

2019-2020 AACR RESEARCH GRANT RECIPIENTS



AACR.org/Funding

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for Cancer Research®
FINDING CURES TOGETHER®

CONGRATULATIONS TO THE 2019-2020 GRANT RECIPIENTS

It is the pleasure of the American Association for Cancer Research (AACR) to recognize the newest class of AACR grant recipients. These outstanding scientists have dedicated their careers to advancing the detection, prevention, and treatment of cancer.

Since its inception in 1993, the AACR grants program has seen incredible growth and awarded more than \$114 million in funding to hundreds of scientists. These grants have funded scientists both domestically and abroad at every career stage. Here, we are recognizing 55 outstanding scientists who have devoted their careers to cancer.

It has been yet another spectacular scientific program spanning the continuum from basic, translational, and clinical research to prevention research. The AACR is proud to present our newest class of recipients.

Congratulations to our newest class of recipients!

FUNDERS

The AACR is thankful to our funding partners, whose generosity and ingenuity have been instrumental to the continued success of the grants program, and to our Scientific Advisory and Review Committees for their tremendous work and invaluable expertise in selecting the most meritorious proposals for funding and providing advice on the progress of research projects.



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2019 GRANT RECIPIENTS FELLOWSHIPS



AACR ANNA D. BARKER BASIC CANCER RESEARCH FELLOWSHIP

The AACR Anna D. Barker Basic Cancer Research Fellowship encourages and supports postdoctoral or clinical research fellows to establish a successful career path in any area of basic cancer research.



Chaoyun Pan, PhD

Postdoctoral Fellow

Winship Cancer Institute of Emory University
Atlanta, GA

The role of kinase-mediated inositol metabolism in chemotherapy resistance

BIOGRAPHY

Dr. Pan received his doctorate from Nanjing University, China, in 2016, where he studied how human cytomegalovirus establishes latent infection by regulating human early response genes and reprogramming the immune system. He is currently a postdoctoral fellow in the laboratory of Dr. Sumin Kang at Emory University studying the role of kinases and related metabolic processes in cancer metastasis and chemotherapy resistance.

SCIENTIFIC STATEMENT

Platinum-based chemotherapy such as cisplatin is the front-line treatment against a wide array of solid tumors. Despite initial therapeutic success, development of resistance presents a major challenge. Metabolic reprogramming to maintain redox balance has previously been linked to cisplatin resistance, but the precise mechanisms by which rewired tumor metabolism regulates redox status in cancer cells to provide cisplatin-resistant tumor growth remain unclear. Dr. Pan's preliminary data showed that inositol-trisphosphate 3-kinase B (ITPKB), a key factor in inositol phosphate metabolism, acts as a synthetic lethal target partner for cisplatin treatment through NOX4 inhibition. He hypothesizes that ITPKB and its metabolite IP4 are critical drivers of cisplatin resistance by balancing redox status through NOX4 regulation. He proposes to elucidate the molecular mechanisms by which the ITPKB-NOX4 axis contributes to cisplatin resistance. Additionally, he aims to validate ITPKB as a novel therapeutic target for cisplatin-resistant cancer treatment.

ACKNOWLEDGEMENT OF SUPPORT

I sincerely thank the grant review committee for selecting me as a recipient for the 2019 AACR Anna D. Barker Basic Cancer Research Fellowship. This prestigious fellowship represents an invaluable opportunity to accomplish my proposed research and develop my career in cancer research.

AACR-CANCER RESEARCH UK TRANSATLANTIC FELLOWSHIP

The AACR-Cancer Research UK Transatlantic Fellowship is a four-year postdoctoral fellowship program to support promising early-stage postdoctoral researchers to pursue their projects both in the U.K. and the U.S. It represents a joint effort from the AACR and CRUK to support exceptional investigators interested in beginning their independent postdoctoral research careers.



Geylani Can, PhD

Postdoctoral Fellow

Harvard Medical School
Boston, MA

Regulation of DNA replication in mitosis

BIOGRAPHY

Dr. Can is a postdoctoral fellow in Dr. Johannes Walter's laboratory at Harvard Medical School. He is currently studying the regulation of DNA replication in mitosis. Dr. Can earned his BS in molecular biology and genetics at the Izmir Institute of Technology, Turkey, and completed his MS thesis at the Karolinska Institute, Sweden. He then joined the Gurdon Institute, University of Cambridge, and in 2018, obtained his PhD investigating the roles of DNA damage checkpoint during the cell cycle.

SCIENTIFIC STATEMENT

DNA must be rapidly and accurately duplicated before each cell division. Failure during replication leads to genomic instability which is a major source of many diseases including cancer. Importantly, the duplication of certain 'difficult-to-replicate' loci such as common fragile sites (CFS) is often not completed until mitosis, and this delay can have detrimental consequences. In fact, CFSs are among the most commonly rearranged genomic loci in cancer genomes, highlighting a causal connection between cancer and late DNA replication. It remains unclear how cells mitigate damage associated with late replication in mitosis. By using an unbiased proteomics approach as well as candidate screening, Dr. Can aims to discover new factors that are required for the regulation of DNA replication in mitosis. The newly identified factors will be analyzed biochemically to reveal their roles in genomic rearrangement at CFSs. Understanding the regulation of DNA replication in mitosis may uncover new targets for anticancer therapies.

ACKNOWLEDGEMENT OF SUPPORT

The 2019 AACR-Cancer Research UK Transatlantic Fellowship will be of tremendous help to realize my ambitions at this early stage of my career development. I feel very grateful to have received this prestigious fellowship and the opportunities that open up to me as a consequence. I am excited to pursue my research on DNA replication in mitosis, and I hope that it will allow me to contribute to advances in cancer treatment in the coming years.

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Alejandro Jimenez-Sanchez, PhD

Postdoctoral Research Fellow

Memorial Sloan Kettering Cancer Center
New York, NY

Integrative single cell time-series for tumor microenvironment remodeling

BIOGRAPHY

Dr. Jimenez-Sanchez received his doctorate at the University of Cambridge, where he used genomics approaches to study the microenvironment of ovarian tumors. He detected pervasive heterogeneity in immune infiltrates within patients and found evidence of oncogenic signaling associated with immune exclusion. He then joined Dr. Dana Pe'er's group at the Sloan Kettering Institute in New York, and Professor Charles Swanton's group at the Francis Crick Institute in London, to study tumor spatio-temporal dynamics in response to immune-combination therapies using single-cell genomics computational methods. Dr. Jimenez-Sanchez's aim is to unleash the potential of the immune system to fight cancer.

SCIENTIFIC STATEMENT

Immunotherapy has revolutionized cancer treatment by targeting tumor-immune interactions and providing durable objective responses in advanced metastatic cancers. However, these therapies have only been effective in a subset of cancer types and patients. Thus, strategies to enhance T-cell infiltration and tumor recognition are needed to potentiate immunotherapy. Single-cell genomics makes it possible to disentangle heterotypic cellular interactions in tumors and reveal mechanisms of response to therapies in an unprecedented manner. Dr. Jimenez-Sanchez is using these approaches to characterize the response to a combination of senescence-inducing therapy and anti-PD1 immunotherapy in lung and pancreatic adenocarcinomas. He is developing computational methods that integrate single-cell transcriptome, epigenome, T-cell receptor profiling, and spatial transcriptomics data across space and time. He will model the tumor microenvironment and tumor evolutionary dynamics in response to senescence-inducing and immunotherapy treatments using tractable mouse models and single-cell data from hundreds of human lung and pancreas tumor samples.

ACKNOWLEDGEMENT OF SUPPORT

I am grateful for the support that the AACR-Cancer Research UK Transatlantic Fellowship is providing for my postdoctoral research. This fellowship is allowing me to bring together the expertise of two world leaders of cancer research into this exciting project and it will be critical for my scientific career development.

AACR-CANCER RESEARCH UK TRANSATLANTIC FELLOWSHIP

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Ching Ting (Justin) Loke, BM BCh, PhD

Research Fellow

University of Birmingham
Birmingham, U.K.

Understanding the clonal structure and chemoresistance of ASXL1/RUNX1 AML

BIOGRAPHY

Dr. Loke trained at the University of Cambridge and the University of Oxford Medical School, and then completed postgraduate hematology training in Birmingham, U.K. His interest is in Acute Myeloid Leukemia (AML). Dr. Loke completed his PhD at the University of Birmingham and was awarded a number of prizes for his studies of the epigenetic deregulation of AML with RUNX1 translocations under Professor Constanze Bonifer. Dr. Loke is currently working at the Queen Elizabeth Hospital and the CRUK Clinical Trials Unit in Birmingham, U.K. and is involved in the management of trials involving patients with AML undergoing allogeneic stem cell transplants.

SCIENTIFIC STATEMENT

The major cause of treatment failure in AML is disease relapse. Genomic profiling of AML patients has shown that mutations in ASXL1 commonly co-occur with RUNX1 mutations, which renders these patients at an increased risk of induction failure and relapse. It is unclear as to why the two mutations co-occur and why they are resistant to treatment. Using samples from patients with these mutations, we will identify the clonal structure of the disease at different timepoints of the disease trajectory. We will also develop a new mouse model of this disease to enable identification of mechanisms of collaboration and novel vulnerabilities of this form of AML. As well as advancing our understanding of the basic biology of this disease, this project will potentially have implications on how we monitor patients with these mutations after therapy and how we treat these patients.

ACKNOWLEDGEMENT OF SUPPORT

This fellowship is vital to my development as a clinician scientist with the aim to develop transformative strategies to help patients with AML. This funding scheme is unique in enabling this transatlantic collaboration which will accelerate research in a number of hematology-oncology research centers internationally.

AACR-CANCER RESEARCH UK TRANSATLANTIC FELLOWSHIP

The AACR-Cancer Research UK Transatlantic Fellowship is a four-year postdoctoral fellowship program to support promising early stage postdoctoral researchers to pursue their projects both in the U.K. and the U.S. It represents a joint effort from the AACR and CRUK to support exceptional investigators interested in beginning their independent postdoctoral research careers.



Hadley Elizabeth Sheppard, PhD

Postdoctoral Fellow

The Institute of Cancer Research
London, U.K.

Drugging brachyury in chordoma

BIOGRAPHY

Dr. Sheppard completed her undergraduate education at the University of California, Davis, and received her PhD in genetics and genomics in the laboratory of Dr. Charles Lin at Baylor College of Medicine. During her PhD studies, Dr. Sheppard was part of the team that mapped a super enhancer regulating T (brachyury) in chordoma. With this finding, she investigated the selectivity of transcriptional CDK inhibitors that act via super enhancers to disrupt master transcription factors like brachyury. Dr. Sheppard is looking forward to continuing her postdoctoral work in chordoma from an increasingly translational perspective in the laboratory of Dr. Paul Workman at the Institute of Cancer Research.

SCIENTIFIC STATEMENT

Dr. Sheppard's project aims to drug brachyury and its genetic regulation in chordoma. Chordoma is a rare primary tumor that develops in the skull base and spine and currently has no targeted therapies. Strong evidence supports the hypothesis that chordoma is driven by expression of the T gene, which encodes the protein brachyury. Dr. Sheppard's proposed research in chordoma is reflected in three aims to: 1) investigate the underlying basis of brachyury dependency in chordoma, 2) advance therapeutic targeting of brachyury using clinical grade transcriptional CDK inhibitors, and 3) develop direct small molecule degraders of brachyury. Progress along these thematically linked aims will advance biological understanding of chordoma and accelerate needed targeted therapies towards the clinic.

ACKNOWLEDGEMENT OF SUPPORT

I am thrilled to receive this fellowship as it facilitates my ability to work in the laboratory of Dr. Paul Workman at the Institute of Cancer Research. With this funding, I will conduct impactful chordoma research that will directly benefit patients while enhancing a collaborative chordoma U.K. research network.

CAREER DEVELOPMENT AWARDS



AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant is a funding initiative to stimulate “high-risk, high-reward” research from early- to mid-career investigators. This novel grant mechanism is intended to promote and support creative, paradigm-shifting cancer research that might not be funded through conventional channels and is intended to catalyze significant scientific discoveries to advance our understanding of cancer and have a potentially transformative impact on future clinical practice.



Liron Bar-Peled, PhD

Assistant Professor

Massachusetts General Hospital
Boston, MA

Deciphering the mechanisms of ferroptosis signaling and death in cancer

BIOGRAPHY

Dr. Bar-Peled received his PhD in biology from the Massachusetts Institute of Technology, where he used advanced cellular and molecular techniques to uncover how nutrients are sensed by the mTORC1 pathway in the laboratory of Dr. David Sabatini. In 2013, he joined the laboratory of Dr. Ben Cravatt to understand how cancer cells respond to oxidative stress. Employing novel chemical, proteomic, and biochemical approaches, Dr. Bar-Peled revealed new druggable components of the NRF2 antioxidant response pathway uncovering new mechanisms by which NRF2 regulates metabolic pathways. In early 2019, Dr. Bar-Peled joined the Center for Cancer Research at Massachusetts General Hospital and the Department of Medicine at Harvard Medical School.

SCIENTIFIC STATEMENT

The overarching goal of this project is to illuminate how ferroptosis (FO), a cell death pathway mediated by oxidative stress, is sensed within cancer cells and the mechanisms by which cancer cells succumb to FO. Lipid peroxides represent physiologically important signaling and damaging molecules which at high levels trigger FO. Consequently, there is strong evidence that induction of FO may be a successful therapeutic approach for the treatment of multiple forms of cancer. Despite its profound basic importance and potential clinical benefit, we know surprisingly little about how lipid peroxides signal and induce FO. Here we propose to develop and employ highly innovative proteomic and metabolomic technologies to test the hypothesis that lipid peroxide modification of proteins is a mechanism for signal transduction and promotes FO.

ACKNOWLEDGEMENT OF SUPPORT

It is a tremendous honor to be awarded this prestigious grant. I am emboldened to undertake creative and cutting-edge research to address fundamental biochemical mechanisms by which cancer cells adapt to metabolic stress. The ultimate goal is to translate these basic discoveries into therapeutic insights for cancer patients.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

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Sahand Hormoz, PhD

Assistant Professor

Dana-Farber Cancer Institute
Boston, MA

***Reconstructing the differentiation dynamics
and genealogy of cancer cells***

BIOGRAPHY

Dr. Hormoz obtained his undergraduate degree from the University of Toronto in engineering science. He then completed his MS and PhD in applied physics at Harvard University with Dr. Michael Brenner. His postdoctoral studies were conducted jointly as a theorist at the Kavli Institute of Theoretical Physics at the University of California, Santa Barbara, with Dr. Boris Shraiman and as an experimental systems and synthetic biologist in the laboratory of Dr. Michael Elowitz at Caltech. Dr. Hormoz is currently an assistant professor with the Department of Data Sciences at the Dana-Farber Cancer Institute and the Department of Systems Biology at Harvard Medical School.

SCIENTIFIC STATEMENT

In a subtype of blood cancers called myeloproliferative neoplasms (MPN), intriguingly, the same mutation can result in drastically different disease phenotypes in different patients. This disconnect between genotype and phenotype is partly because the same mutation can have different consequences depending on the identity of the hematopoietic cell in which the mutation first occurs and the extent to which the population of mutated cells expands. We aim to: 1) identify the disease-initiating cancer stem cell and characterize its differentiation dynamics in each patient by sequencing the full transcriptome and the cancer mutations of individual cells, and 2) reconstruct the genealogy of the cancer cells (and infer the history of disease progression) in each patient from the pattern of accrued somatic mutations in individual cancer cells. Our proposal will answer some of the most outstanding and fundamental questions about where MPN originates, and how it manifests itself in each patient.

