AACR RESEARCH GRANT RECIPIENTS
2021-2022

AACR American Association for Cancer Research®

FINDING CURES TOGETHER®

CONGRATULATIONS
TO THE 2021-2022 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 34 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 $131 million in funding to over 800 scientists. These grants have funded scientists 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.

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LBCA® — Lobular Breast Cancer Alliance

LUSTGARTEN FOUNDATION — PANCREATIC CANCER RESEARCH

MERCK — INVENTING FOR LIFE

MIRATI THERAPEUTICS

MPM — Powering Breakthroughs in Life Sciences

novocure®

OMF — OCULAR MELANOMA FOUNDATION

Pfizer

What would Willie want — Foundation — www.QuadW.org

St. Baldrick's FOUNDATION — Conquer Childhood Cancers

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AACR FELLOWSHIP TO FURTHER DIVERSITY, EQUITY, AND INCLUSION IN CANCER DISPARITIES RESEARCH

The AACR Fellowship to Further Diversity, Equity, and Inclusion in Cancer Disparities Research has been established to support postdoctoral or clinical research fellows conducting disparities research and to establish a successful career path in this field. Eligibility is limited to members of racial or ethnic groups that have been shown to be underrepresented in the cancer-related sciences workforce.
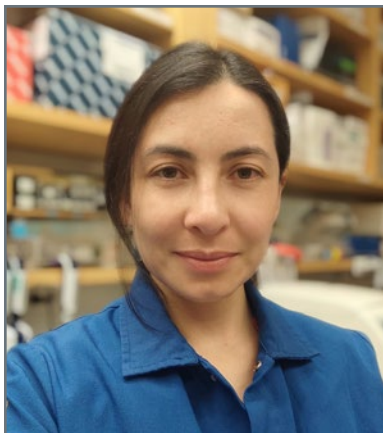
Ana Estrada-Florez, PhD
Postdoctoral Fellow

University of California, Davis
Davis, California

Identification of predisposition and progression gastric cancer biomarkers in Latinos

SCIENTIFIC STATEMENT OF RESEARCH
Gastric cancer (GC) represents a leading cause of incidence and mortality in Latinos. Latinos are ~2-fold more likely to be diagnosed and die of GC when compared to Non-Latino Whites. This research project aims to identify variants associated with GC risk in patients of Latino ancestry. Whole-exome sequencing of 500 patients diagnosed with early-onset GC and/or who had a family history of cancer was performed to identify novel and previously reported mutations in GC. A selection of variants with predicted impact on the phenotype will be tested in gastric preneoplasia biopsies using duplex sequencing, a highly sensitive method to detect rare mutations with ultra-depth sequencing. Variants with likely functional consequences for tumor initiation and/or progression will be selected to generate isogenic gastric organoids to investigate their effect on proliferation, differentiation, and gene expression. This study aims to generate a body of knowledge useful for the prevention, diagnosis, and treatment of GC.

BIOGRAPHY
Ana Estrada-Florez is a Postdoctoral Researcher in the Carvajal-Carmona Lab at the UC Davis Genome Center. She received a MSc in Biology from the University of Tolima in 2012 and a PhD in Biomedical Sciences from the University of Caldas in 2019. During her MS and PhD, her research used epidemiology approaches, exome sequencing, and genome-wide association studies to dissect the role of environmental and genetic factors in thyroid cancer risk. Her current research is focused on the genetics of gastric cancer, the second most common cause of cancer death worldwide, with the highest incidence in Asia and Latin America.

ACKNOWLEDGMENT OF SUPPORT
As a Latina born and educated in Colombia, I am honored with this outstanding fellowship to continue working in this relevant field. My goal is to contribute toward closing the gap of research in minority populations, to improve the health and wellbeing of my ethnic group, and the community in general.

AACR FELLOWSHIP TO FURTHER DIVERSITY, EQUITY, AND INCLUSION IN IMMUNO-ONCOLOGY RESEARCH

The AACR Fellowship to Further Diversity, Equity, and Inclusion in Immuno-oncology Research has been established to support postdoctoral or clinical research fellows to conduct immuno-oncology research and to establish a successful career path in this field. Eligibility is limited to members of racial or ethnic groups that have been shown to be underrepresented in the cancer-related sciences workforce.

Natasha Pinto Medici, PhD
Postdoctoral Fellow

Yale University
New Haven, Connecticut

RNA splicing hijacks anti-tumor immunity in pancreatic cancer

SCIENTIFIC STATEMENTS OF RESEARCH
Pancreatic ductal adenocarcinoma (PDAC) is a devastating disease due to diagnosis at an advanced stage and resistance to all current available therapies. However, the development of resistance is unattributed to additional mutations, suggesting that non-mutational mechanisms help these tumors thrive while blocking immune surveillance. Therefore, there is an unmet need to understand the molecular pathology and immunology of PDAC to develop novel therapeutics. Transcriptional regulation has received extensive attention as a mechanism of therapeutic resistance, but RNA Splicing (RS), a more widespread and potent mechanism of gene regulation and protein diversity, is still poorly understood in therapeutic resistance and immune response. Dr. Natasha Pinto Medici's research will help toward the understanding of RS, which has the potential to uncover novel mechanisms that cancer cells use to transform and thrive. Moreover, her research will help guide the combination of therapies with anti-splicing therapy to restore immune cell activity and sensitivity in therapy-resistant cancers.

BIOGRAPHY
Dr. Pinto Medici is a Postdoctoral Fellow in the laboratory of Dr. Luisa Escobar-Hoyos in the Department of Therapeutic Radiology at Yale University. Originally from Brazil, Dr. Pinto Medici obtained her undergraduate and master's degrees in immunology from Universidad Federal do Rio de Janeiro. After being awarded a competitive Brazilian fellowship for studies abroad, she came to the USA and obtained her PhD in molecular genetics and microbiology from Stony Brook University. As a trained immunologist, she understands that the immune system contributes to disease prognosis. Currently, she researches the molecular regulation of immunity in pancreatic cancer, a deadly and undruggable malignancy.

ACKNOWLEDGMENT OF SUPPORT
I am honored to be awarded with this AACR fellowship. As a Latina, I feel proud and grateful to have my research valued. With this award, I hope to expand my studies in the immunology of pancreatic cancer to improve therapy and bring hope to patients and their families.

AACR-LOBULAR BREAST CANCER ALLIANCE
INVASIVE LOBULAR CARCINOMA RESEARCH FELLOWSHIP

The AACR-Lobular Breast Cancer Alliance Invasive Lobular Carcinoma Research Fellowship is a joint effort to support and encourage innovative research projects with direct applicability and relevance to invasive lobular breast carcinoma (ILC). This fellowship supports postdoctoral or clinical research fellows working on mentored ILC research projects to help establish a successful career path in the field.

