

AACR RESEARCH GRANT RECIPIENTS 2020-2021



AACR.org/Funding

AACR American Association
for Cancer Research®
FINDING CURES TOGETHER®

CONGRATULATIONS TO THE 2020-2021 GRANT RECIPIENTS

The American Association for Cancer Research (AACR) is proud to present the newest class of AACR grant recipients.

This year's scientific grant projects span the continuum from basic, translational, and clinical research as well as prevention and disparities research. This year's class is comprised of 55 outstanding scientists who 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 \$117 million in funding to hundreds of scientists. These grants have funded scientists both domestically and abroad at every career stage.

Congratulations to our newest grant recipients!

FUNDERS

The AACR would like to thank our funding partners, whose generosity and support have been instrumental to the continued success of our grants program, and 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.



What Would Willie Want



The John and Elizabeth
Leonard Family Foundation



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AACR-ASTRAZENECA STIMULATING THERAPEUTIC ADVANCES THROUGH RESEARCH TRAINING (START) GRANT

The AACR-AstraZeneca Stimulating Therapeutic Advances through Research Training (START) Grant represents an exciting initiative to encourage and support collaboration between academia and industry. The combined academic and industry training provided through this program will be invaluable to young investigators, allowing them to attain a comprehensive research experience.



Francesca Citron, PharmD, PhD

Postdoctoral Research Fellow

University of Texas MD Anderson Cancer Center
Houston, Texas

Unraveling the mechanism of DPY30 in pancreatic cancer

BIOGRAPHY

Dr. Citron obtained her PharmD degree in 2014 and her PhD in molecular biomedicine in 2018 at the University of Trieste, Italy. Her PhD research, under the mentorship of Dr. Gustavo Baldassarre at CRO-Aviano NCI, focused on the role of microRNAs as possible biomarkers in breast and head and neck cancers. After receiving several awards, Dr. Citron moved to The University of Texas MD Anderson Cancer Center to join the laboratory of Giulio Draetta, MD, PhD. Currently, she is studying the role of chromatin modulators in maintaining DNA stability and shaping pancreatic cancer progression.

SCIENTIFIC STATEMENT

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease characterized by silent onset and diagnosis in advanced stages, and it represents an urgent unmet clinical need. Improved understanding of factors driving PDAC progression is required to identify novel therapeutic concepts that may impact patient outcomes. Dr. Draetta's lab previously applied a robust shRNA-based in vivo screening platform to PDAC patient-derived xenograft models to identify epigenetic dependencies. Screens in multiple models identified members of the COMPASS-like complex as critical mediators of DNA stability essential for PDAC maintenance. This research will characterize genomic instability induced upon COMPASS-like complex silencing and uncover the mechanisms that underlie the role of COMPASS-like complex to sustain PDAC tumor growth. Given the paucity of therapeutic options available for PDAC, this research will greatly advance our ability to define a novel therapeutic strategy to target this DNA damage response that is highly specific for pancreatic cancer cells.

ACKNOWLEDGMENT OF SUPPORT

I am honored and grateful to receive the 2020 AACR-AstraZeneca START Grant. This represents a milestone in my training that will support my eventual transition to independent research. This funding inspires me to fulfill my responsibility to patients and to ask impactful questions to advance oncology practice.

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Francisca Nunes de Almeida, PhD

Postdoctoral Fellow

Columbia University
New York, New York

Targeting DNA damage repair in neuroendocrine prostate cancer

BIOGRAPHY

Dr. Nunes de Almeida completed her undergraduate studies in biochemistry at the University of Porto and a master's in biology at Uppsala University. During her PhD, Dr. Nunes de Almeida joined the laboratory of Franck Pichaud at the MRC Laboratory for Molecular and Cell Biology at University College London, where she investigated the mechanisms that regulate epithelial cell polarity in *Drosophila*. She is now a postdoctoral fellow in the laboratory of Cory Abate-Shen at the Irving Cancer Research Center at Columbia University, studying the role of DNA damage repair in lineage plasticity and treatment resistance in prostate cancer.

SCIENTIFIC STATEMENT

In prostate cancer, adenocarcinoma cells can transdifferentiate into neuroendocrine cells upon treatment with androgen receptor (AR)-targeted therapies, leading to a highly aggressive and metastatic disease. Dr. Nunes de Almeida aims to investigate the role of DNA damage repair (DDR) genes in this process of transdifferentiation. She hypothesizes that DDR genes drive differentiation from adenocarcinoma to neuroendocrine prostate cancer, leading to a more aggressive disease. She reasons that by targeting DDR genes it will be possible to reduce neuroendocrine transdifferentiation, improving the outcome for men with lethal prostate cancer. To address this hypothesis, Dr. Nunes de Almeida will use genetically engineered mouse models as tools to model a subtype of lethal prostate cancer and to validate novel drug therapies. Ultimately, this project will contribute to the development of novel and alternative treatments for patients with lethal prostate cancer, thus having a significant impact on improving prostate cancer patient care.

ACKNOWLEDGMENT OF SUPPORT

Receiving the 2020 AACR-AstraZeneca START grant is a unique opportunity to develop my postdoctoral project in an environment that fosters a culture of collaboration between industry and academia. I am truly honored and grateful to receive this career-defining fellowship.

AACR-BAYER STIMULATING THERAPEUTIC ADVANCES THROUGH RESEARCH TRAINING (START) GRANT

The AACR-Bayer Stimulating Therapeutic Advances through Research Training (START) Grant represents an exciting initiative to encourage and support collaboration between academia and industry. The combined academic and industry training provided through this program will be invaluable to young investigators, allowing them to attain a comprehensive research experience.



Dobeen Hwang, PhD

Postdoctoral Associate

The Scripps Research Institute
Jupiter, Florida

Dual payload ADCs designed for mitigating cancer resistance

BIOGRAPHY

Dr. Hwang received her PhD at Seoul National University under the supervision of Dr. Junho Chung. Her research focused on discovering and engineering antibodies through phage display technology for use as cancer therapeutics and medical imaging tools. Since joining Dr. Christoph Rader's laboratory at The Scripps Research Institute in 2017, she has continued to work in the field of antibody therapy, specifically on the development of next-generation antibody-drug conjugates (ADCs) for cancer therapy. She has devoted a particular focus to developing new conjugation technologies for the generation of site-specific ADCs and new antibody carriers to improve their tumor tissue penetration.

SCIENTIFIC STATEMENT

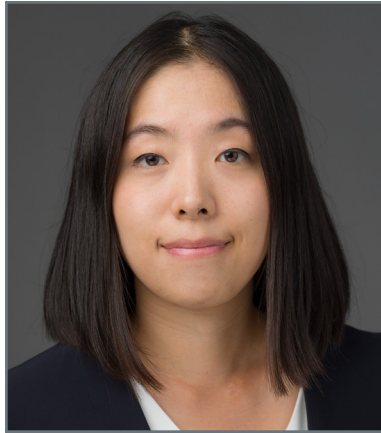
ATP-binding cassette (ABC) transporters contribute to multidrug resistance (MDR) by pumping cytotoxic drugs out of cancer cells, which has been a major impediment in the treatment of cancers. Among ABC transporters, multidrug resistance protein 1 and multidrug resistance-associated protein 1 have been extensively investigated and are implicated in refractory and resistant (R/R) cancer in response to chemotherapy and antibody-drug conjugates (ADCs). As these transporters are potential targets for developing more efficacious cancer treatments, Dr. Hwang proposes developing dual-payload ADCs designed to mitigate MDR in cancer cells by selectively co-delivering anti-cancer drugs and MDR inhibitors to cancer cells without harming healthy tissues expressing ABC transporters acting in physiological roles. Blocking MDR activity through an inhibitor will prompt the accumulation of the co-delivered anti-cancer drug and kill tumor cells at lower ADC dosing. She hopes this platform will offer new treatment options to R/R cancer patients.

ACKNOWLEDGMENT OF SUPPORT

I am very honored to have been selected for the AACR-Bayer START Grant and appreciate the support of my mentors for this proposal. This award will allow me to acquire insight into industrial drug discovery and development, continue my research on antibody-based cancer therapeutics, and greatly facilitate my career development.

AACR-BAYER STIMULATING THERAPEUTIC ADVANCES THROUGH RESEARCH TRAINING (START) GRANT

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Mari Nakamura, PhD

Postdoctoral Fellow

University of California, San Diego
San Diego, California

Defining molecular dependencies of pancreatic adenosquamous carcinoma

BIOGRAPHY

Dr. Nakamura obtained her BSc, MSc, and PhD from the University of Tokyo in Japan. She is currently a postdoctoral fellow in Dr. Tannishtha Reya's laboratory at the University of California, San Diego. Her research focuses on understanding the molecular mechanisms regulating pancreatic cancer progression and aims to identify novel therapeutic targets for the disease.

SCIENTIFIC STATEMENT

Pancreatic cancer is one of the deadliest types of cancer, with a five-year survival rate in the single digits. There are multiple subtypes of this malignancy, including adenosquamous carcinoma of the pancreas (ASCP), a highly aggressive tumor with the poorest clinical outcome out of all pancreatic cancers. Given recent studies showing that a considerable proportion of pancreatic cancers exhibit adenosquamous features, the need to better characterize ASCP and to explore its molecular dependencies is of great importance. Using a new mouse model that develops ASCP as well as patient-derived samples, Dr. Nakamura plans to uncover the key molecular drivers that govern the formation and progression of ASCP tumors. This study will potentially reveal new biomarkers and therapeutic targets of ASCP that would enable patient stratification and the development of subtype-specific treatments.

ACKNOWLEDGMENT OF SUPPORT

The AACR-Bayer START Grant provides me with an important opportunity to explore the therapeutic vulnerabilities of ASCP, an aggressive subtype of pancreatic cancer that has thus far not been investigated thoroughly. I am honored to receive this support and hope to use this opportunity to gain exciting insights for the field.

2020 CAREER DEVELOPMENT AWARDS



AACR NEXTGEN GRANT FOR TRANSFORMATIVE CANCER RESEARCH

The AACR NextGen Grant for Transformative Cancer Research represents the AACR's flagship funding initiative to stimulate highly innovative research from young investigators. This grant mechanism is intended to promote and support creative, paradigm-shifting cancer research that may not be funded through conventional channels.



Karuna Ganesh, MD, PhD

Assistant Member

Memorial Sloan Kettering Cancer Institute
New York, New York

Dissecting regenerative plasticity of metastasis stem cells

BIOGRAPHY

Dr. Ganesh is a physician-scientist and assistant member at Memorial Sloan Kettering Cancer Center in the Molecular Pharmacology Program and Gastrointestinal Oncology Service. She received her MD/PhD from the University of Cambridge/MRC Laboratory of Molecular Biology, UK, studying mechanisms of antibody diversification with the late Professor Michael Neuberger. She trained in internal medicine at Beth Israel Deaconess Medical Center and in medical oncology at Memorial Sloan Kettering Cancer Center, where she completed a postdoctoral fellowship with Dr. Joan Massagué. Her laboratory studies mechanisms of regenerative plasticity in metastasis.

SCIENTIFIC STATEMENT

Despite advances in cancer therapeutics, metastasis remains the principle cause of cancer death. Using novel patient-derived organoid models of metastatic colorectal cancer, Dr. Ganesh's group recently demonstrated that disseminating colorectal cancers (CRC) undergo a dynamic phenotypic switch from a tumor initiating cancer stem cell state to a distinct metastasis stem cell (MetSC) state that is required for metastasis initiation and therapy resistance. In this proposal she will integrate transcriptomic and epigenetic analyses of patient samples with mechanistic dissection in cutting-edge patient-derived organoid models and orthotopic transplantation mouse models of metastatic colorectal cancer. By combining clinically relevant patient-derived models with immunologically intact mouse models, she seeks to define the molecular mechanisms that underpin the phenotypic plasticity of metastatic cancer. Her goal is to identify crucial signaling nodes required for metastatic plasticity that can be therapeutically targeted to improve outcomes for patients with advanced cancer.

ACKNOWLEDGMENT OF SUPPORT

I am deeply honored to have been selected as a 2020 AACR NextGen Grant for Transformative Cancer Research recipient. This grant will provide critical funds to enable us to pursue an ambitious program of research to better understand and treat advanced cancers.

AACR NEXTGEN GRANT FOR TRANSFORMATIVE CANCER RESEARCH

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Matthew H. Spitzer, PhD

Assistant Professor

University of California, San Francisco
San Francisco, California

Metabolic dynamics of anti-tumor T cells in breast cancer

BIOGRAPHY

Dr. Spitzer completed his graduate training in immunology at Stanford University in the laboratories of Drs. Edgar Engleman and Garry Nolan. There, he developed experimental and analytical methods to model the state of the immune system and immune responses to cancer using high dimensional single-cell data. Dr. Spitzer then moved to UCSF as a Parker Fellow and a Sandler Faculty Fellow, where he is currently an assistant professor in the Departments of Otolaryngology-Head and Neck Surgery and of Microbiology & Immunology, as well as an investigator of the Parker Institute for Cancer Immunotherapy and the Chan Zuckerberg Biohub.

SCIENTIFIC STATEMENT

Immunotherapy has revolutionized oncology over the last decade. However, responses in breast cancer remain infrequent and transient. Elucidating the mechanisms governing effective anti-tumor immunity will be imperative to rationally improve the efficacy of these treatments. T cells are central to productive anti-tumor immune responses, and the field of immunometabolism has linked T cell metabolic activity to their differentiation and effector function. Modulation of T cell metabolism, therefore, represents a promising strategy to augment responses to immunotherapy. Leveraging new methods developed by Dr. Spitzer and his lab members, they will quantify metabolic adaptations along with markers of T cell differentiation and function at the single-cell level. Through parallel studies in mouse models and primary patient biospecimens, they will understand the metabolic requirements of T cells during tumor eradication. These studies will pave the way to develop more durable and broadly effective immunotherapies for breast cancer patients.

ACKNOWLEDGMENT OF SUPPORT

I am so appreciative for the support of our work through a 2020 AACR NextGen Grant for Transformative Cancer Research. This grant will provide essential funds and resources to achieve our goal of improving immunotherapy for breast cancer through a deeper understanding of T cell metabolic function.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant supports early- to mid-career investigators employing highly innovative approaches to major problems or challenges in cancer research.