ACKNOWLEDGEMENT OF SUPPORT

I am thrilled to be a recipient of the AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant and to work closely with the AACR. This award recognizes the importance of innovative research and gives my lab the freedom to tackle fundamental questions in blood cancers using creative and risky approaches that otherwise would not be possible.

INDEPENDENT INVESTIGATOR GRANTS



AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grant represents a joint effort to promote and support innovative research focused on Tumor Treating Fields. This grant is intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Gerben R. Borst, MD, PhD

Clinician Scientist (Assistant Professor)

The Netherlands Cancer Institute
Amsterdam, Netherlands

Uncovering and exploiting interphase effects of Tumor Treating Fields

BIOGRAPHY

Dr. Borst is trained as a radiation oncologist at the Netherlands Cancer Institute. During this training he obtained his PhD and performed a fellowship at the Institute of Cancer Research, London. During this fellowship, he studied the effect of radiotherapy-induced G2 cell cycle arrest abrogation. After his training, Dr. Borst did a postdoctoral fellowship at the Princess Margaret Cancer Centre in Toronto studying the effect of PARP inhibition on radiotherapy outcome. Currently, he is treating patients with primary brain tumors and brain metastasis, and his research group is focusing on combining different modalities to increase the effect of cancer treatment.

SCIENTIFIC STATEMENT

TTFIELDS are low-intensity intermediate-frequency alternating electric fields used to treat cancer patients. Clinical trials demonstrated the effectiveness of TTFIELDS in patients with glioblastoma. It is postulated that TTFIELDS interfere with proper formation of the mitotic spindle, eventually activating the spindle assembly checkpoint (SAC), and triggering apoptosis. More recent data suggest that TTFIELDS may also affect replication fork integrity and inhibition of ionizing radiation-induced DNA damage repair. These observations are cell cycle phase dependent, whereas the impact of TTFIELDS on the cell cycle distribution is not fully elucidated. More research is needed to investigate the underlying mechanism of how TTFIELDS are related to cell cycle changes. This research of the cell cycle effect and connection to the earlier observations is important for developing novel strategies with increased efficacy.

ACKNOWLEDGEMENT OF SUPPORT

The 2019 AACR-Novocure Tumor Treating Fields Research Grant will support us to elucidate the working mechanism of Tumor Treating Fields. This support is of utmost importance to find new ways to increase the efficacy of Tumor Treating Fields and thereby improve treatment outcome of cancer patients.

NEUROENDOCRINE TUMOR RESEARCH FOUNDATION-AACR GRANT

The Neuroendocrine Tumor Research Foundation-AACR Grant represents a joint effort to promote and support innovative cancer research. This grant supports independent junior and senior investigators to develop and study new ideas and innovative approaches that have direct application and relevance to neuroendocrine tumors.



Ali Azhdarinia, PhD

Associate Professor

University of Texas Health Science Center at Houston
Houston, TX

Tumor-specific delivery of temozolomide to overcome resistance in gastroenteropancreatic neuroendocrine tumors

BIOGRAPHY

Dr. Azhdarinia is an associate professor of molecular medicine in the Brown Foundation Institute of Molecular Medicine at the University of Texas Health Science Center. Dr. Azhdarinia received his bachelor's degree in biology from the University of Houston, followed by completion of his master's degree and PhD in pharmacology from the University of Texas Graduate School of Biomedical Sciences. His research training was in the area of contrast agent development with a focus on radiopharmaceutical development. Dr. Azhdarinia's research interests are in utilizing molecular targeting strategies for the detection and treatment of cancer.

SCIENTIFIC STATEMENT

Traditional chemotherapeutics induce systemic toxicities that limit treatment protocols to conservative clinical endpoints instead of seeking long-term tumor regression and cure. Given the goal of maximizing therapeutic index, drug delivery systems have been used to actively target cytotoxics and reduce off-target effects. Image-guided drug delivery is uniquely suited to enhance the therapeutic index of chemotherapy agents based on its intrinsic ability to monitor and quantify drug distribution. To demonstrate the translational feasibility of this approach, the clinical positron emission tomography agent, ⁶⁸Ga-DOTA-TOC, will be used as the foundation for developing a peptide-drug conjugate with the DNA alkylating agent, temozolomide (TMZ). Receptor-mediated TMZ delivery may overcome the effects of neuroendocrine tumor heterogeneity, potentially making it a universal, tumor-specific chemotherapy agent for somatostatin receptor subtype 2-positive tumors. Targeted TMZ delivery may also produce sufficiently high tumor doses capable of overcoming resistance mechanisms in a manner that is not possible with systemic administration.

ACKNOWLEDGEMENT OF SUPPORT

The 2019 Neuroendocrine Tumor Research Foundation-AACR Grant will allow my laboratory to develop a drug delivery approach that uniquely combines clinically proven imaging and therapy moieties into a single agent. The funding critically supports my long-term goal of introducing new precision therapies for patients with neuroendocrine tumors.

TEAM SCIENCE AWARDS



AACR-JOHNSON & JOHNSON LUNG CANCER INNOVATION SCIENCE GRANT

The AACR-Johnson & Johnson Lung Cancer Innovation Science Grant represents a joint effort to address the need for promoting and supporting collaborative cancer research in areas that include digital therapeutics and smoking cessation biomarkers/behavioral phenotyping to bolster our understanding of how lung cancer can be successfully intercepted.



Lead Principal Investigator

Paul M. Cinciripini, PhD

Margaret & Ben Love Chair in Clinical Cancer Care in honor of Dr. Charles A. LeMaistre & Chair Department of Behavioral Science

The University of Texas MD Anderson Cancer Center Houston
Houston, TX



Co-Principal Investigator

Charles Green, PhD

Associate Professor

University of Texas Health Science Center at Houston
Houston, TX

Genetic substrates of a novel neural biomarker for smoking cessation

SCIENTIFIC STATEMENT

We have previously demonstrated that electroencephalogram (EEG) assessment of reward sensitivity can be measured using neural responses associated with natural reward or smoking cues, that low intrinsic reward sensitivity (IRS-) smokers are less likely to quit smoking than those high in intrinsic reward sensitivity (IRS+), and that varenicline offsets this deficit. We have also shown that differences in reward sensitivity relate directly to activity in reward centers in the brain (striatum, dLPFC) and are associated with variation in the *CHRNA3* rs578776 SNP. The present study will extend our previous work by examining genetic correlates of reward sensitivity (IRS+/-) to select markers that previously predicted the IRS construct as well as those related to cessation, withdrawal, and medication response, and then validating this marker set on a prospectively collected sample of smokers. The goal is to develop a genetic proxy for the EEG assessment of reward sensitivity that can be applied easily in the clinical setting.

ACKNOWLEDGEMENT OF SUPPORT

The AACR-Johnson & Johnson Lung Cancer Innovation Science Grant is important to our research program in smoking cessation because it will allow us to leverage nearly 800 existing genetic samples to predict reward sensitivity, validate this marker set on a subsequent prospective sample of smokers, and construct a custom chip that can be used by future scientists to identify the reward sensitivity construct.

AACR-JOHNSON & JOHNSON LUNG CANCER INNOVATION SCIENCE GRANT

The AACR-Johnson & Johnson Lung Cancer Innovation Science Grant represents a joint effort to address the need for promoting and supporting collaborative cancer research in areas that include digital therapeutics and smoking cessation biomarkers/behavioral phenotyping to bolster our understanding of how lung cancer can be successfully intercepted.



Lead Principal Investigator

Mary E. Cooley, PhD, RN, FAAN

Nurse Scientist

Dana-Farber Cancer Institute
Boston, MA



Co-Principal Investigator

Peter Castaldi, MD, MSc

Assistant Professor

Brigham and Women's Hospital
Boston, MA



Co-Principal Investigator

Sun S. Kim, PhD

Associate Professor

University of Massachusetts Boston
Boston, MA

A digitally-enhanced smoking cessation intervention for high-risk smokers

SCIENTIFIC STATEMENT

Lung cancer remains the leading cause of cancer death. Although effective early detection methods are available, uptake remains low. Lung cancer screening in combination with smoking cessation improves mortality above lung cancer screening alone. However, research has focused on integrating smoking cessation interventions into lung cancer screening programs. The primary goal of this study is to leverage digital technology to engage high-risk smokers in an innovative video-phone based smoking cessation program that introduces lung cancer screening as an option to enhance lung health. Efforts are underway to identify high-risk individuals through use of more precise methods such as risk prediction tools and/or genomic analyses to optimize the use of lung cancer screening technology. A secondary goal of this proposal is to gather information about smokers' perceptions of lung cancer risk, their interest in actual receipt of calculated scores, and then the best way to present this information to enhance understanding.

ACKNOWLEDGEMENT OF SUPPORT

This award will allow our research team to combine our complementary skills to test an innovative intervention that seeks to engage high-risk smokers in behaviors that promote lung health, detect lung cancer sooner, and save more lives.

2020 GRANT RECIPIENTS FELLOWSHIPS



AACR-AMGEN FELLOWSHIP IN CLINICAL/TRANSLATIONAL CANCER RESEARCH

The AACR-Amgen Fellowship in Clinical/Translational Cancer Research represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct clinical and/or translational cancer research and to establish a successful career path in this field.



Shanmugapriya Thangavadivel, PhD

Postdoctoral Researcher

The Ohio State University Comprehensive Cancer Center
Columbus, OH

Characterization and elimination of residual CLL following BTKi therapy

BIOGRAPHY

Dr. Thangavadivel obtained her PhD at the Medical University Innsbruck, Austria, in 2016. Her PhD work focused on the chemokine network and autophagy mechanism in multiple myeloma. She then spent a year as a postdoctoral fellow at The Lerner Research Institute, Cleveland Clinic Foundation. In 2017, she joined the Experimental Hematology Laboratory at The Ohio State University. Dr. Thangavadivel is currently working on mutational, epigenetic, and biochemical features of tumor cells along with the surrounding bone marrow microenvironment in chronic lymphocytic leukemia (CLL) patients.

SCIENTIFIC STATEMENT

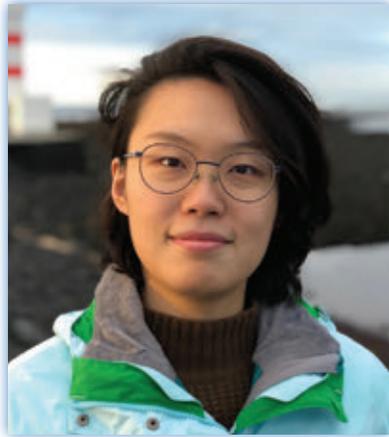
Ibrutinib has been a transformative therapy for CLL. Most patients who achieve complete remission after treatment with ibrutinib have persistent, low-level disease called minimal residual disease (MRD). These residual cells ultimately are responsible for clinical relapse. The aim of this proposal is to study the changes in CLL cells and the microenvironment, which will help develop strategies to target these residual cells. Dr. Thangavadivel proposes to use next generation sequencing methods to identify mutational status and epigenetic changes in CLL cells which will help distinguish specific clones and understand biological differences. Dr. Thangavadivel will investigate the changes in the microenvironment and immune cells to understand how MRD cells have altered signaling pathways that enable these cells to escape the effects of ibrutinib. The availability of sensitive and specific methods to quantify residual disease may allow individualized therapy in the future.

ACKNOWLEDGEMENT OF SUPPORT

I am honored and grateful to receive the 2020 AACR-Amgen Fellowship in Clinical/Translational Cancer Research. This award will support my research to identify new strategies to eliminate minimal residual disease in CLL. This fellowship will also promote my career development as an independent researcher in the field of hematologic malignancies.

AACR ANNA D. BARKER BASIC CANCER RESEARCH FELLOWSHIP

The AACR Anna D. Barker Basic Cancer Research Fellowship encourages and supports postdoctoral or clinical research fellows to establish a successful career path in any area of basic cancer research.



Conghui Yao, PhD

Postdoctoral Research Fellow

Harvard Medical School
Boston, MA

Metabolic regulation of anti-tumor immunity in obesity

BIOGRAPHY

Dr. Yao completed her undergraduate study in chemical biology at Peking University in China. She received her PhD at Washington University in St. Louis, where she studied the cancer cell metabolome using cutting-edge mass spectrometry and advanced bioinformatic analysis. After completing her graduate training, Dr. Yao joined Harvard Medical School as a postdoctoral research fellow under the co-mentorship of immunologist Dr. Arlene Sharpe and cancer biologist Dr. Marcia Haigis. Dr. Yao's research focuses on the metabolic interplay between tumor and immune system. In addition to her enthusiasm for science, Dr. Yao is a big fan of basketball and pop music.

SCIENTIFIC STATEMENT

On average, ~10% of cancer cases in men and ~20% in women are attributed to obesity. As ~70% adults in the United States are considered overweight or obese, understanding the fundamental effects of these conditions on immune response in the context of cancer is crucial. Recent advances in immunotherapies using checkpoint blockade have proven the effectiveness of modulating T cell function to combat cancer. Yet, extensive efforts are needed to elucidate the underlying mechanism and confounding factors in patients. Dr. Yao is interested in studying how obesity reshapes the metabolic environment of tumors and its impact on CD8+ T cell mediated anti-tumor response. In this research proposal, Dr. Yao will combine comprehensive metabolomic profiling with syngeneic mouse tumor models to interrogate the effects of obesity on anti-tumor immunity.

ACKNOWLEDGEMENT OF SUPPORT

I want to thank the review committee for granting me the 2020 AACR Anna D. Barker Basic Cancer Research Fellowship. I am thrilled and honored to have this opportunity to conduct my research in cancer immunology. With the support from this fellowship, I hope that my research will provide new insights in the field of cancer biology and contribute to the development of novel cancer therapies.

AACR-ASTRAZENECA BREAST CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Breast Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct breast cancer research and establish a successful career path in this field.



Monish Ram Makena, PhD

Postdoctoral Research Associate

Johns Hopkins University School of Medicine
Baltimore, MD

A novel mechanism of resistance in receptor positive breast cancer

BIOGRAPHY

Dr. Makena left his family in India and traveled to the United States to pursue impactful research that would benefit patients. His PhD thesis at Texas Tech University investigated the efficacy of novel drug combinations in pediatric cancers. Currently, Dr. Makena is a postdoctoral fellow in the Department of Physiology at the Johns Hopkins School of Medicine, where he is exploring a novel link between calcium signaling and breast cancer. Dr. Makena's research spans immunology, molecular biology, pharmacology, and physiology. Dr. Makena's career goal is to be a translational scientist, and develop novel treatment options to enhance the quality of life of cancer patients.