Candace Frerich, PhD
Postdoctoral Researcher

University of Texas Southwestern Medical Center
Dallas, Texas

Modulation of glucocorticoid receptor activity to prevent ILC progression

SCIENTIFIC STATEMENT OF RESEARCH
The mechanisms driving tumor growth and progression in invasive lobular carcinoma (ILC) remain unknown. Selective Glucocorticoid Receptor Modulators (SGRMs), compounds that bind to the body's stress hormone receptor, glucocorticoid receptor (GR), inhibit estrogen receptor positive (ER+) invasive ductal carcinoma (IDC) growth in vivo. SGRMs are particularly appealing clinically because they are without metabolic side effects. Late metastasis of ILC to serosal surfaces is particularly deadly. Dr. Frerich's overall hypothesis is that GR activation in ILC will improve patient outcome by slowing tumor growth and inhibiting serosal metastases. Her preliminary data are consistent with this hypothesis, demonstrating that GR/*NR3C1* expression correlates with improved ILC patient overall survival and GR activation in vitro slows proliferation of ILC cells. She will test the hypothesis that GR liganding by dexamethasone (Dex; agonist) or SGRMs (modulators) slows proliferation and reduces cell adhesion using 2D and 3D in vitro and in vivo ILC models.

BIOGRAPHY
Dr. Candace Frerich received a Bachelor of Science in Biochemistry from Angelo State University in San Angelo, TX where she studied the phylogenetics of Texas bat species. She received her PhD in Biomedical Sciences from the University of New Mexico Health Science Center in Albuquerque, NM. There she studied oncogenic Myb transcription factors in salivary gland adenoid cystic carcinoma while working in the laboratory of Scott Ness, PhD. Dr. Frerich then joined the lab of Suzanne Conzen, MD at the University of Texas Southwestern Medical Center where she now studies the role of the glucocorticoid receptor in lobular breast cancer.

ACKNOWLEDGMENT OF SUPPORT
I sincerely appreciate the support of AACR and LBCA. As a postdoctoral researcher, I am thankful for this opportunity and will work diligently to improve ILC patient treatment.

2021 CAREER DEVELOPMENT AWARDS

AACR CAREER DEVELOPMENT AWARD TO FURTHER DIVERSITY, EQUITY, AND INCLUSION IN PANCREATIC CANCER RESEARCH

The AACR Career Development Award to Further Diversity, Equity, and Inclusion in Pancreatic Cancer Research has been established to support the development and diversity of talent working in pancreatic cancer research. Eligibility is limited to members of racial or ethnic groups that have been shown to be underrepresented in the cancer-related sciences workforce.

Luisa Escobar-Hoyos, MSc, PhD
Assistant Professor

Yale University
New Haven, Connecticut

RNA splicing: the "missing link" in pancreatic cancer pathogenesis and immunity

SCIENTIFIC STATEMENT OF RESEARCH
Pancreatic cancer (PC) is a highly aggressive and lethal cancer that is resistant to currently available therapies. The Escobar-Hoyos laboratory recently discovered that PCs are exquisitely susceptible to a range of therapies directed at RNA splicing. However, it is unknown how alterations in RNA splicing drive PC tumorigenesis or impact therapeutic responses. Thus, identification of the role of aberrant RNA splicing in PC tumorigenesis could reveal novel therapeutic targets. Our long-term goal is to identify, design, and test novel mechanistic-based targeted therapies for highly aggressive tumors such as PC. The main objective of this project is to characterize the role of RNA splicing factor mutations in PC pathogenesis and treatment response. These results will uncover a fundamental, yet novel non-mutational mechanism required for PC pathogenesis and tumor maintenance: altered RNA splicing.

BIOGRAPHY
Dr. Escobar-Hoyos is a tenure-track Assistant Professor in the Departments of Therapeutic Radiology, Molecular Biophysics, and Biochemistry at Yale University. Her laboratory's mission is to identify, design, and test novel biomarker- and mechanistic-based targeted therapies for pancreatic cancer and other aggressive tumors. Her laboratory has revealed aberrant RNA splicing and transcription programs that drive tumorigenesis, promote aggressive behavior and therapeutic resistance in tumor cells. These studies provided pre-clinical data that is now being translated into phase 1 and 2 clinical trials. Before starting at Yale University, she conducted her postdoctoral training at Sloan Kettering Cancer Center and doctoral studies at Stony Brook University.

ACKNOWLEDGMENT OF SUPPORT
I am thrilled and honored to be an awardee of the 2021 AACR Career Development Award to Further Diversity, Equality, and Inclusion in Pancreatic Cancer Research. The funded studies will provide novel and fundamental understanding of the processes that cause pancreatic cancer and lead to the development of novel and effective therapies against this disease.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

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

Iok In Christine Chio, PhD
Assistant Professor

The Trustees of Columbia University in the City of New York
New York, New York

Redox-based strategies for pancreatic cancer early detection

SCIENTIFIC STATEMENT OF RESEARCH
Pancreatic ductal adenocarcinoma (PDA) remains incurable, largely due to delayed diagnosis. It is estimated that progression from initiation to overt cancer requires 12 years. This long latency presents a window of opportunity for diagnosis if a cancer-specific biomarker can be identified and sensitively detected. *KRAS* is mutated in 95% of PDA and induces metabolic reprogramming and generation of reactive oxygen species (ROS). While ROS are highly labile, the Chio lab recently found that one of their oxidation products is stable on proteins and specifically enriched in PDA cells. Using mouse models and patient sera, the Chio lab proposes to apply chemical proteomic tools to identify oxidation products that will discriminate between PDA and benign disease such as pancreatitis. These experiments will set up a discovery pipeline for the exploration of new diagnostics and contribute to the development of early detection and therapeutic strategies in the clinic.

BIOGRAPHY
Dr. Christine Chio is an Assistant Professor of Genetics and Development in the Institute for Cancer Genetics at Columbia University Medical Center. Dr. Chio earned her PhD at the University of Toronto studying the interplay between innate immunity and cancer development under the mentorship of Dr. Tak Wah Mak. Subsequently, she joined the lab of Dr. David Tuveson at Cold Spring Harbor Laboratory to pursue her postdoctoral training. Since then, her research has focused on understanding the role of cellular redox regulation, particularly in the development of pancreatic cancer.

ACKNOWLEDGMENT OF SUPPORT
The AACR-MPM Oncology Charitable Foundation Transformative Cancer Research Grant will catapult our efforts to address an important knowledge gap in cancer redox biology and to develop effective, redox-based early detection strategies for pancreatic cancer and other malignancies.

