aggressive subtypes. HGSC was long thought to arise in the ovary itself but has recently been shown to arise from epithelial cells in the fallopian tube. This new understanding of the cell of origin has shifted studies of ovarian cancer pathogenesis, prevention and early detection towards a focus on the fallopian tube. In order to study how cells in the fallopian tube undergo transformation from a normal to cancerous state, and to develop robust methods for prevention and early detection of HGSC, it is essential to have good, genetically-engineered mouse models of HGSC that arise from the correct cell of origin and accurately mimic the process of transformation. However, all current mouse models are complicated by the fact that over time, the mice develop not only ovarian cancer, but also other cancers.

The goal of Dr. Perets' research is to develop a new mouse model that overcomes this problem by employing a more specific approach to induce deletion of tumor suppressor genes in fallopian tube cells. Her team will then use this new murine model to test new ovarian cancer prevention methods, which are especially needed by women with BRCA1/2 mutations which predispose to ovarian cancer; and to gain an in-depth understanding of how ovarian cancer initiates in the fallopian tube. This model will enhance pre-clinical testing of new diagnostic and therapeutic approaches for ovarian cancer.

BEVERLEY LIBRACH ABSHEZ INITIATIVE FOR OVARIAN AND FEMALE REPRODUCTIVE SYSTEM CANCERS - $100,000 per year for 3 years

Ziv Shulman, PhD, Weizmann Institute of Science

The physiological role of patient-derived antibodies in ovarian cancer progression

About the Investigator:

Dr. Shulman's research focuses on understanding the mechanism of the immune response, with the goal of developing new ways to improve protective immunity from infectious disease and cancer. He received his BSc degree from the Hebrew University of Jerusalem, his PhD degree from the Weizmann Institute, and he was a postdoctoral fellow at the Rockefeller University in New York City. He is currently a Senior Scientist (equivalent to an Assistant Professor in the US or Canada) in the Department of Immunology at the Weizmann Institute of Science in Rehovot, Israel.

About the Research:

Ovarian cancer is the gynecological malignancy that is most difficult to treat. Patients may be diagnosed at an advanced stage of disease, when current therapies are not as active as they are against early stage disease. While the body mounts a robust immune response to ovarian cancer, efforts to develop therapies based on that response have so far been unsuccessful.

The goal of Dr. Shulman's research is to develop new therapeutic approaches that leverage the robust immune response that occurs in patients with high-grade serous ovarian cancer (HGSC). They examine the antibody immune response against the tumor in order to expose new targets on its surface and new naturally occurring therapeutic antibodies. Dr. Shulman and his team will use mouse models to test whether patient-derived antibodies, generated in high-grade serous ovarian carcinoma (HGSC) tumors, can initiate an effective anti-tumor response. They will characterize that response and the mechanisms that tumor cells may adopt to evade it in order to optimize this approach. This antibody-based biological treatment will provide a much needed novel treatment for fighting ovarian cancer.

Israel Cancer Research Fund

THE LEN & SUSAN MARK INITIATIVE for OVARIAN and UTERINE/MMMT CANCERS - Phase III - awarded $100,000/year for 3 years

Sol Efroni, PhD, Bar-Ilan University

Early detection of ovarian cancer using a blood sample

About the Investigator:

Dr. Efroni studies how the immune response fights cancer. His approach combines biochemical and computational analyses to define how the immune response transitions from a normal to disease state. Dr. Efroni received his BA degree from Tel-Aviv University, his MA degree from the Hebrew University of Jerusalem, and his PhD degree from the Weizmann Institute of Science, and was a postdoctoral fellow at the US National Cancer Institute of the National Institutes of Health in Bethesda, Maryland. He is currently an Associate Professor in the Faculty of Life Sciences at Bar-Ilan University in Ramat Gan, Israel.

About the Research:

Outcomes in ovarian cancer depend on timely diagnosis and access to appropriate surgery and systemic therapy. However, robust screening methods for early detection of ovarian cancer are currently not available. Disease is often diagnosed late, which makes effective treatment more challenging.

The goal of Dr. Efroni's research is to develop a method for early detection of ovarian cancer. The immune response monitors changes in the body, in order to defend against infectious disease and cancer. The immune cells that fight cancer circulate in the blood stream and with careful analysis they can be used to report on a great variety of clinically important conditions. Dr. Efroni proposes to leverage this natural surveillance system to detect ovarian cancer in the earliest stages of development. Starting with a simple blood sample, his team will identify a molecular signature that is the hallmark of disease by analyzing the changes in the expression and sequence of genes critical to the immune response to ovarian cancer. Success in this effort will provide a reliable and much-needed tool for ovarian cancer screening.

Israel Cancer Research Fund

THE LEN & SUSAN MARK INITIATIVE for OVARIAN AND UTERINE/ MMMT CANCERS - Phase III - awarded $100,000/year for 3 years

Keren Levanon, MD, PhD,
Chaim Sheba Medical Center

Predicting and overcoming resistance to first-line chemotherapy in ovarian cancer

About the Investigator:

Dr. Levanon is a physician-scientist and medical oncologist who focuses on patients with gynecological malignancies. She received her B. Med., M.D. and Ph.D. degrees from Tel Aviv University, and she was a postdoctoral fellow at Mass General Hospital and the Dana-Farber Cancer Institute in Boston, Massachusetts. She is currently a Senior Medical Oncologist and Head of the Ovarian Cancer Research Laboratory at Chaim Sheba Medical Center at Tel HaShomer, in Tel Aviv.