SCIENTIFIC STATEMENT

Most breast cancers are estrogen receptor positive and treated with targeted endocrine therapy. Unfortunately, many patients develop resistance, and there is an urgent need to better understand underlying mechanisms and identify new targets for treatment. We describe a new role for calcium signaling in maintaining genomic integrity that drives survival and chemotherapy resistance in hormone receptor positive breast cancer. We found that the Secretory Pathway Ca^{2+} -ATPase-2 (SPCA2) has the unusual ability to activate entry of calcium into cancer cells. When calcium entry is blocked, cancer cells accumulate reactive oxygen species, develop breaks in one or both strands of DNA, stop dividing, and die. As a result, cancer cells become more sensitive to drugs that damage DNA. This proposal seeks to understand how SPCA2 regulates the ATM/ATR-p53 DNA damage response pathway, identify the source of reactive oxygen species, and evaluate the effectiveness of drugs that target this pathway.

ACKNOWLEDGEMENT OF SUPPORT

This fellowship boosted my confidence, strengthened my professional credentials, and enhanced my motivation to become a translational scientist. Furthermore, this fellowship will cover my salary, and enable me to attend the AACR Annual Meeting, which is a valuable opportunity for a trainee in cancer research.

AACR-ASTRAZENECA BREAST CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Breast Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct breast cancer research and establish a successful career path in this field.



Naiara Perurena, PhD

Postdoctoral Research Fellow

Brigham and Women's Hospital
Boston, MA

Understanding and combating therapeutic resistance in HER2+ breast cancer

BIOGRAPHY

Dr. Perurena obtained her PharmD from the University of Navarra, Spain, in 2010 after completing an internship at St. George's Hospital in the United Kingdom. She completed her MSc (2011) and PhD (2015) under the supervision of Dr. Fernando Lecanda at the Center for Applied Medical Research, University of Navarra. During her PhD training, she studied molecular mechanisms of metastasis and received a fellowship to join Dr. Mikala Egeblad's laboratory at Cold Spring Harbor Laboratory as a visiting student. Since 2016, Dr. Perurena has been a postdoctoral research fellow in the laboratory of Dr. Karen Cichowski at Brigham and Women's Hospital/Harvard Medical School.

SCIENTIFIC STATEMENT

Resistance to HER2 inhibitors remains a major challenge. Currently, there are no cures for metastatic HER2+ breast cancer. In addition, while many individuals with localized disease initially respond to HER2-directed therapies, a subset of patients with no overt signs of metastasis may still relapse. Therefore, there is an urgent need to 1) understand the mechanisms that underlie resistance to current treatments, 2) identify robust biomarkers of therapeutic resistance, and 3) develop improved, and more importantly, curative therapies. Dr. Perurena aims to define the role of two new tumor and metastasis suppressor RasGAPs in anti-HER2 resistance. The overall goals of the project are to 1) determine how the loss of these proteins precisely promotes resistance to anti-HER2 therapies using in vitro and in vivo models, and 2) identify new targets in these RasGAP-deficient tumors by performing a negative selection CRISPR/Cas9 screen to develop more effective combination therapies.

ACKNOWLEDGEMENT OF SUPPORT

I am truly honored and grateful to be a recipient of the AACR-AstraZeneca Breast Cancer Research Fellowship. This distinction offers me an extraordinary opportunity to address major challenges in breast cancer treatment and will be invaluable for the development of my scientific career.

AACR-ASTRAZENECA CLINICAL IMMUNO-ONCOLOGY RESEARCH TRAINING FELLOWSHIP

The AACR-AstraZeneca Clinical Immuno-oncology Research Training Fellowship Program is designed to encourage exceptional clinical research by bridging close collaboration between academia and industry. Selected clinical researchers will be provided with real-world experience in early-stage and/or late-stage clinical development at the facilities of AstraZeneca in Gaithersburg, MD.



Justin A. Chen, MD

Clinical Fellow

University of California, Davis
Davis, CA

Late-stage clinical development in immuno-oncology

BIOGRAPHY

Dr. Chen obtained his BS in biomedical engineering at the University of California, Davis, graduating with highest honors and departmental awards for research and academic achievement. He then earned his MD at Albert Einstein College of Medicine, and completed internal medicine residency training at Stanford University. Currently, Dr. Chen is a hematology/oncology fellow at the University of California, Davis, and is enrolled in the Mentored Clinical Research Training Program, which grants a MAS degree in clinical research upon completion. His academic interests include immuno-oncology, early phase therapeutics, and applications of next-generation sequencing.

SCIENTIFIC STATEMENT

Research Activities at AstraZeneca

During the research year at AstraZeneca, Dr. Chen will be paired with an AstraZeneca clinical team member who will serve as his mentor, and he will shadow the mentor on their various activities, including meetings with project and study teams. This includes discussions on various topics (e.g., drug development strategy and execution, regulatory strategy implementation, statistics, marketing, clinical operations) with key stakeholders. Research conducted during this year will provide Dr. Chen with the opportunity to gain experience in drug development and understand challenges in late-stage clinical research in immuno-oncology. Additional focus areas may also be provided (e.g., preclinical research, biomarker discovery).

ACKNOWLEDGEMENT OF SUPPORT

I am thrilled and grateful to have been selected for the AACR-AstraZeneca Clinical Immuno-oncology Research Training Fellowship. This award offers me the opportunity to explore clinical trial design and execution from a unique perspective, complementing my prior research experience and further developing my career in investigational immuno-oncology.

AACR-ASTRAZENECA CLINICAL IMMUNO-ONCOLOGY RESEARCH TRAINING FELLOWSHIP

The AACR-AstraZeneca Clinical Immuno-oncology Research Training Fellowship Program is designed to encourage exceptional clinical research by bridging close collaboration between academia and industry. Selected clinical researchers will be provided with real-world experience in early-stage and/or late-stage clinical development at the facilities of AstraZeneca in Gaithersburg, MD.



Nicholas Tschernia, MD

Hematology/Oncology Fellow

The University of North Carolina School of Medicine
Chapel Hill, NC

Early-stage clinical development in immuno-oncology

BIOGRAPHY

Dr. Tschernia is a second-year hematology/oncology fellow at the University of North Carolina at Chapel Hill. He has a background in tumor immunology, which was fostered in the laboratory of Dr. William Murphy at the University of Nevada, Reno, where Dr. Tschernia studied combinations of immune agonists in murine models of melanoma. He went on to complete medical school at the University of Nevada School of Medicine, during which time he participated in the National Institutes of Health - Medical Research Scholars Program (MRSP). The MRSP afforded him the opportunity to work in the laboratory of Dr. Crystal Mackall, where he developed novel Chimeric Antigen Receptor (CAR) T-cell therapies targeting pediatric sarcomas and was involved in the first intent-to-treat Phase 1 study of CARs targeting CD19 in pediatric B-cell ALL. Dr. Tschernia went on to complete his internal medicine residency at the University of Rochester before moving on to his current fellowship at the University of North Carolina. He has a clinical interest in bone marrow transplant and is intent on developing a career centered on bridging the divide between novel cellular therapies in pre-clinical development and the patients who need them.

SCIENTIFIC STATEMENT RESEARCH

Activities at AstraZeneca

During the research year at AstraZeneca, Dr. Tschernia will be paired with an AstraZeneca clinical team member who will serve as his mentor and he will shadow the mentor on their various activities, including meetings with project and study teams. This includes discussions on various topics (e.g., drug development strategy and execution, regulatory strategy implementation, statistics, marketing, clinical operations) with key stakeholders. Research conducted during this year will provide Dr. Tschernia with the opportunity to gain experience in drug development and understand challenges in early-stage clinical research in immuno-oncology. Additional focus areas may also be provided (e.g., preclinical research, biomarker discovery).

ACKNOWLEDGEMENT OF SUPPORT

The 2020 AACR-AstraZeneca Clinical Immuno-oncology Research Training Fellowship represents the ideal synergy between academia and industry, fostering the energy and dedication emboldened within early physician-scientists, and provides the ideal avenue of dedicated training to ensure our success. I am both humbled and overwhelmed with gratitude at this unique career-defining opportunity.

AACR-ASTRAZENECA IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

The AACR-AstraZeneca Immuno-oncology Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct immuno-oncology research and establish a successful career path in this field.



Maria Casanova-Acebes, PhD

Postdoctoral Fellow

Icahn School of Medicine at Mount Sinai
New York, NY

Macrophage determinants of therapy resistance in cancer

BIOGRAPHY

Dr. Casanova-Acebes is a postdoctoral fellow at the Icahn School of Medicine at Mount Sinai in the laboratory of Dr. Miriam Merad. She received her PhD in cellular biology and genetics under the supervision of Dr. Andrés Hidalgo at the Universidad Autónoma de Madrid. Her PhD studies focused on understanding the mechanisms that drive neutrophil aging and how the removal of aged neutrophils triggers the homeostatic release of hematopoietic progenitors from the bone marrow. After a successful PhD, Dr. Casanova-Acebes joined the Merad laboratory in 2015 after being awarded a fellowship from the Human Frontiers Science Program, one of the most prestigious international grants for postdoctoral researchers. Dr. Casanova-Acebes is now studying the contribution of tissue resident and monocyte-derived macrophages in lung adenocarcinoma, and ways to manipulate them to harness anti-tumor immunity.

SCIENTIFIC STATEMENT

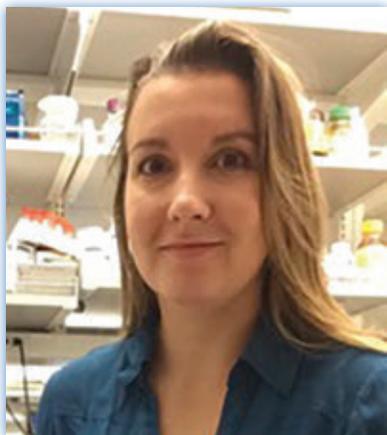
The unprecedented response of advanced lesions to checkpoint blockade has established the definitive role of T cell immunity in NSCLC treatment. Only a small subset of patients responds to PD-1 blockade, and there is now a worldwide effort to understand the mechanisms of response and resistance. The contribution of macrophages to immunotherapy is not yet established, but their critical role in tumor biology makes it highly likely they will influence the response to PD-1 blockade. The goal of this project is to identify novel and relevant macrophage determinants of therapy resistance in lung cancer. By using high dimensional tissue mapping by CyTOF, scRNAseq, and multiplex imaging, Dr. Casanova-Acebes will extensively map human early NSCLC at baseline and in response to PD-1 blockade. This will determine the macrophage composition of NSCLC and elucidate how macrophage subsets influence, and are influenced by, PD-1 immunotherapy. Our studies will also help to identify the molecular program of macrophages that promotes tumor growth and immune evasion.

ACKNOWLEDGEMENT OF SUPPORT

I would like to express my very great appreciation to the AACR for granting me an AACR-AstraZeneca Immuno-oncology Research Fellowship. Receiving this grant will help me identify the macrophage determinants that promote therapy resistance. As a soon-to-be principal investigator, this grant will be pivotal in laying the groundwork for my future career in cancer immunology and starting my independent career in the right direction.

AACR-ASTRAZENECA IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

The AACR-AstraZeneca Immuno-oncology Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct immuno-oncology research and establish a successful career path in this field.



Leah Schmidt, PhD

Postdoctoral Fellow

Fred Hutchinson Cancer Research Center
Seattle, WA

Elucidating effects of the lung tumor microenvironment on T cell therapy

BIOGRAPHY

Dr. Schmidt earned her BSc in biochemistry at McMaster University in Canada, where she studied recombinant vaccines against cancer and HIV in the laboratory of Dr. Jonathan Bramson. She completed her PhD training in biology under the mentorship of Dr. Tyler Jacks at the Massachusetts Institute of Technology, where she researched how natural killer cells influence lung cancer progression and how they can be leveraged therapeutically. Dr. Schmidt is currently conducting her postdoctoral work in the laboratory of Dr. Phil Greenberg at the Fred Hutchinson Cancer Research Center, studying the role of the tumor microenvironment in shaping the outcomes of adoptive T-cell therapies.

SCIENTIFIC STATEMENT

Immune checkpoint therapy (ICT) is a front line treatment for lung adenocarcinoma (LUAD); however, 'non-T cell inflamed' signatures predict poor responses to ICT in ~50% of patients. Adoptive cellular therapy (ACT) with T cells engineered to express T-cell receptors specific for tumor antigens is an approach that circumvents the need for endogenous T-cell responses. ACT against LUAD faces unique hurdles for the safe eradication of disease; a deeper understanding of complex interactions between therapeutic cells and the lung tumor microenvironment (TME) will be crucial for developing successful treatment strategies that enhance function and mitigate toxicity. Dr. Schmidt will leverage physiologically-relevant preclinical models to probe the role of the evolving TME in shaping ACT outcomes, compare these findings to human LUAD analyses, and uncover prognostic markers and combinatorial strategies to safely enhance ACT efficacy against refractory tumors, with the ultimate goal of informing ongoing and future clinical LUAD ACT studies.

ACKNOWLEDGEMENT OF SUPPORT

I am proud and grateful to be an AACR-AstraZeneca Immuno-oncology Research Fellowship recipient. In addition to providing crucial financial support during a pivotal and transformative phase in my scientific career, this award offers equally critical professional opportunities to connect and interact as a member of the cancer immunology community of scientists.

AACR-ASTRAZENECA LUNG CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Lung Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct lung cancer research and establish a successful career path in this field.



Ezequiel Carlos Dantas, MD, PhD

Postdoctoral Fellow

Weill Cornell Medical College
New York, NY

Metabolic regulation of lung cancer cachexia by STAT-3

BIOGRAPHY

Dr. Dantas is a postdoctoral associate at Weill Cornell Medical College under the mentorship of Dr. Marcus Goncalves and Dr. Lewis Cantley. He obtained his MD-PhD from The University of Buenos Aires where he was awarded the summa cum laude distinction for his studies on the regulation of immune function by extracellular acidosis under the supervision of Dr. Jorge Geffner. During his PhD studies, he also characterized the antiviral activity of the Histidine-Rich Glycoprotein, with a particular focus on its effect on HIV-1 infection. In 2017, Dr. Dantas was awarded the prestigious Fulbright Scholarship to study ex-vivo tissue culture techniques at the National Institutes of Health with Dr. Leonid Margolis. In 2019, Dr. Dantas joined Dr. Goncalves and Dr. Cantley to pursue the development of new clinical strategies for the treatment and early detection of cachexia in lung cancer patients.

SCIENTIFIC STATEMENT

The cancer-associated cachexia syndrome (CACS) is a systemic metabolic syndrome featuring body weight loss due to skeletal muscle and white adipose tissue wasting. In non-small cell lung cancer (NSCLC), approximately 50% and 75% of patients with early and advanced-stage disease, respectively, are affected. Despite being a devastating condition both to patients and their families, there is no FDA approved treatment. Preliminary data from our laboratory suggest that in the LKB1/KRAS (KL) model of lung cancer, cachexia is associated with strong activation of STAT-3 in tumor, liver, and muscle. In this project, we propose to identify the cells and cytokines responsible for the onset of this systemic syndrome. Additionally, we have previously described that hypoketonemia is a feature of cachexia in KL mice, but the impact of STAT-3 activation in the metabolic phenotype of CACS remains understudied. We hypothesize that the JAK2/IRAK1 inhibitor pacritinib will be able to ameliorate CACS by modulating inflammation in the tumor microenvironment while also reducing STAT-3 activation in the periphery.

ACKNOWLEDGEMENT OF SUPPORT

I would like to express my most sincere gratitude to the AACR selection committee for selecting my proposal for funding. As an early career scientist, this gives me the opportunity to begin the path towards becoming an independent researcher while doing science to improve the lives of patients. I hope that the results of this project will lead to new therapeutic approaches for a pathology that has none.