AACR-MPM ONCOLOGY CHARITABLE FOUNDATION TRANSFORMATIVE CANCER RESEARCH GRANT

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

Eirini Papapetrou, MD, PhD
Associate Professor

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

G protein signaling as a novel target for splicing factor-mutant cancers

SCIENTIFIC STATEMENT OF RESEARCH
Recurrent hotspot somatic mutations in genes encoding splicing factors (SFs) are very commonly found in myelodysplastic syndrome (MDS) and in other cancers at varying frequencies but remain undruggable and the mechanisms by which they drive malignancy remain elusive. We recently discovered a novel convergent effector of SF mutations, a long isoform of *GNAS* (the gene encoding the alpha subunit of the stimulatory G protein, Gαs), as a novel target for MDS and other SF-mutant cancers. The goal of the study is to investigate Gαs as a therapeutic target and evaluate therapeutic interventions that inhibit signaling downstream of its long form (Gαs-L) using iPSC-derived and primary MDS cells in in vitro and in vivo functional assays.

BIOGRAPHY
Eirini Papapetrou, MD, PhD, is an Associate Professor of Oncological Sciences at the Icahn School of Medicine at Mount Sinai. Dr. Papapetrou's research program seeks to uncover new disease mechanisms and therapeutic targets for myeloid neoplasms. Her laboratory pioneered the development of iPSC models of myeloid malignancies. Dr. Papapetrou is the recipient of several awards, including the American Society of Gene and Cell Therapy Outstanding New Investigator Award, Damon Runyon-Rachleff Innovation Award, Pershing Square Sohn Prize, and is an elected member of the American Society for Clinical Investigation.

ACKNOWLEDGMENT OF SUPPORT
I am honored and grateful to receive this award, which will enable my laboratory to embark on a new and exciting direction in cancer biology of evaluating a new therapeutic target for cancers with splicing factor mutations.

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.

Robbie J. Majzner, MD
Assistant Professor

The Board of Trustees of the Leland Stanford Junior University
Stanford, California

SCIENTIFIC STATEMENT OF RESEARCH
The overarching goal of the Majzner lab is to generate immunotherapies for pediatric cancer while studying fundamental mechanisms of tumor resistance through three focus areas:

1. CAR T-cell platform development: Major impediments prevent the deployment of CAR T-cells for solid tumors. The laboratory leverages insights from clinical trials and preclinical models to engineer solutions to overcome these obstacles.

2. Defining the immunobiology of GD2: GD2 has been a known target in pediatric oncology for over 20 years, but little is known about its biology. The laboratory has demonstrated that GD2 is an immune-checkpoint molecule and continues to explore its basic role in tumor biology and immune modulation.

3. Preclinical development of novel approaches for pediatric immunotherapy: The Majzner lab is centrally focused on improving outcomes for children with cancer through the translation of novel immunotherapies. The ultimate manifestation of this goal will be when our findings are translated to the clinic.

BIOGRAPHY
Robbie Majzner is an Assistant Professor of Pediatrics in the Division of Hematology, Oncology, Stem Cell Transplantation & Regenerative Medicine at Stanford University School of Medicine. After graduating with a BA from Columbia University, Dr. Majzner attended Harvard Medical School, where he developed an interest in pediatric oncology. He completed his residency training in pediatrics at New York Presbyterian-Columbia and fellowship training in pediatric hematology-oncology at Johns Hopkins and the National Cancer Institute. During his fellowship at the NCI and a subsequent instructorship at Stanford, he became interested in developing new methods to harness the pediatric immune system to target childhood cancer which is now the broad focus of his laboratory group.

ACKNOWLEDGMENT OF SUPPORT
The AACR-St. Baldrick's Foundation Pediatric Cancer Research Grant will support efforts in my laboratory to develop new therapies for children with incurable cancers. This work will focus on engineering new platform technologies capable of unleashing the power of CAR T cells for children with solid tumors.

2021 INDEPENDENT RESEARCH GRANTS

AACR INNOVATION GRANT TO FURTHER DIVERSITY, EQUITY, AND INCLUSION

The AACR Innovation Grant to Further Diversity, Equity, and Inclusion Grant has been established to support the development of highly talented cancer researchers. Eligibility is limited to members of racial or ethnic groups that have been shown to be underrepresented in the cancer related sciences. This grant promotes research into finding new treatment options for cancers with high unmet medical need, encouraging innovation and translation of ideas from basic research into novel drugs.

M. Andres Blanco, PhD
Assistant Professor

The Trustees of the University of Pennsylvania
Philadelphia, Pennsylvania

Evaluating KAT6A as a novel target for non-APL AML differentiation therapy

SCIENTIFIC STATEMENT OF RESEARCH
Acute myeloid leukemia (AML) is a disease of blocked differentiation in which blasts fail to mature and proliferate continuously. Differentiation therapy, which aims to reactivate latent maturation programs and induce cell cycle exit, is curative in the promyelocytic (APL) AML subtype but not in other AML subtypes. Recently, Dr. Blanco's laboratory identified the histone acetyltransferase KAT6A as a novel driver of differentiation arrest in non-APL AML. KAT6A is actionable and a small molecule inhibitor (WM-1119) has recently been developed. The goal of Dr. Blanco's funded project is to evaluate whether targeting of KAT6A represents a high potential strategy for non-APL AML differentiation therapy. His group will first test the in vivo therapeutic efficacy of WM-119 in AML mouse models. He will then determine the responsiveness of clinical patient samples from diverse AML subtypes to WM-1119 using ex vivo assays for self-renewal, proliferation, and myeloid transcriptional programs.

BIOGRAPHY
Dr. Blanco received his BA from Cornell University where he double majored in biological sciences and philosophy. He then received his PhD in molecular biology from Princeton University where he studied the molecular basis of cancer metastasis in the laboratory of Yibin Kang. Dr. Blanco then conducted his postdoctoral research at Harvard Medical School and Children's Hospital Boston in the laboratory of Yang Shi. His postdoctoral research focused on the role of chromatin modifications in cell fate regulation. In 2018, Dr. Blanco started his laboratory at the University of Pennsylvania where his group studies the epigenetic regulation of cancer cell fate decisions.

ACKNOWLEDGMENT OF SUPPORT
This award will provide critical support for my lab's research on the role of the gene KAT6A in driving differentiation arrest in acute myeloid leukemia. This support will allow us to make rapid progress on this project and generate data that will make it highly competitive for federal grant funding.

AACR-ANNA D. BARKER BASIC CANCER RESEARCH FELLOWSHIP

The AACR Anna D. Barker Basic Cancer Research Fellowship encourages and supports postdoctoral or clinical research fellows to establish a successful career path in cancer research.
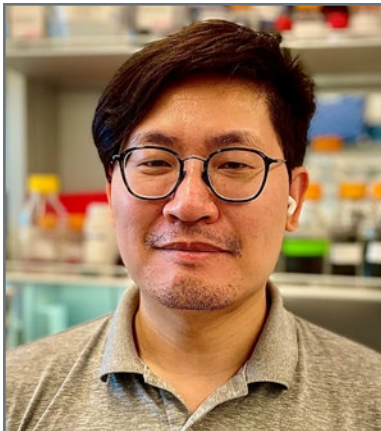
Hsiwen Yeh, PhD
Postdoctoral Fellow

The Rockefeller University
New York, New York

The role of mitochondrial glutathione in tumor initiation and progression

SCIENTIFIC STATEMENT OF RESEARCH
Cancer cells exhibit dramatic alterations in cellular metabolism to support cell growth, proliferation, and survival. However, the role of metabolism in late-stage tumor progression is less studied. Yet, it is emerging as a new avenue for the identification of innovative targets for drug development in cancer therapy. Through organellar proteomics and metabolomics approaches, mitochondrial antioxidants have been identified as major contributors to cancer dissemination. Dr. Yeh aims to elucidate the roles of compartmental antioxidants during tumor progression and uncover clues for disease pathogenesis and potential therapeutic targets for cancer.