Sara J. Buhrlage, PhD

Assistant Professor

Dana-Farber Cancer Institute
Boston, Massachusetts

Bivalent DUB recruiters for targeted protein stabilization

BIOGRAPHY

Dr. Buhrlage is an assistant professor in Dana-Farber's Cancer Biology Department and Harvard Medical School's Biological Chemistry and Molecular Pharmacology Department. Her research group focuses on the development of small molecule modulators of deubiquitylating enzymes (DUBs) for cancer therapy. Prior to joining as a faculty member in 2015, Dr. Buhrlage ran the medicinal chemistry core laboratory at Dana-Farber. Dr. Buhrlage completed a PhD in organic chemistry in 2008 under the direction of Professor Anna Mappat the University of Michigan and trained for two years in medicinal chemistry at the Broad Institute.

SCIENTIFIC STATEMENT

The two main classes of proteins that promote development and progression of cancer are oncogenic proteins and tumor suppressor proteins. Nearly all precision oncology drugs developed in recent decades function by blocking the activity of oncogenic proteins. In contrast, pharmacological strategies to increase levels of tumor suppressors have remained largely elusive. Dr. Buhrlage proposes to develop a novel class of agents, bivalent deubiquitinase (DUB) proximity inducing molecules, that can selectively stabilize targeted proteins. This new drug development paradigm is enabled by her group's recent success in developing selective DUB ligands for several members of the enzyme family. The successful completion of this proposal has the potential to transform cancer clinical care by delivering a completely new strategy for one of the most prolific undruggable oncology classes, tumor suppressors.

ACKNOWLEDGMENT OF SUPPORT

I'd like to sincerely thank the AACR and MPM for the opportunity to pursue this "high-risk, high-reward" research project. As an early career investigator, the chance to pursue this type of project could propel my career. We will pursue the research aggressively and are optimistic we'll credential a new cancer treatment paradigm.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant supports early- to mid-career investigators employing highly innovative approaches to major problems or challenges in cancer research.



Robert Eil, MD

Assistant Professor

Oregon Health & Science University
Portland, Oregon

Targeting the ionic checkpoint on T cell antitumor function

BIOGRAPHY

Dr. Eil is a surgeon-scientist focused on applying immunotherapy to cancers involving the liver, pancreas, and bile ducts. During his surgical training, Dr. Eil completed a research fellowship at the Surgery Branch of the National Cancer Institute, focusing on T cell biology and tumor immunology. Following his clinical fellowship in surgical oncology (MSKCC), he returned to Oregon Health & Science University with appointments in the Departments of Surgery and Cellular, Developmental and Cancer Biology. Dr. Eil's multidisciplinary expertise provides a unique perspective on alleviating suppression of T cell function in cancer to improve the lives and outcomes of patients.

SCIENTIFIC STATEMENT

Dramatic responses can be seen in some patients following the receipt of cancer immunotherapy in the form of immune checkpoint blockade or T cell transfer. However, owing to tumor induced T cell dysfunction, resistance to treatment is common. Dr. Eil's work demonstrated for the first time that potassium (K⁺) is elevated within cancers and deters T cell antitumor functions (Eil et al, Nature 2016; Science 2019). To test the hypothesis that cancer cell death suppresses T cell function through K⁺ sensitive signal transduction he will 1) determine the functional significance of cancer cell death byproducts for inflammasome and T cell activation in human Intrahepatic Cholangiocarcinoma (ICC), 2) define the mechanism underlying K⁺ control of T cell function, and 3) assess the impact of interventions to reprogram T cell K⁺ transport as cancer immunotherapeutics.

ACKNOWLEDGMENT OF SUPPORT

Receipt of this 2020 AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant represents a critical milestone in my development as an independent scientist. I am thrilled to have the opportunity to pursue this exciting line of investigation with the potential to apply ground-breaking immune-based treatments to patients with treatment-resistant cancers.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant supports early- to mid-career investigators employing highly innovative approaches to major problems or challenges in cancer research.



Hani Goodarzi, PhD

Assistant Professor

University of California, San Francisco
San Francisco, California

Discovering and targeting cancer-engineered pathways of metastasis

BIOGRAPHY

Dr. Hani Goodarzi is an assistant professor at the University of California, San Francisco. With a dual background in computational and experimental cancer biology, he brings a multidisciplinary approach to studying tumor progression. His research is focused on developing strategies that enable an unbiased search for previously unknown pathways of metastasis. By developing novel technologies for genome-wide measurement of hard-to-quantify RNA molecules, he has made key discoveries about the role of oncRNA, tRNAs, and tRNA fragments in cancer metastasis. On the computational front, Dr. Goodarzi is focused on building network analytical models that help elucidate key pathways and processes that drive human disease. In 2017, he was awarded the Martin and Rose Wachtel Award in Cancer Research for his contributions to cancer research and was recently named a Kimmel Scholar. He was previously a recipient of the prestigious Blavatnik Award for Young Scientists as well as the Tri-institutional Breakout Prize.

SCIENTIFIC STATEMENT

Cancer is fundamentally a disease of disordered gene expression. Revealing the regulatory pathways that are hijacked by cancer cells to drive pathologic gene expression programs is a crucial step towards understanding oncogenesis. However, given our current understanding of cancer progression as an evolutionary process, there is a largely unexplored possibility that cancer cells may engineer their own regulatory pathways. The discovery and characterization of such cancer-emergent regulatory mechanisms forms the foundation of the research proposed by Dr. Goodarzi and his team. Their recent discovery of orphan non-coding RNAs (oncRNAs) as a cancer-specific class of small RNAs with regulatory potential provides an opportunity for a systematic search for functional neo-regulators of gene expression in cancer cells. In addition to providing much needed insight into tumor evolution, this research also nominates novel targets that are solely active in cancer cells and whose targeted inhibition is unlikely to elicit on-target systematic toxicity.

ACKNOWLEDGMENT OF SUPPORT

The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant provides a unique opportunity for my team to tackle a high-risk, high-reward project. In addition to providing support and resources, this represents a vote of confidence in our approach from the leaders in the field.

AACR-ST. BALDRICK'S FOUNDATION PEDIATRIC CANCER RESEARCH GRANT

The recipient of the AACR-St. Baldrick's Foundation Pediatric Cancer Research Grant is chosen from among several outstanding junior faculty investigators at the level of assistant professor who have been nominated by the recipient of the AACR-St. Baldrick's Foundation Award for Outstanding Achievement in Pediatric Cancer Research. This program represents the first time that an AACR scientific achievement award has been linked to a research grant opportunity.



Jarno Drost, PhD

Principal Investigator

Princess Máxima Center for Pediatric Oncology
Utrecht, Netherlands

BIOGRAPHY

Dr. Drost received his MSc degree in biomedical sciences at the Free University of Amsterdam (with honors). In 2012, he obtained his PhD at the Netherlands Cancer Institute (lab of Dr. Reuven Agami). He then joined the lab of Dr. Hans Clevers (Hubrecht Institute) as a post-doctoral fellow and got acquainted with organoid technology. In 2016, Dr. Drost started his research group at the Princess Máxima Center for Pediatric Oncology and OncoCode Institute, where he studies the molecular alterations underpinning childhood solid tumors, with a primary focus on renal and rhabdoid tumors.

SCIENTIFIC STATEMENT

Kidney tumors are among the most common solid tumors in children, comprising distinct subtypes that differ in many aspects. Although overall survival rates of certain subtypes have considerably increased over the past decades, some subtypes still carry a dismal outcome profile. In particular, rhabdoid tumors, which can appear in the kidney, the brain, and soft tissues, remain one of the big challenges in childhood cancer. All this creates an urgent need for the development of new (and less toxic) therapies. Dr. Drost's research group at the Princess Máxima Center studies the molecular mechanisms underlying the development of childhood kidney and rhabdoid tumors with the aim of identifying novel therapies. Dr. Drost pioneered the use of organoid technology in childhood cancer and succeeded in growing organoids from a spectrum of pediatric tumors. His group uses these organoid models as a screening platform to find drugs that specifically target tumor cells. Furthermore, he combines organoid and mouse models with (singlecell) next generation sequencing, gene editing, and lineage tracing technologies to study the molecular mechanisms underpinning tumorigenesis.

ACKNOWLEDGMENT OF SUPPORT

The AACR-St. Baldrick's Foundation Pediatric Cancer Research Grant offers the support to further develop ongoing, as well as initiate new, research lines. It also provides international exposure for my research, allowing me to initiate new international collaborations in the field of childhood cancer, as I believe that a collaborative approach is vital for a successful research career.

BREAST CANCER RESEARCH FOUNDATION-AACR NEXTGEN GRANT FOR TRANSFORMATIVE CANCER RESEARCH

The AACR NextGen Grant for Transformative Cancer Research represents the AACR's flagship funding initiative to stimulate highly innovative research from young investigators. This grant mechanism is intended to promote and support creative, paradigm-shifting cancer research that may not be funded through conventional channels. The Breast Cancer Research Foundation generously supports this grant.



Jeremy C. Borniger, PhD

Assistant Professor

Cold Spring Harbor Laboratory
Cold Spring Harbor, New York

Neuromodulation of subcortical circuits driving breast cancer progression

BIOGRAPHY

Dr. Borniger is an assistant professor with dual appointments in the neuroscience and cancer divisions at Cold Spring Harbor Laboratory. He received his bachelor's degree in biological anthropology from Indiana University – Bloomington. He then went on to complete a PhD in neuroscience at The Ohio State University, focusing on distal communication between breast cancer and the brain. Dr. Borniger then completed a BRAIN Initiative postdoctoral fellowship with Dr. Luis de Lecea at Stanford University, where he applied cutting-edge techniques to assess neural circuit activity in mouse models of cancer.

SCIENTIFIC STATEMENT

Dr. Borniger's experiments will map how tumor development (premalignancy to malignancy and metastasis) alters brain-wide neural activity using light-sheet tomography to visualize cFos expression and distribution throughout the entire brain in an unbiased fashion. Then, the team will use scRNA-seq to "trap" and transcriptionally profile activated neurons. Finally, using optogenetics they will examine how manipulation of these circuits alters the intra-tumor immune response and sleep/wake behavior. This is based on the growing body of work demonstrating links between sleep/wake states, stress, and immunity. This work will directly investigate how mammary tumors in the periphery reshape neuronal activity across the entire brain to alter sleep/wake behavior and, reciprocally, causally test the role these neuronal ensembles play in the tumor's ability to evade the immune system and modulate systemic physiology. Precise targeting of neural-cancer and neuro-immune interactions will provide new opportunities for improving outcomes of difficult-to-treat malignancies.

ACKNOWLEDGMENT OF SUPPORT

This award provides essential funding for my laboratory as an early stage investigator. This support will allow my group to tackle pressing questions regarding the basic biology of breast cancer by using a suite of systems neuroscience techniques, with the ultimate goal of identifying targets for validation or preventative therapy.

2020 INDEPENDENT INVESTIGATOR GRANTS



AACR-THE MARK FOUNDATION FOR CANCER RESEARCH “SCIENCE OF THE PATIENT” (SOP) GRANT

The AACR-The Mark Foundation for Cancer Research “Science of the Patient” (SOP) Grant represents a joint effort to stimulate novel research aimed at understanding the influence of the biology of the host (i.e., patient) on the genesis, development, treatment, and survivorship of cancer.



Gregory L. Beatty, MD, PhD

Associate Professor

University of Pennsylvania
Philadelphia, Pennsylvania

Impact of liver biology on cancer immunity

BIOGRAPHY

Dr. Beatty is an associate professor of medicine in the Division of Hematology/Oncology at the University of Pennsylvania. He is Director of Clinical and Translational Research for the Pancreatic Cancer Research Center at the University of Pennsylvania. He trained at Bucknell University (BS, chemical engineering, 1995) and the University of Pennsylvania (immunology, PhD, 2000; MD, 2004; residency 2004-2006; medical oncology fellow, 2006-2010). In 2012, he joined the faculty and now leads a discovery laboratory that uses mouse models, human tissues, and clinical trials to study mechanisms of resistance to immunotherapy with the priority to develop new treatment strategies.

SCIENTIFIC STATEMENT

Dr. Beatty's project addresses the liver as a determinant of the efficacy of cancer immunotherapy. The liver is central to establishing immune tolerance and is continuously exposed to cancer cells and factors released by cancer. This connection between cancer and the liver has emerged as a critical element of cancer metastasis and immune evasion. His group has found that hepatocytes, the chief functional cells of the liver, are instructed by cancer to support liver metastasis and has identified several molecular determinants that initiate this biology. However, it remains unclear how to therapeutically intervene on the liver as a strategy to enhance the immune response to cancer and to prevent metastasis. His goal is to define determinants of the liver response to human cancer and to interrogate mechanisms by which the liver coordinates immune dysfunction. In doing so, he aims to identify novel therapeutic targets and new treatments for patients with cancer.

ACKNOWLEDGMENT OF SUPPORT

I am so thrilled to receive this grant award, which allows my research team and me to conduct studies on the connection between the liver, cancer, and immunity. Support from the AACR and The Mark Foundation will allow us to be innovative and to follow our vision of broadening the efficacy of immunotherapy.

AACR-THE MARK FOUNDATION FOR CANCER RESEARCH “SCIENCE OF THE PATIENT” (SOP) GRANT

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**Marcus DaSilva Goncalves,
MD, PhD**

Assistant Professor

Weill Cornell Medicine
New York, New York

Targeting insulin to improve endometrial cancer

BIOGRAPHY

Dr. Goncalves is an endocrinologist and basic scientist at Weill Cornell Medicine in New York. He holds degrees in biomedical engineering from the Johns Hopkins University and MD/PhD degrees from the University of Pennsylvania. He completed his postgraduate medical training at the joint program among Weill Cornell Medicine, New York Presbyterian Hospital, and Memorial Sloan Kettering Cancer Center. His research focuses on the interactions between cancer and the hormones that regulate systemic metabolism. In his specialized clinical practice, he regularly treats patients with cancer experiencing hyperglycemia, weight loss, and other complications that may arise from their disease or care.