AACR-ASTRAZENECA LUNG CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Lung Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct lung cancer research and establish a successful career path in this field.



Shilpa Singh, PhD

Postdoctoral Fellow

Virginia Commonwealth University School of Medicine
Richmond, VA

Novel therapeutic strategy to target lung cancer with p53 mutations

BIOGRAPHY

Dr. Singh completed her B. Pharm. in 2008 from Mumbai University, India. Dr. Singh received her MSc (Pharmaceutical Sciences) in 2012 and her PhD (Biochemistry) in 2018 from Virginia Commonwealth University. Her PhD work focused on investigating contributions of oncogenes (MDM2 and gain of function p53 mutation) in the deregulation of normal or cancer cell proliferation. Currently, she is working on unveiling vulnerabilities of oncogenic mutant p53-driven DNA replication and mitosis in cancer cells in an effort to uncover novel unexplored therapeutic strategies targeting mutant p53-containing lung cancer.

SCIENTIFIC STATEMENT

Tumorigenic p53 mutations termed gain-of-function (GOF) p53 mutations are frequently found in all types of human lung cancers, particularly in solid tumors. As targeting the mutant p53 protein itself presents technical challenges, preventing expression of downstream GOF p53 transcriptional targets that establish GOF p53 dependency may offer powerful avenues in the development of novel precision therapies. Dr. Singh plans to use a uniquely designed reporter system where expression of mCherry/luciferase genes are driven by a specifically engineered promoter responsive only to GOF p53 and not WT p53. Utilizing this system, the goal of the project will be to screen chemical libraries to identify inhibitors of GOF p53-mediated transactivation. The chemicals with the ability to inhibit GOF p53-specific transcription will then be used to study the impact on growth and survival of lung cancer cells expressing GOF p53 in in vitro and in vivo assays.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to receive the AACR-AstraZeneca Lung Cancer Research Fellowship. This fellowship will support a project that utilizes the novel observation of dependence of lung cancer cells on endogenously expressing GOF p53 and thus would allow targeting of many lung cancer patients who have cancers with GOF p53.

AACR-ASTRAZENECA LYMPHOMA RESEARCH FELLOWSHIP

The AACR-AstraZeneca Lymphoma Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct lymphoma research and establish a successful career path in this field.



Zachary Epstein-Peterson, MD

Medical Oncology Fellow

Memorial Sloan Kettering Cancer Center
New York, NY

Oncogenic mechanisms and therapeutic targeting of IDH2 mutations in AITL

BIOGRAPHY

Dr. Epstein-Peterson is a medical oncology fellow at Memorial Sloan Kettering Cancer Center conducting clinical-translational research in the laboratory of Dr. Andrew Intlekofer. Dr. Epstein-Peterson aims to define and target metabolic pathways in lymphoma with a focus on angioimmunoblastic T-cell lymphoma, a rare and aggressive subtype of non-Hodgkin lymphoma. Additionally, his clinical focus, mentored by Dr. Steven Horwitz, is in the care of patients with T-cell and cutaneous lymphomas. Dr. Epstein-Peterson received his BA in classics from the Johns Hopkins University and his MD from Harvard Medical School. He completed his internal medicine residency at NewYork-Presbyterian Weill Cornell Medical Center followed by chief residency at Memorial Sloan Kettering Cancer Center.

SCIENTIFIC STATEMENT

Peripheral T-cell lymphomas (PTCL) are a heterogeneous group of aggressive malignancies that comprise ~10-15% of non-Hodgkin lymphoma (NHL). In contrast to B-cell NHL, the biology of PTCL remains poorly understood and outcomes are poor, with 5-year overall survival rates of less than 30% in response to standard therapies. Angioimmunoblastic T-cell lymphoma (AITL), one of the most common subtypes of PTCL, exhibits recurrent somatic mutations at arginine 172 (R172) of the metabolic enzyme isocitrate dehydrogenase 2 (IDH2) in 20-30% of patients. Cancer-associated IDH2 R172 mutations produce high levels of the oncometabolite 2-hydroxyglutarate (2HG), which disrupts gene expression programs and blocks normal T-cell differentiation. We hypothesize that targeted inhibition of mutant IDH2 may offer an effective new therapeutic strategy to treat IDH2-mutant AITL. To test this hypothesis, we will pursue a series of investigations using primary patient samples and patient-derived xenografts. These studies will pave the way for the clinical development of mutant IDH2 inhibitors in AITL with the ultimate goal of improving outcomes for patients.

ACKNOWLEDGEMENT OF SUPPORT

I am deeply humbled and honored to receive funding through the 2020 AACR-AstraZeneca Lymphoma Research Fellowship. This fellowship will enable us to pursue investigations that we hope will better define basic disease biology and ultimately translate into better outcomes for patients with T-cell lymphomas. Personally, the fellowship will allow me to develop critical skills as a translational researcher as I transition from fellow to independent faculty investigator.

AACR-ASTRAZENECA LYMPHOMA RESEARCH FELLOWSHIP

The AACR-AstraZeneca Lymphoma Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct lymphoma research and establish a successful career path in this field.



Timothy J. Voorhees, MD

Hematology and Oncology Fellow

The University of North Carolina School of Medicine
Chapel Hill, NC

Pilot study of anti-PD-1 therapy following CD30 directed CAR-T cell therapy

BIOGRAPHY

Dr. Voorhees graduated from the University of Michigan with a BSc in cellular and molecular biology. He completed his medical school and internal medicine training at The Ohio State University Wexner Medical Center. Dr. Voorhees is currently completing his hematology and oncology fellowship at the University of North Carolina. He has been supported by the UNC-Duke Immunotherapy T32 and has been the recipient of several clinical and research achievement awards during his fellowship. His research is mentored by Dr. Jonathan Serody, Director Bone Marrow Transplant and Cellular Therapy, and he is clinically mentored by Dr. Anne Beaven, Lymphoma Program Director.

SCIENTIFIC STATEMENT

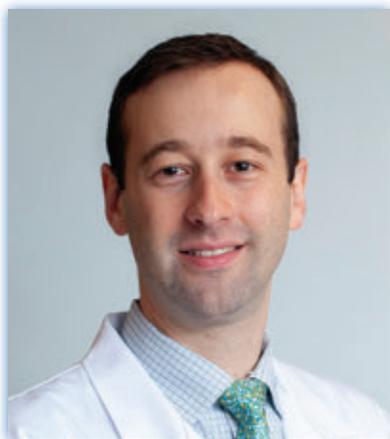
Hodgkin Lymphoma is a B-cell malignancy characterized by CD30+ multinucleated Reed-Sternberg cells within an extensive, ineffective immune infiltrate. Our institution has experience with administering autologous CD30 directed chimeric antigen receptor T-cells (CD30.CAR-T) to patients with relapsed or refractory Hodgkin Lymphoma. While clinical response rates to CD30.CAR-T therapy are high, some patients have developed recurrent disease. In those with Hodgkin Lymphoma recurrence after CD30.CAR-T therapy, we have observed a surprisingly high clinical response rate with re-challenge of anti-PD-1 therapy. The proposed research is a prospective pilot study to determine the clinical activity and immunomodulatory effect of anti-PD-1 therapy in patients with relapsed Hodgkin Lymphoma after CD30.CAR-T therapy. All patients will have prior anti-PD-1 exposure before CAR-T therapy. Positive clinical response and/or strong immunomodulatory effects would provide rationale for combining CD30.CAR-T therapy and anti-PD-1 therapy sequentially in a future prospective trial.

ACKNOWLEDGEMENT OF SUPPORT

I am very honored to be awarded the 2020 AACR-AstraZeneca Lymphoma Research Fellowship. This award will provide essential support to complete my research focusing on anti-PD-1 therapy after CD30.CAR-T therapy in Hodgkin Lymphoma and will provide a strong foundation as I transition from a fellow to an independent investigator.

AACR-BRISTOL MYERS SQUIBB IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

The AACR-Bristol Myers Squibb Immuno-oncology Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct immuno-oncology research and establish a successful career path in this field.



Chris Nabel, MD, PhD

Postdoctoral Fellow

Massachusetts Institute of Technology's
Koch Institute for Integrative Cancer Research
Cambridge, MA

Metabolic and immune profiling of kras-subsets in lung adenocarcinoma

BIOGRAPHY

Dr. Nabel obtained his MD and PhD in cell and molecular biology at the University of Pennsylvania studying APOBEC enzymology in the laboratory of Dr. Rahul Kohli. He completed internal medicine training at Brigham and Women's Hospital and is a medical oncology fellow at the Massachusetts General Hospital Cancer Center, where he sees patients with the Center for Thoracic Cancers. Dr. Nabel is a postdoctoral fellow in the laboratory of Dr. Matthew Vander Heiden at Massachusetts Institute of Technology's Koch Institute for Integrative Cancer Research, where he studies the metabolic basis of lung cancer biology and cancer cell proliferation.

SCIENTIFIC STATEMENT

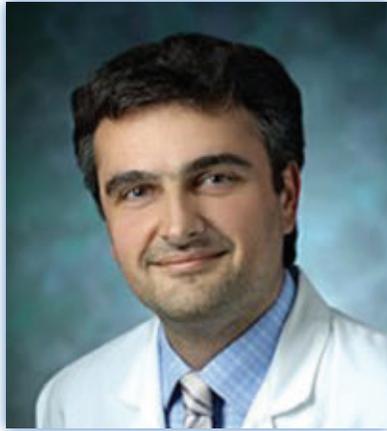
Treatment options for patients with lung adenocarcinoma have improved in recent years, but unfortunately these advances have not benefited patients with KRAS-driven adenocarcinoma. Patients with combined mutations in KRAS and STK11/LKB1 (KL) have among the worst overall survival even when compared to other KRAS-subsets such as KRAS and TP53 (KP). LKB1 is a serine-threonine kinase with numerous targets, including the energy sensor AMPK and influences cell metabolism. To explore the consequences of LKB1-mutation on the metabolic and immune components of the tumor microenvironment, Dr. Nabel and colleagues will use mass spectrometry-based methods to quantify absolute metabolite levels in the tumor interstitial fluid of KP and KL mouse tumors to study the effects of these metabolic changes on cancer cell proliferation and immunologic activation. Using Multiplex Fluorescence Immunohistochemistry, they will further evaluate differing immune cell populations in human patient tumor samples with KP and KL mutations.

ACKNOWLEDGEMENT OF SUPPORT

I am greatly appreciative for the 2020 AACR-Bristol Myers Squibb Immuno-oncology Research Fellowship. As a medical oncologist-in-training, I am dedicated to a career leading an independent basic science research group that will improve treatments for cancer patients through discovery. This fellowship allows me to bridge the gap between trainee and independent investigator.

AACR-CONQUER CANCER FOUNDATION OF ASCO YOUNG INVESTIGATOR AWARD FOR TRANSLATIONAL CANCER RESEARCH

The AACR-Conquer Cancer Foundation of ASCO Young Investigator Award for Translational Cancer Research provides funding to physician-scientists to encourage and promote quality research in clinical oncology.



Dimitrios Mathios, MD

Resident

The Johns Hopkins University School of Medicine
Baltimore, MD

Cell-free DNA analyses for early detection of brain tumors

BIOGRAPHY

Dr. Mathios received his medical degree from Athens Medical School in Greece and then joined the Johns Hopkins Neurosurgery Department as a postdoctoral fellow with primary focus in cancer immunotherapy and cancer genetics. He entered the neurosurgery residency program at Johns Hopkins in 2014 and is currently a 5th year resident. Dr. Mathios has a strong interest in neuro-oncology and is focusing his two year research fellowship on efforts to non-invasively diagnose patients with brain tumors via liquid biopsy approaches under the mentorship of Dr. Victor Velculescu at Johns Hopkins Kimmel Cancer Center.

SCIENTIFIC STATEMENT

Early detection of patients with brain tumors has the potential to increase survival and improve quality of life. Additionally, noninvasive disease monitoring via plasma-based liquid biopsy approaches during the course of treatment obviates the need for risky, invasive procedures, which are routinely performed for the sole purpose of assessing treatment response. However, attempts to develop a plasma-based liquid biopsy assay for brain tumors have largely failed. This work proposes to use a new approach that combines genetic and epigenetic features of circulating tumor DNA and utilizes a machine learning approach to distinguish patients with brain tumors from disease free individuals.

ACKNOWLEDGEMENT OF SUPPORT

This award recognizes the major challenges that brain tumor patients face daily during their treatment and provides the necessary support towards development of a liquid biopsy approach for earlier and less invasive diagnosis of brain tumors. With the generous support of AACR-Conquer Cancer Foundation of ASCO, I will be able to explore my research interests and set the basis for my future physician-scientist career.

AACR-GENENTECH CANCER DISPARITIES RESEARCH FELLOWSHIP

The AACR-Genentech Cancer Disparities Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct cancer disparities research and establish a successful career path in this field.



Tyler A. Allen, PhD

Postdoctoral Associate

Duke Cancer Institute
Durham, NC

Interrogating ancestry-related alternative splicing variation in metastasis

BIOGRAPHY

Dr. Allen is a molecular and cell biologist and cancer health disparities researcher with expertise in cancer metastasis. He is a postdoctoral fellow in the Patierno/Freedman/George laboratory in the Duke Cancer Institute, and his work focuses on understanding the role of alternative RNA-splicing in metastasis. He earned his PhD from the College of Veterinary Medicine in Comparative Biomedical Sciences at North Carolina State University, where he was an NCI predoctoral fellow. Dr. Allen holds BS degrees in biology and plant biology, also from North Carolina State University.

SCIENTIFIC STATEMENT

Prostate cancer (PCa) is the most frequently diagnosed solid malignancy in men. Epidemiological studies have shown African-American men to be at higher risk for developing prostate cancer and experience a higher death rate as compared to other ethnic groups. In patients with PCa, metastasis cases remain the leading cause of death, yet the underlying mechanisms of metastasis remain poorly understood. Accumulating studies suggest alternative RNA-splicing (ARS) plays a critical role in metastasis, warranting further investigation into this field. Dr. Allen hypothesizes that metastatic PCa cells use ARS during the metastasis process, enabling them to travel successfully and seed secondary sites. Additionally, he hypothesizes that differences in race-related ARS contribute to disparities in prostate cancer metastasis and mortality rates. To test this hypothesis, patient-matched primary and metastatic PCa tissue will be molecularly interrogated for ARS variation between the primary and secondary tumor sites. Tissues from equal numbers of patients of African or European ancestry will be analyzed to determine ancestry-related ARS differences between primary and metastatic tissue.

ACKNOWLEDGEMENT OF SUPPORT

It is an honor to be selected for the AACR-Genentech Cancer Disparities Research Fellowship. This fellowship supports a study with significant impact on not only health disparities, but also the molecular understanding of the metastasis process. I am thankful for the award and look forward to helping advance the field with the support of AACR and Genentech.

AACR-GENENTECH CANCER DISPARITIES RESEARCH FELLOWSHIP

The AACR-Genentech Cancer Disparities Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct cancer disparities research and establish a successful career path in this field.