BIOGRAPHY
Dr. Yeh received his PhD at National Defense Medical Center in Taiwan, where he studied cancer metastasis and gene regulation. After completing his graduate training, he joined Rockefeller University as a Postdoctoral Research Fellow. Dr. Yeh's research focuses on the role of oxidative metabolism in tumorigenesis.

ACKNOWLEDGMENT OF SUPPORT
Receiving the AACR Anna D. Barker Basic Cancer Research Fellowship is a great honor. The fellowship represents an excellent opportunity to achieve my research goals of providing new insights in the field of cancer metabolism and identifying prognostic and therapeutic strategies to prevent cancer metastasis.

AACR-ASTRAZENECA BREAST CANCER RESEARCH FELLOWSHIP

The AACR Breast Cancer Research Fellowships represent a joint effort to encourage and support postdoctoral or clinical research fellows to conduct breast cancer research and to establish a successful career path in this field.
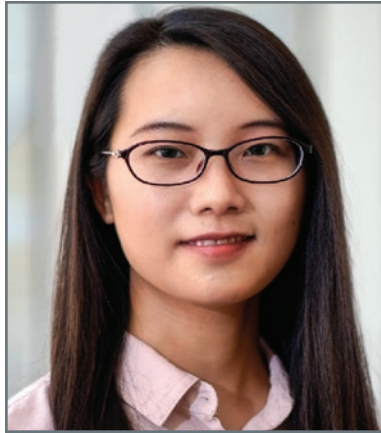
Qin Luo, PhD
Postdoctoral Associate

Baylor College of Medicine
Houston, Texas

Boosting Immunogenic Cell Death to Enhance Breast Cancer Immunotherapy

SCIENTIFIC STATEMENT OF RESEARCH
Immune checkpoint blockade therapy (ICBT) has relatively limited use in breast cancer patients due to the lack of pre-existing immunity in the tumor microenvironment. Dr. Luo and her colleagues previously found ORIN1001 suppressing the RNase activity of endoplasmic reticulum (ER) stress sensor IRE1a promotes the immunogenic lytic cell death in combination with taxane, releasing inflammatory factors and danger-associated molecular patterns (DAMPs) which act as alarm signals to activate the adaptive immunity. As a result, ORIN1001 and taxane convert PD-L1-negative immune-cold breast tumors, which have no response to ICBT at all, to PD-L1-high-expressing immune-hot ones that are highly sensitive to ICBT. Triplet combination therapy with ORIN1001, taxane, and pembrolizumab elicits a very strong anti-tumor immune response that could generate long-term durable responses in patients. Dr. Luo will establish the mechanism of how ORIN1001 induces inflammasome-dependent pyroptotic cell death in combination with taxane and design a mechanism-based novel breast cancer immunotherapy.

BIOGRAPHY
Dr. Luo is currently a Postdoctoral Associate in the Department of Molecular and Cellular Biology at Baylor College of Medicine. Her long-standing interest has always been in cancer immunology and tumor microenvironment. She got her PhD at the Institute of Biomedical Sciences (Fudan University, China) where she found Neutrophil Extracellular Traps (NETs) and cancer-associated fibroblasts fuel hepatocellular carcinoma (HCC) initiation and metastasis. Now she expands her research and training to breast cancer stress responses and immunotherapy and aims to develop mechanism-based novel therapies to transform metastatic breast cancer into a manageable chronic disease.

ACKNOWLEDGMENT OF SUPPORT
I am extremely honored to receive the 2022 AACR Breast Cancer Research Fellowship. This provides critical support for me to develop the mechanisms of how ORIN1001 and taxane convert PD-L1-negative immune-cold breast tumors to immune-hot ones. Also, this support sets me on the path towards an independent scientific career.

AACR-ASTRAZENECA BREAST CANCER RESEARCH FELLOWSHIP

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

Minh Tung Phung, PhD
Postdoctoral Fellow

The Regents of the University of Michigan
Ann Arbor, Michigan

Early-onset breast cancer and research on the environment

SCIENTIFIC STATEMENT OF RESEARCH
Early-onset breast cancer (EOBC) is the most common cancer among young adult women. The incidence rates are higher among Black compared to White individuals and among people living in urban compared to rural areas. The impact of environmental exposures on EOBC risk is notably understudied. The investigators will establish a population-based case-control study in Michigan to examine the impact of environmental factors on EOBC risk and disparities by race/ethnicity and other social determinants of health. Cases are Non-Hispanic Black and White EOBC patients aged 25-44 (n=675). Controls (n=2,025) are cancer-free participants in the Michigan Cancer and Research on the Environment Study (MI-CARES). The environmental exposures of interest include personal-level factors (e.g., personal care products, smoking, pesticides, insecticides) and location-related factors (e.g., air pollution, per- and polyfluoroalkyl substances, metals, dioxane). Given that many exposures are modifiable, this study has tremendous potential to identify EOBC primary prevention opportunities and improve health equity.

BIOGRAPHY
Dr. Phung obtained his MPH from the University of Auckland and will be receiving his PhD in epidemiology from the University of Michigan in April 2022. His MPH thesis developed and validated a risk prediction model for breast cancer survival in New Zealand. His PhD research focused on identifying novel risk factors for ovarian cancer and developing a risk stratification model to assist with precision prevention. He will be a Postdoctoral Research Fellow at the University of Michigan starting May 2022, focusing on breast and ovarian cancer research under the supervision of Dr. Leigh Pearce.

ACKNOWLEDGMENT OF SUPPORT
I am extremely honored to receive the AACR Breast Cancer Research Fellowship. This fellowship will advance my research and goal to become an independent researcher in cancer epidemiology. This fellowship will also provide opportunities to build a foundation in research on environmental factors and early-onset breast cancer.

AACR-ASTRAZENECA CLINICAL IMMUNO-ONCOLOGY RESEARCH TRAINING FELLOWSHIP

AACR-AstraZeneca Clinical Immuno-oncology Research Training Fellowship program is designed to encourage exceptional clinical research by bridging close collaboration between academia and industry. Selected clinical researchers will be provided with real-world experience in clinical development at a Astrazeneca facility in Gaithersburg, MD.