About the Research:

About half of patients with advanced-stage ovarian cancer receive a standard chemotherapy regimen coupled with surgery to remove the tumor. Although initial response rates are high, residual disease cells remain and lead to relapse following the initial therapy. The remaining cells are frequently resistant to the drugs used in the first rounds of chemotherapy, and they will not respond to subsequent treatment with the same agents. Very little is known about these drug-resistance mechanisms.

The goal of Dr. Levanon's research is to provide early feedback about the response to treatment that will guide clinical decision-making toward personalized, potentially curative, therapy. Dr. Levanon proposes to define the gene expression programs that correlate with drug resistance, and to seek circulating factors that can distinguish good-responders from poor-responders in blood samples of patients taken over the course of chemotherapy. Taken together, these approaches will generate a clinically-useful tool for prediction of response to front-line treatment in real-time, and will highlight druggable recurrent resistance pathways in ovarian cancer patients.

Israel Cancer Research Fund

THE LEN & SUSAN MARK INITIATIVE for OVARIAN AND UTERINE/ MMMT CANCERS - Phase III - awarded $100,000/year for 3 years

Eylon Yavin, PhD, Hebrew University of Jerusalem

Imaging ovarian cancer by cpFIT-PNAs

About the investigator:

Dr. Yavin's research focuses on the design and synthesis of diagnostic and therapeutic molecules, known as Peptide Nucleic Acids, or "PNAs", that exert their effects by binding to specific nucleic acid sequences in a cell. Dr. Yavin received his BSc degree from the Hebrew University of Jerusalem, his MSc and PhD degrees from the Weizmann Institute of Science, and was a postdoctoral fellow at the California Institute of Technology in Pasadena, California. He is currently an Associate Professor in the School of Pharmacy at the Hebrew University of Jerusalem.

About the Research:

Treatment for ovarian cancer typically involves surgery that removes the ovaries as well as the omentum; a thin fold of abdominal tissue that encases the stomach, large intestine, and other abdominal organs. Surgery is coupled with chemotherapy to kill tumor cells. If surgery is not completely effective, residual tumor tissue that remains may result in relapse. There is an unmet need to develop novel diagnostic approaches for identification of malignant foci during the course of surgery.

The goal of Dr. Yavin's research is to develop an approach that will enable a surgeon to recognize and remove small clusters of ovarian cancer in the course of surgery. Building on his expertise in the chemistry of PNA therapeutics/diagnostics, he proposes to develop a technology that uses a PNA molecular sensor specific for a tumor cell marker (RNA). The PNA lights up upon RNA binding thereby distinguishing tumor from normal cells. His team has already shown that tumor cells can be detected in fresh human surgical samples within minutes of being sprayed with tumor-specific "cpFIT-PNA" probes. Dr. Yavin and his collaborators will now further test this method in a mouse model of ovarian cancer, as a step toward advancing this technology to the clinic for the benefit of ovarian cancer patients.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Naama Barkai, PhD, Weizmann Institute

The Contribution of Histone Chaperone to Nucleosome Exchange within Cells

About the Investigator:

Dr. Barkai's research focuses on revealing general design principles that guide the function and evolution of biochemical circuits in normal and cancer cells. She received her B.Sc. and PhD in Physics from the Hebrew University of Jerusalem and carried out postdoctoral research at Princeton University in the US. She is currently Professor and Chair of the Department of Molecular Genetics at the Weizmann Institute.

About the Research:

Histone chaperones play critical roles in DNA-related processes and genome integrity. Expression of one of these chaperones, FACT, increases in tumor cells, where it correlates with tumor aggressiveness and poor prognosis. Tumor cells are more dependent on FACT than normal cells, and altering FACT levels leads to corresponding changes in oncogene-induced transformation. This makes FACT of interest to cancer research as it may present novel therapeutic potential. The rapid changes that occur in response to FACT regulation have, however, been difficult to study with existing technologies.

Dr. Barkai's laboratory has recently established a novel approach that overcomes this methodological barrier. In this project, she proposes to use this method to follow the consequences of FACT depletion and replenishment on the dynamic interactions of histones throughout the human genome. FACT function will be linked to specific histone interactions by analyzing appropriate mutants, establishing a link between the structure of FACT and its activities that will reveal the mechanistic basis of its action within cells. The results of this research may benefit future drug development efforts that target this oncogenic factor.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Ittai Ben-Porath, PhD, Hebrew University of Jerusalem

Roles of p16 and senescence in the epidermal UV radiation response and early tumorigenesis

About the Investigator:

Dr. Ben-Porath studies the genetic mechanisms that determine tumor growth and metastasis. He received his BSc and PhD from the Hebrew University of Jerusalem, and then carried out postdoctoral research at the MIT Whitehead Institute before joining the Department of Developmental Biology and Cancer Research in the Faculty of Medicine at Hebrew University, where he is now an Associate Professor.

About the Research:

Epidermal tumors are among the most common human cancers. Most of these tumors are caused by exposure to ultra-violet (UV) radiation from the sun. The initial step in tumor development involves excessive cell proliferation and formation of premalignant lesions, which can progress to squamous cell carcinomas. These are highly prevalent tumors, management of which requires surgery and therapy, and some become malignant and deadly.