SCIENTIFIC STATEMENT

The incidence and mortality rate of endometrial cancer are increasing due, in part, to the obesity epidemic. Obesity dramatically increases the risk of death from endometrial cancer, more so than any other cancer type. There are a variety of systemic changes that occur in the obese state that favor tumor initiation and progression. One of these factors, hyperinsulinemia, activates tumor phosphatidylinositol 3-kinase (PI3K) activity, which has been directly implicated in the pathogenesis of endometrial cancer. Therefore, dietary and pharmacologic strategies that lower insulin levels or block PI3K function may be effective anti-cancer agents in this setting. In this proposal, Dr. Goncalves will use mouse models and human clinical trials to test if a very low carbohydrate diet will reduce tumor insulin signaling, increase markers of cell death, and enhance the efficacy of PI3K inhibitors in endometrial cancer.

ACKNOWLEDGMENT OF SUPPORT

I am honored to receive the 2020 AACR-The Mark Foundation for Cancer Research “Science of the Patient” (SOP) Grant. Host factors are often overlooked in clinical trials and basic research. This unique grant provides critical support for us to highlight the role of diet and insulin in endometrial cancer progression.

AACR-THE MARK FOUNDATION FOR CANCER RESEARCH “SCIENCE OF THE PATIENT” (SOP) GRANT

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Daniel L. Marks, MD, PhD

Professor

Oregon Health & Science University
Portland, Oregon

Autonomic dysfunction in cancer cachexia

BIOGRAPHY

Dr. Marks received medical and graduate training at the University of Washington, then completed his pediatric residency at the University of Utah and a fellowship in pediatric endocrinology at OHSU. He is currently Senior Associate Dean for Research at OHSU. He is also Professor and Ray Hickey Chair for Pediatric Research and Director of the Papé Family Pediatric Research Institute. His current investigations are focused on the neuroendocrine control of body weight. He has a particular interest in the brain mechanisms of disease-associated cachexia, with emphasis on cachexia in cancer patients and children with chronic disease.

SCIENTIFIC STATEMENT

A variety of cancers produce profound changes in the brain that severely compromise both quality of life and survival. In particular, a constellation of weight loss, muscle wasting, adipose tissue reprogramming, and anorexia comprise a debilitating condition known as cachexia that is found in ~80% of patients with pancreatic ductal adenocarcinoma (PDAC). Dr. Marks’s group has demonstrated that signaling between the tumor and the central nervous system (CNS) is critical for metabolic, behavioral, and neurocognitive complications during tumor growth. They have developed new models and compelling preliminary data demonstrating that preautonomic and neuroendocrine neurons located in the hypothalamus are activated early in the course of PDAC development and provide a robust catabolic output to peripheral tissues. These same pathways demonstrate remarkable phenotypic plasticity during the evolution of cachexia. These pathways provide novel therapeutic options for cachexia and include drugs that are already in clinical practice or advanced clinical trials.

ACKNOWLEDGMENT OF SUPPORT

I am grateful to the AACR and The Mark Foundation for Cancer Research for the generous support offered by this award. We believe that the work supported by this grant will improve the lives of patients with cancer and point the way to new treatments for cachexia in cancer patients.

AACR-THE MARK FOUNDATION FOR CANCER RESEARCH “SCIENCE OF THE PATIENT” (SOP) GRANT

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**Fatemeh Momen-Heravi,
DDS, PhD, MPH, MS**

Assistant Professor

Columbia University
New York, New York

Biological mechanism and risk factor of head and neck cancer in blacks

BIOGRAPHY

Dr. Momen-Heravi is an assistant professor at Herbert Irving Comprehensive Cancer Center and the College of Dental Medicine at Columbia University. She received her DDS from Tehran University, master of public health in biostatistics from Harvard University, and PhD in molecular biology/biotechnology from the University of Westminster, UK. She received residency training in periodontics at Columbia University and performed postdoctoral research in molecular biology at Harvard Medical School and the University of Massachusetts Medical School. Her lab at Columbia University combines computational biology and advanced biostatistical methods with wet lab techniques to identify signaling mechanisms and tumor vulnerabilities in head and neck cancer and lung cancer. Her group also works on novel genome editing modalities based on CRISPR/CAS and exosomes as precision medicine tools to treat cancer.

SCIENTIFIC STATEMENT

Head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer worldwide. With a five-year survival rate of fifty percent, precision therapy advances are desperately needed for HNSCC patients. Population-based studies have identified disparities between racial groups in HNSCC treatment and survival, especially for patients with African ancestry. This disparity exists even after controlling for social determinants of health and access to care. Due to a lack of understanding of genomic and transcriptomic drivers of head and neck cancer in black patients, a subset of targetable mutations or pathways could be missing for black populations. This project is aimed to fill this gap by characterizing the molecular features of HNSCC tumors specifically in patients with African ancestry, as defined computationally (rather than by self-reporting). These analyses will result in an unbiased estimate of the relation of ancestry/race and HNSCC molecular features. In addition to genomic alterations, the project will also identify transcriptomic changes associated with HNSCC. Pathway analysis and integration of omics data will uncover tumor vulnerabilities in Black patients for therapeutic targeting, with the ultimate goal of developing personalized therapies and reducing health disparities.

ACKNOWLEDGMENT OF SUPPORT

It is an honor to receive the AACR-The Mark Foundation for Cancer Research “Science of the Patient” (SOP) Grant. The grant supports the important mission of reducing health disparities in head and neck cancer. Our research will transform the lives of many minority patients by understanding their specific risk factors and developing new personalized treatment.

AACR-THE MARK FOUNDATION FOR CANCER RESEARCH “SCIENCE OF THE PATIENT” (SOP) GRANT

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Liuqing Yang, PhD

Associate Professor

University of Texas MD Anderson Cancer Center
Houston, Texas

Liver PAH defect provokes immune resistance

BIOGRAPHY

Dr. Liuqing Yang was recruited to the Department of Molecular and Cellular Oncology at MD Anderson Cancer Center in 2013. He is a Cancer Prevention and Research Institute of Texas Scholar and an awardee of the Wilson S. Stone Memorial Award, Andrew Sabin Family Foundation Fellow Award, AACR-Bayer Innovation and Discovery Grant, AACR NextGen Stars Award, President’s Recognition of Faculty Excellence Award, and Faculty Scholar Award. He is trying to find better treatments for acquired resistance to immunotherapy by thinking about the metabolic microenvironment in a new way.

SCIENTIFIC STATEMENT

Acquired resistance to immunotherapy refers to a scenario where patients have an initial response to immunotherapy but later exhibit a reduced response to the treatment, raising major clinical concerns. Furthermore, the majority of cancer patients exhibit hepatitis following immune checkpoint blocker treatment. The molecular mechanism of immunotherapy-associated hepatic impairment and its effects on a patient’s metabolic microenvironment remain elusive. This research project aims to demonstrate the signaling events triggered by immune checkpoint blockers in hepatocytes and altered metabolic microenvironment-dependent acquired immune resistance, dissecting the interplay between the liver and the tumor microenvironment post-immunotherapy. This research will also investigate whether cancer patients undergoing immune checkpoint blocker treatment should avoid an Aspartame- and protein-rich diet, which will broadly impact current clinical management considerations. Furthermore, the proposed studies may pave the way for formulations using clinically administered liver enzyme enhancers to restore immune balance post-immune checkpoint blocker treatment to overcome acquired immune resistance.

ACKNOWLEDGMENT OF SUPPORT

We are immensely thankful for the support provided by the AACR and The Mark Foundation. Our studies are aimed at improving clinical outcomes for a wide range of patients undergoing immunotherapeutic cancer treatments, and the discoveries made with the support of this grant will be critical to future considerations for immunotherapy.

2021 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.



Ferran Nadeu, PhD

Postdoctoral Researcher

Institut d'Investigacions Biomèdiques
August Pi i Sunyer (IDIBAPS)
Barcelona, Spain

Tracking the progression and transformation of chronic lymphocytic leukemia

BIOGRAPHY

Dr. Nadeu received his PhD in biomedicine from the University of Barcelona under the mentorship of Dr. Elías Campo. He has contributed to a better understanding of the heterogeneous genomic landscape of chronic lymphocytic leukemia and its influence on patient outcomes. He has also been involved in the identification of novel non-coding driver mutations, the (epi)genomic characterization of mantle cell lymphoma, the use of cell-free DNA for the genomic profiling of diffuse large B-cell lymphoma, and the development of new bioinformatic algorithms to characterize B cell tumors from next-generation sequencing data.

SCIENTIFIC STATEMENTS

Chronic lymphocytic leukemia (CLL) is a common disease that represents a paradigmatic model of cancer evolution. The disease may have a long stable phase, spontaneously regress, progress to an aggressive disease, or even transform into aggressive mature B-cell lymphoma. Recent large-scale genomic/epigenomic studies have revealed the complex genomic alterations of the disease. However, the information generated is insufficient to explain the influence of genomic/epigenomic changes in the progression and transformation of CLL. Understanding these driving forces is essential to design biologically oriented therapeutic strategies. In this project, Dr. Nadeu proposes to decode the complex evolutionary paths of CLL through an integrative genomic/transcriptomic/epigenomic analysis of sequential tumor samples from a selected cohort of patients. The tumors will be examined using standard and low-input whole-genome and transcriptome sequencing as well as epigenome sequencing. This global characterization will be combined with single-cell genomics, spatial transcriptomics, and epigenomic approaches.

ACKNOWLEDGMENT OF SUPPORT

I am deeply honored to be awarded the 2021 AACR-Amgen Fellowship in Clinical/Translational Cancer Research. My most sincere gratitude to the AACR, Amgen, and its scientific review committee. This award boosts my postdoctoral fellowship, setting the path towards an independent scientific career. I hope the results of this project will translate into better management strategies for patients.

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 to establish a successful career path.



Xue-Yan He, PhD

Postdoctoral Fellow

Cold Spring Harbor Laboratory
Cold Spring Harbor, New York

Targeting stress-induced neutrophil extracellular traps prevents metastasis

BIOGRAPHY

Dr. He obtained her PhD at the Model Animal Research Center of Nanjing University, where she identified the role of tumor suppressor p53 in the tumor microenvironment. She started her postdoctoral study on breast cancer immune response at the cancer center of Cold Spring Harbor Laboratory, with a fellowship awarded by New York State. Currently, her goal is to understand how stress promotes breast cancer recurrence via modifying immune response.

SCIENTIFIC STATEMENT

Emerging evidence has shown a link between chronic stress and tumor metastatic recurrence, which is the leading cause of cancer-related deaths. Since stress is difficult to avoid, especially in cancer patients, it is imperative to understand how stress causes metastasis in order to better identify therapeutic regimens for stressed patients. Dr. He's project aims to delineate the mechanisms of how elevated stress hormone glucocorticoids contribute to tumor metastasis via neutrophil extracellular traps (NETs)—structures of DNA and protein expelled by neutrophils—in different organs and how these stress-induced NETs influence cancer therapies. To accomplish this Dr. He will 1) determine how stress-triggered NETs promote breast cancer metastasis in mouse models and 2) establish the mechanism by how glucocorticoids induce NETs to promote metastasis using RNA-seq, ChIP-seq and in vitro screening.

ACKNOWLEDGEMENT OF SUPPORT

I am very grateful and greatly honored to be selected for the AACR-AstraZeneca Breast Cancer Research Fellowship. Receiving this fellowship will help advance my postdoctoral training in understanding the mechanisms underlying tumor progression and targeting them for therapeutic benefit and lay a solid foundation for my scientific career development.

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 to establish a successful career path.



Samantha Van Nest, PhD

Postdoctoral Associate

Weill Cornell Medicine
New York, New York

The impact of hypoxia on radiation induced anti-cancer immunity

BIOGRAPHY

Dr. Van Nest has dedicated her career to advancing the next generation of radiation therapy, advocating for personalized and systemic treatment approaches. She obtained her PhD from the University of Victoria, where she established Raman Spectroscopy as a technique for tracking radiobiological responses. She is currently a postdoctoral associate in the Department of Radiation Oncology at Weill Cornell Medicine. Her research operates at the interface between radiobiology and immunology, investigating the impact of radiation on the immunopeptidome and potential exposure of neoantigens to promote anti-tumor immunity.

STATEMENT

A profound challenge limiting the success of immunotherapy in breast cancer is the inherently low immunogenicity of this disease. Radiation therapy has been shown at the preclinical level to enhance antitumor immunity by exposing tumor antigens which can be recognized by T cells, converting a previously immune hidden tumor into one which can be systemically targeted. However, breast cancers commonly develop hypoxia, which has been implicated in suppressing antigen processing and presentation. Dr. Van Nest is determining the impact of radiation on enhancing anti-tumor immunity through exposure of neoantigens and, in particular, the impact of hypoxia on this process. This work will provide key evidence for targeting hypoxia in order to enhance response to radiation therapy in combination with immunotherapy in breast cancer.

ACKNOWLEDGEMENT OF SUPPORT

It is truly an honor to receive the AACR-AstraZeneca Breast Cancer Research Fellowship and have the opportunity to advance our understanding of the role of hypoxia in radiation induced immunogenicity. It is my hope to provide important rationale for targeting hypoxia in the context of this novel treatment approach.

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 to establish a successful career path.



Raphael Mattiuz, PhD

Postdoctoral Fellow

Icahn School of Medicine at Mount Sinai
New York, New York

Determining the regulation and role of mreg DC in tumor immunity

BIOGRAPHY

Dr. Mattiuz completed his PhD at the Centre d'Immunologie de Marseille-Luminy (Aix-Marseille University, France), where he studied the role of type 1 conventional dendritic cells in breast cancer immunosurveillance. He is currently conducting his postdoctoral work under the supervision of Dr. Miriam Merad at the Precision Immunology Institute at the Icahn School of Medicine at Mount Sinai, determining the regulation and role of mreg DCs in tumor immunity in mice and patients.

SCIENTIFIC STATEMENT

The key steps leading to subversion of the immune system and tumor escape are still obscure. Dr. Merad's laboratory recently identified a molecular state of dendritic cells (DCs) upon tumor antigen uptake named 'mature DCs enriched in immunoregulatory molecules' (mreg DCs). mreg DCs express not only maturation genes associated with T cell stimulation, but also genes associated with immunoregulation. These results suggest that the balance of the mreg DC regulatory and activation program will determine the behavior of tumor-specific T cells. During his fellowship, Dr. Mattiuz proposes to build on these findings to determine some of the molecular drivers of the regulatory module expressed by mreg DCs and exploit this knowledge to enhance DC immunogenicity and antitumor immunity. Then, he will determine the significance of the spatial distribution of mreg DCs to T cell dependent antitumor immunity (in the tumor microenvironment versus the tumor draining lymph node).