Max Jameson-Lee, MD, PhD
Fellow

University of Pittsburgh
Pittsburgh, Pennsylvania

RESEARCH ACTIVITIES AT ASTRAZENECA
During the research year at AstraZeneca, Dr. Jameson will be paired with an AstraZeneca 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. Jameson with the opportunity to gain experience in drug development and understand challenges in late-stage clinical research. Additional focus areas may also be provided (e.g., preclinical research, biomarker discovery, real-world evidence).

BIOGRAPHY
Max Jameson-Lee MD, PhD is currently a Hematology/Oncology Fellow at UPMC Hillman Cancer Center in Pittsburgh. He completed his medical training and thesis work at Virginia Commonwealth University and the University of Virginia, with a focus on immunology and cancer. During residency, he combined his interests in patient care, immunology, and bioinformatics to create minor antigen prediction pipelines for stem cell transplant patients, correlating predicted antigen loads with graft vs host disease. During this fellowship he developed clinical trials combining targeted and immunotherapy in melanoma to drive active T cells into tumor microenvironments in high-risk patients.

ACKNOWLEDGMENT OF SUPPORT
I am excited to participate in the AACR AstraZeneca Clinical Immuno-Oncology Fellowship. Working with industry partners on clinical trial design, while performing translational research will be a foundational experience for me as an early phase clinical trialist.

AACR-ASTRAZENECA OVARIAN CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Ovarian Cancer Research Fellowships represent a joint effort to encourage and support postdoctoral or clinical research fellows to conduct ovarian cancer research and to establish a successful career path in this field.

Ksenija Nesic, PhD
Research Officer

Walter and Eliza Hall Institute of Medical Research
Parkville, Australia

CRISPR screens to find novel targets to overcome PARP inhibitor resistance

SCIENTIFIC STATEMENT OF RESEARCH

Homologous recombination (HR) DNA repair deficiency is a frequent event in ovarian cancer (OC). While PARP inhibitors (PARPi) are a powerful targeted therapy for HR deficient OC, most women eventually stop responding and die from their disease. Understanding mechanisms of PARPi action and resistance are critical to improving outcomes for women with OC. To address this, Dr Ksenija Nesic is using genome-wide CRISPR screens to identify both novel PARPi resistance mechanisms and PARPi synergy targets in three OC cell line models with different HR defects. Completion of all three screens will generate a comprehensive picture of PARPi synergy and resistance pathways across HR deficient ovarian cancer. Screen hits validated in vitro will then be explored in vivo using a highly characterized cohort of OC patient-derived xenograft models. These findings will be vital for ensuring that the unprecedented PARPi outcomes will be available for a greater proportion of women with OC.

BIOGRAPHY

Dr. Ksenija Nesic graduated with a Bachelor of Science from the University of Melbourne in 2012 and went on to complete a masters degree with Professor David Thorburn at the Murdoch Children's Research Institute (Melbourne, Australia), where she developed a sequencing-based test for mitochondrial DNA mutations in children with mitochondrial disease. In 2020, she completed her PhD in Professor Clare Scott's group at WEHI (Melbourne, Australia), where she studied diverse mechanisms of PARP inhibitor resistance in ovarian carcinoma PDX and cell line models. She is now continuing this work as a post-doctoral researcher in the Scott laboratory.

ACKNOWLEDGMENT OF SUPPORT

The AACR-AstraZeneca Ovarian Cancer Research Fellowship is giving me the opportunity to complete fundamental research started during my PhD, with the potential to improve outcomes for many women diagnosed with ovarian cancer. I am extremely grateful for the support that this fellowship provides and excited about the research to come.

AACR-ASTRAZENECA OVARIAN CANCER RESEARCH FELLOWSHIP

The AACR-AstraZeneca Ovarian Cancer Research Fellowships represent a joint effort to encourage and support postdoctoral or clinical research fellows to conduct ovarian cancer research and to establish a successful career path in this field.

Anna Salvioni, PharmD, PhD
Postdoctoral Fellow

University Cancer Institute
Toulouse Oncopole
Toulouse, France

HRD effect on T-cell exhaustion in ovarian cancer

SCIENTIFIC STATEMENT OF RESEARCH
Ovarian cancer is the most lethal gynecologic malignancy. Despite its immunogenic nature, response rates to immune checkpoint blockade monotherapy are low. Patients with Homologous Recombination Deficiency (HRD), whose tumors display higher infiltration by T cells, do not experience a significant response to anti-PD-1 treatment. As previous work of our team identified two populations of antigen-specific exhausted CD4 and CD8 T cells as key players in response to anti-PD-1 treatment in epithelial malignancies, we aim to characterize these populations in tumors exhibiting or not HRDs. Taking advantage of pre-therapy tumor samples collected from a cohort of patients treated at our institution, we set out to define the exhaustion profile of tumor-infiltrating lymphocyte populations and how HRDs shape the immune landscape of tumors, by flow-cytometry, multiplex immunohistochemistry, and transcriptomic approaches. The results of this study will be key for the identification of efficient combination therapies for the treatment of ovarian cancer.

BIOGRAPHY
Dr. Salvioni completed her Pharmacy training at the University of Padua, Italy, and her PhD at Paul Sabatier University in Toulouse, France. Her PhD research, both in Toulouse and at the University of California Berkeley, as a visiting student, focused on adaptive immunity mechanisms in host-pathogen interactions. She is currently a Postdoctoral Researcher at the University Cancer Institute of Toulouse Oncopole and the Cancer Research Center of Toulouse, where she studies the impact of Homologous Recombination Deficiency on T-cell exhaustion in ovarian cancer, in order to provide the basis for efficient combination therapies able to prevail over resistance to immunotherapy.

ACKNOWLEDGMENT OF SUPPORT
I am honored and grateful to be a recipient of the AACR-AstraZeneca Ovarian Cancer Research Fellowship. This grant provides an invaluable opportunity to study the influence of Homologous Recombination Deficiency on T-cell exhaustion in ovarian cancer and it is pivotal for my path towards being an independent researcher in onco-immunology.

AACR-BRISTOL MYERS SQUIBB
CANCER DISPARITIES RESEARCH FELLOWSHIP

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

Kara Cicero, MD, MPH
Postdoctoral Fellow

The Trustees of Columbia University in the City of New York
New York, New York

Prevalence & Risk Factors of MGUS in a Black Sub-Saharan African Population

SCIENTIFIC STATEMENT OF RESEARCH
Multiple myeloma and its precursor, monoclonal gammopathy of undetermined significance (MGUS), both occur twice as often within Black populations compared to Whites, suggesting that racial disparities lie within the development of MGUS, not progression to malignancy. However, few studies have been conducted on MGUS within African cohorts. In collaboration with ICAP and local partners, Cicero, et al. will determine the prevalence of MGUS in a population of Black men and women in Eswatini. They will perform protein electrophoresis, immunofixation, and free light chain quantification on plasma samples from a nationally representative repository that has been stored at -80°C since 2016. They will also assess the relationship between HIV status and MGUS by employing univariable and multivariable logistic regressions, controlling for age, gender, and socioeconomic status. They expect their results to be applicable not just to those in sub-Saharan Africa, but also to populations of African descent here in the US.