Dr. Ben-Porath propose a new view of the early formation of these tumors, suggesting that UV light induces the accumulation in exposed regions of epidermal keratinocytes that enter a state termed “senescence”, marked by activity of a protein named p16. Whereas this senescent state blocks the ability of damaged cells to multiply and form tumors themselves, recent work from Dr. Ben-Porath's lab showed that when senescent cells accumulate in the skin they can stimulate the formation of pre-cancerous lesions by secreting factors that cause neighboring cells to proliferate. He now plans to test whether UV-induced senescence in the skin in fact promotes epidermal tumorigenesis. Furthermore, the study will test whether recently identified “senolytic” drugs, which specifically kill senescent cells can eliminate UV-induced senescent keratinocytes and suppress early epidermal cancer. This novel treatment approach may affect disease management of many patients and reduce progression to malignancy.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Benjamin Berman, PhD, Hebrew University of Jerusalem

Tracking DNA methylation loss to understand the origins and evolution of a tumor

About the Investigator:

The goal of Dr. Berman's research is to understand the genomic patterns of DNA methylation and other epigenomic markers that underlie gene regulation in human development and disease. Dr. Berman is a native of Los Angeles who received his BA and PhD at the University of California at Berkeley, then joined the faculty at the University of Southern California and Cedars-Sinai Medical Center, first as Director of Bioinformatics for the USC/Norris Comprehensive Cancer Center Sequencing Core, and subsequently as an independent investigator funded by the US National Cancer Institute. In 2019, he transplanted his lab to the Hebrew University of Jerusalem, where they could take advantage of large existing research programs in DNA methylation and liquid biopsy. Dr. Berman is currently an Associate Professor in the Department of Developmental Biology and Cancer Research at the Faculty of Medicine of Hebrew University of Jerusalem and the Institute for Medical Research Israel-Canada (IMRIC).

About the Research:

Epigenetic changes do not alter DNA sequence but do alter chemical DNA modifications that affect basic cellular processes. Loss of the DNA modification 5-methylcytosine is one of the most widely recognized epigenetic changes in cancer cells, and Dr. Berman's lab recently showed how this process affects cells during normal aging as well. Recent evidence suggests that these epigenetic changes in cancer can not only affect gene expression but also alert immune cells that normally respond to tumors.

Dr. Berman's laboratory has developed analytical tools to analyze methylation patterns from large scale sequencing data from individual patients. They will develop computational tools to use these DNA methylation loss patterns to infer a cancer cell's origin and evolutionary history, taking advantage of new technologies that analyze single cells to identify consequences of methylation loss for expression of genes that promote and prevent cancer. This may lead to identification of new cancer biomarkers and an understanding of which drugs can target cancers that exhibit characteristic methylation patterns. Dr. Berman's lab will devise new tests for detection of these biomarkers in circulating cell-free DNA (sometimes referred to as a "liquid biopsy").

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Rony Dahan, PhD, Weizmann Institute of Science

Dendritic cell targeted agonists for cancer immunotherapy

About the Investigator:

Dr. Dahan studies the mechanisms that control the activity of both natural and therapeutic antibodies. He received his BSc and PhD degrees from the Technion and carried out postdoctoral research at Rockefeller University in New York City. He is currently an Assistant Professor in the Department of Immunology at the Weizmann Institute, where he launched this exciting research project with support from an ICRF Research Career Development Award (RCDA) funded 2018-2021.

About the Research:

The immune response fights cancer, and considerable effort has been devoted to developing strategies that will stimulate immune cells to eliminate tumors from the body. Therapeutic antibodies that stimulate the CD40 receptor on B cells were initially thought to herald the next generation of cancer immunotherapies, with considerable promise for treating hematological malignancies, such as chronic lymphocytic leukemia; and solid tumors, such as pancreatic ductal adenocarcinoma. However, clinical trials showed that toxicity occurred at high antibody doses, and low doses have little effect.

The goal of Dr. Dahan's research is to develop a platform for immunotherapy with CD40 antibodies that bypasses this dose-limiting toxicity. He and his team have successfully engineered novel "bi-specific" antibodies that activate both CD40 and the dendritic cells that attack the tumor. Dr. Dahan now proposes to optimize these first generation bi-specific antibodies so that they effectively enlist the immune response to attack the tumor. The research promises to produce an optimized human antibody for cancer immunotherapy that will enable translation of this approach into the clinic, for treatment of cancers of the blood and solid tissues.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Michael Elkin, PhD,
Hadassah-Hebrew University Medical Center

Metabolic endotoxemia: a new molecular link between obesity and breast cancer

About the Investigator:

Dr. Elkin is an expert in tumor biology, diabetes and diabetic complications. He received his BSc, MSc and PhD degrees from the Hebrew University, and carried out postdoctoral research in the US National Institute of Dental Research of the US National Institutes of Health. He is currently an Associate Professor in the Department of Oncology at the Hadassah Medical Organization and a member of the Faculty of Medicine at the Hebrew University of Jerusalem.

About the Research:

Obese women have a higher risk of bearing breast tumors that are resistant to therapies, and once diagnosed obese women have worse clinical outcomes than their lean counterparts, as cancer is more likely to recur and associated with higher death rates. The estimated global prevalence of obesity in women is approximately 40%, and breast cancer is the most commonly diagnosed cancer in females, making it important to elucidate the mechanistic link between breast cancer and obesity. Obesity is associated with metabolic endotoxemia — the chronic presence of extremely low (but biologically significant) levels of bacterial endotoxin in circulation of obese individuals. However, it is not known whether metabolic endotoxemia is an important determinant of accelerated tumor progression and/or resistance to therapy in obese breast cancer patients.