Rania Bassiouni, PhD

Postdoctoral Scholar Research Associate

University of Southern California
Los Angeles, CA

Alpha-catenin loss contributes to racial disparity in breast cancer

BIOGRAPHY

Dr. Bassiouni is a translational cancer researcher with an interest in integration of genomic and molecular techniques to interrogate and reduce cancer health disparities. She is a postdoctoral scientist at the University of Southern California working under the mentorship of Dr. John Carpten. Her research focuses on elucidating molecular mechanisms underlying aggressive triple-negative breast cancer in African-American patients, and defining therapeutic opportunities to reverse this disparity. Previously, Dr. Bassiouni received her PhD in biomedical sciences from the University of Central Florida, where she trained in cancer biology and pre-clinical therapeutic development.

SCIENTIFIC STATEMENT

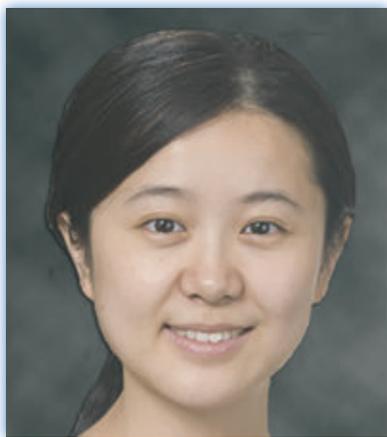
Triple-negative breast cancer (TNBC) is recognized as an aggressive, treatment-resistant, and poor-prognosis disease. For reasons not well understood, African-American (AA) women are disproportionately affected by TNBC, with higher rates of incidence and mortality than Caucasian women. In an effort to distinguish biological factors that contribute to this disparity, Dr. Bassiouni has identified loss of the tumor suppressor alpha-catenin to be associated with poor survival of AA TNBC patients. Dr. Bassiouni's study will utilize a racially-diverse panel of patient-derived tissues to model and study alpha-catenin loss in TNBC. The study will examine the molecular and cellular consequences of alpha-catenin loss that could contribute to aggressive disease, as well as whether the resulting phenotype presents therapeutic opportunities for treatment of AA TNBC.

ACKNOWLEDGEMENT OF SUPPORT

I am greatly honored to be awarded the 2020 AACR-Genentech Cancer Disparities Research Fellowship. With this support, I aim to advance our understanding of cancer health disparities and to ultimately benefit patients disproportionately burdened by disease.

AACR-GENENTECH IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

The AACR-Genentech Immuno-oncology Research Training Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct immuno-oncology research and establish a successful career path in this field.



Wei Wang, PhD

Postdoctoral Fellow

University of Wisconsin Carbone Cancer Center
Madison, WI

Mechanism of immunosuppression in papillomavirus induced neoplastic disease

BIOGRAPHY

Dr. Wang earned her bachelor's degree in 2011 from Huazhong University of Science and Technology in China. She graduated from the Cellular and Molecular Pathology program at the University of Wisconsin-Madison in 2016. Dr. Wang's PhD work under the mentorship of Dr. Paul Sondel focused on the role of natural killer (NK) cells in antibody-based immunotherapies. Her past work suggested that NK cell receptor variations between patients could potentially serve as new biomarkers for patients' response to Rituximab, Dinutuximab, and IL2 therapies for neuroblastoma, follicular lymphoma, and renal cell carcinoma respectively. Dr. Wang joined Dr. Paul Lambert's laboratory in 2018 as a postdoctoral trainee and since then has been working on the role of stress keratin 17 in host immune response using mouse papillomavirus (MmuPV1) as a model. Her recent work demonstrated that K17 expression was critical for papilloma persistence in a T cell-dependent manner, and that the lack of K17 in mice led to significantly increased CD8+ T cell infiltration.

SCIENTIFIC STATEMENT

Dr. Wang's current research focuses on understanding how papillomavirus evades the host immune response to establish persistent infection. Her recent work indicated that stress keratin 17 is a key regulator to prevent T cell infiltration in mouse papillomavirus-induced lesions. Dr. Wang's proposed research will address the molecular mechanisms underlying the K17 expression and T cell infiltration, using mouse papillomavirus, MmuPV1, as a model. Interestingly, stress keratin 17 has been found upregulated in a variety of human squamous cell carcinomas, not just limited to HPV+ cancers. Her current and proposed work will also be expanded to other types of cancers to understand the role of stress keratin 17 and immune regulation. The insights gained from these studies may lead to discovery of potentially targetable pathways to improve T cell infiltration and efficacy of existing immunotherapies.

ACKNOWLEDGEMENT OF SUPPORT

The 2020 AACR-Genentech Immuno-oncology Research Fellowship will support my proposed study of investigating mechanisms of immune response regulation by K17 in cancer and help me transition to an independent researcher with the goal of applying what I learn from this study to improve current immunotherapy efficacy.

AACR-INCYTE IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

The AACR-Incyte Immuno-oncology Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct immuno-oncology research and establish a successful career path in this field.



Nicoletta Cieri, MD, PhD

Postdoctoral Fellow

Dana-Farber Cancer Institute
Boston, MA

Addressing AML with vaccine-induced polyclonal leukemia-specific T cells

BIOGRAPHY

Dr. Cieri attended medical school at San Raffaele University in Italy, where she also obtained her PhD. With Dr. Chiara Bonini as her mentor, she focused on dissecting the impact of T-cell state and function in adoptive immune-gene therapy approaches as well as allogeneic hematopoietic stem cell transplantation (allo-HSCT) for leukemias. Dr. Cieri then moved back to the clinic and completed hematology residency at Milan University in Italy. She joined Dr. Catherine Wu's laboratory at the Dana-Farber Cancer Institute in 2019, where she is studying the complex interplay between T cells and leukemia upon allo-HSCT.

SCIENTIFIC STATEMENT

Relapse from acute myeloid leukemia (AML) after allo-HSCT remains an unmet clinical challenge. AML recurrence after transplant is the leading cause of mortality, with limited and unsatisfactory post-relapse treatment options. With this project, Dr. Cieri aims to devise an immunotherapeutic strategy centered on potentiating the beneficial graft-versus-leukemia effect of donor-derived T cells in the context of allo-HSCT. The study combines AML vaccination as a means to in vivo prime donor T cells against leukemic antigens, with in silico prediction of AML neoepitopes and ex vivo T-cell expansion, using novel cutting-edge biomaterials, and subsequent adoptive transfer of AML-reactive T cells. The successful completion of this study is expected to provide the groundwork for a new strategy to treat AML by targeting multiple patient-specific mutations through the adoptive transfer of therapeutic T cells providing long-term immune surveillance against disease recurrence.

ACKNOWLEDGEMENT OF SUPPORT

I am humbled and thrilled to have been selected as a recipient of the 2020 AACR-Incyte Immuno-oncology Research Fellowship. This invaluable support and recognition represents a key milestone in my career development as a physician-scientist, and I am truly committed to the development of innovative immunotherapeutic approaches for cancer.

AACR-OCULAR MELANOMA FOUNDATION FELLOWSHIP, *in honor of Robert C. Allen, MD*

The AACR-Ocular Melanoma Foundation Fellowship, in honor of Robert C. Allen, MD, represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct ocular/uveal melanoma research and establish a successful career path in ophthalmology, ocular oncology, uveal melanoma biology, or a similar field.



Anna Han, PhD

Postdoctoral Fellow

Thomas Jefferson University
Philadelphia, PA

Targeting metabolism as a therapeutic approach in uveal melanoma

BIOGRAPHY

Dr. Han received her PhD at the University of Tennessee, Knoxville, where she built her research career in cancer metabolism. She commenced post-doctoral training in 2017 at the Sidney Kimmel Cancer Center at Thomas Jefferson University under the supervision of Dr. Andrew Aplin. Her research interests include 1) understanding of specific metabolic characteristics of uveal melanoma (UM), 2) investigating the metabolic functions of BRCA1-associated protein 1 (BAP1) in UM, 3) the correlation between metabolism and dormancy in UM, and 4) targeting mechanisms of intrinsic resistance to targeted therapies in UM.

SCIENTIFIC STATEMENT

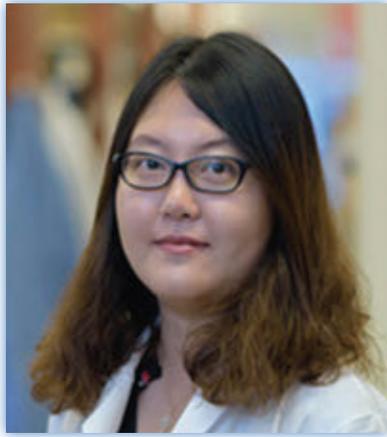
Uveal melanoma (UM) is the most common eye melanoma in adults. Although primary UM tumors can be efficaciously treated with radiation and enucleation, about 50% of patients eventually develop metastasis. Currently, there are no U.S. FDA-approved targeted therapeutic options for UM. Many previous pre-clinical studies in other cancer types revealed that targeting metabolism can be a promising strategy; however, this approach has remained largely unexplored in UM. Dr. Han will study the UM-specific metabolism aspect of UM-specific genetic mutations. She will identify distinctive metabolic characteristics of UM that might serve as therapeutic vulnerabilities, and study the metabolic changes correlated with BAP1 mutations in UM. Dr. Han expects to provide a new rationale and supporting pre-clinical evidence to further pursue promising metabolic targets that are involved in UM tumorigenesis and progression. Dr. Han's ultimate aim is to translate the findings from these studies into new clinical trials for the patients.

ACKNOWLEDGEMENT OF SUPPORT

By driving this proposal, I will directly benefit from my sponsor's expertise in cancer metabolism, specifically in uveal melanoma. I will develop molecular skills, and critical thinking abilities, and learn to communicate my science. This will allow me to achieve my ultimate aspiration of becoming an independent researcher with my own laboratory.

AACR-PFIZER BREAST CANCER RESEARCH FELLOWSHIP

The AACR-Pfizer Breast Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct breast cancer research and establish a successful career path in this field.



Yudan Chi, PhD

Research Fellow

Memorial Sloan Kettering Cancer Center
New York, NY

***The microenvironmental landscape of
breast cancer leptomeningeal metastasis***

BIOGRAPHY

Dr. Chi received her bachelor's degree in veterinary medicine at the Northeast Agriculture University, China, followed by her PhD at the Chinese Academy of Sciences. At MSKCC, Dr. Chi is a scholar of the Alan and Sandra Gerry Metastasis and Tumor Ecosystems Center and is studying the microenvironmental landscape of breast cancer leptomeningeal metastasis.

SCIENTIFIC STATEMENT

Leptomeningeal metastasis (LM) represents a bleak complication of cancer resulting in rapid neurologic disability and death. Through single-cell RNA sequencing of clinical breast cancer specimens, Dr. Chi recently identified a cancer-specific iron transport system LCN2/SLC22A17 as an essential mediator of LM growth. She proposes to uncover the evolutionary dynamics that underlie breast cancer metastasis into the leptomeninges. In particular, she will focus on the mechanisms that allow cancer cells to overcome the inflammatory and hypoferremic microenvironment of LM. To accomplish this, she will characterize cancer cell-immune cell interactions employing analysis of clinical samples as a tool for discovery. Mouse models and in vitro studies will allow for mechanistic dissection of iron transport. Together, this research aims to determine the microenvironmental evolution of breast cancer metastasis in the central nervous system.

ACKNOWLEDGEMENT OF SUPPORT

It is my great honor to receive the 2020 AACR-Pfizer Breast Cancer Research Fellowship, which will facilitate my project in cancer research. This fellowship will also provide very important support for me to further explore leptomeningeal metastasis from mechanism to treatment.

AACR-SWIM ACROSS AMERICA CANCER RESEARCH FELLOWSHIP

The AACR-Swim Across America Cancer Research Fellowship represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct cancer research and establish a successful career path.



Manisha Jalan, DPhil

Research Scholar

Memorial Sloan Kettering Cancer Center
New York, NY

Alternate DNA repair pathways in homologous recombination-deficient cancers

BIOGRAPHY

Dr. Jalan's research training over the last decade across three continents has primarily been focused on understanding the mechanisms utilized by cells to maintain genome integrity. Having completed her bachelor's degree from St. Xavier's College in India and master's degree from the University of Sheffield in the U.K., Dr. Jalan went on to pursue her doctorate at the University of Oxford mentored by Professor Matthew Whitby. There, she identified genetic factors required during recombination dependent replication restart in yeast. Currently employed as a research scholar at Memorial Sloan Kettering Cancer Center, Dr. Jalan is working with Dr. Simon Powell to understand DNA damage response in mammalian cells.

SCIENTIFIC STATEMENT

Genome instability has long been considered the primary driver of most cancer types. It is well established that double strand breaks (DSBs) in DNA, if not repaired faithfully, can lead to mutations and chromosomal rearrangements and even cell death. Homologous recombination (HR) has long been the preferred method to deal with DSBs due to its error-free nature. Thus, in HR-deficient tumors, there must exist several alternate repair pathways to keep cells alive, some of which have recently been recognized. This project aims to develop a high throughput assay to test if DNA breaks can be repaired using an alternative template other than DNA, to ensure genome stability. The proposed studies will identify novel and interesting factors that could stimulate novel therapeutic approaches by exploiting synthetic lethality in HR-deficient cancers.

ACKNOWLEDGEMENT OF SUPPORT

It is my great privilege to receive the 2020 AACR-Swim Across America Cancer Research Fellowship. I would like to thank the review committee and my mentor Dr. Powell for supporting my application. This prestigious award is an important step in my career to build the foundation to be an independent researcher.

AACR-TRIPLE NEGATIVE BREAST CANCER FOUNDATION RESEARCH FELLOWSHIP

The AACR-Triple Negative Breast Cancer Foundation Research Fellowship represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct triple negative breast cancer research and establish a successful career path in this field.



Laura Sipe, PhD

Postdoctoral Fellow

University of Tennessee Health Science Center
Memphis, TN

Novel pre-clinical model to identify genetic modifiers of TNBC

BIOGRAPHY

Dr. Sipe earned her PhD from the University of Virginia in 2018, where she demonstrated critical effects of sympathetic innervation of adipose tissue. To integrate her expertise in physiology and metabolism with the tumor microenvironment, Dr. Sipe joined the University of Tennessee Health Science Center to study obesity and breast cancer in the laboratory of Dr. Liza Makowski. With co-mentoring by Dr. Rob Williams, Dr. Sipe will examine genetic determinants of triple negative breast cancer using a unique murine genetic reference population which will allow for unprecedented findings of genetic modifiers of triple negative breast cancer.

SCIENTIFIC STATEMENT

Triple negative breast cancer (TNBC) is an aggressive breast cancer subtype with very poor outcomes. The goal of this proposal is to discover novel genes that predict TNBC vulnerability and disease progression, a critical step to improving predictive and personalized treatments. Current barriers to progress in the field are limitations in pre-clinical models that use a single inbred genetic background. Dr. Sipe has developed a novel murine model by crossing an established TNBC strain into the background of the largest genetic reference population. This approach will allow Dr. Sipe to interrogate TNBC phenotypes across a diverse and well characterized genetic background. Much like patients, this “humanized” pre-clinical model has differing severity of TNBC phenotypes. Using cutting-edge systems genetics methods, including the comparison of murine and human TNBC genotypes and phenotypes, this work will shed light on critical mediators of TNBC that could be targeted for novel therapeutic approaches.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to accept this 2020 AACR-Triple Negative Breast Cancer Foundation Research Fellowship and complete the proposed work to generate a “humanized” model of TNBC. At the culmination of this proposal, we will identify novel genes that impact TNBC severity, spearheading new avenues of independent research and ultimately improving TNBC outcomes.