ACKNOWLEDGMENT OF SUPPORT

It is a great honor to become an AACR-AstraZeneca Immuno-oncology fellow. I am truly grateful to the committee for selecting my research project. It is a crucial step to pursue my research career. I am really looking forward to contributing to the AACR mission by my research in enhancing patient antitumor immunity.

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.



Joseph Minhow Chan, MD, PhD

Medical Oncology Fellow

Memorial Sloan Kettering Cancer Center
New York, New York

Uncovering drivers of small cell transformation at single-cell level

BIOGRAPHY

Dr. Chan completed his MD/PhD at Columbia University College of Physicians and Surgeons, where he studied computational biology and developed new methods to model the topology of viral evolution and identify recurrent FGFR-TACC fusions in glioblastoma multiforme. He is currently a medical oncology and postdoctoral research fellow at Memorial Sloan Kettering Cancer Center, where he aims to leverage single-cell technologies to understand how neuroendocrine lineage plasticity in lung and prostate cancer mediates metastasis and therapeutic resistance and how the tumor microenvironment can impact this tumor-intrinsic process.

SCIENTIFIC STATEMENT

In lung adenocarcinoma (LUAD), neuroendocrine transformation to small cell lung cancer (SCLC) is associated with metastasis and resistance to targeted therapies. This lineage plasticity often leads to LUAD and SCLC subclones with shared ancestry admixed in the same tumor. Single-cell RNA sequencing (scRNA-seq) in samples of combined LUAD/SCLC histology presents an ideal platform to capture intratumoral heterogeneity and transitional subpopulations between histologies. We hypothesize that under RB1 and TP53 loss, Notch signaling and key transcription factors mediate neuroendocrine transformation. We will 1) leverage scRNA-seq in samples of combined LUAD/SCLC histology to identify molecular markers of subclonal populations and 2) validate predicted transcriptomic drivers of neuroendocrine plasticity in preclinical *in vitro* and *in vivo* models, including an EGFR+ LUAD patient-derived xenograft that undergoes neuroendocrine transformation after osimertinib treatment. The long-term goal is to identify drug targets to reverse or prevent plasticity as a form of resistance in an aggressive disease subtype with no known optimal therapeutic regimen.

ACKNOWLEDGMENT OF SUPPORT

I am deeply humbled and grateful to be supported by the 2021 AACR-AstraZeneca Lung Cancer Research Fellowship. I hope this award will provide me with a critical platform to become a successful independent investigator who combines computational biology, single-cell technologies, and translational domain knowledge to create meaningful clinical impact in the lives of my cancer patients.

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.



Joseph G. Schroers-Martin, MD

Postdoctoral Fellow

Stanford University
Stanford, California

Noninvasive early detection & characterization of post-transplant lymphoma

BIOGRAPHY

Dr. Schroers-Martin worked as a software developer and pursued bioinformatics and virology training before receiving his medical degree from the University of Hawai'i. He completed internal medicine residency followed by a post-doctoral research year at Stanford University. As a clinical hematology and oncology fellow at Stanford, he utilizes cell-free DNA to study the early detection and biology of lymphomas.

SCIENTIFIC STATEMENT

Patients receiving solid organ transplants are at high risk for cancer, with up to 25% of deaths after heart transplantation due to malignancy. The most common cause of death is post-transplant lymphoproliferative disorder (PTLD), an aggressive lymphoma associated with immunosuppression. There is no established clinical method to screen patients for this cancer. In collaboration with several transplant centers, Dr. Schroers-Martin will use "liquid biopsies" to evaluate early PTLD detection via DNA shed by emerging lymphomas and associated viruses.

ACKNOWLEDGMENT OF SUPPORT

The 2021 AACR-AstraZeneca Lymphoma Research Fellowship is a great honor, and I am deeply grateful for this opportunity to continue my work in noninvasive cancer detection and lymphomagenesis. This critical support will provide a foundation for my transition from fellow to independent translational investigator.

AACR-BAYER CLINICAL ONCOLOGY RESEARCH (CORE) TRAINING FELLOWSHIP

The AACR-Bayer Clinical Oncology Research (CORE) 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 clinical development at a Bayer facility in Cambridge, MA.



Praful Ravi, MB, BChir, MRCP

Fellow in Hematology, Oncology

Dana-Farber Cancer Institute
Boston, Massachusetts

BIOGRAPHY

Dr. Ravi received his medical degree at the University of Cambridge and obtained his MRCP in London before completing a residency in internal medicine at the Mayo Clinic. He then completed a fellowship in medical oncology at Dana-Farber Cancer Institute, and recently became an instructor of medicine at the Lank Center for Genitourinary Oncology at Dana-Farber and Harvard Medical School. He treats patients and performs clinical research in genitourinary cancers and is interested in conducting clinical trials and identifying biomarkers that may ultimately enable personalization of cancer therapy to each patient.

RESEARCH ACTIVITIES AT BAYER

During the research year at Bayer, Dr. Ravi will be paired with a Bayer scientist 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. Ravi with the opportunity to gain experience in drug development and understand challenges in early-stage and late-stage clinical research. Additional focus areas may also be provided (e.g., preclinical research, biomarker discovery).

ACKNOWLEDGMENT OF SUPPORT

I am delighted and honored to receive the AACR-Bayer CORE Training Fellowship. This will provide dedicated time and funding for me to pursue further training in drug development and clinical trial design and will therefore be invaluable to my overall career development as a clinical investigator in genitourinary cancers.

AACR-BRISTOL MYERS SQUIBB CANCER DISPARITIES RESEARCH FELLOWSHIP

The AACR-Bristol Myers Squibb 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.



Kyle A. Cottrell, PhD

Postdoctoral Research Scholar

Washington University in St. Louis
St. Louis, Missouri

Addressing breast cancer disparities by targeting ADAR

BIOGRAPHY

Dr. Cottrell received his PhD in molecular cell biology from Washington University in St. Louis, where he studied post-transcriptional regulation by microRNAs and RNA binding proteins. He currently works as postdoctoral research scholar at Washington University in St. Louis, where he focuses on the role of RNA editing in triple-negative breast cancer.

SCIENTIFIC STATEMENT

Triple-negative breast cancer (TNBC), the deadliest form of breast cancer, affects Black/African American women at twice the rate of white women. Broadly applicable targeted therapies are needed to address the disparities associated with TNBC. Dr. Cottrell and his colleagues have previously found that many TNBC cell lines are dependent on the expression of the RNA editing enzyme ADAR. During this study, Dr. Cottrell will identify the factors required for ADAR-dependence and then develop a classification model to predict which tumors will be sensitive to ADAR inhibition. This work will advance our understanding of ADAR-dependence such that ADAR-dependent TNBC can be accurately classified, thus opening the door to treating this deadly form of breast cancer and reducing the disparate effects of TNBC on Black/African American women.

ACKNOWLEDGMENT OF SUPPORT

I am truly honored to receive the 2021 AACR-Bristol Myers Squibb Cancer Disparities Research Fellowship. This support will allow me to elucidate the mechanisms of ADAR-dependency in triple-negative breast cancer and will hopefully lead to an effective therapy that will reduce the disparate effects of this disease.

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 to establish a successful career path.



Kelly P. Burke, MD, PhD

Hematology-Oncology Fellow

Dana-Farber Cancer Institute
Boston, Massachusetts

Dissecting CTLA-4 and PD-1 cooperation in tumor immunity and adverse events

BIOGRAPHY

Dr. Burke obtained her MD and PhD in immunology from the Johns Hopkins School of Medicine where she studied the T cell response against the hepatitis C virus. She completed her internal medicine residency at Massachusetts General Hospital and is a medical oncology fellow at the Dana-Farber Cancer Center. Dr. Burke is a post-doctoral fellow at Harvard Medical School, where she studies the development of protective anti-tumor immunity and the development of adverse events.

SCIENTIFIC STATEMENT

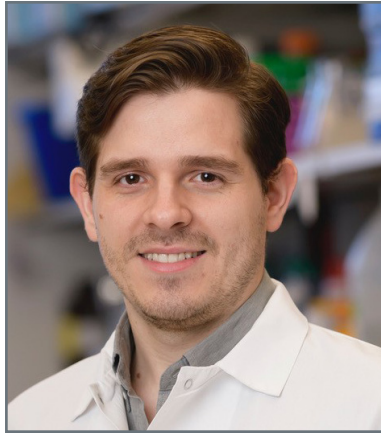
Immune checkpoint blockade (ICB) targeting CTLA-4 and PD-1 has had remarkable clinical success but carries a risk of developing inflammation in organs that clinically resembles autoimmune disease, known as immune-related adverse events (“irAEs”). Dr. Burke will apply genetic approaches in mouse models to isolate how loss of CTLA-4 and PD-1 signaling alters the function of CD4+ regulatory or non-regulatory T cells during tumor growth or the development of spontaneous inflammation. She will also apply these models toward testing strategies to blunt the development of spontaneous inflammation to improve our understanding of anti-tumor immunity and unintended adverse events.

ACKNOWLEDGMENT OF SUPPORT

I am tremendously honored to be the recipient of the 2021 AACR-Bristol Myers Squibb Immuno-oncology Research Fellowship. This support will advance my research and goal to become an independent investigator at the intersection of clinical oncology and basic mechanisms in immuno-oncology.

AACR-EXELIXIS RENAL CELL CARCINOMA RESEARCH FELLOWSHIP

The inaugural AACR-Exelixis Renal Cell Carcinoma Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct renal cell carcinoma research and to establish a successful career path.



Rodrigo Romero, PhD

Postdoctoral Fellow

Memorial Sloan Kettering Cancer Center
New York, New York

Modeling renal cell carcinomagenesis using engineered renal organoids

BIOGRAPHY

Dr. Romero completed his PhD in biology at the Massachusetts Institute of Technology, where he researched how the antioxidant response influences lung cancer progression and how the activation of this response leads to therapeutically targetable vulnerabilities. He is currently conducting his postdoctoral work at the Memorial Sloan Kettering Cancer Center, studying the role of the tumor microenvironment in shaping effective or dysfunctional anti-tumor T cell responses.

SCIENTIFIC STATEMENT

The clinical success of angiogenesis and immune checkpoint inhibitors over the past several years has led to significant improvement in the treatment of renal cell carcinoma (RCC). Genomic studies have identified recurrent genomic aberrations enriched in RCC; however, the functional consequences of alteration of these and other genes in the development of primary, metastatic disease, or therapy-resistant disease are ill defined. A thorough characterization of the complex interactions between mutational background and the renal tumor microenvironment (TME) will be critical to identify treatment strategies that enhance tumor control. Dr. Romero is set to leverage a new generation of preclinical models that aim to recapitulate the distinct immune contexts of different patient populations and compare these findings to human RCC analyses, which may guide development of improved immunotherapies and combination therapies.

ACKNOWLEDGMENT OF SUPPORT

I would like to express my utmost gratitude to be selected as the 2021 AACR-Exelixis Renal Carcinoma Research Fellowship recipient. In addition to providing crucial financial support during this transformative phase of my scientific career, this grant will be instrumental in providing opportunities to build foundations in renal and tumor immunology.

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.



Francisco Cartujano, MD

Research Assistant Professor

University of Rochester
Rochester, New York

Advancing smoking cessation and physical activity among Latinos

BIOGRAPHY

Dr. Cartujano received his MD from Universidad Autónoma del Estado de Morelos and completed his research fellowship at the University of Kansas Medical Center. Dr. Cartujano has been trained in participatory research to address tobacco-related disparities. Specifically, he has worked in the development and implementation of culturally and linguistically appropriate mobile interventions for smoking cessation among Latinos in the United States and Latin America. Currently, Dr. Cartujano is a research assistant professor at the University of Rochester Medical Center (URMC) and the Assistant Director of Community Outreach and Engagement at Wilmot Cancer Institute, part of URMC.

SCIENTIFIC STATEMENT

Of the 55 million Latinos that reside in the United States, 6 million are current smokers. Latinos experience multiple barriers to healthcare access that result in tobacco-related disparities. Overcoming these disparities demands innovative, accessible, effective, and culturally appropriate solutions. Dr. Cartujano will study the synergism of smoking cessation and physical activity in a mobile intervention. The primary goal of this study is to develop and assess the feasibility, acceptability, and preliminary impact of *Deja de fumar, ¡ejercitándote!* (Quit Smoking by Exercising!), a mobile intervention to promote smoking cessation and physical activity among Latinos. *Deja de fumar, ¡ejercitándote!* will integrate four components: 1) a 12-week text messaging coaching program with interactive capabilities, 2) wearable devices to monitor physical activity, 3) an online dashboard that manages participants' incoming and outgoing data from both the text messaging program and wearable devices, and 4) nicotine replacement therapy.

ACKNOWLEDGMENT OF SUPPORT

As a Mexican immigrant and a medical doctor, I have an unwavering commitment to address tobacco-related disparities among Latinos. I am extremely honored to be awarded the 2021 AACR-Genentech Cancer Disparities Research Fellowship. This grant will advance smoking cessation and physical activity among Latinos. ¡Muchas gracias!

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.



Valentina Zavala, PhD

Postdoctoral Researcher

University of California, Davis
Davis, California

Identification of non-European functional variants in breast cancer

BIOGRAPHY

Dr. Zavala earned her doctorate in molecular and cellular biology at Pontificia Universidad Católica de Chile, studying the effect of up-regulated microRNAs on BRCA1 expression in breast cancer. In 2018, she joined the Fejerman Lab at the University of California, San Francisco, where she was trained in integrative genomics through the study of the genetic factors that contribute to breast cancer risk in Latinas. In 2020, Dr. Zavala moved with the Fejerman Lab to the University of California, Davis, where she continues her research focusing on understanding the molecular mechanisms that link population-specific genetic variants to breast cancer biology in Latinas.