Dr. Elkin hypothesizes that the continued presence of subclinical levels of bacterial endotoxin enhances the malignant phenotype of breast cancer cells. This may occur both directly and through adverse activation of other cells in the tumor microenvironment and adjacent adipose tissue. His team will test this using newly-established experimental tools, in model systems and primary clinical samples. The anticipated results have the potential to be translated into clinical benefit for breast cancer patients with elevated body weight.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Ayelet Erez, MD, PhD, Weizmann Institute of Science

Preventing cancer cachexia by regulating amino acid metabolism

About the Investigator:

Dr. Erez's research focuses on understanding the contribution of the urea cycle to the metabolic changes that accompany disease pathogenesis, especially of cancer. She received her BSc and MD degrees from the Technion, and after completing a Residency in Pediatrics she obtained a PhD in Cancer Genetics from Tel Aviv University. After postdoctoral and fellowship training in Genetics at Baylor College of Medicine, she joined the faculty at the Weizmann Institute, where she is now an Associate Professor.

About the Research:

Cancer-associated cachexia is evident as ongoing loss of skeletal muscle, with or without loss of fat mass, that cannot be entirely reversed by conventional nutrition support. The onset of cancer-associated cachexia not only decreases the quality of life but also has other negative consequences for a cancer patient, as it increases both the toxicity of chemotherapy and complications from surgeries.

The goal of the proposed research is to understand the mechanism underlying the abnormal homeostatic state in which cachexia begins. In healthy individuals, muscle breakdown leads to flow of amino acids into the liver where excess nitrogen is converted to urea by the urea cycle, for disposal as urea in the urine. Dr. Erez proposes that abnormal cross-talk between the tumor, liver, and muscles occurs in cancer patients, leading to abnormal nitrogen metabolism that contributes to the tumor-induced metabolic alterations characteristic of cachexia. To test this, the initiation and progression of cancer-associated cachexia will first be characterized in mouse models, detailing changes in both metabolism and gene expression. The relevance of these findings to human disease will be evaluated in a retrospective analysis of electronic medical records of cancer patients with and without cachexia. This study may identify new biochemical biomarkers for diagnosing, monitoring, and treating cancer-associated cachexia, which would have profound impact on cancer patients.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Dan Levy, PhD, Ben Gurion University of the Negev

Role of lysine methylation in the regulation of mitotic events under replication stress

About the Investigator:

The major focus of Dr. Levy's research is to elucidate the biological role of lysine methylation in the modulation of intracellular signaling pathways. Dr. Levy received his BSc degree from the Hebrew University of Jerusalem, his MSc from Tel Aviv University, and his PhD in Molecular Genetics from the Weizmann Institute of Science. After postdoctoral research at Stanford, he joined the Department of Microbiology, Immunology and Genetics in the Faculty for Health Sciences of Ben Gurion University of the Negev, where he is now an Associate Professor.

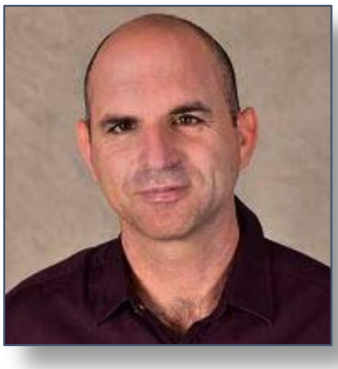
About the Research:

Tumor cells exhibit uncontrolled DNA replication and cell division. Cancer treatment is currently shifting toward personalized approaches in which therapy is based upon understanding of changes that occur in specific cancers. One change that frequently occurs is an increase in activity of the enzyme Aurora-B, which has an essential role in normal cell division.

Dr. Levy's preliminary data suggest that Aurora-B is subjected to a chemical modification (methylation), which could modulate its enzymatic activity and the regulation of cell cycle progression. If so, inhibition of methylation could reduce Aurora-B activity. He and his team will test this possibility. Successful completion of this project will have broad implications for both basic and translational research, as it will provide new understanding of how cancer progresses and identify a novel therapeutic target for therapy in patients with tumors characterized by elevated Aurora-B activity.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years



David Meiri, PhD, Technion

Antitumoral effects of a distinct combination of cannabinoids via the Notch1 pathway in T-ALL

About the Investigator:

Dr. Meiri's laboratory investigates the vast therapeutic potential of naturally-occurring cannabinoids and other bioactive components in various *cannabis* species. He received his BSc and MSc degrees from Tel Aviv University, where he obtained a PhD in Plant Sciences before turning his focus to cancer research as postdoctoral fellow in the University Health Care Network, Canada. He is currently an Assistant Professor of Biology at the Technion.

About the Research:

Cannabis is already being used by cancer patients, primarily as palliative care to alleviate pain and stimulate appetite while preventing nausea and vomiting. Recently, phytocannabinoids, the unique active compounds of the cannabis plant, have been shown to have therapeutic potential, and accumulating pre-clinal and clinical data suggest the right plant components can actually exert antitumoral effects on specific tumors.