BIOGRAPHY
After graduating Cum Laude from Cornell University, Kara Cicero attended Tulane University School of Medicine, where she was inducted into the Alpha Omega Alpha Honor Medical Society. She also pursued a joint MPH in Global Health Systems and Development, where she received the Ling and Jessop Awards for teaching local healthcare workers in Malawi. During her Internal Medicine residency at Columbia University, she developed an interest in oncology and is now a clinical fellow in Hematology and Medical Oncology at Columbia. Throughout her training, she has been involved in numerous research endeavors focused on hematologic malignancies within global oncology.

ACKNOWLEDGMENT OF SUPPORT
I am thrilled to receive the Cancer Disparities Fellowship and grateful for the opportunity to lead my first major project! I hope that our study will deepen our understanding of the racial disparities surrounding MGUS and multiple myeloma in an understudied population that is also most likely to be affected.

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.

Sung-Min Hwang, PhD

Postdoctoral Associate

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

Decoding ER stress signaling in ovarian cancer-reactive T cells

SCIENTIFIC STATEMENT OF RESEARCH

Ovarian cancer (OvCa) is a highly immunosuppressive malignancy that is refractory to standard treatments and all current forms of immunotherapy. We have uncovered that harsh conditions in the ovarian tumor microenvironment compromise the protein-folding capacity of the endoplasmic reticulum (ER) in intratumoral T cells, causing abnormal ER stress response activation of the IRE1α-XBP1s branch causes severe intratumoral T cell dysfunction in OvCa. However, the precise molecular mechanisms by which IRE1α-XBP1s signaling governs global effector profiles in intratumoral T cells facing ER stress remains largely unexplored. Dr. Hwang's aim is to explore how XBP1s operates as a novel transcriptional regulator controlling the expression of factors required for optimal T cell activation, differentiation, and anti-tumor function. This project is expected to uncover a novel regulator of T cell function in ovarian tumors and pave the way for developing the next generation of effective CAR T cell immunotherapies for OvCa.

BIOGRAPHY

Dr. Hwang completed his PhD from the Pohang University of Science and Technology, Republic of Korea. During his PhD studies, he developed a variety of genetically engineered mice and experimental models to understand the molecular mechanisms regulating the differentiation and activity of T cells in autoimmunity and cancer. He is currently a Postdoctoral Fellow at the Weill Cornell Medicine in New York City, where he is developing new forms of adoptive cellular immunotherapies based on ovarian cancer-reactive T cells lacking endoplasmic reticulum stress sensors, which are expected to have increased persistence and enhanced protective function in the harsh ovarian tumor microenvironment.

ACKNOWLEDGMENT OF SUPPORT

Receiving the 2022 AACR Immuno-oncology Research Fellowship is a great honor and a key milestone in developing a career in cancer research. I sincerely thank the AACR for funding my project to foster a comprehensive understanding of the tumor microenvironment as a critical impediment to the success of immunotherapy in ovarian cancer.

AACR-CONQUER CANCER®, THE ASCO FOUNDATION YOUNG INVESTIGATOR AWARD FOR TRANSLATIONAL CANCER RESEARCH

The AACR-Conquer Cancer Foundation of ASCO Young Investigator Award for Translational Cancer Research provides funding to promising investigators to encourage and promote quality research in clinical oncology. The purpose of this jointly supported award is to fund a physician-scientist during the transition from a fellowship program to a faculty appointment.

Adrienne Long, MD, PhD
Clinical Fellow

The Board of Trustees of the
Leland Stanford Junior University
Stanford, California

Using thymic tissue to identify high-affinity TCRs targeting Ewing sarcoma

SCIENTIFIC STATEMENT OF RESEARCH

Checkpoint inhibitors have revolutionized how we treat adult cancers but have shown little efficacy against pediatric tumors due to their low mutational burden. One alternative approach is to use T cells engineered to express a T cell receptor (TCR) with defined specificity against oncofetal antigens (developmental proteins expressed by tumors but not by healthy, post-natal tissue). To date, the development of such therapies has been largely limited by the difficulty in isolating high-affinity TCRs that target oncofetal antigens. This is because oncofetal antigens are non-mutated self-peptides, and thus inherently less immunogenic. Dr. Long is poised to use fundamentals of central tolerance and T cell development to create novel methods that will redefine how the field identifies high-affinity cancer-specific TCRs, and specifically identify high-affinity TCRs with a strong potential for clinical translation in the treatment of Ewing sarcoma.

BIOGRAPHY

Dr. Long is a pediatric oncologist developing novel immunotherapies for children with cancer. She received her BS and MD from Northwestern, and a PhD while working with Dr. Crystal Mackall at the NIH. For her thesis, Dr. Long was the first to define T cell exhaustion as a major limiter of CAR efficacy. She completed a pediatrics residency at Boston Children's Hospital and a hematology/oncology fellowship at Stanford. In 2022, she will be a Stanford instructor and will continue her post-doctoral research with Dr. Mark Davis, studying how thymic selection, designed to prevent autoimmunity, may contribute to poor antitumor immunity in children.

ACKNOWLEDGMENT OF SUPPORT

The generous support of the AACR-Conquer Cancer Foundation of ASCO will be instrumental in helping me become an independent physician-scientist that translates novel immunotherapies into the clinic. Their funding also highlights the importance of developing immunotherapies for pediatric solid tumors and provides the necessary support towards making this a reality.

AACR-INCYTE IMMUNO-ONCOLOGY RESEARCH FELLOWSHIP

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

Yun Ha Hur, DVM, PhD
Postdoctoral Associate

The Rockefeller University
New York, New York

How the aging tumor microenvironment impacts cancer

SCIENTIFIC STATEMENT OF RESEARCH
Squamous cell carcinomas (SCCs), metastatic cancers of stratified epithelial tissues, are among the most common malignancies. They occur when epithelial stem cells acquire oncogenic mutations to form tumor-initiating cells (TIC). While initially thought to be rooted in the accumulation of genetic mutations, there is a growing appreciation of the importance of the tissue microenvironment in driving cancer. With rising SCC incidences in the aging population, this begs the question of whether age-related changes in the tumor microenvironment contribute to tumor susceptibility and how. One dramatic change in the aged microenvironment lies in immune function, raising the possibility that impaired crosstalk between TICs and immune cells is responsible for the rise in cancer susceptibility. During her fellowship, Dr. Hur proposes to identify age-related differences in cell types and gene expression in the TIC: immune cell niche and gain insights into the functional importance of their crosstalk involved in SCC formation, maintenance, and metastasis.