SCIENTIFIC STATEMENT

Despite the advances in the discovery of disease risk-associated genetic variants in diverse populations, Hispanic/Latinx individuals remain underrepresented in GWAS and transcriptome databases. Multiple variants located in the 6q25 locus near the estrogen receptor 1 gene (ESR1) have been associated with breast cancer risk in several studies, showing subtype-specific associations including a Hispanic/Latinx-specific protective variant. The proposed study is based on the hypothesis that this region harbors multiple population- and subtype-specific breast cancer risk variants with a cis effect on gene expression in Latinas. Dr. Zavala will use an approach that integrates germline data from the Peruvian Genomics of Breast Cancer Study (PEGEN-BC), a breast cancer case series of highly Indigenous American patients, with transcriptomic data from BC tumors from these same patients.

ACKNOWLEDGMENT OF SUPPORT

It is an honor to receive the 2021 AACR-Genentech Cancer Disparities Research Fellowship. This opportunity will allow me to advance knowledge about germline effects on tumor biology in an understudied population and will provide me with the resources to continue developing as a scientist and take my career to the next level.

AACR-GENENTECH IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

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



Anup Kumar Singh, PhD

Postdoctoral Fellow

La Jolla Institute for Immunology
San Diego, California

Studying the potential of targeting TET enzymes in cancer immunotherapy

BIOGRAPHY

Dr. Singh obtained his PhD from the Jawaharlal Nehru University, India. In his graduate research work he studied the epigenetic basis of therapy resistance in cancer stem cells at the Central Drug Research Institute, India. In his early postdoctoral training at the City of Hope Beckman Research Institute he studied the role of TET family of enzymes in somatic cell reprogramming and cancer. He is currently a postdoctoral fellow at the La Jolla Institute for Immunology where he is studying the role of TET proteins in immunotherapy resistance in cancer cells.

SCIENTIFIC STATEMENT

Cancer immunotherapy harnesses the immune system to boost immune responses. CAR T-cell based immunotherapy is remarkably effective against hematopoietic cancers but not against solid tumors, apparently because CAR T cells become “exhausted” much like normal CD8⁺ T cells responsive to standard peptide/MHC ligands. TET enzymes are dioxygenases that oxidize 5-methylcytosine (5mC) in DNA to 5-hydroxymethylcytosine (5hmC) and other DNA demethylation intermediates. We have already shown in mouse models that TET loss-of-function in tumor-infiltrating T cells (TILs), induced either by acute TET deletion or inhibition of TET function, improves tumor rejection. We have traced this to an improved ability of splenic CD4⁺ and CD8⁺ TILs to promote tumor regression. Tet deficiency also impairs the function of T regulatory (Treg) cells due to decreased stability of Foxp3 expression. In this proposal, I will define the mechanisms underlying the ability of TET deficiency to improve tumor rejection through effects on these two cell types.

ACKNOWLEDGMENT OF SUPPORT

I am honored to receive an AACR-Genentech Immuno-oncology Research Fellowship. This support and recognition from the AACR and Genentech will help me extend my prior research on cancer stem cells, TET enzymes, and epigenetic regulation to the field of cancer immunology and establish an independent research career.

AACR-INCYTE LYMPHOMA RESEARCH FELLOWSHIP

The AACR-Incyte 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.



Antonin Papin, PhD

Postdoctoral Fellow

Joan & Sanford I. Weill Medical College
of Cornell University
New York, New York

Role of the linker histones H1 in lymphomas

BIOGRAPHY

Dr. Papin completed his PhD training in Nantes, France, where he worked on the role of the microenvironment in the expansion of B cell lymphomas and especially on deciphering the dialog between the monocytes/macrophages and mantle cell lymphoma cells. He now studies the role of the linker histone H1 at Weill Cornell Medical College.

SCIENTIFIC STATEMENT

B cell-lymphomas (BCL) are the seventh most common tumor type in the United States and are often incurable for patients that fail chemotherapy. Among the mutational landscape of BCL, including diffuse large B cell lymphomas (DLBCL), approximately 30% of cases have mutations in the linker histone H1 genes. However, molecular mechanisms by which H1 mutations induce lymphoma are unknown. The main role of histone H1 proteins is to bind to linker DNA between nucleosomes thereby causing compaction of chromatin and gene silencing. Importantly, H1 mutations occur most frequently in the very aggressive MCD subtype of DLBCL, where co-occurrence of BCL2 overexpression and H1E mutations identify a subset with poor outcome. Thus, strategies to overcome resistance or treat relapsed H1 mutated lymphomas are an unmet medical need. This research project proposes to define the biologic role of H1 mutations in lymphomagenesis and identify new therapeutic strategies for targeting H1 mutant in lymphoma patients.

ACKNOWLEDGMENT OF SUPPORT

It is a real honor for me to receive the AACR-Incyte Lymphoma Research Fellowship. I warmly thank the AACR and Incyte for funding my project to study lymphoma and develop new therapeutic options for lymphoma patients.

AACR-JOHN AND ELIZABETH LEONARD FAMILY FOUNDATION BASIC CANCER RESEARCH FELLOWSHIP

The AACR-John and Elizabeth Leonard Family Foundation Basic Cancer Research Fellowship represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct basic cancer research and establish a successful career path.



Siddhant U. Jain, PhD

Research Fellow

Dana-Farber Cancer Institute
Boston, Massachusetts

Probing the dysregulation of SWI/SNF and PRC1/2 interplay in tumorigenesis

BIOGRAPHY

Dr. Jain received his PhD in biomolecular chemistry under the supervision of Dr. Peter Lewis at the University of Wisconsin-Madison, where he studied the biochemical mechanisms underlying the “oncohistones” found in pediatric cancers and characterized the oncoprotein, EZHIP (CXorf67). He is a postdoctoral research fellow in Dr. Cigall Kadoch’s lab at Dana-Farber Cancer Institute, where he studies the biochemical functions of the SWI/SNF family of chromatin remodelers in normal cells and in cancers.

SCIENTIFIC STATEMENT

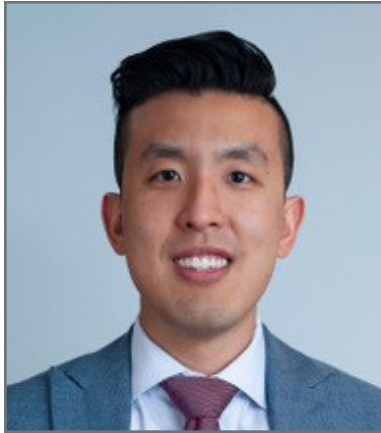
Approximately 20% of human cancers contain mutations in the subunits of SWI/SNF family of chromatin remodeling complexes. SWI/SNF complexes activate transcription by regulating nucleosome positioning and providing access to transcriptional machinery. Notably, synovial sarcomas are uniformly driven by the SS18-SSX fusion oncoprotein, which leads to genomic redistribution of SWI/SNF complexes. Dr. Jain aims to combine protein biochemistry, genomics, and chemical biology approaches to investigate the mechanism, which aberrant targeting of oncogenic SWI/SNF complexes containing the fusion protein drives cancer-specific transcriptional changes.

ACKNOWLEDGMENT OF SUPPORT

I am honored and grateful to have received the 2021 AACR-John and Elizabeth Leonard Family Foundation Basic Cancer Research Fellowship. This invaluable support provides me with an opportunity to address some outstanding questions about these aggressive pediatric sarcomas and will substantially potentiate my current scientific aims and future career trajectory.

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 to establish a successful career path.



Albert E. Kim, MD

Neuro-oncology Fellow

Massachusetts General Hospital
Boston, Massachusetts

Noninvasive identification of oncogenic drivers in breast cancer brain mets

BIOGRAPHY

Dr. Kim attended medical school at the Medical College of Georgia. He completed neurology residency training at Washington University in St. Louis and is a neuro-oncology fellow at the Dana-Farber/Partners Cancer Care Program. In July 2021, he will become an instructor at the Massachusetts General Hospital Cancer Center, where he will see patients at the Pappas Center of Neuro-Oncology. Dr. Kim is a post-doctoral fellow in the laboratories of Priscilla Brastianos at MGH Brain Tumor Center and Elizabeth Gerstner at MGH Martinos Center, where he uses Omics-based techniques and medical imaging to define and target genomic and metabolic pathways for brain metastases.

SCIENTIFIC STATEMENT

A feared complication of metastatic breast cancer is the development of brain metastases (BM) due to the substantial morbidity and limitations in current treatments. While precision medicine approaches for BM have recently demonstrated promising responses, many patients are not able to benefit from this treatment paradigm as molecular analysis of BM tissue is not usually feasible. To answer this question, Dr. Kim will apply genomic profiling and deep learning (DL) methods to a rich dataset comprised of breast cancer BM tissues, patient-matched brain MRI's, and cell-free DNA samples, to develop techniques that reveal therapeutic targets within a patient's BM. His hope is that these findings will shift current paradigms – for example, a lumbar puncture and MRI, instead of tissue from a neurosurgical resection, may be opportunities to non-invasively identify oncogenic drivers for a BM and longitudinally monitor breast cancer evolution.

ACKNOWLEDGMENT OF SUPPORT

I am deeply humbled and honored to be a recipient of the AACR-Pfizer Breast Cancer Research Fellowship. As an oncologist-in-training, I am dedicated to a career leading a translational group that facilitates precision medicine for patients with brain metastases. This award provides critical support for my transition to independence.

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.



Anushree Gulvady, PhD

Postdoctoral Fellow

Dana-Farber Cancer Institute
Boston, Massachusetts

Metastasis-promoting tumor-induced microenvironmental alterations

BIOGRAPHY

Dr. Gulvady earned her bachelor's and master's degrees in Microbiology from the University of Mumbai, India. She then joined the laboratory of Dr. Christopher E. Turner at SUNY Upstate Medical University, where she investigated focal adhesion proteins, Hic-5 and Paxillin in regulating critical aspects of tumor migration and completed her PhD in 2018. To acquire an understanding of tumor heterogeneity and metastasis, she joined the laboratory of Dr. Kornelia Polyak at the Dana-Farber Cancer Institute, where she will be using genome-wide CRISPR screens, preclinical mouse models and human TNBC samples, to improve patient risk stratification and guide treatment design.

SCIENTIFIC STATEMENT

The overwhelming majority of triple-negative breast cancer (TNBC)-related deaths are due to treatment-resistant metastatic disease. Understanding the mechanisms underlying disease progression and metastasis is therefore crucial for improved outcomes. Tumor heterogeneity is a major obstacle in our understanding and treatment of cancer. Tumors can be heterogeneous among different patients, within the same patient at different stages of disease, and cells within the same tumor can also display startling heterogeneity. Current efforts have been focusing on genome sequencing of bulk tumors to identify the drivers of disease. However, previous research from the lab indicates that the interactions among cancer cells within tumors and not just mutant genes per se, drives tumor progression. This research using preclinical mouse models of heterogeneity and human TNBC samples aims to identify novel targets within the immune and lymphovascular microenvironments, to gain mechanistic insight into subclonal cooperation and metastatic progression towards improving patient outcome.

ACKNOWLEDGMENT OF SUPPORT

I am extremely grateful and honored to receive the AACR-Triple Negative Breast Cancer Foundation Research Fellowship. This opportunity will facilitate a deeper understanding of how heterogeneity within tumors contributes to disease progression and alters treatment outcomes in TNBC- a direct bridge to the clinic.

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.



Rutulkumar Patel, MS, PhD

Postdoctoral Associate

Duke University Medical Center
Durham, North Carolina

Radiosensitizing rhabdomyosarcoma by targeting metabolic vulnerabilities

BIOGRAPHY

Dr. Patel received his MS from the Illinois Institute of Technology, and PhD from Case Western Reserve University. His PhD dissertation project was funded by NASA to study the impact of space radiation on the hematopoietic system. Following graduation, he joined the laboratory of Dr. David Kirsch, a well-renowned radiation oncologist in the care of patients with bone and soft tissue sarcomas at Duke University. As a postdoctoral associate, Dr. Patel studies metabolic vulnerabilities of rhabdomyosarcomas. The goal is to radiosensitize sarcomas through metabolic interventions and translate the findings into clinical trials for rhabdomyosarcomas patients.

SCIENTIFIC STATEMENT

Despite aggressive treatment of sarcomas and progress in understanding the genomic landscape of this disease, the five-year survival of patients with metastatic rhabdomyosarcoma (RMS) remains 30%. Understanding how RMS cells use nutrients to fuel growth in local vs. metastatic disease may provide unique opportunities to target RMS. Dr. Patel uses a primary mouse model of RMS that utilizes mutations that most frequently occur in human embryonal RMS. His preliminary data showed that sarcomas rely on glucose and glutamine for survival, but after radiation therapy these sarcomas switch to utilize glutamine preferentially. Dr. Patel's work shows that inhibition of glutamine metabolism radiosensitizes RMS. His goal is to understand how glutamine deprivation radiosensitizes sarcomas and to determine the therapeutic potential of targeting central carbon metabolism in RMS.

ACKNOWLEDGMENT OF SUPPORT

The 2021 AACR-QuadW Foundation Fellowship for Clinical/Translational Sarcoma Research provides necessary funding to pursue pharmacological inhibition of glutaminase as a therapeutic avenue for rhabdomyosarcoma patients in the future. The funding will also provide preliminary data for future grant applications and help with my training as I take a path towards becoming an independent investigator.

THE BOSARGE FAMILY FOUNDATION-WAUN KI HONG SCHOLAR AWARD FOR REGENERATIVE CANCER MEDICINE

The Bosarge Family Foundation-Waun Ki Hong Scholar Award for Regenerative Cancer Medicine represents a joint effort to encourage and support postdoctoral or clinical research fellows to conduct novel and provocative research in the field of regenerative cancer medicine and to establish a successful career path.



Jessica E.S. Shay, MD, PhD

Research Fellow

Massachusetts General Hospital
Boston, Massachusetts

Leveraging ketone bodies for intestinal repair after cancer therapy

BIOGRAPHY

Dr. Shay pursued her MD/PhD at the University of Pennsylvania where she completed her thesis under Dr. Celeste Simon, investigating the hypoxic response to inflammation and tumor progression in models of colitis-associated colon cancer. After completing her training in internal medicine at Johns Hopkins Hospital, she pursued a research-oriented gastroenterology fellowship at Massachusetts General Hospital. Under the mentorship of Omer Yilmaz at the Koch Institute for Integrative Cancer Research at MIT, she is currently investigating the influence of host nutrient-derived metabolites on intestinal stem cell function.