The goal of this project is to identify phytocannabinoids active against T-cell acute lymphoblastic leukemia (T-ALL). Dr. Meiri's team has recently identified a specific cannabis extract that kills T cell leukemia cells in which mutation of the Notch1 oncogene promotes cell proliferation, as occurs in more than half of all cases of adult T-AL. Building on those results, they have isolated three unique phytocannabinoid compounds that, when co-administered, synergistically replicate this effect. They now proposed to optimize therapy of T-ALL with these combined phytocannabinoids, by examining the efficacy and safety of treatment. They will also learn how these compounds affect the Notch signaling pathway, which is dysregulated in a number of cancer types, in experiments that will pave the way for the establishment of a new drug therapy for the treatment of Notch-dependent cancers.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Niv Papo, PhD, Ben Gurion University of the Negev

Map ligand binding selectivity landscapes toward engineering target-specific inhibitors

About the Investigator:

Dr. Papo develops high affinity proteins using a combination of experimental and computational methodologies to bind to and antagonize a variety of disease-related targets. He received his BSc and MSc degrees from the Hebrew University of Jerusalem, and his PhD in biochemistry from the Weizmann Institute. He worked on protein engineering as a postdoc at Stanford, and then joined the faculty at Ben Gurion University of the Negev in Beer Sheva, where he is now an Associate Professor.

About the Research:

Matrix Metalloproteinases (MMPs) comprise a large family of enzymes whose abnormal activities have been implicated in cancer progression. Despite extensive efforts, there are currently no clinically approved therapeutic agents that are specific for individual MMPs. Difficulty in generating them are almost certainly due to the similarity in structures of the many enzymes in this large family.

The goal of this project is to engineer novel inhibitors for these well-established chemical targets in cancer therapy. To do so, Dr. Papo and his team will screen large compound libraries for inhibitors that are selective for one or a subset of MMPs, and carry out computational analysis of binding specificity. This analysis will use tools they have developed that make this a one-step, cost-effective process. They will evaluate the ability of these engineered inhibitors to function as MMP antagonists using in vitro, cell-based and pre-clinical studies. Based on these results, they will devise approaches to enhance specificity that make these inhibitors useful in the clinic.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Rina Rosin-Arbesfeld, PhD, Tel Aviv University

Targeting Wnt signaling in hematological malignancies

About the Investigator:

Dr. Rosin-Arbesfeld's research focuses on molecular and biochemical aspects of the Wnt signal transduction pathway. She received her B.Sc., M.Sc. and Ph.D. degrees at Tel Aviv University, and carried out postdoctoral research at Britain's Medical Research Council Laboratory of Molecular Biology in Cambridge, UK. She is currently an Associate Professor in the Department of Clinical Microbiology and Immunology at the Sackler Faculty of Medicine at Tel Aviv University.

About the Research:

Most cancer cells have undergone changes in one or more pathways that signal cells to limit proliferation. One of those most commonly deregulated is the Wnt signaling pathway that enables cells to communicate via well-characterized receptors on the cell surface. Dysregulation of the Wnt pathway is implicated in the pathogenesis of various cancer types, including solid tumors and hematological malignancies. Studies that have connected the expression and function of the Wnt pathway to solid tumors, especially colorectal cancer, have led to development of a number of therapeutics. However, not much is known about how the Wnt signaling pathway functions in the bloodstream. This lack of knowledge limits opportunities to treat hematological malignancies, such as leukemia and lymphoma, using therapeutics targeted to the Wnt pathway.

The goal of Dr. Rosin-Arbesfeld's research is to determine how the Wnt pathway promotes development of hematological malignancies. Her laboratory has demonstrated that mature white blood cells secrete factors critical to Wnt signaling, and that these factors are active in the bloodstream. They propose to investigate the specific class of cells that secrete these factors, to establish how these factors function, and to identify the cells that are affected by them. Successful completion of this project will increase our understanding of how hematological malignancies occur, and will lead to new strategies to treat hematological cancers with Wnt-targeted therapies.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Ruth Scherz-Shouval, PhD,
Weizmann Institute of Science

Dissecting the stromal landscape of colitis-associated cancer

About the Investigator:

Dr. Scherz-Shouval's research focuses on understanding how a cancer cell alters the local environment to support tumor growth. She received her BSc degree from the Hebrew University of Jerusalem, and her PhD in Cell Biology from the Weizmann Institute. After postdoctoral training at the MIT Whitehead Institute, she returned to the Weizmann, where she is now a Senior Scientist and head of an independent laboratory in the Department of Biomolecular Sciences.

About the Research:

For tumors to expand, metastasize, and evade immune surveillance, cancer cells must recruit normal, non-cancerous cells that provide a suitable local neighborhood for cancer cell proliferation. The recruited cells are collectively termed the tumor microenvironment. Cells in the microenvironment are reprogrammed to support the tumor at the expense of its host, and this can cause local inflammation at the site of the tumor. Inflammation, in turn, drives tumor development and can lead to very aggressive disease. This is evident in patients with inflammatory bowel disease (IBD), where chronic inflammation of the colon causes a condition known as "colitis" and puts patients at high risk of developing colitis-associated colon cancer.

The goal of Dr. Scherz-Shouval's research is to learn how to block the pro-tumorigenic factors that are activated by colitis. Many of these factors are produced by a cell type known as fibroblast, which provides the structural support for tissues including the intestines and skin. During inflammation, fibroblasts are activated and they secrete factors that cause local inflammation and stimulate growth of pre-cancerous cells. Dr. Scherz-Shouval and her team will learn how fibroblasts are activated, and identify the changes that they undergo in the process leading from IBD to colon cancer. This will provide a deeper understanding of how tumors develop into systemic malignancies and guide development of new therapies for IBD patients at risk for colitis-associated colon cancer.