AACR-QUADW FOUNDATION FELLOWSHIP FOR CLINICAL/TRANSLATIONAL SARCOMA RESEARCH

The AACR-QuadW Foundation Fellowship for Clinical/Translational Sarcoma Research represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct translational or clinical sarcoma research and establish a successful career path in this field.



Jenna M. Gedminas, MD

Solid Tumor Oncology Fellow

Children's Hospital of Philadelphia
Philadelphia, PA

***Targeting the oncogenic driver of
desmoplastic small round cell tumor***

BIOGRAPHY

Dr. Gedminas completed her undergraduate education at the University of Florida and received her MD from the Chicago Medical School at Rosalind Franklin University of Medicine and Science, followed by residency training in pediatrics at Advocate Children's Hospital. Following completion of her fellowship in pediatric hematology and oncology at Helen DeVos Children's Hospital/Michigan State University, Dr. Gedminas received additional training as a pediatric solid tumor fellow at the Children's Hospital of Philadelphia, where she now continues as an instructor in the Division of Oncology. She conducts sarcoma research in the laboratory of Dr. Patrick Grohar.

SCIENTIFIC STATEMENT

Desmoplastic small round cell tumor (DSRCT) is a rare and aggressive soft tissue sarcoma, most commonly seen in adolescent and young adult males. DSRCT is defined by a single recurrent mutation, EWS-WT1, a dysregulated transcription factor, that alters the expression of more than 1500 genes. Dr. Gedminas' previous work defined DSRCT cells as absolutely dependent on EWS-WT1 for survival. Dr. Gedminas' current work will exploit this dependency as a therapeutic vulnerability using the small molecule lurbinectedin which she has shown to inhibit the expression of EWS-WT1 based on preliminary data. The goal of this study is to elucidate the mechanism of EWS-WT1 suppression by lurbinectedin to guide the administration of this compound and identify novel combination therapies. This will be a major step forward for this disease as there are currently no clinical trials for new agents for DSRCT and no accepted effective standard of care.

ACKNOWLEDGEMENT OF SUPPORT

The AACR-QuadW Foundation Fellowship for Clinical/Translational Sarcoma Research provides me with essential support to continue my work developing novel therapeutic approaches for desmoplastic small round cell tumor while I continue the path toward becoming an independent investigator in the field of pediatric sarcoma.

CAREER DEVELOPMENT AWARDS



AACR GERTRUDE B. ELION CANCER RESEARCH AWARD

With generous support from GlaxoSmithKline, the AACR Gertrude B. Elion Cancer Research Award encourages and supports tenure-eligible junior faculty to conduct research focused on cancer etiology, diagnosis, treatment, or prevention.



Kaysia Ludford, MD

Assistant Professor

The University of Texas MD Anderson Cancer Center
Houston, TX

Interplay between ethnicity & biology in response to checkpoint inhibition

BIOGRAPHY

Dr. Ludford is a third year hematology-oncology fellow at MD Anderson Cancer Center. Upon completion of her fellowship in June 2020, she will join the faculty of the General Oncology and Gastrointestinal Medical Oncology Departments at MD Anderson. She obtained BA degrees in chemistry and Spanish from Vassar College, an MSc in chemistry from the University of Michigan, and an MD from Yale University School of Medicine. Dr. Ludford completed her internal medicine training at Brigham and Women's Hospital. Her overarching career goals are to provide clinical oncological care to medically underserved populations and to contribute to the global mission of reducing cancer disparities through scientific inquiry. Dr. Ludford enjoys spending time with family, traveling, and keeping up with her toddler son.

SCIENTIFIC STATEMENT

Checkpoint inhibitors (CPI) have revolutionized oncology, resulting in improved outcomes for large numbers of patients across a wide range of cancers. The clinical trials that led to U.S. Food and Drug Administration approval of these drugs have suboptimal representation of racial/ethnic minorities (<1-3% Blacks and Hispanics in some trials and failure to report race in the others). As such, it is unclear whether CPI reliably benefit these patients. Unlike cytotoxic therapies, checkpoint inhibitors rely heavily on the host's own immune system which in turn is strongly impacted by environmental and host-related factors such as the microbiome and genetic variations. Consequently, race/ethnicity and social determinants of health have a more direct connection to host immune status and response to immunotherapies. The overarching goal of our research program is three-fold: (i) to identify disparities in the response and outcomes of patients treated with checkpoint inhibitors, (ii) to investigate the biological mechanisms driving observed differences, and (iii) to design clinical interventions to reduce disparities in immune-oncology. In a retrospective study of 44 patients with acral melanoma, we showed that both non-White and White patients have low tumor mutation burden, which ordinarily would be anticipated to yield low responses to CPI. Surprisingly however, non-White patients had high response rates of 58%, 6-fold higher than White patients. Interestingly, this response was not associated with significant increase in overall survival. For this proposal, we will focus on dissecting this provocative observation of differential response.

ACKNOWLEDGEMENT OF SUPPORT

It is a distinct honor to have been selected to receive the 2020 AACR Gertrude B. Elion Cancer Research Award. This award will be invaluable in helping me establish my academic career, providing resources to carry out the biological studies to investigate how immune-biology and ethnicity impact response to immunotherapies.

AACR-NOVOCURE CAREER DEVELOPMENT AWARD FOR TUMOR TREATING FIELDS RESEARCH

The AACR-Novocure Career Development Award for Tumor Treating Fields Research represents a joint effort to promote and support early-career investigators who are conducting innovative research focused on Tumor Treating Fields. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Narasimha Kumar Karanam, PhD

Instructor

UT Southwestern Medical Center
Dallas, TX

Harnessing E2F-Rb-CDK4/6 axis for novel combination therapy with TFields

BIOGRAPHY

Dr. Karanam received his master's degree in biochemistry from the University of Hyderabad, India. He then joined the Center for Cellular and Molecular Biology in Hyderabad, India, as a research assistant. This is where his interest in cancer research began. He subsequently pursued his PhD in cancer biology at the University of Greifswald, Germany, with Professor Uwe Volker. As a postdoctoral fellow in Dr. Michael Story's laboratory, he examined the role of miRNAs in head and neck cancer progression. Dr. Karanam is currently an instructor at UT Southwestern Medical Center, where his research includes the interrogation of TFields mechanisms of action for therapeutic benefit.

SCIENTIFIC STATEMENT

Tumor treating fields (TFields) are low-intensity, intermediate frequency, alternating electric fields that are applied to tumor regions and cells using non-invasive arrays. Initial mechanism described for TFields-induced cell death has been via the disruption of mitosis and later it was found that TFields cause replication stress and inhibit the DNA damage repair process due to decreased expression of genes involved in the Fanconi anemia pathway and cell cycle checkpoint. However, the exact cause of the downregulation of these genes has been elusive. Preliminary quantitative proteomics data identified a novel role for TFields through the CDK-Rb-E2F axis. The goal of this project is to explore TFields-induced proteome and metabolome changes in lung and pancreatic cancers using in vitro and in vivo models. Moreover, this project will test novel combination therapy options targeting deregulated CDK-Rb-E2F axis using E2F and CDK4/6 inhibitors together with TFields.

ACKNOWLEDGEMENT OF SUPPORT

I am deeply honored to receive the AACR-Novocure Career Development Award for Tumor Treating Fields Research. This award affords me the opportunity to understand the system level effects of TFields exposure through trans-omics approaches in order to find novel combination therapies that can be translated into tangible benefits for cancer patients.

AACR-NOVOCURE CAREER DEVELOPMENT AWARD FOR TUMOR TREATING FIELDS RESEARCH

The AACR-Novocure Career Development Award for Tumor Treating Fields Research represents a joint effort to promote and support early-career investigators who are conducting innovative research focused on Tumor Treating Fields. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Chirag B. Patel, MD, PhD

Assistant Professor

Stanford University
Stanford, CA

Increasing glioblastoma cell membrane permeability with TTFields

BIOGRAPHY

Dr. Patel earned BS/MSE degrees in biomedical engineering from Johns Hopkins University and MD/PhD degrees from the MD Anderson/UT-Houston Graduate School of Biomedical Sciences and UT-Houston Medical School. He completed adult neurology residency at the University of California, Los Angeles, and postdoctoral and clinical fellowships in molecular imaging and adult neuro-oncology, respectively, at Stanford University. He is now a clinical assistant professor of neurology and, by courtesy, of radiology at Stanford University. Dr. Patel's laboratory studies the mechanisms of alternating electric fields (tumor treating fields [TTFields]) in human glioblastoma, with an aim to develop novel combination strategies for improved efficacy in this invariably lethal cancer.

SCIENTIFIC STATEMENT

The first demonstrated clinical efficacy of tumor treating fields (TTFields) was in glioblastoma. Compared to adjuvant chemotherapy alone, adjuvant chemotherapy and 200 kHz TTFields prolonged overall survival from 15 to 21 months and increased the 5-year survival rate from 5% to 13%. How TTFields potentiate the effects of chemotherapy against cancer is not completely understood. A recent finding that TTFields increase glioblastoma cell membrane permeability may help to explain some of the anti-cancer effects of TTFields. This project will (1) determine the optimal TTFields frequency for cell membrane permeabilization in glioblastoma and non-cancer cells; (2) identify the size of maximal membrane disruption due to TTFields; and (3) quantify the amount of chemotherapy entering and retained in glioblastoma upon TTFields exposure. If additional optimal TTFields frequency besides 200 kHz for disruption of glioblastoma cellular membrane integrity is found, then alternating it with the FDA-approved 200 kHz frequency may result in improved control in glioblastoma.

ACKNOWLEDGEMENT OF SUPPORT

I am grateful to receive an AACR-Novocure Career Development Award for Tumor Treating Fields Research from the AACR and Novocure. This award will help me transition to independence by expanding on my previous studies focused on novel mechanisms of action of TTFields in glioblastoma, from a translational perspective.

BREAST CANCER RESEARCH FOUNDATION-AACR CAREER DEVELOPMENT AWARD FOR TRANSLATIONAL BREAST CANCER RESEARCH

The Breast Cancer Research Foundation-AACR Career Development Award for Translational Breast Cancer Research represents a joint effort to promote and support innovative research designed to accelerate the discovery, development, and application of new agents to treat breast cancer and/or for pre-clinical research with direct therapeutic intent.



Isaac Harris, PhD

Assistant Professor

The University of Rochester Medical Center
Rochester, NY

***Uncovering the roles of extracellular GSH
in triple-negative breast cancer***

BIOGRAPHY

Dr. Harris obtained his BE in chemical engineering in 2008 from the University of Toronto. He received his PhD with Dr. Tak Mak at the Princess Margaret Cancer Centre in 2013, where he studied antioxidants using mouse models of breast cancer. Dr. Harris completed his postdoctoral training with Dr. Joan Brugge at Harvard Medical School, where he developed a high-throughput drug screening platform to understand selective vulnerabilities in breast cancers upon inhibition of antioxidants. In 2019, Dr. Harris joined the Department of Biomedical Genetics at the University of Rochester Medical Center and Wilmot Cancer Institute as an assistant professor.

SCIENTIFIC STATEMENT

Breast cancers use antioxidants to quench oxidative stress and survive. The most aggressive subtype of breast cancer, triple-negative breast cancer (TNBC), has a higher occurrence in younger women and has the poorest outcome. Unfortunately, TNBC lacks targeted therapies, highlighting the need for novel treatment strategies to combat this disease. Using mouse modeling and high-throughput drug screening, the Harris laboratory will elucidate the extent to which circulating glutathione, the most abundant antioxidant in the body, supports TNBC survival. This research will illuminate a completely novel mechanism of antioxidant supply and usage in TNBC. It will broaden our knowledge of the interplay between breast cancer and its surrounding metabolic environment. Finally, these studies have the potential to reveal an entirely new set of unrealized targets and therapeutic strategies for TNBC.

ACKNOWLEDGEMENT OF SUPPORT

It is an honor to receive the 2020 Breast Cancer Research Foundation-AACR Career Development Award for Translational Breast Cancer Research. Our laboratory focuses on understanding the roles of antioxidants in breast cancer. The immense support from this award will drive us forward in interrogating circulating antioxidants and developing novel therapeutic strategies for TNBC.

BREAST CANCER RESEARCH FOUNDATION-AACR CAREER DEVELOPMENT AWARD FOR TRANSLATIONAL BREAST CANCER RESEARCH

The Breast Cancer Research Foundation-AACR Career Development Award for Translational Breast Cancer Research represents a joint effort to promote and support innovative research designed to accelerate the discovery, development, and application of new agents to treat breast cancer and/or for pre-clinical research with direct therapeutic intent.



Sheheryar Kabraji, BM BCh

Physician

Dana-Farber Cancer Institute
Boston, MA

Overcoming residual disease in HER2+ breast cancer

BIOGRAPHY

Dr. Kabraji received his medical degree from Oxford University Medical School and completed internal medicine residency at Massachusetts General Hospital. He completed his medical oncology fellowship in the Dana-Farber/Partners Hematology/Oncology Fellowship Program, and post-doctoral research in Dr. Sridhar Ramaswamy's laboratory at Mass General Cancer Center, where he developed an assay to detect quiescent cancer cells in tissues. Dr. Kabraji is a breast medical oncologist at the Susan F. Smith Center for Women's Cancers, Dana-Farber Cancer Institute, and instructor in medicine at Harvard Medical School. Dr. Kabraji studies how cancer cell quiescence promotes drug resistance in localized and metastatic breast cancer.

SCIENTIFIC STATEMENT

Outcomes for HER2-positive (HER2+) breast cancer have been transformed by effective HER2-targeting therapies. However, local and distant recurrences of HER2+ breast cancer still occur after treatment due to surviving tumor cells known as residual disease (RD). Based on previous work, we hypothesize that RD, despite effective HER2-inhibition, is facilitated by quiescent cancer cells that promote an immune-exhausted microenvironment. To test this hypothesis, we will first investigate the immune response associated with residual disease after HER2-inhibition in patients and mouse models. Next, we will determine how quiescent cancer cells promote immune evasion in the setting of RD. Finally, we will evaluate combined quiescent cancer cell inhibition and immune checkpoint blockade to eliminate residual disease after HER2 inhibition in HER2+ breast cancer. Results from this proposal will suggest how to target quiescent cancer cells to potentiate the anti-tumor immune response and eliminate residual disease in HER2+ breast cancer.

ACKNOWLEDGEMENT OF SUPPORT

I am deeply grateful to be a recipient of the 2020 Breast Cancer Research Foundation-AACR Career Development Award for Translational Breast Cancer Research. This award will support my transition to becoming an independent investigator tackling an understudied mechanism of drug resistance in breast cancer: cancer cell quiescence.

INDEPENDENT INVESTIGATOR GRANTS



AACR-BAYER INNOVATION AND DISCOVERY GRANT

AACR-Bayer Innovation and Discovery Grant promotes the key tenets of the Bayer Grants4Targets™ Initiative, providing new treatment options for cancers with high unmet medical need, encouraging innovation, and translation of ideas from basic research into novel drugs, and fostering collaborations between excellent academic groups and the pharmaceutical industry.