SCIENTIFIC STATEMENT

Due to continuous regeneration every five-seven days, the gastrointestinal tract is susceptible to the cytotoxic/static effects of nearly all cancer therapies. Although advances have been made, cancer therapies continue to result in intestinal epithelial injury and mucositis, thereby limiting effectiveness through dose reduction and impairing patient quality of life. As such, there is a clear need for scientific discoveries that increase intestinal healing and regeneration to allow more effective cancer therapies for improved patient outcomes. The mechanisms by which host nutritional state influences intestinal regeneration remains incompletely characterized. However, work in the Yilmaz lab has previously demonstrated that fasting has a profound impact on intestinal stem cell function in young and aged mice and can improve the age-associated decline in tissue regeneration, in part through the production of ketone bodies. Dr. Shay seeks to mechanistically delineate the signaling and energetic roles of ketone body metabolites to enhance therapeutic options for intestinal regeneration.

ACKNOWLEDGEMENT OF SUPPORT

The Bosarge Family Foundation-Waun Ki Hong Scholar Award for Regenerative Cancer Medicine provides me protected time to pursue important research investigating the influence of host nutrient-derived metabolites on the regenerative capacity of intestinal stem cells that will lay the groundwork for a research-oriented career as a physician-scientist.

2021 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.



Alison M. Taylor, PhD

Assistant Professor

Columbia University
New York, New York

The role of chromosome 3 arm aneuploidy in lung squamous cell carcinoma

BIOGRAPHY

Dr. Taylor obtained her BS in biology at the Massachusetts Institute of Technology and her PhD in genetics at Harvard Medical School in the laboratory of Dr. Leonard Zon. She completed her postdoctoral fellowship focusing on cancer functional genomics at the Dana-Farber Cancer Institute and Broad Institute with Dr. Matthew Meyerson. In January 2020, Dr. Taylor joined Columbia University's Herbert Irving Comprehensive Cancer Center and Department of Pathology and Cell Biology as assistant professor. The goal of her research program is to understand the role of aneuploidy, whole chromosome or chromosome arm imbalance, in the development of cancer.

SCIENTIFIC STATEMENT

Aneuploidy, including the gain or loss of whole chromosomes or chromosome arms, is a near-universal feature of cancer. However, the role of aneuploidy in tumor pathogenesis remains an unanswered question in cancer biology. To directly test the effects of cancer aneuploidy alterations in human cells, Dr. Taylor developed a genome engineering approach to delete chromosome arms in vitro. With this technology, the Taylor lab will uncover the function of specific aneuploidy alterations in tumorigenesis. Here, the lab will focus on chromosome 3p deletion and chromosome 3q gain, alterations that occur at high frequency in lung squamous cell carcinoma (SCC) and SCCs of other tissues. This research aims to determine how aneuploidy affects the pro-tumorigenic phenotypes of differentiation and invasiveness, as well as how different chromosomal regions contribute to aneuploidy-induced phenotypes. This work could ultimately lead to identification of novel therapeutic targets and bring new insights into the biology of cancer aneuploidy.

ACKNOWLEDGMENT OF SUPPORT

I am very honored to be this year's recipient of the AACR Gertrude B. Elion Cancer Research Award. With this award and with the AACR's resources for all stages of research, the AACR and GlaxoSmithKline are providing critical support as I establish my independent career as a cancer researcher in the field of aneuploidy.

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.



Gerben Borst, MD, PhD

Clinician Scientist

University of Manchester
Manchester, United Kingdom

Unraveling the cell cycle effect of TTFields towards synergistic strategies

BIOGRAPHY

Dr. Borst obtained his MD at the University of Antwerp and his PhD at the University of Amsterdam. He completed his clinical training in the Department of Radiation Oncology at the Netherlands Cancer Institute. After additional training at the Hokkaido University, Japan, the Institute of Cancer Research, U.K., the Princess Margaret Cancer Centre, Canada, and the University of California, San Francisco, Dr. Borst developed his translational research group investigating novel insights in the treatment response of brain tumors. In July 2020, Dr. Borst started a clinical-academic position at the University of Manchester and The Christie NHS Foundation Trust.

SCIENTIFIC STATEMENT

Glioblastoma is the most common primary malignant brain tumor in adults with a dismal prognosis despite an aggressive treatment regimen. Tumor Treating Fields (TTFields) are a novel noninvasive treatment modality utilizing alternating electric fields demonstrating an increase in overall survival. More research is needed to fully understand the mechanism, the timing, and sequence of TTFields-induced effects to further improve its efficacy. Dr. Borst's group is studying the effect of TTFields with a specific interest on cell cycle distribution. Advanced time lapse experiments will study TTFields in relation to cell cycle duration/transitions, cell morphology, and cell death. In addition, clinically relevant in vivo models will be introduced providing essential validation and insights in its working mechanism.

ACKNOWLEDGMENT OF SUPPORT

The AACR-Novocure Career Development Award will enable the setup of advanced research elucidating insights for further knowledge and improvement of efficacy of TTFields treatment. This work will subsequently lead to novel translational studies that are needed to improve the treatment outcome of patients with brain tumors.

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.



Jared A. Weis, PhD

Assistant Professor

Wake Forest University
Winston-Salem, North Carolina

Characterizing effects of TTFields on cell-extracellular matrix biophysics

BIOGRAPHY

Dr. Weis is an assistant professor of biomedical engineering at Wake Forest School of Medicine. He received his BS in biomedical engineering from Washington University in St. Louis and his MS and PhD in biomedical engineering from Vanderbilt University. He was a postdoctoral fellow at the Vanderbilt University Institute of Imaging Science and a research assistant professor of biomedical engineering at Vanderbilt University prior to joining Wake Forest. His research group focuses on developing novel analysis approaches in cancer that combine mechanistic computational modeling with non-invasive imaging data to explore the response to cancer therapy.

SCIENTIFIC STATEMENT

Tumor Treating Fields (TTFields) are thought to exhibit primarily anti-mitotic effects on cancer cells. However, recent data supports an emerging role modulating cancer cell-extracellular matrix (ECM) phenotypic biophysics, representing an important yet underexplored mechanism of the therapeutic impact TTFields on cancer cell motility, mechanical invasion, and ECM structural architecture. Using primary and metastatic brain tumor 3D culture systems, Dr. Weis will examine mechanistic biophysical and mechanical characterization of the response to TTFields and stromal influences from the tumor microenvironment that potentiate response. Interrogating 3D cell culture systems with a hybrid computational imaging approach, he will use live-cell microscopy imaging and data-driven mechanistic computational modeling to characterize the phenotypic biophysical cellular and microenvironmental response to TTFields. The overall goal of the research is to provide new mechanistic insight into the cell-ECM biophysical effects of TTFields therapy and provide for precision evaluation approaches to predict patient response and optimize TTFields therapy.

ACKNOWLEDGMENT OF SUPPORT

I am honored to receive this AACR-Novocure Career Development Award for Tumor Treating Fields Research. This award will support and promote my research using hybrid experimental and computational approaches to better understand TTFields therapy response. This early-career investigator support is invaluable for establishing my career as a cancer researcher.

AACR-OCULAR MELANOMA FOUNDATION CAREER DEVELOPMENT AWARD, in honor of Robert C. Allen, MD

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



Roger Olofsson Bagge, MD, PhD

Associate Professor

Goteborgs Universitet (University of Gothenburg)
Gothenburg, Sweden

IHP and immunotherapy for uveal melanoma metastasis - the SCANDIUM-II trial

BIOGRAPHY

Dr. Bagge is a senior consultant surgeon at Sahlgrenska University Hospital and an associate professor at the University of Gothenburg, Sweden. He is responsible for isolated hyperthermic perfusion in Sweden and treats all patients requiring either isolated limb perfusion or isolated hepatic perfusion. Dr. Bagge is also a research group leader at the Wallenberg Center for Molecular and Translational Medicine. He conducts both clinical and preclinical research, with a special focus on treatments for both cutaneous and ocular melanoma. He has published more than 70 papers and is currently the main supervisor for six PhD students.

SCIENTIFIC STATEMENT

Metastatic uveal melanoma is a cancer with poor prognosis and unmet need for new and effective therapies. There has been a revolution in the treatment of metastatic melanoma with the emergence of immune checkpoint inhibitors. Despite the success in cutaneous melanoma, the results in the treatment of uveal melanoma are very limited. In this research project, Dr. Bagge will investigate a new treatment regimen for uveal melanoma patients with liver metastases combining a locoregional treatment, isolated hepatic perfusion with melphalan, with the immune checkpoint inhibitors ipilimumab and nivolumab. During isolated hepatic perfusion, the liver is surgically isolated from the systemic circulation, allowing a high concentration of melphalan to be perfused through the liver with minimal systemic toxicity. The translational aspects of the trial will further delineate the immunological mechanisms of the treatment using FACS and genomic analysis of tumor and blood from the patients.

ACKNOWLEDGMENT OF SUPPORT

I am truly honored and grateful to be the recipient of the 2021 AACR-Ocular Melanoma Foundation Career Development Award, in honor of Robert C. Allen, MD. This recognition is extremely important in our joint quest to address the unmet need for effective treatments for patients with metastatic ocular melanoma.

BREAST CANCER RESEARCH FOUNDATION-AACR CAREER DEVELOPMENT AWARD TO PROMOTE DIVERSITY AND INCLUSION

The Breast Cancer Research Foundation-AACR Career Development Award to Promote Diversity and Inclusion represents a focused effort to encourage and support investigators from diverse backgrounds that are underrepresented in the cancer related sciences workforce and to foster their career advancement.



Kimberley Lee, MD, MHS

Assistant Member

H. Lee Moffitt Cancer Center & Research Institute
Tampa, Florida

The role of adjuvant endocrine therapy in racial disparities in survival

BIOGRAPHY

Dr. Lee is an assistant member in the Departments of Breast Oncology and Health Outcomes and Behavior at Moffitt Cancer Center. Dr. Lee received her MD and MHS in general epidemiology from Johns Hopkins University. Most recently, she completed a medical oncology fellowship at Johns Hopkins Sidney Kimmel Cancer Center. Dr. Lee's research focuses on how individual and systems-level factors contribute to disparities in health outcomes for people with breast cancer. Her goal is to develop multi-level interventions to address risk factors for poor outcomes, ultimately leading to greater health equity and improved outcomes for all.

SCIENTIFIC STATEMENT OF RESEARCH

Black women continue to experience worse survival outcomes from breast cancer compared to other racial groups. This disparity exists for the hormone-receptor positive form of breast cancer that requires long-term treatment with adjuvant endocrine therapy (AET). To experience the full survival benefits of AET, it must be initiated, adhered to, and taken daily for 5 to 10 years (AET pathway). There is a dearth of research on how these steps interplay to impact racial disparities in outcomes for women with breast cancer. To address this gap, Dr. Lee will investigate how the entire AET pathway influences outcomes and then identify multi-level risk factors for non-adherence to each step of the pathway. She will use a mixed-methods approach to understand barriers to the pathway using population level real world data and qualitative interviews with Black breast cancer survivors.

ACKNOWLEDGEMENT OF SUPPORT

I am honored to have been selected as a recipient of the 2021 Breast Cancer Research Foundation-AACR Career Development Award to Promote Diversity and Inclusion. This award will help establish my research career, providing opportunity and support to conduct my research in breast cancer disparities.

BREAST CANCER RESEARCH FOUNDATION-AACR CAREER DEVELOPMENT AWARD TO PROMOTE DIVERSITY AND INCLUSION

The Breast Cancer Research Foundation-AACR Career Development Award to Promote Diversity and Inclusion represents a focused effort to encourage and support investigators from diverse backgrounds that are underrepresented in the cancer related sciences workforce and to foster their career advancement.



Joshua Saldivar, PhD

Assistant Professor

Oregon Health & Science University
Portland, Oregon

Oncogenic ATR signaling during MYC-induced reprogramming in breast cancer

BIOGRAPHY

Dr. Saldivar received his PhD at Ohio State University, where he studied the origins of genomic instability in premalignant cells. He completed his postdoctoral work at Stanford University, where he uncovered a cell cycle checkpoint pathway controlling the S to G2 transition. He is currently an assistant professor in the Division of Oncological Sciences and a member of the Cancer Early Detection Advanced Research Center at Oregon Health & Science University. His lab studies the mechanisms driving reprogramming in the early stages of cancer.

SCIENTIFIC STATEMENT OF RESEARCH

Breast cancer stem cells drive tumor malignancy and therapeutic resistance. These abnormal cells emerge following oncogene-induced reprogramming of committed cell types into stem cells, a poorly understood phenomenon. Expression of oncogenes, such as MYC, can activate super-enhancers that drive stem cell transcription programs leading to dedifferentiation. The transcriptional coactivator Mediator links super-enhancers to target promoters within large transcription hubs and promotes MYC activity at super-enhancers, suggesting Mediator facilitates reprogramming. Dr. Saldivar has uncovered an unexpected link between large transcription hubs and ATR, a replication stress-response kinase that is needed for MYC-driven cancers. His group will use a combination of time-lapse confocal imaging and single-cell sequencing to uncover a potential oncogenic role of ATR signaling within these hubs during MYC-induced reprogramming and breast cancer stem cell emergence. The outcomes of this work may pave the way for new therapeutic strategies utilizing ATR inhibitors to target cancer stem cells.

ACKNOWLEDGEMENT OF SUPPORT

I am deeply honored to be selected as a recipient of the 2021 Breast Cancer Research Foundation-AACR Career Development Award to Promote Diversity and Inclusion. As an early career investigator, this award will enable me to conduct research focused on the mechanisms of oncogenic reprogramming in breast cancer.

LUSTGARTEN FOUNDATION-AACR CAREER DEVELOPMENT AWARD FOR PANCREATIC CANCER RESEARCH, in Honor of John Robert Lewis

The Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research, in Honor of John Robert Lewis, represents a joint effort to encourage and support early career scientists engaged in pancreatic cancer research who are members of racial or ethnic groups that have been shown to be underrepresented in the cancer related sciences workforce.



Avery D. Posey, Jr., PhD

Assistant Professor

University of Pennsylvania
Philadelphia, Pennsylvania

The role of Tn antigen in pancreatic cancer: Driver, suppressor, and target

BIOGRAPHY

Dr. Posey is an assistant professor in the Department of Systems Pharmacology and Translational Therapeutics, a member of the Parker Institute for Cancer Immunotherapy, and a research health scientist at the Philadelphia Veterans Administration Medical Center. Dr. Posey holds a PhD in genetics from the University of Chicago, a BS in biochemistry from the University of Maryland, Baltimore County (UMBC), and a second BS in bioinformatics from UMBC. Dr. Posey completed postdoctoral training in the laboratory of Dr. Carl June, where he generated glycosylation-specific chimeric antigen receptors to precisely target tumor-glycoforms of MUC1.