Israel Cancer Research Fund

PROJECT GRANT - awarded $60,000/year for 3 years

Joel Yisraeli, PhD, Hebrew University of Jerusalem

Developing a small molecule inhibitor for Igf2bp1 — a novel targeted therapy for lung carcinoma

About the Investigator:

Dr. Yisraeli's group studies the role of RNA binding proteins in helping mediate RNA localization, stability, and translation during development, cell migration, and in different kinds of cancer. He received his BA from Princeton University, his PhD degree in Microbiology from the Hebrew University, and carried out postdoctoral research in Developmental Biology at Harvard University. He is currently an Associate Professor of Developmental Biology and Cancer Biology at the Hebrew University of Jerusalem.

About the Research:

In most tumors, genes that regulate cell division are "dysregulated": genes that stimulate division ("oncogenes") are activated when they should not be. This results in uncontrolled proliferation of the tumor cells. Dysregulation usually occurs as the result of mutations in key oncogenes and tumor suppressor genes. In lung cancer, the KRAS oncogene frequently carries mutations that cause it to promote continued rounds of cell division. In addition, activity of KRAS is further enhanced by a second mechanism. The mRNA that encodes KRAS interacts with an RNA binding protein, Igf2bp1, resulting in increased levels of KRAS and enhanced KRAS activity.

The goal of Dr. Yisraeli's proposal is to develop a new therapy for treatment of lung cancer by inhibiting KRAS and other pro-oncogenic RNAs that are bound by Igf2bp1 in cancer cells. By screening a large library (27,000 compounds), his team identified a lead compound that inhibits binding of KRAS mRNA to Igf2bp1. This destabilizes the mRNA that encodes KRAS, diminishes KRAS protein levels, and inhibits growth of lung adenocarcinoma cells in culture. Additional RNAs, encoding other oncogenic proteins, are also degraded by administration of the compound. He now proposes to develop enhanced, second-generation molecules and test them in pre-clinical mouse models, where they are predicted to inhibit tumor progression and metastasis. This may lead to novel, pharmaceutical-grade precisely targeted compounds that can be used clinically, either as primary or adjuvant therapies for patients suffering from lung carcinoma.

Israel Cancer Research Fund

ACCELERATION GRANT - awarded $70,000/ year for 2 years

Blood Brain Barrier (BBB) disruption by low-pulsed electric fields for antibody delivery to brain metastases

Yael Mardor, PhD
Sheba Medical Center/
Tel Aviv University

Itzik Cooper, PhD
Sheba Medical Center/
Interdisciplinary Center, Herzliya

Shirley Sharabi, PhD
Sheba Medical Center

About the Investigators:

Dr. Mardor, the Principal Investigator, is an expert in Magnetic Resonance Imaging and drug delivery into the brain, with emphasis on brain and brain tumors. She received her BS and MS degrees from Tel Aviv University, and completed her PhD in Nuclear Physics at Tel Aviv University in collaboration with the US Brookhaven National Laboratory. She is currently the Chief Scientist and Head of the Magnetic Resonance Research Group at the Advanced Technology Center of Sheba Medical Center and an Associate Professor at Tel Aviv University Medical School. She is joined on this project by Co-Investigators Itzik Cooper, PhD, of Sheba Medical Center/Interdiscplinary Center, Herzliya; and Shirley Sharabi, PhD, of Sheba Medical Center.

About the Research:

From 15%-35% of breast cancer patients develop brain metastases. Though there are effective treatments for metastatic breast cancer, treating brain metastases has been limited by what is known as the blood-brain barrier (or BBB). This is a natural barrier that prevents both small and large molecules in the bloodstream from entering into the brain. Drs. Mardor, Sharabi and Cooper have worked together to pioneer a safe and non-invasive approach for disrupting the BBB by short, non-invasive, and repeated electrical field treatments, which allows both small and large molecules to enter the brain.

The goal of this research project is to develop a platform that causes transient disruption of the BBB that permits efficient delivery of the antibody Herceptin to the brain. Herceptin specifically targets breast cancer cells that carry high levels of the HER-2 protein on the cell surface. Intravenous administration of Herceptin can control breast cancer that has metastasized essentially anywhere in the body except the brain, where the blood brain barrier inhibits access by Herceptin. Success in the proposed research will provide new hope for breast cancer patients. More generally, the ability to efficiently disrupt the BBB to administer therapeutics may change the treatment paradigm for other cancer patients as well, including those suffering from primary brain tumors and other types of tumors that metastasize to the brain.

Israel Cancer Research Fund

POST-DOCTORAL FELLOWSHIP - awarded $30,000/year for 3 years

Aviad Ben-Shmuel, PhD,
Weizmann Institute of Science

Elucidating the modulation of Natural Killer cells by the cancer stroma

About the Investigator:

Dr. Ben-Shmuel is working to understand how the immune response to a tumor is influenced by the non-cancerous cells that inhabit it. Dr. Ben-Shmuel received his B.Sc. in Biotechnology at Bar-Ilan University, and continued there for graduate research in Molecular Immunology under the supervision of Dr. Mira Barda-Saad. He is currently carrying out postdoctoral training with Dr. Ruth Scherz-Shouval at the Weizmann Institute. As a postdoctoral fellow, Dr. Ben-Shmuel is working to determine how cells that surround a tumor can suppress the immune response to a tumor. His postdoctoral training will provide him with the technical and intellectual expertise necessary to study the complexities of solid tumors and will lay the foundation for a future as an independent researcher.

About the Research:

Most solid tumors are surrounded by non-cancerous cells, which form a region known as the cancer stroma. The non-cancerous cells in the stroma can have profound influences on tumor development. Immune cells usually attack a tumor and limit its growth, but stromal cells are able to suppress that normal immune response.