BIOGRAPHY
Dr. Hur received her DVM from Seoul National University in South Korea and completed her PhD in the laboratory of Dr. Richard Cerione at Cornell University. During her graduate training, she discovered that embryonic stem cells generate extracellular vesicles which help maintain pluripotency in recipient embryonic stem cells. She is currently conducting her postdoctoral work under the supervision of Dr. Elaine Fuchs at Rockefeller University, where she is studying how the aging tumor microenvironment impacts cancer progression.

ACKNOWLEDGMENT OF SUPPORT
It is an honor to be a recipient of the AACR Immuno-oncology Research Fellowship. This opportunity will allow me to contribute to advance knowledge about the roles that the tumor microenvironment plays in cancer, also providing me with the resources to pursue my career as an independent researcher.

AACR-MERCK CANCER DISPARITIES RESEARCH FELLOWSHIP

The AACR-Merk Cancer Disparities Research Fellowships represent an effort to encourage and support postdoctoral or clinical research fellows to conduct cancer disparities research and to establish a successful career path in this field.
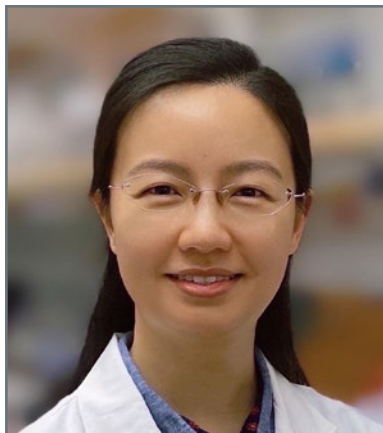
Yuanyuan Fu, PhD
Postdoctoral Fellow

University of Hawaii
Honolulu, Hawaii

Targeting Colorectal Cancer Disparity in Native Hawaiians/Pacific Islanders

SCIENTIFIC STATEMENT OF RESEARCH
Colorectal cancer (CRC) is the third most common cancer diagnosed and the second most common cause of cancer deaths among Americans. Native Hawaiians (NH)/Pacific Islanders (PI) are a unique racial/ethnic group in the US and exhibit many disproportionate health issues. In particular, they suffer from elevated CRC incidence and elevated mortality rates. Genetic factors contributing to colorectal pathobiology have not been systemically studied within NH/PI. The proposed study aims to investigate if genetic differences contribute to the health disparities observed between NH/PI and other ethnic groups, which could be targeted as promising biomarkers to improve CRC diagnosis and prognosis in NH/PI. By analyzing the transcriptome profiling data with clinicopathological information and exploring specific biological mechanisms underlying the development of CRC in NH/PI patients, this study will provide valuable insights into CRC susceptibility and targets of intervention, with the goal of positively impacting health outcomes in the unique NH/PI population.

BIOGRAPHY
Dr. Yuanyuan Fu completed her PhD in cancer epidemiology at the University of Hawaii Cancer Center. Here, she conducted research on the biological role and clinical implication of several novel non-coding RNAs in cancers. She started her postdoctoral study on clinical and genetic cancer research in the Department of Quantitative Health Sciences at the University of Hawaii, John A. Burns School of Medicine. Currently, Dr. Fu's research goal is to understand how genetic factors contribute to colorectal cancer disparities in the unique population of Native Hawaiians/Pacific Islanders.

ACKNOWLEDGMENT OF SUPPORT
The AACR Cancer Disparities Research Fellowship will enable advanced research on colorectal cancer disparities in Native Hawaiians/Pacific Islanders. The study will help identify the ethnic-specific genetic effects on tumor progression and target them for therapeutic benefit and lay a solid foundation for my scientific career development.

AACR-MERCK CANCER DISPARITIES RESEARCH FELLOWSHIP

The AACR-Merk Cancer Disparities Research Fellowships represent an effort to encourage and support postdoctoral or clinical research fellows to conduct cancer disparities research and to establish a successful career path in this field.

Melanie Stall, MD
Fellow

The University of Texas
Southwestern Medical Center
Dallas, Texas

Perceptions of LEP Parents of Children with Cancer on Care and Support

SCIENTIFIC STATEMENT OF RESEARCH
Patients and families with limited English proficiency (LEP) face unique challenges within the healthcare system and perceive healthcare discrimination or lower quality of medical care related to a lack of fluency in English. Dr. Stall aims to elevate the voices of families with LEP navigating the stressful pediatric cancer illness experience by exploring and characterizing their perceptions of communication, support, and medical care received during treatment. To delve into this complicated topic with depth and nuance, Dr. Stall will conduct semi-structured interviews with parents with LEP using a certified medical interpreter at multiple time points during treatment. She aims to use findings from this study to identify areas of improvement to develop interventions that improve the illness and treatment experience of patients and families with LEP.

BIOGRAPHY
Dr. Stall received her medical degree from Wright State University Boonshoft School of Medicine. She then completed her Pediatric Residency at the University of Tennessee Health Science Center at Le Bonheur Children's Hospital and St. Jude Children's Research Hospital. During residency she developed an interest in qualitative research, specifically studying prognostic communication language in children with advanced cancer. Dr. Stall is approaching her final year of Pediatric Hematology-Oncology Fellowship at the University of Texas Southwestern Medical Center at Children's Health where she will remain as an instructor to continue working on her research.

ACKNOWLEDGMENT OF SUPPORT
It is an honor to receive the AACR-Merck Cancer Disparities Research Fellowship. Navigating pediatric cancer is difficult at best, and after witnessing the added struggles of my patients and families with limited English proficiency, I am grateful that this award will allow me to identify ways to improve their experience.

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.

Zhenna Xiao, PhD
Postdoctoral Fellow

The University of Texas MD Anderson Cancer Center
Houston, Texas

Single Cell Genomic Evolution of HER2-Resistance in Breast Cancer

SCIENTIFIC STATEMENT OF RESEARCH
HER2 positivity accounts for 15-20% of breast cancer and has traditionally been associated with poor prognosis. While HER2-targeted therapies significantly improve clinical outcomes, many patients develop resistance and progress to metastatic disease and death. Dr. Xiao aims to delineate the genomic evolution and transcriptional reprogramming of the tumor cells and the tumor microenvironment during HER2-targeted therapy resistance using high-throughput single-cell DNA and RNA sequencing methods. Completion of the proposed proposal will greatly improve our fundamental understanding of the resistance to HER2-targeted therapy and is expected to identify new therapeutic targets in the tumor, stromal and immune cells that can be exploited to overcome resistant disease in HER2-positive breast cancer patients and predict therapeutic response.

BIOGRAPHY
Dr. Xiao obtained her PhD at UT MD Anderson UT Health Graduate School of Biomedical Sciences, where she studied deubiquitinating enzymes that promote breast cancer progression and migration via regulating protein stability. She is currently a Postdoctoral Fellow in the Department of Genetics at MD Anderson Cancer Center. Her research mainly focuses on delineating the role of clonal evolution and intratumor heterogeneity in therapy resistance in human breast cancer using single-cell genomics.