SCIENTIFIC STATEMENT

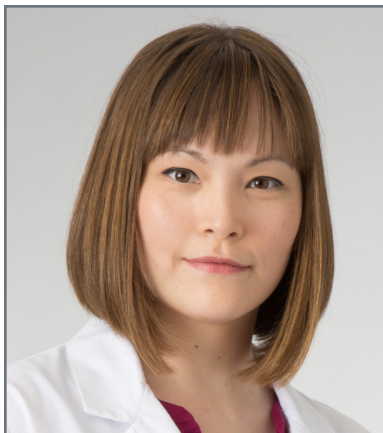
Pancreatic adenocarcinoma (PDAC) is a poorly immunogenic tumor characterized by low mutational burden and limited responses to immunotherapies. PDAC tumors, similar to other solid tumors, exhibit alterations of cellular glycosylation, including the abundant expression of the truncated O-glycan Tn antigen, which is the ligand for the macrophage galactose-type lectin (MGL) expressed by tolerogenic antigen presenting cells and M2-phenotype macrophages. In this study, we will study the role of the Tn antigen in the pathogenesis of PDAC. We will perform single-cell RNA sequencing of tumor immune infiltrate and bone marrow to understand whether and how the Tn antigen shapes the PDAC immune microenvironment as well as the systemic immune composition. Lastly, we will adoptively transfer anti-Tn CAR-T cells to mice bearing heterogeneous Tn+ PDAC tumors to test whether disrupting the MGL-Tn axis will decrease the local immunosuppression within the tumor and improve anti-tumor responses in PDAC tumors.

ACKNOWLEDGMENT OF SUPPORT

I am grateful to accept the Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research, in honor of John Robert Lewis. This award will support and expand my laboratory's scientific enterprise. Importantly, we will investigate an underappreciated immune axis in pancreatic cancer and devise therapeutic strategies to eventually benefit patients.

LUSTGARTEN FOUNDATION-AACR CAREER DEVELOPMENT AWARD FOR PANCREATIC CANCER RESEARCH, in Honor of Ruth Bader Ginsburg

The Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research, in Honor of Ruth Bader Ginsburg, represents a joint effort to support the career advancement of a female scientist engaged in pancreatic cancer research.



Dannielle Engle, PhD

Assistant Professor

The Salk Institute for Biological Studies
La Jolla, California

The role of CA19-9 in pancreatic cancer progression and metastasis

BIOGRAPHY

Dr. Engle received her BA in biological sciences and Asian & Middle Eastern studies from Northwestern University. She completed her doctorate in biology in the laboratory of Dr. Geoffrey Wahl at the University of California, San Diego and the Salk Institute for Biological Studies. After completing her postdoctoral fellowship in the laboratory of Dr. David Tuveson at the Cambridge Research Institute in England and Cold Spring Harbor Laboratory, Dr. Engle was recruited to start her own laboratory at the Salk Institute. Dr. Engle is also the recipient of an NCI Career Transition Award, the Theodore T. Puck Award, and other notable distinctions.

SCIENTIFIC STATEMENT

Metastasis is a major contributor to pancreatic cancer mortality. Recently, Dr. Engle discovered that the aberrant glycan CA19-9 accelerated pancreatic tumor progression and increased metastatic dissemination in mice. Dr. Engle and her team will identify systemic signals responsible for priming the pre-metastatic niche for pancreatic cancer dissemination. Using the post-translational CA19-9 modification, secreted ligands that are aberrantly glycosylated and potentiate metastatic dissemination will be identified using a combination of *in vivo* and advanced organoid co-culture approaches. To intercept these pro-metastatic signals, the receptors responsible for communicating these cues in distal microenvironments will be genetically targeted. E-selectin, a known CA19-9 receptor, will be abrogated in a cell-type specific manner to assess the impact on metastatic dissemination and gene expression programs. CA19-9 ligands and receptors may serve as future targets for therapeutic intervention. This comprehensive program will elucidate the cell intrinsic and extrinsic roles of CA19-9 in pancreatic cancer metastasis.

ACKNOWLEDGMENT OF SUPPORT

Having lost close family members to pancreatic cancer, it has been my dream to start a dedicated pancreatic cancer research lab. The Lustgarten-AACR Career Development Award, in honor of Ruth Bader Ginsburg will enable me to harness my personal and scientific passion to make inroads against this devastating disease.

2021 INDEPENDENT INVESTIGATOR GRANTS



AACR-BAYER INNOVATION AND DISCOVERY GRANT

The 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.



Daniel A. Harki, PhD

Associate Professor

University of Minnesota Twin Cities
Minneapolis, Minnesota

Harnessing N-Myc signaling by chemical degradation of aurora kinase A

BIOGRAPHY

Dr. Harki received a BA in biology and in chemistry from West Virginia University where he performed organic synthesis research with Dr. Kay Brummond. He then pursued a PhD in chemistry from Penn State University on the development of antiviral nucleosides with Dr. Blake Peterson, followed by postdoctoral studies at the California Institute of Technology investigating the regulation of transcription factor signaling in cancer with pyrrole-imidazole polyamides with Dr. Peter Dervan. Dr. Harki joined the Department of Medicinal Chemistry at the University of Minnesota in 2009 and is currently a Northrop Professor. Research in the Harki laboratory focuses on the development of novel chemical probes and therapeutics.

SCIENTIFIC STATEMENT

N-Myc is a transcription factor whose aberrant activation results in the expression of genes that drive cancer growth and proliferation. High N-Myc levels are correlated with poor therapeutic outcomes in neuroblastomas; therefore, N-Myc is a promising target for developing neuroblastoma therapies. A chemical strategy to rapidly deplete N-Myc protein levels through the targeted protein degradation of Aurora-A was developed in preliminary studies. The novel Aurora-A degraders were found to inhibit the growth of MYCN-amplified neuroblastoma cells with good potency. This project involves chemical optimizations of Aurora-A/N-Myc-degrading compounds to generate second-generation compounds with improved potency, selectivity, and drug-like properties. The anticipated outcome of this work is the identification of a pre-clinical drug candidate that can be advanced in future studies.

ACKNOWLEDGMENT OF SUPPORT

The long-term goal of the project is to develop a new therapy for the treatment of childhood neuroblastomas. I am very grateful to receive an AACR-Bayer Innovation and Discovery Grant to support our drug discovery efforts.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

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Daniel Herranz, PharmD, PhD

Assistant Professor

Rutgers University
New Brunswick, New Jersey

A novel mitochondrial uncoupling drug in the treatment of leukemia

BIOGRAPHY

Dr. Herranz obtained his PhD at the Spanish National Cancer Research Center, working on the role of Sirt1 in metabolism, cancer, and aging under the supervision of Dr. Manuel Serrano. For his postdoctoral training, he joined Dr. Adolfo Ferrando's Lab at Columbia University, where he focused on the transcriptional and metabolic dependencies of T-cell leukemia. In 2017, he established his own independent research program at Rutgers Cancer Institute of New Jersey, where he has already made significant contributions uncovering novel enhancer regions in leukemia as well as novel therapeutic targets for the treatment of this disease.

SCIENTIFIC STATEMENT

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematologic malignancy. Despite advances in treatments, 20-50% of patients relapse and ultimately die, highlighting the need to discover novel therapies. Dr. Herranz's group previously demonstrated the synergistic effects of concomitantly targeting NOTCH1 signaling and either autophagy or glutaminolysis in vivo. In this context, mitochondria are specialized organelles critically involved in the control of bioenergetic and biosynthetic pathways. Thus, they hypothesized that directly targeting mitochondria may be an effective antileukemic therapy. Indeed, preliminary results using a novel mitochondrial uncoupling drug uncovered very potent antileukemic intrinsic effects. However, leukemic cells treated with this drug as single agent eventually became resistant and relapsed. Thus, this project aims to dissect the mechanisms of resistance to mitochondrial uncoupling as well as to identify synergisms with currently used chemotherapeutic drugs in T-ALL patients. The results from this project might translate into improved therapies for the treatment of leukemia in the near future.

ACKNOWLEDGMENT OF SUPPORT

My long-term goal is to become a leader in leukemia translational studies. This AACR-Bayer Innovation and Discovery Grant is widely recognized as an extremely prestigious award, bestowed only to the most innovative projects. Thus, it will be instrumental to consolidate my career as well as to propel our studies using mitochondrial uncoupling drugs.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

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**Fatemeh Momen-Heravi,
DDS, PhD, MPH, MS**

Assistant Professor

Columbia University Medical Center
New York, New York

SafeExo platform for lung-specific drug delivery and gene editing

BIOGRAPHY

Dr. Momen-Heravi received a DDS from Tehran University, Iran, an MPH from Harvard University, and a PhD in molecular biology/biotechnology from the University of Westminster, U.K. She pursued residency training in periodontics at Columbia University and performed postdoctoral research in molecular biology at Harvard Medical School and the University of Massachusetts Medical School. She is currently an assistant professor at the Herbert Irving Comprehensive Cancer Center and the College of Dental Medicine at Columbia University. Her lab works on novel genome editing modalities based on CRISPR/Cas and exosomes as precision medicine tools to treat cancer. Her group also combines computational biology and advanced biostatistical methods with wet lab techniques to identify signaling mechanisms and tumor vulnerabilities in head and neck cancer and lung cancer.

SCIENTIFIC STATEMENT

Using the latest developments in gene editing, direct targeting of oncogenic mutations with CRISPR/Cas is a highly innovative therapeutic approach. Like all genetic tools, the CRISPR/Cas machinery must be delivered directly to target cells' nuclei without unwanted immunogenicity or off-target effects to be safe and effective. However, current delivery platforms such as adenovirus, lentiviral vectors, and synthetic delivery methods are immunogenic, induce off-target effects, are toxic, and lack tissue tropism toward the lung. Exosomes are small vesicles shed by all cells in the cellular microenvironment that carry and deliver biomacromolecules. Dr. Momen-Heravi's lab has recently developed a novel customizable delivery platform based on engineered exosomes (safeEXO) which are devoid of endogenous nucleic acids, express endogenous Cas protein, and have targeting moieties toward lung tissue, called safeExo-CAS. The group will optimize the use of this delivery platform to deliver CRISPR/Cas machinery to lung tissues to treat lung cancer.

ACKNOWLEDGMENT OF SUPPORT

I am honored to be an awardee of the AACR-Bayer Innovation and Discovery Grant. This funding provides a pathway to develop our novel exosome-based therapeutic platform into novel therapeutics to treat lung cancer. I extend my gratitude to the AACR and Bayer for supporting innovation in cancer research.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

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Jill P. Smith, MD

Professor

Georgetown University
Washington, District of Columbia

Targeted nanoparticle for early diagnosis & treatment of pancreatic cancer

BIOGRAPHY

Dr. Smith is a professor of medicine at the Lombardi Comprehensive Cancer Center at Georgetown University. She was the former Director of Clinical & Translational Research at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH). Dr. Smith also practices at the Washington DC Veterans Affairs Medical Center. As a clinical scientist, Dr. Smith has dedicated her entire academic career to patient care, teaching, and conducting research. Her passion has been bench-to-bedside translational research. Her basic science research has focused on G-protein-coupled receptors, in particular cholecystikinin receptors and their role in gastrointestinal cancers. She was elected the first female president of the American Pancreatic Association.

SCIENTIFIC STATEMENT

Mutant KRAS is the primary driver mutation identified in most human pancreatic cancers. Although mutant KRAS can be silenced in vitro by RNAi, attempts to target KRAS in vivo have been met with obstacles and, therefore, this oncogene has been labeled as “untargetable”. The cholecystikinin-B receptor (CCK-BR) is not found in normal pancreas but becomes overexpressed in precancerous PanIN lesions and in pancreatic cancer. Dr. Smith’s group has developed a biodegradable fluorescent polyplex nanoparticle that selectively targets the CCK-BR that can carry a siRNA payload to inhibit growth of human pancreatic cancer in mice. In this project, fluorescent CCK-BR targeted nanoparticles will be used to deliver mutant KRAS siRNA to high grade PanINs using the mutant Kras (LSL-KrasG12D/+;P48-Cre) mouse model in order to prevent PanIN progression. Next, the KRAS siRNA loaded nanoparticles will be used to treat orthotopic established pancreatic cancer in immune competent mice.

ACKNOWLEDGMENT OF SUPPORT

The outcome of our work could lead to a new approach for targeting KRAS in pancreatic cancer. This fluorescent target-specific nanoparticle, or theranostic agent, can be developed for both treatment (therapy) and early detection (diagnosis) of high grade PanIN-3 lesions in order to prevent pancreatic cancer. We would like to acknowledge support for this project from the 2021 AACR-Bayer Innovation and Discovery Grant.

AACR-BAYER INNOVATION AND DISCOVERY GRANT

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Jing Yang, PhD

Professor

University of California, San Diego
La Jolla, California

Targeting EPHA2/LYN mechanotransduction to inhibit breast cancer metastasis

BIOGRAPHY

Dr. Yang obtained her PhD in molecular cancer biology with Dr. Sally Kornbluth at Duke University. In 2000, Dr. Yang became a Damon Runyon Cancer Research Foundation postdoctoral fellow with Dr. Robert Weinberg at the Whitehead Institute for Biomedical Research. Dr. Yang joined the faculty of University of California, San Diego in 2006 and is currently a professor in the Department of Pharmacology, Pediatrics and Moores Cancer Center at the University of California, San Diego. Her work identified epithelial-mesenchymal transition as being critical for tumor invasion and metastasis. Her group continues to study epithelial-mesenchymal plasticity in tumor progression.