Dr. Ben-Shmuel is investigating the regulatory role of the cancer stroma on tumor-infiltrating lymphocytes. He is focusing on a class of cells known as Natural Killer (NK) cells, which provide the front line of immune defense against cancer growth and metastases. Identification of the circuits which modulate the function of NK cells will open the door to developing novel therapies that counteract the inhibitory effect of the stroma on the immune response to cancer.

Israel Cancer Research Fund

POST-DOCTORAL FELLOWSHIP - awarded $30,000/year for 3 years

Adi Reches, PhD, Hebrew University of Jerusalem

RNA modification as a regulator of leukemia growth and potential therapeutic target

About the Investigator:

Dr. Reches is interested in understanding the role of RNA-based mechanisms in cellular transformation and utilizing these mechanisms to identify new possible cancer therapies. She received her B.Sc. in Life Science at the Hebrew University of Jerusalem, and continued there for graduate research under the supervision of Dr. Ofer Mandelboim in the Department of Immunology, focusing on how the immune system protects from cancer. She is currently carrying out postdoctoral training with Dr. Daphna Nachmani in the Department of Genetics at the Hebrew University. As a postdoctoral fellow, Dr. Reches is investigating how modification of RNAs critical to protein synthesis affects proliferation of leukemia cells, and whether the modification pathways may provide a new therapeutic target. Her goal is to become an independent researcher, applying the expertise she developed during postdoctoral training to identify molecular pathways that may serve as novel targets for cancer therapy.

About the Research:

Rapid and unregulated proliferation is a hallmark of cancer cells, especially leukemia. To support this rapid proliferation, cells must accelerate synthesis of proteins. Protein synthesis is carried out by complex molecular machines, called ribosomes, which themselves consist of both protein and RNA. Modification of the RNA components of the ribosome occurs in cancer cells, but the pathways that generate the “cancer-ribosome” are not well described.

Dr. Reches is working to identify the modifications in ribosomal RNAs that are key to the rapid proliferation of leukemic cells. She will focus on the pathway that modifies RNA by adding a methyl group (CH_3) to the backbone of RNA molecules, and use cutting-edge techniques to identify the sites of modification and how they change during transition from normal to leukemic cells. She will then ask if leukemic cell proliferation can be controlled by eliminating critical steps in those pathways, with the goal of identifying novel targets for new therapies for leukemia.

Israel Cancer Research Fund

CLINICAL RESEARCH CAREER DEVELOPMENT AWARD (CRCDA) - awarded $49,500/year for 3 years

Amit Tirosh, MD, Sheba Medical Center/ Tel Aviv University

The role of oncometabolites in von Hippel Lindau-related pancreatic cancer

About the Investigator:

Dr. Tirosh is an expert in the genetics of endocrine tumors and their clinical management. He received his MD degree from the Hebrew University of Jerusalem, was a Resident in Internal Medicine and Endocrinology at Assaf-Harofe and Rabin Medical Centers in Israel, and then a Fellow in Genetics of Endocrine Disease and Cancer Bioinformatics at the National Cancer Institute of the US National Institutes of Health. He is currently Head of the Neuroendocrine Oncology Genomics Laboratory at Sheba-Tel HaShomer Hospital and an Associate Professor of Medicine in the Sackler Faculty of Medicine at Tel Aviv University.

About the Research:

von Hippel-Lindau syndrome is a rare disease that causes tumors and cysts to grow in the body, at sites including the brain and spinal cord, kidneys, pancreas, and adrenal glands. The tumors are usually benign (non-cancerous); but, some tumors, such as those in the pancreas and kidney, can become cancerous. von Hippel-Lindau disease is caused by mutations in the *VHL* gene, which normally functions to prevent cells from growing and dividing too rapidly or in an uncontrolled way. This gene normally functions to enable cells to sense levels of oxygen, and cells with a mutant *VHL* gene falsely sense low oxygen levels.

Dramatic changes in the pathways that cells use to metabolize nutrients occur during the development of cancer. These changes can affect both cell growth and the immune response to the tumor. Dr. Tirosh has found that distinct changes in metabolism characterize pancreatic tumors that developed in individuals with von Hippel-Lindau disease, and he has identified a specific small molecule metabolite that may mediate the effects of the *VHL* mutation. Dr. Tirosh hypothesizes that this small molecule is a pro-tumor metabolite, that accelerates tumor proliferation and suppresses the immune response to the tumor in pancreatic cancer patients with VHL. His team will test these hypotheses. If correct, this small molecule is a potential target for treatment of pancreatic cancers (and possibly other cancers) in VHL patients.

Israel Cancer Research Fund

RESEARCH CAREER DEVELOPMENT AWARD (RCDA) - awarded $49,500/year for 3 years

Joshua Grolman, PhD, Technion

The role of extra-cellular matrix plasticity in immune modulation of the tumor microenvironment

About the Investigator:

Dr. Grolman studies the physical properties of the extracellular matrix, focusing on how it regulates cellular morphology to determine function in cancer and the immune response. He received his BS in Biochemistry at the University of Massachusetts at Amherst and his PhD in Materials Science and Engineering at the University of Illinois, Urbana-Champaign. In 2020, following postdoctoral training in Biomedical Engineering at Harvard, he became an Assistant Professor in the Department of Materials Science and Engineering at the Technion.