James L. Chen, MD

Assistant Professor

The Ohio State University Comprehensive Cancer Center
Columbus, OH

***Deciphering mechanisms of sorafenib sensitivity
in desmoid tumors***

BIOGRAPHY

Dr. Chen is a dually-appointed faculty member in the Departments of Internal Medicine and Biomedical Informatics. He is a recognized expert in the treatment of sarcoma and a translational bioinformatician. Along with serving as medical director for clinical and research informatics at the James Comprehensive Cancer Center, at the Ohio State University, Dr. Chen is active clinically and serves as principal investigator for several investigator-initiated sarcoma trials. His laboratory focuses on developing novel biomarkers and workflows for repurposing drugs in cancer using bioinformatics techniques. Dr. Chen chairs several national cancer workgroups in ASCO, the ALLIANCE Clinical Trials Group, and the Oncology Research Information Exchange Network (ORIEN).

SCIENTIFIC STATEMENT

Desmoid tumors are rare tumors that are frequently recurrent and locally invasive. Desmoid patients often experience chronic pain, organ dysfunction, decrease in quality of life, and even death. Unfortunately, desmoid treatment remains a case of trial-and-error with no established biomarkers to predict treatment response. The oral drug, sorafenib, has emerged as a powerful front-line strategy. Although sorafenib reduces the risk of disease progression, less than a third of patients have an objective response. Thus, predictive biomarkers are critically needed to better identify sorafenib responders. We have collected numerous desmoid tumors as part of our sarcoma biobanking program. We plan to use the Biobank and desmoid patient-derived cell lines and examine their response before and after treatment with sorafenib. This will allow us to understand what genes are involved in sensitivity. If successful, we hope to test out these genetic biomarkers in a clinical trial.

ACKNOWLEDGEMENT OF SUPPORT

I am very grateful for this funding opportunity as it will provide critical data for better understanding how to tailor treatment for our patients with desmoid tumors.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

AACR-Bayer Innovation and Discovery Grant promotes the key tenets of the Bayer Grants4Targets™ Initiative, providing new treatment options for cancers with high unmet medical need, encouraging innovation, and translation of ideas from basic research into novel drugs, and fostering collaborations between excellent academic groups and the pharmaceutical industry.



Nicholas A. Graham, PhD

Assistant Professor

University of Southern California
Los Angeles, CA

Proteomic approaches to improve therapeutic targeting of PRMTs in glioma

BIOGRAPHY

Dr. Graham is an assistant professor of chemical engineering at the University of Southern California. He received a BS in chemical engineering and French from Washington University in St. Louis, followed by an MS and PhD in chemical engineering from Caltech with Dr. Anand Asthagiri. He then completed an NIH-supported postdoctoral fellowship in molecular and medical pharmacology at the University of California, Los Angeles, with Dr. Thomas Graeber before joining the University of Southern California. His laboratory uses systems biology approaches including mass spectrometry-based proteomics and metabolomics to study cancer, aging, and diabetes.

SCIENTIFIC STATEMENT

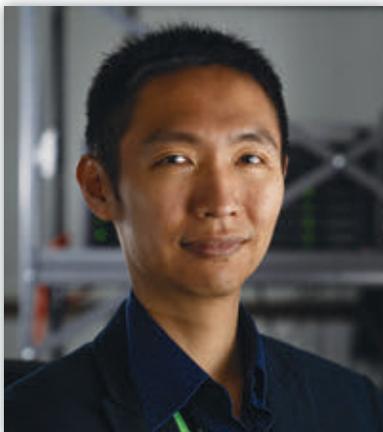
Gliomas, particularly high-grade glioblastomas, are aggressive brain cancers that have remained largely refractory to targeted therapeutic approaches. An emerging therapeutic approach is ‘collateral lethality’, whereby passenger deletion of a gene creates a druggable, tumor-specific vulnerability. One such collateral lethal interaction involves inhibition of the protein arginine methyltransferase 5 (PRMT5) in tumors with deletion of the 5-methylthioadenosine phosphorylase (MTAP) gene. However, there remain important mechanistic questions that need to be answered before PRMT5 inhibitors can be successfully clinically translated. Using a novel proteomic approach to globally measure how PRMT5 inhibitors regulate the protein arginine methylome, the Graham Lab will seek to identify the mechanistic basis of collateral lethality between PRMT5 inhibitors and MTAP deletion in patient-derived gliomasphere cultures. This project will thus advance brain tumor therapeutic research by enabling translational efforts to test PRMT5 inhibitors in glioblastoma, a deadly brain cancer in desperate need of new therapeutic options.

ACKNOWLEDGEMENT OF SUPPORT

I am extremely grateful for the support provided by the 2020 AACR-Bayer Innovation and Discovery Grant. Support from this grant will allow my lab to use proteomic approaches to test new therapeutic approaches for patients suffering from the deadly brain cancer glioblastoma.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

AACR-Bayer Innovation and Discovery Grant promotes the key tenets of the Bayer Grants4Targets™ Initiative, providing new treatment options for cancers with high unmet medical need, encouraging innovation, and translation of ideas from basic research into novel drugs, and fostering collaborations between excellent academic groups and the pharmaceutical industry.



Willy Hugo, PhD

Assistant Professor

UCLA David Geffen School of Medicine
Los Angeles, CA

Targeting the residual disease in MAPK inhibitor treated melanoma

BIOGRAPHY

Dr. Hugo earned his PhD in computational biology from the National University of Singapore in 2011 and published multiple high impact papers on the mechanisms of resistance to targeted- and immunotherapy in melanoma during his postdoctoral training under the mentorship of Dr. Roger Lo at the University of California, Los Angeles (UCLA). Currently, Dr. Hugo is an assistant professor at the Department of Medicine, UCLA. His laboratory is studying the role of the interaction between tumor cells and the immune/stromal cells in the tumor microenvironment and how such interaction influences the development of resistance toward targeted- and immunotherapies in cancer.

SCIENTIFIC STATEMENT

About 50% of all melanomas harbor a mutated form of the gene BRAF. The introduction of mutant-specific BRAF inhibitors and their combinations with MEK inhibitors (hereafter referred to together as MAPK pathway inhibitors or MAPKi) has significantly improved mutant BRAF melanoma patients' survival, yet this therapy rarely results in complete eradication of a patient's tumor. One of the most reported resistance-conferring adaptations under MAPKi is the emergence of melanoma cells with diminished melanocytic phenotype, as evidenced by low expression of the MITF protein and high expression of the AXL protein. As such, most of the recent studies to overcome MAPKi resistance have been focusing on finding ways to suppress the MITF-low, AXL-high melanoma cells. Intriguingly, based on our melanoma patient-derived data, MAPKi-treated patient tumors do not show the MITF-low, AXL-high phenotypic switch as frequently as observed in the wet lab experimental setup. This observation has an important clinical implication: we may have been trying to overcome a resistance mechanism that is not prevalent in real patient tumors. We posit that the discrepancy is driven by the presence of immune and stromal cells in patient tumors. Thus, this proposal plans to test for novel therapeutic vulnerabilities of MAPKi-treated melanoma cells in the presence of relevant immune/stromal cells and their factors in order to accurately model the emergence of MAPKi resistance in melanoma patients.

ACKNOWLEDGEMENT OF SUPPORT

The 2020 AACR-Bayer Innovation and Discovery Grant will allow me to study and test novel therapeutic targets in MAPK inhibitor resistant melanoma. Importantly, this project will dissect the development of MAPK inhibitor resistance phenotype in the presence of immune and other normal cells, which can better mimic the true environment in which tumors grow. With this grant support, I am confident that our team can discover novel therapeutic opportunities that can be exploited to improve the efficacy and durability of MAPK inhibitor therapy in melanoma patients.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

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Edward L. Schwartz, PhD

Professor of Medicine and Molecular Pharmacology

Albert Einstein College of Medicine
New York, NY

A novel druggable target for tumors with a mutant RB1 tumor suppressor gene

BIOGRAPHY

Dr. Schwartz received a doctorate in pharmacology and toxicology from Michigan State University and did postdoctoral training in the Department of Pharmacology at Yale University. Dr. Schwartz uses his expertise in cancer biology and experimental therapeutics toward the identification of new targets for drug design and development for the treatment of cancer. His current research focuses on agents that induce tumor cell death by novel mechanisms, including the regulation of proteins that control the cell cycle and the modulation of cell signaling.

SCIENTIFIC STATEMENT

The RB1 tumor suppressor gene is mutated and inactivated in highly aggressive tumors, including virtually all small cell lung cancers, where its loss, along with TP53, is required and sufficient for tumorigenesis. While it is known that RB1 mutant cells fail to arrest at the G1/S checkpoint, this information has not led to effective strategies, as it is challenging to develop targeted drugs for tumors that are driven by the loss of gene function.

Skp2 is a substrate recruiting subunit of an SCF E3 ubiquitin ligase and is a repression target of pRb. In mice in which lung and prostate tumorigenesis was driven by the loss of RB1, the concurrent knockout of Skp2 completely blocked tumor growth and metastasis, thereby validating Skp2 as a potential drug target in RB1-deficient tumors. The objective of this proposal is to design, synthesize and test small molecule inhibitors of Skp2, a downstream actionable target in RB1-deficient cancers.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to be an awardee of the AACR-Bayer Innovation and Discovery Grant. This funding provides a pathway to translate our mechanistic findings to the discovery of novel therapeutics to treat tumors that are deficient in the RB1 tumor suppressor gene, aggressive cancers for which there are no effective drugs. I extend my gratitude to the AACR and Bayer for their support.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

AACR-Bayer Innovation and Discovery Grant promotes the key tenets of the Bayer Grants4Targets™ Initiative, providing new treatment options for cancers with high unmet medical need, encouraging innovation, and translation of ideas from basic research into novel drugs, and fostering collaborations between excellent academic groups and the pharmaceutical industry.



Shobha Vasudevan, PhD

Associate Professor

Massachusetts General Hospital Cancer Center
Boston, MA

***Targeting post-transcriptional regulation
underlying chemoresistance***

BIOGRAPHY

Dr. Vasudevan is an associate professor of medicine at Massachusetts General Hospital Cancer Center and Harvard Medical School. Her research is focused on the role of RNA mechanisms underlying resistant cancers as a basis for designing new therapies. Her laboratory discovered that quiescent cells use specialized post-transcriptional mechanisms to promote gene expression important for cancer persistence. Dr. Vasudevan completed her doctorate with Dr. Stuart Peltz at Rutgers University-UMDNJ and her postdoctoral fellowship with Dr. Joan Steitz at Yale University. She has received several awards including from the RNA Society, Leukemia and Lymphoma Society, Cancer Research Institute, V Foundation, and Leukemia Research Foundation.

SCIENTIFIC STATEMENT

Our studies showed that stress-induced, post-transcriptional mechanisms drive distinct gene expression that allow therapy survival in resistant cancers. This includes cytokines and immune receptors that block apoptosis and anti-tumor immunity. We re-purposed small molecules that are used to suppress cytokines in fibrosis and a non-toxic kinase inhibitor to block stress signals and prevent resistance in leukemia. These pathways are observed in refractory triple negative breast cancer, suggesting an avenue to improve current therapies. The goal is to target the post-transcriptional expression of survival regulators that are induced by therapy stress signals using our inhibitors to curb refractory triple negative breast cancer. We will combine our inhibitors with clinical therapies, in patient samples and syngeneic models and patient derived xenografts in immune-competent mice, to test if the inhibitors block resistance and restore anti-tumor immunity. This study will test new resistance inhibitors in vivo, and improve therapy against resistant breast cancer.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to receive the AACR-Bayer Innovation and Discovery Award, which will enable us to progress our findings toward clinical applications. This can complement current therapies to improve patient outcomes and promote collaboration with the AACR community.

AACR-BRISTOL MYERS SQUIBB MIDCAREER FEMALE INVESTIGATOR GRANT

The AACR-Bristol Myers Squibb Midcareer Female Investigator Grant represents a joint effort to encourage and support mid-career female physician-scientists and researchers to conduct immuno-oncology research and to foster their career advancement toward becoming senior investigators.



Laura D. Wood, MD, PhD

Associate Professor and Associate Director of Research Affairs in the Division of Gastrointestinal and Liver Pathology

The Johns Hopkins University School of Medicine
Baltimore, MD

Defining the immune microenvironment in Pancreatic IPMNs

BIOGRAPHY

Dr. Wood received her BS in biology from the College of William & Mary. She then earned both her MD and PhD from Johns Hopkins University School of Medicine. Dr. Wood completed residency in anatomic pathology and a fellowship in gastrointestinal and liver pathology also at Johns Hopkins Hospital. She now leads her own research laboratory focused on molecular characterization of pancreatobiliary neoplasms and signs out clinical gastrointestinal pathology specimens.

SCIENTIFIC STATEMENT

Pancreatic cancer arises through non-invasive precursor lesions that are curable if detected and treated early. One precursor lesion, intraductal papillary mucinous neoplasm (IPMN), is a key target for clinical intervention and can serve as a model for premalignant pancreatic neoplasia. We propose to comprehensively analyze the immune microenvironment in a genomically characterized cohort of IPMNs, allowing correlation of the immune microenvironment with various features of the genomic landscape, including somatic mutations in specific driver genes, tumor mutational burden, and quality and quantity of predicted neoantigens. In addition, we will utilize an organoid model of IPMN to identify tumor infiltrating lymphocytes (TILs) specifically targeting these neoplasms. Taken together, these studies will define the immune response to these pancreatic precursor lesions, providing critical insights into the biology of pancreatic tumorigenesis. The results will create an important foundation to develop immunological strategies to prevent the malignant progression of IPMNs.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to receive the AACR-Bristol Myers Squibb Midcareer Female Investigator Grant. I greatly appreciate this support at this critical stage in my career, which will enable our group to perform exciting new studies integrating cancer genomics, tumor immunology, and novel in vitro models of pancreatic neoplasia.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grant represents a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Carsten Hagemann, PhD

Privatdozent (Assistant Professor)

Universitätsklinikum Würzburg
Würzburg, Germany

Overcoming the blood brain barrier drug delivery hurdle with TTFields

BIOGRAPHY

Since his early studies of biology at the Justus-Liebig-University Gießen, Germany, Dr. Hagemann has been interested in cellular signaling and tumor biology. His PhD was awarded for work on Raf mediated signaling in 1999 by the Julius-Maximilians-University Würzburg, Germany. During his postdoctoral training at Leicester University, his research expanded to stress activated kinases. In 2002, Dr. Hagemann became head of the Tumorbiology Research Laboratory in the Department of Neurosurgery, University Hospital Würzburg. Since 2015, he has been Privatdozent (assistant professor equivalent) for experimental neurosurgery, focusing on molecular growth mechanisms of glioblastoma multiforme, developing new drug delivery systems and TTFields.

SCIENTIFIC STATEMENT

Despite the availability of potent therapeutics, a great number of CNS disorders such as glioblastoma still pose a major problem in modern medicine. Owing to the presence of the blood-brain barrier (BBB), many potential drugs are unable to reach the brain. However, the advent of TTFields as an effective, clinically-approved glioblastoma treatment opened unexplored areas in both BBB and TTFields research. We demonstrated the feasibility of transiently opening the BBB in vitro and in vivo via TTFields. Tight junction proteins claudin-5 and occludin were delocalized from the membranes of murine brain microvascular endothelial cells. Moreover, BBB integrity was compromised leading to increased permeability in vitro and in vivo. Nonetheless, the mechanisms by and through which it takes place remain yet to be understood. Therefore, this study aims to investigate these mechanisms for future clinical translation in human 2D and 3D cell culture models and an organotypic ex vivo system.