SCIENTIFIC STATEMENT

Increasing matrix stiffness in breast tumors is a prognostic marker of distant metastasis and poor survival. In addition to biochemical pathways, an equally promising therapeutic avenue to combat breast tumor metastasis is to target novel mechanotransduction pathways. Previous work from the lab of Dr. Yang identified a novel mechanotransduction pathway that, in response to mechanical cues in the tumor microenvironment, promotes epithelial-mesenchymal transition (EMT) and thereby impinges on tumor invasion and metastasis. Mechanistically, her group identified a mechanosensitive EPHA2/LYN protein complex that functions upstream of the EMT transcription factor TWIST1 to promote its nuclear localization to trigger EMT and metastasis. In this proposal, she aims to use both genetic and pharmacological approaches to inhibit the EPHA2/LYN signaling to determine the efficacy to inhibit breast tumor invasion and metastasis. Activation of LYN and EPHA2 in response to tumor rigidity makes regulators of this mechanotransduction pathway novel targets for anti-metastasis therapeutics.

ACKNOWLEDGMENT OF SUPPORT

I am so grateful and honored to receive the 2021 AACR-Bayer Innovation and Discovery Grant. This support will allow us to push our basic cancer research discovery from the bench side to be one step closer to clinical translation. Thank you for supporting innovative cancer research.

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.



Andrea Schietinger, PhD

Associate Member

Memorial Sloan Kettering Cancer Center
New York, New York

Targeting molecular drivers of T cell dysfunction for cancer immunotherapy

BIOGRAPHY

Dr. Schietinger is an associate member of the Immunology Program at Memorial Sloan Kettering Cancer Center. She aims to understand when, why, and how immune cells become unresponsive to tumors. Her lab utilizes genetic cancer mouse models that mimic cancer development in patients to investigate T cell responses over the course of tumor development, and define the molecular and epigenetic mechanisms that are responsible for the failure to control and eliminate tumors. Dr. Schietinger received her PhD from the University of Chicago and University of Munich, Germany, and conducted her postdoctoral training at the University of Washington.

SCIENTIFIC STATEMENT

The immune system has enormous power to detect and eliminate pathogens. However, harnessing this power to fight cancer has proven challenging. Tumor specific T cells are found in human tumors but are dysfunctional, allowing tumors to grow unimpeded. Dr. Schietinger's group recently found that T cell dysfunction and therapeutic reprogrammability are epigenetically encoded. They propose to design and test innovative approaches to decode and reprogram tumor specific T cells for cancer immunotherapy. They will (1) employ CRISPR-mediated editing approaches to identify and target molecular drivers of T cell dysfunction and (2) identify the phenotypic, functional, and epigenetic states of human tumor-infiltrating T cells and test whether surface proteins can be used as biomarkers of the underlying epigenetic programs to predict which patients are likely to benefit from immunotherapeutic interventions.

ACKNOWLEDGMENT OF SUPPORT

The 2021 AACR-Bristol Myers Squibb Midcareer Female Investigator Grant award will allow us to conduct bold, high-risk high-reward science needed to design transforming immunotherapeutic reprogramming strategies for all cancer patients.

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.



Spencer J. Collis, PhD

Reader

University of Sheffield
Sheffield, United Kingdom

TTFields-based DDRi combinations to overcome spatiofunctional heterogeneity

BIOGRAPHY

Dr. Collis a molecular and cell biologist with over 20 years' research experience in DNA damage response and genome stability. Following his PhD at Cancer Research UK (CRUK)'s Paterson Institute, he carried out his postdoctoral training at the Johns Hopkins University and CRUK's London Research Institute. In 2009, he established his own laboratory at the University of Sheffield and was subsequently awarded a prestigious CRUK Senior Cancer Research Fellowship. He is currently a reader in genome stability. He has been awarded over £2M in competitive grant funding, published 38 papers, sit on numerous journal editorial boards and funding panels, and has trained over 20 post-graduate students and post-doctoral researchers.

SCIENTIFIC STATEMENT

DNA damaging chemoradiotherapy is standard-of-care treatment for post-surgical management of glioblastoma. However, even with the integration of the recently approved Tumor Treating Fields (TTFields) therapy, only 13% of patients survive more than five years. This is a consequence of spatial heterogeneity, temporal tumor evolution, and inherently resistant glioma stem-like (GSC) sub-populations, therefore highlighting an urgent need to develop more effective TTFields-based therapeutic strategies. Dr. Collis's group has recently developed novel clinically and surgically relevant ex vivo GSC models that reflect spatiofunctional heterogeneity and post-surgical residual disease. In collaboration with Novocure, they have established the capability to deliver TTFields to these models. Using focused functional and genome-scale approaches, he will establish whether functionally and spatially distinct tumor sub-populations demonstrate differential responses to TTFields therapy and will identify universal or specific DNA damage response-based therapeutic vulnerabilities to facilitate rationally designed TTFields-based approaches to help improve current survival rates for patients with this deadly disease.

ACKNOWLEDGMENT OF SUPPORT

The AACR-Novocure Tumor Treating Fields Research Grant will be instrumental in allowing us to further define how TTFields therapy interacts with the various subpopulations within tumors, as well as the postsurgical resistant stem cell niche responsible for tumor recurrence. This will help us to identify potential drug combinations that could further improve its clinical effectiveness.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

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Maurizio D'Incalci, MD

Laboratory Head

Humanitas University
Rozzano, Italy

TTFields in mesothelioma: mechanisms and novel rational drug combinations

BIOGRAPHY

Dr. D'Incalci obtained his medical degree *cum laude* from the University of Milan. He then specialized in pharmacology and in oncology. He subsequently worked in the Molecular Pharmacology Laboratory of the National Cancer Institute. He has been chief of the Cancer Chemotherapy Laboratory and of the Oncology Department at the Mario Negri Institute, Italy. Currently, he is a professor at the Humanitas University and head of the Cancer Pharmacology Laboratory at the Humanitas Research Hospital. He is the author of 536 scientific publications and 44 book chapters of cancer pharmacology.

SCIENTIFIC STATEMENT

The clinical activity demonstrated by Tumor Treating Fields (TTFields) in association with standard chemotherapy in patients with malignant pleural mesothelioma (MPM) led Dr. D'Incalci to investigate the mechanisms that underlie this interaction. The availability of well characterized patient-derived MPM cell lines growing both *in vitro* and *in vivo* with different degrees of sensitivity to TTFields renders the performance of comparative studies possible to identify those mechanisms that are crucial for antitumor activity. Dr. D'Incalci hypothesizes that the selectivity of TTFields against MPM cells is related to the modulation of genes/pathways involved in cell proliferation/survival. TTFields might also alter cell membrane permeability, increasing drug uptake *in vitro*, and modulate drug distribution *in vivo* by interacting with the tumor microenvironment. The elucidation of the mode of action of TTFields and the identification of effective combinations of TTFields with selected anticancer drugs will help design novel clinical studies in a rational fashion.

ACKNOWLEDGMENT OF SUPPORT

The AACR-Novocure Tumor Treating Fields Research Grant will allow my research group to investigate the mode of action of TTFields and to identify mechanism-based effective combinations of TTFields with antitumor drugs against malignant pleural mesothelioma potentially applicable in the clinic.

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.



Chang-Young Jang, PhD

Professor

Sookmyung Women's University
Seoul, South Korea

Identification of new target of TTFs in mitosis for therapeutic application

BIOGRAPHY

Dr. Jang received his PhD in biochemistry from Korea University, South Korea. His postdoctoral research at Stanford University focused on deeper mechanistic understanding of mitotic progression. Dr. Jang is currently a professor in the College of Pharmacy at Sookmyung Women's University. His current research is focused on the communication between DNA damage response and mitotic exit checkpoint and the role of mitotic structures in mitotic catastrophe.

SCIENTIFIC STATEMENT

Tumor treating fields (TTFs) therapy is a novel anticancer treatment that disrupts mitosis in tumor cell through perturbing dipole moment of α/β -tubulin and concomitant spindle microtubule polymerization. Dr. Jang's team identified Aurora B-MCAK as a target pathway of TTFs in spindle dynamics. Since Aurora B is an enzymatic component of chromosomal passenger complex (CPC) and regulates chromosome condensation, spindle attachment, and cytokinesis, his study will provide insights on TTFs-induced mitotic catastrophe through disrupting microtubule polymerization and cytokinesis. In preliminary data, he also showed TTFs-induced chromosome misalignment, centrosome disorganization, and two distinct mitotic defects in various cancer cell lines. In this project, Dr. Jang is studying the mechanism underlying TTFs-induced Aurora B activation and centrosome dysfunction to identify the targets and TTFs-sensitizers for implementation in combination therapy. In addition, he plans to categorize cancer cell lines into two groups to deduce the biomarkers from their genetic background for personalized therapy.

ACKNOWLEDGMENT OF SUPPORT

I am very honored to receive the AACR-Novocure Tumor Treating Fields Research Grant. This support will enable my group to translate our basic science discoveries into new treatment strategies and improve the efficacy of TTFs treatment in glioblastoma and other cancer patients.

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.



Sara G.M. Piccirillo, PhD

Assistant Professor

University of New Mexico
Albuquerque, New Mexico

The impact of Tumor-Treating Fields on residual disease in glioblastoma

BIOGRAPHY

Dr. Piccirillo received her PhD in translational and molecular medicine from the University of Milan-Bicocca, Italy. For her post-doctoral training, she moved to the University of Cambridge, U.K. She was then recruited to the University of Texas Southwestern Medical Center as a faculty member of internal medicine. In 2019, she joined the University of New Mexico Health Sciences Center as a tenure-track assistant professor in the Department of Cell Biology and Physiology and as a full member of the Comprehensive Cancer Center.

SCIENTIFIC STATEMENT

Areas of residual disease represent the source of the recurrent tumor that is fatal for glioblastoma (GBM) patients. However, targeting the residual disease is not offered as part of the standard of care because these areas are difficult to identify and, to date, they have not been characterized during disease progression. Dr. Piccirillo previously contributed to the development of a multiple-sampling scheme that allows objective identification of the residual disease in the sub-ventricular zone (SVZ) of GBM patients. Her work revealed that in 65% of cases the SVZ contains treatment-resistant cancer stem-like cells; thus, investigating residual disease in this area may hold the key to developing a valid therapeutic target for many patients. In this study, Dr. Piccirillo and her research group are set to examine the impact of Tumor Treating Fields (TTFields) on treatment-resistant cancer stem-like cells isolated from the SVZ of GBM patients using single-cell transcriptomics and functional phenotyping analysis.

ACKNOWLEDGMENT OF SUPPORT

I am extremely honored to receive the 2021 AACR-Novocure Tumor Treating Fields Research Grant. This support will provide us with the necessary resources to examine the impact of TTFields on mechanisms contributing to the ability of cancer stem-like cells to overcome treatment and seed the recurrent tumor in GBM patients.

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.



Claudio E. Tatsui, MD

Associate Professor

University of Texas MD Anderson Cancer Center
Houston, Texas

Tumor Treating Fields in the therapy of spinal metastases

BIOGRAPHY

Dr. Tatsui obtained his medical degree at Federal University of Parana, Brazil. Upon completing his neurosurgical residency, he came to the U.S. to pursue further specialization and research. He completed clinical fellowships in complex spine reconstructive surgery at the University of Miami and in neurosurgical oncology at the MD Anderson Cancer Center. He currently holds the position of associate professor in the Department of Neurosurgery at MD Anderson Cancer Center. His practice and research is focused in development of innovative treatments for patients suffering from spinal metastasis.

SCIENTIFIC STATEMENT

In this research, Dr. Tatsui's group will investigate the therapeutic application of tumor treating fields (TTFs) to inhibit cell growth in 3D cultures derived from cell lines and fresh surgical specimens of spinal metastasis. His group plans to identify the most effective inhibitory frequencies for different types of spinal tumors and test the influence of titanium pins to evaluate if the increased electrical conductivity induced by metal improves the anti-proliferative effect of TTFs in the 3D culture. Lastly, he will develop subcutaneous tumors in the flank of nude mice and deliver the most effective inhibitory TTF frequency as identified in vitro for that specific cell type to validate the hypothesis that in vitro data can be used for therapy planning. These concepts have the potential to generate important data supporting clinical translation for the use of TTF in the post-operative management of radiation refractory spinal metastasis.

ACKNOWLEDGMENT OF SUPPORT

I am very grateful to receive the 2021 AACR-Novocure Tumor Treating Fields Research Grant. Tumor growth remodels the bony microenvironment, creating changes in tissue anisotropic properties thus far never explored in the context of TTFs application. This research support will allow build up knowledge to develop new treatment strategies for spinal metastasis.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

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Suhe Wang, MD, PhD

Research Associate Professor

University of Michigan
Ann Arbor, Michigan

Natural electrical fields treatment to induce immune modulation in NSCLC

BIOGRAPHY

Dr. Wang obtained her MD and PhD from Fujian Medical University, China, and the University of Strathclyde, Scotland, respectively. She completed her post-doctoral training under the mentorship of Dr. J Paul Banga at King's College London, U.K., and under the mentorship of Dr. James R. Baker, Jr. at the University of Michigan. Dr. Wang's main research interest is the application of nano-medicine to vaccines, cancers, and autoimmune diseases. Her research has been widely published and supported by the DOD, NIH, and US Thyroid Research Council.

SCIENTIFIC STATEMENT OF RESEARCH

15-30% of non-small cell lung cancer (NSCLC) is associated with KRAS mutations, however, targeted therapies are not available for KRAS-mutated NSCLC. Patients with KRAS mutations benefit less from chemotherapies and have a worse prognosis. Dr. Wang hypothesizes that TTFs therapy could lead to the release of neo-antigens from tumors and induce a unique anti-tumor immune response against KRAS mutation-mediated immunosuppression, which may increase the efficacy of immunotherapy by modulating the tumor microenvironment and eliciting effective and specific anti-tumor immune responses to kill lung epithelial cells that have undergone lung adenocarcinoma-specific mutations. In this study, she will test the hypothesis in a mouse model of inducible lung adenocarcinoma with KRAS activating mutations. An immune monitoring system will be established to analyze immune modulation after TTFs treatment compared to conventional radiation treatment. Both specific immune responses and cytotoxic immune cells will be analyzed.

ACKNOWLEDGEMENT OF SUPPORT

Tumor Treating Fields (TTFs) invented by Novocure have not been applied to KRAS-mutated NSCLC, a subtype of lung cancer with a poor prognosis. By completing this study, we hope that TTFs can be added as an effective treatment against KRAS-mutated NSCLC.



615 Chestnut Street, 17th Floor • Philadelphia, PA 19106-4404
215-440-9300 • 866-423-3965 Toll Free
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