About the Research:

Mammalian cell morphology is a key determinant of function. It is regulated by cues from the local microenvironment mediated by cell-cell interactions, soluble signaling molecules, and adhesion of receptors on each cell to the extracellular matrix that cushions cells and supports tissues. Many of these properties are interconnected. While cellular mechanics play a major role in all biological processes, techniques currently available to measure force vectors in biological materials and timescales are inadequate.

The goal of Dr. Grolman's research project is to developing new materials that make it possible to measure the forces that cells experience in developing tumors and during the response to immunotherapy. His team tackles these issues by synthesizing novel polymeric architectures and asking how they affect nano-scale stress and strain in 3D, using techniques that include super-resolution live-cell imaging. This will improve understanding of disease states and therapeutic opportunities dependent upon cell and tissue architecture.

Israel Cancer Research Fund

RESEARCH CAREER DEVELOPMENT AWARD (RCDA) - awarded $49,500/year for 3 years

Asaf Madi, PhD, Tel Aviv University

Improving durable response rates following checkpoint blockade therapy

About the Investigator:

Dr. Madi studies the molecular signaling that occurs in the tumor microenvironment in response to immunotherapy and immune cell interactions. He completed his Ph.D. studies at Tel Aviv University in collaboration with the Weizmann Institute of Science in Computational Immunology, where he studied B cell and T cell repertoires. Dr. Madi then continued to do a postdoctoral fellowship at Harvard Medical School, Brigham and Women Hospital and the Broad Institute of Harvard and MIT, Boston, USA where he mainly focused on the study of T-cell differentiation and cancer immunology. In 2018 he joined Tel Aviv University, where he is now an Assistant Professor at the Department of Pathology in the School of Medicine.

About the Research:

Anti-tumor immunotherapy enlists the patient's own immune response to fight cancer. The immune response involves many different cell types, and for the immune system to remember its previous encounters with cancer and with infectious disease a special class of cells, called "memory T cells", must be activated.

The goal of Dr. Madi's proposal is to identify these memory cells at the earliest stage of their development and determine the signals required for their activation. To do so, his team will use advanced technologies and computational methods to examine gene expression in single cells to identify key regulators that are expressed during differentiation from naïve states, when cells do not recognize the tumor; to memory states, when they readily attack the tumor. These studies will reveal potential targets for therapeutic translation.

Israel Cancer Research Fund

RESEARCH CAREER DEVELOPMENT AWARD (RCDA) - awarded $49,500/year for 3 years

Noga Ron-Harel, PhD, Technion

Engaging cellular metabolism to enhance T cell immunotherapy in aged patients

About the Investigator:

Dr. Ron-Harel studies the metabolic regulation of T lymphocytes. She received her BA from the Technion in Chemistry and Biology, and her PhD from the Weizmann Institute in Neuroimmunology. In 2018, after postdoctoral training in Immunometabolism at Harvard Medical School, she returned to the Technion as an Assistant Professor in the Faculty of Biology.

About the Research:

Aged cancer patients are less tolerant to the detrimental side effects of classical therapies than younger patients and could greatly benefit from more specific therapeutic approaches. This is especially the case for immunotherapy, as the immune response may weaken with age. Strikingly, most preclinical and clinical studies do not include aged patients or animals. and the available information on response to immunotherapy in the aged is sparse and mostly retrospective.

Dr. Ron-Harel proposes to investigate cellular and systemic effects of aging on immunotherapy. T lymphocytes play a central role in the immune defense against cancer. Dr. Ron-Harel's previous studies identified metabolic dysfunction in aged T cells and demonstrated that supplementation with deficient metabolites improves T cell activation and survival. This proposal builds on those studies to identify metabolic barriers impairing T cell therapy in the aged. This could lead to the development of novel therapeutic approaches that improve therapeutic outcomes by enhancing the metabolic fitness of aged T cells.

Israel Cancer Research Fund

RESEARCH CAREER DEVELOPMENT AWARD (RCDA) - awarded $49,500/year for 3 years

Efrat Shema, PhD, Weizmann Institute of Science

Deciphering the epigenome of gliomas driven by oncohistones and IDH mutations

About the Investigator:

Dr. Shema's research focuses on understanding human genome regulation by development and application of novel single-molecule-based technologies to visualize the epigenome. She received her BSc degree from the Hebrew University of Jerusalem and her PhD from the Weizmann Institute. In 2017, after postdoctoral training at Massachusetts General Hospital and the Broad Institute of MIT and Harvard, she returned to the Weizmann Institute, where she is now an Assistant Professor in the Department of Biological Regulation.

About the Research:

Malignant gliomas are aggressive tumors of the central nervous system, which are very challenging to treat. Genes are packaged by proteins called histones, which regulate gene activity, and sequencing studies have revealed that many malignant gliomas carry mutations in genes that encode histones, particularly histone H3. Identification of these characteristic histone mutations has made it possible to define clinically specific glioma subtypes, suggesting that the mutant histones drive development of the tumors. However the underlying mechanisms by which these mutations drive disease are currently poorly understood.

The goal of Dr. Shema's research is to identify new drug targets and improve future treatments for glioma patients. To reach this goal, she has recently developed a novel single-molecule technology to study changes in modifications of histones and related proteins that regulate gene expression. Her team will apply this technology to elucidate how alterations in histone H3 create ‘oncohistones’ that may drive development of pediatric glioma, and how recurrent mutations in the IDH protein may drive development of adult glioma. These analyses will yield new data on genome regulation in cancer, and open the way to new therapeutic opportunities.