ACKNOWLEDGEMENT OF SUPPORT

Our engagement in TTFields research led to the discovery of potential of TTFields to transiently open the blood-brain barrier. Support by the AACR-Novocure Tumor Treating Fields Research Grant enables us to translate this observation into future clinical practice, offering a solution to the current CNS drug delivery problem to treat brain tumors and other diseases.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

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Sandeep Mittal, MD, FRCSC, FACS

Professor

Virginia Tech
Roanoke, VA

Epigenetic modifications induced by TTFIELDS in patient-derived GBM cells

BIOGRAPHY

Dr. Mittal is professor and chief of neurosurgery at Virginia Tech Carilion School of Medicine and Carilion Clinic. He received his medical degree from McGill University in Canada. He completed neurosurgery residency and a postdoctoral research fellowship at the Montreal Neurological Institute at McGill University. He subsequently completed a fellowship in epilepsy surgery, followed by another fellowship in neuro-oncological surgery. Dr. Mittal directs the Translational Neurosurgery Research Laboratory located at the Fralin Biomedical Research Institute at Virginia Tech. His primary clinical and research interests are related to developing novel therapies for brain tumors and epilepsy. An accomplished clinician-scientist, Dr. Mittal has authored over 150 peer-reviewed publications.

SCIENTIFIC STATEMENT

Tumor-treating fields (TTFIELDS) are low-intensity, alternating electrical fields that produce anti-mitotic effects and cell death in glioblastoma (GBM). Epigenetic modifications in cancer cells (e.g. methylation or acetylation of DNA or proteins) induced by TTFIELDS remain unknown and may serve as prognostic or therapeutic response markers (e.g. hypermethylation of the MGMT promoter in GBM). We will determine whether TTFIELDS decrease the prevalence of epigenetic markers of TMZ resistance using patient-derived GBM cell lines. Aim 1: Determine if in vitro TTFIELDS regulate the expression of MGMT by altering transcriptional activity of the MGMT gene. Aim 2: Determine if in vitro TTFIELDS alteration of cell morphology and the actin cytoskeleton is associated with changes in global histone acetylation, and if it can be manipulated with HDAC inhibitors. These studies will significantly expand the current understanding of TTFIELDS therapy for the treatment of patients with GBM and will reveal novel TTFIELDS mechanisms of action.

ACKNOWLEDGEMENT OF SUPPORT

The 2020 AACR-Novocure Tumor Treating Fields Research Grant will allow us to investigate an important aspect of TTFIELDS that has largely remained unexplored thus far. That is, do TTFIELDS delay the development of temozolomide resistance in patients with glioblastoma? We thank the AACR and Novocure for supporting this valuable and highly clinically relevant research.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grant represents a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Debabrata Saha, PhD

Associate Professor

UT Southwestern Medical Center
Dallas, TX

Evaluating efficacy of TTFIELDS and radiotherapy in preclinical tumor model

BIOGRAPHY

Dr. Saha has been working in the field of cancer biology for more than 20 years and has developed expertise specifically in the area of tumor cell resistance to radiation and chemotherapy. He received his master's in biochemistry from the University of Calcutta, India and his PhD in chemistry from the University of Nebraska, Lincoln. As a postdoctoral fellow at Vanderbilt Medical Center in Nashville he carried out research on cell signaling and radiation therapy. After joining UT Southwestern Medical Center, Dr. Saha further expanded his research in the field of cancer radiotherapy in preclinical cancer models.

SCIENTIFIC STATEMENT

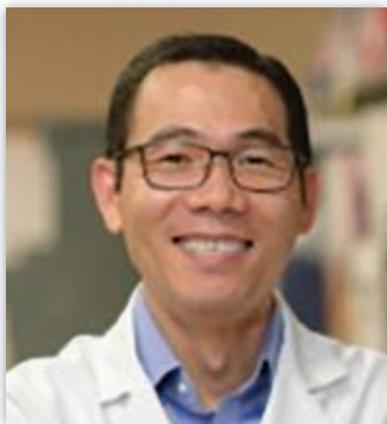
Dr. Saha's laboratory is studying a novel function of a tumor suppressor protein DAB2IP on chromosomal instability in prostate and renal cancer models. Recent results from his laboratory provided compelling evidence that DAB2IP protein plays a significant role in modulating the spindle assembly checkpoint function and in safeguarding normal cells against chromosomal instability. Dr. Saha also discovered that DAB2IP enhances the response to radiation in cancer cells, and that prostate cancer patients lacking DAB2IP had worse survival after radiation therapy. In addition, his laboratory is developing novel tumor models for cancer radiobiology and performing animal irradiation experiments to understand the mechanism of radio-resistance in cancer cells. Over the years, Dr. Saha has developed expertise in screening and evaluating small molecule inhibitors as radio-sensitizers in multiple cancer models.

ACKNOWLEDGEMENT OF SUPPORT

I am extremely grateful to receive the 2020 AACR-Novocure Tumor Treating Fields Research Grant. Because cancers can rarely be controlled by single therapy modality, TTFIELDS can be more effective in a combinatorial regimen because of its impact on multiple signaling pathways. I will be testing the efficacy of TTFIELDS with radiation and anti PD-L1 therapy.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grants represent a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields (TTFields; intermediate frequency, low intensity, alternating electric fields) that disrupt cell division in cancer cells. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



David D. Tran, MD, PhD

Associate Professor

University of Florida College of Medicine
Jacksonville, FL

Molecular mechanism of resistance to Tumor Treating Fields in glioblastoma

BIOGRAPHY

Dr. Tran is associate professor, chief of the Division of Neuro-Oncology, and associate director of the Preston A. Wells, Jr. Brain Tumor Center at the McKnight Brain Institute of the University of Florida. He received his MD-PhD degrees from the Mayo Clinic College of Medicine in 2005 and completed his oncology and neuro-oncology fellowship at Washington University School of Medicine in St. Louis in 2011. He is a leader in cancer precision medicine and an NCI-funded investigator. He has authored many seminal publications in cancer research and serves as principal investigator of several national trials in brain tumors.

SCIENTIFIC STATEMENT

Glioblastoma (GBM) is the deadliest brain cancer in adults. Tumor-treating fields (TTF) were recently approved for the treatment of GBM and mesothelioma. TTF are low-intensity alternating electric fields that disrupt chromosomal segregation leading to apoptosis. Unfortunately, treatment resistance develops in most TTF responders. Yet, its mechanism remains largely unexplored. The research team has generated GBM cells with relative resistance to TTF and, applying an innovative computational algorithm, identified the Prostaglandin E2 Receptor (PTGER3) as a master regulator of TTF resistance. In this proposal, we will determine the mechanism by which PTGER3 regulates TTF resistance. First, we will determine how PTGER3 regulates resistance through a nuclear stemness factor network. Next, we will determine whether PTGER3 regulates GBM-initiating cells to promote TTF resistance in vitro and in vivo using patient-derived xenografts and tumor samples. These findings will provide new opportunities to improve therapeutic efficacy of this novel highly effective anti-cancer treatment.

ACKNOWLEDGEMENT OF SUPPORT

It is my distinct honor to receive the prestigious 2020 AACR-Novocure Tumor Treating Fields Research Grant. It will provide my team the necessary resources to investigate the mechanism of how tumor cells develop resistance to this novel cancer therapeutic modality and to identify methods to overcome it.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grant represents a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. These grants are intended to provide a deeper understanding of the mechanisms of action of this novel anti-cancer treatment modality and to accelerate the development of new treatment strategies to advance therapeutic options for cancer.



Christopher Douglas Willey, MD, PhD

Professor

The University of Alabama at Birmingham
Birmingham, AL

Exploring Novo-TTF in advanced patient derived GBM models with multi-omics

BIOGRAPHY

Dr. Willey completed a bachelor's degree at Duke University, where he majored in biomedical engineering. He matriculated to the Medical University of South Carolina in the Medical Scientist Training Program (MSTP) culminating in a combined MD and PhD degree. After his internship, he completed radiation oncology residency at Vanderbilt University in the American Board of Radiology Leonard B. Holman Pathway Fellowship Program. Following residency, he became a physician-scientist in radiation oncology at the University of Alabama at Birmingham. He is currently a tenured professor with a research focus on cancer cell biology and kinase signaling in patient-derived models of cancer.

SCIENTIFIC STATEMENT

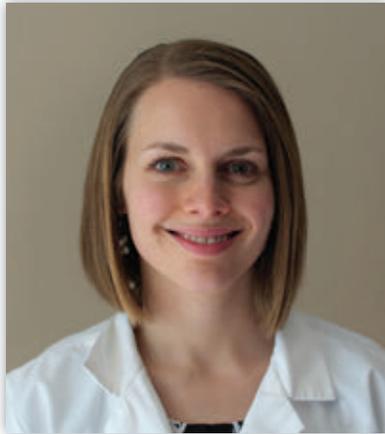
Glioblastoma (GBM) has incredibly poor outcomes (5-year survival <4%) despite maximal safe surgical resection, irradiation, temozolomide, and Tumor Treating Fields (TTF) with patients displaying inherent or acquired resistance (typically within 6 months). Unfortunately, GBM research has relied on highly artificial models under major growth-promoting conditions that select for highly proliferative tumors that no longer resemble the patient's tumor. To address this, we used patient-derived models of cancer (PDMC) coupled with comprehensive molecular profiling to build reliable models. In this AACR-Novocure project, we will investigate tumor microenvironmental (TME) stressors (hypoxia and nutrient deprivation) on derivative PDMC's (spheroids and 3D matrix-embedded tumors) in terms of molecular biology (transcriptome and kinome similarity) and treatment response fidelity. In Aim 1, we will examine TTF efficacy in our panel of GBM PDMCs; in Aim 2, we will determine whether TTF efficacy is altered by the TME. This work will identify key signaling pathways associated with TTF response.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to receive this AACR-Novocure Tumor Treating Fields Research Grant and will investigate TTF-resistance mechanisms in advanced patient-derived models of glioblastoma. This support will allow us to identify new targets and biomarkers to enhance the efficacy of Tumor Treating Fields and improve outcomes in this terrible disease.

AACR-PLGA FUND AT THE PEDIATRIC BRAIN TUMOR FOUNDATION RESEARCH GRANT TO OPTIMIZE DRUG DOSING STRATEGIES FOR PEDIATRIC LGA/LGG PATIENTS

The AACR-PLGA Fund at the Pediatric Brain Tumor Foundation Research Grant to Optimize Drug Dosing Strategies for Pediatric LGA/LGG Patients represents a joint effort to promote and support innovative and collaborative research focused on the most common forms of pediatric brain cancer – low grade glioma/astrocytoma.



Karisa C. Schreck, MD, PhD

Assistant Professor

The Johns Hopkins University School of Medicine
Baltimore, MD

Functional engagement and effect of RAF-targeted therapies in glioma

BIOGRAPHY

Dr. Schreck is an assistant professor of neurology and oncology at the Johns Hopkins University School of Medicine. She received her BS from the New Jersey Institute of Technology, where she majored in biomedical engineering and played varsity soccer. She went on to obtain her MD/PhD from Johns Hopkins University with a focus on the role of neural developmental pathways in glioblastoma. She completed residency in neurology at Johns Hopkins University followed by a fellowship in the joint NIH-Hopkins neuro-oncology fellowship program. The focus of her research is the use of RAF-targeted therapy in brain tumors and mechanisms of resistance.

SCIENTIFIC STATEMENT

Genomic characterization has revealed that pediatric low-grade astrocytoma (PLGA) shares some molecular drivers with pediatric and adult high-grade glioma, specifically activating BRAF-fusion or point mutations. Utilization of RAF and MEK inhibitors (RAFi/MEKi) against these oncogenes is promising in PLGA, but very little is known about blood-brain barrier penetration, target inhibition in brain, combination with other modalities, or biomarkers of response. Dr. Karisa Schreck and collaborator, Dr. Jean Mulcahy Levy, propose to determine RAFi/MEKi penetration and target engagement in non-enhancing and enhancing brain tumor tissue from children and adults with glioma by leveraging biospecimens from ongoing clinical trials. Biospecimens will be used to determine intra-tumoral drug concentrations, functional ERK inhibition, and correlation with response to treatment. The investigators will also identify a kinome signature for treatment sensitivity using pre-/post- treatment specimens and serial blood samples. These data will help inform future trial design and drug dosing in patients with PLGA.

ACKNOWLEDGEMENT OF SUPPORT

I am appreciative of the Pediatric Brain Tumor Foundation and AACR's partnership to support my research. This award provides funding to study BRAF inhibitor entry and function in gliomas using clinical trial specimens from patients. This will enable us to design smarter clinical trials and novel drugs against glioma.

NEUROENDOCRINE TUMOR RESEARCH FOUNDATION-AACR GRANT

The Neuroendocrine Tumor Research Foundation-AACR Grant represents a joint effort to promote and support innovative cancer research. This grant supports independent junior and senior investigators to develop and study new ideas and innovative approaches that have direct application and relevance to neuroendocrine tumors.



Etay Ziv, MD, PhD

Assistant Attending Radiologist

Sloan Kettering Institute for Cancer Research
New York, NY

Emergence of high-grade and treatment-resistant pancreatic NET subclones

BIOGRAPHY

Dr. Ziv is an interventional radiologist at Memorial Sloan Kettering Cancer Center and Director of the Laboratory for Interventional Oncology. His research efforts are focused on understanding neuroendocrine tumor evolution and transformation using a combination of computational techniques and cell line models. He is a recipient of the 2019 Gary Becker Young Investigator Award from the Society of Interventional Radiology. He earned a dual MD, PhD degree at Columbia University, where his dissertation focused on developing machine learning tools to understand the structure and function of gene networks. He completed his intern year at Mount Sinai University, and his residency and fellowship at the University of California, San Francisco.

SCIENTIFIC STATEMENT

Well-differentiated pancreatic neuroendocrine tumors (pNETs) represent a heterogeneous group of tumors with variable degree of aggressiveness. Treatment response and overall prognosis is largely determined by tumor grade. It is unknown when and how high-grade tumors arise in the overall course of the disease and in relation to treatment. This proposal seeks to resolve these issues by exploiting recent advances in tumor evolution biology. Using multi-region sampling from primary and metastatic sites over multiple time points, Dr. Ziv's team will reconstruct tumor phylogeny to determine the timing of the emergence of high grade subclones and to identify subclones selected for after therapy. By tracing the subclonal origin of high grade and treatment resistant tumors, this proposal will have important consequences regarding the role of tumor debulking, optimal treatment sequencing, and predictive biomarkers. Moreover, the findings will shed light on pNET tumor evolution, a poorly understood but important aspect of pNETs.

ACKNOWLEDGEMENT OF SUPPORT

We are very grateful for the 2020 Neuroendocrine Tumor Research Foundation-AACR Grant that will enable us to catalog the subclonal evolution of pancreatic neuroendocrine tumors in order to decipher when and how the most aggressive subclones emerge.



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