ACKNOWLEDGMENT OF SUPPORT
It is my great honor and pleasure to be a recipient of the AACR Breast Cancer Research Fellowship. This fellowship will not only support the proposed research work but will also provide me with an invaluable opportunity to pursue my career objective toward becoming an independent cancer research investigator.

AACR-QUADW FOUNDATION SARCOMA RESEARCH FELLOWSHIP IN MEMORY OF WILLIE TICHENOR

AACR-QuadW Foundation Sarcoma Research Fellowship in Memory of Willie Tichenor represents a joint effort to encourage and support a postdoctoral or clinical research fellow to conduct translational or clinical sarcoma research and to establish a successful career path in this field.

Qiqi Yang, PhD
Research Fellow

Massachusetts General Hospital
Boston, Massachusetts

Reversing multidrug resistance by targeting the PIK3CA/AKT pathway in RMS

SCIENTIFIC STATEMENT OF RESEARCH

Rhabdomyosarcoma (RMS) is a common childhood cancer of muscle. Although treatment has improved the 5-year overall survival to 70%, treatment is often aggressive and has long-term debilitating effects on children. Moreover, a large fraction of patients eventually develop relapse disease that cannot be killed by conventional therapy. Our group has recently identified a new combination therapy of Olaparib PARP inhibitor and DNA damaging agent Temozolomide (OT) for the treatment of RMS that is in clinical trial evaluation at MGH and Dana-Farber Cancer Institute (NCT01858168). Despite these successes, drug resistance to this same combination therapy has been reported in other cancers, raising concerns that drug resistance may also develop in a fraction of RMS patients in our trial. My work will identify the mechanisms by which RMS develop therapy resistance and identify new drugs that re-sensitize these tumors to chemotherapy.

BIOGRAPHY

Dr. Qiqi Yang completed her PhD training in the Department of Biological Sciences at the National University of Singapore under the guidance of Dr. Zhiyuan Gong, a world-recognized pioneer in using zebrafish as a model of hepatocellular carcinoma (HCC). After, she joined the laboratory of Dr. David Langenau at Massachusetts General Hospital and Harvard Medical School. As a postdoctoral research fellow, Dr. Yang's work focuses on identifying and dynamically imaging new therapies for the treatment of therapy-resistant, pediatric rhabdomyosarcoma.

ACKNOWLEDGMENT OF SUPPORT

I would like to express my sincerest gratitude to AACR and the QuadW Foundation. I am deeply honored to have been selected for the Sarcoma Research Fellowship that honors the memory of Willie Tichenor. This funding support will allow me to continue my work to find new therapies for rhabdomyosarcoma.

2022 CAREER DEVELOPMENT AWARDS

AACR-ASTRAZENECA CAREER DEVELOPMENT AWARD FOR PHYSICIAN-SCIENTISTS, IN HONOR OF JOSÉ BASELGA

The AACR-AstraZeneca Career Development Award for Physician-Scientists, in Honor of José Baselga has been established to honor the life and legacy of Dr. José Baselga, who was a scientific leader and supportive mentor to an entire generation of physician-scientists. The intent of this program is to encourage and support junior physician-scientists to conduct research and bolster the development of innovative targeted therapeutics.

Kipp Weiskopf, MD, PhD
Whitehead Fellow

Whitehead Institute for Biomedical Research
Cambridge, Massachusetts

Unbiased Discovery of Macrophage-Directed Immunotherapies for Cancer

SCIENTIFIC STATEMENT OF RESEARCH
Macrophages are often the predominant infiltrating immune cell in tumors, yet their potential to act as effectors of cancer immunotherapy has been underappreciated. The CD47/SIRPa interaction is a macrophage immune checkpoint, and therapies that block this interaction demonstrate the tremendous potential of macrophages to attack cancer. However, the receptors and signaling pathways that regulate macrophage activation against cancer remain poorly understood relative to other immune cell types. In this study, Dr. Weiskopf takes an unbiased approach to identify novel immune checkpoints that regulate macrophages in the tumor microenvironment. Moreover, he will employ an ambitious, multi-pronged strategy to discover new small molecules and biologics that activate macrophages to attack cancer. Overall, he aims to understand the fundamental biology that underlies macrophage activation and develop many new macrophage-directed immunotherapies that benefit patients with cancer.

BIOGRAPHY
Kipp Weiskopf, MD, PhD is a Valhalla Fellow at Whitehead Institute for Biomedical Research, where he leads a research laboratory focused on macrophage-directed therapies for cancer. He is concurrently appointed as a medical oncology fellow at Dana-Farber Cancer Institute. Dr. Weiskopf previously earned his medical and graduate degrees at Stanford University. As a member of Irving Weissman's laboratory, he characterized the CD47/SIRPa axis as a macrophage immune checkpoint. He is an inventor on over 15 U.S. patents and is a co-founder of ALX Oncology. Dr. Weiskopf previously trained at Brigham and Women's Hospital and is board-certified in Internal Medicine.

ACKNOWLEDGMENT OF SUPPORT
Dr. Baselga was a champion of cancer research and a fierce advocate for cancer patients. It is a tremendous honor to be supported by this award, which memorializes Dr. Baselga's lifetime of contributions to oncology. Drawing inspiration from his example, I strive for our research to be transformative for patients.

AACR-DEBBIE'S DREAM FOUNDATION CAREER DEVELOPMENT AWARD FOR GASTRIC CANCER RESEARCH

The AACR-Debbie's Dream Foundation Career Development Award for Gastric Cancer Research represents a joint effort to encourage and support junior faculty to conduct gastric cancer research and to establish a successful career path in this field.

Moritz Eissmann, PhD
Assistant Professor

La Trobe University
Bundoora, Australia

Identification of therapeutic vulnerabilities that promote clonal fitness and metastatic spread of gastric cancer cells in vivo

SCIENTIFIC STATEMENT OF RESEARCH
When gastric cancer (GC) progresses to metastatic disease, the prognosis drastically declines. 48% and 15% of metastatic GC patients have lesions in the liver and the lung respectively, with a dismal median survival of two months. This is primarily due to the lack of therapies that efficiently eliminate metastases. We have developed the first of its kind GC mouse model that is genetically defined, can be conducted in immune-competent mice, and shows reproducible orthotopic primary tumor growth with synchronous liver and lung metastasis formation. Our forerunner studies demonstrate that Stat3 signaling promotes metastatic potential to these sites. Here, we aim to discover the transcriptional traits of dominant metastatic cancer clones in the Stat3 high versus low tumor microenvironment and reveal novel therapeutic vulnerabilities to more effectively tailor treatments that suppress metastatic spread and associated mortality.

BIOGRAPHY
After receiving his Master of Science degrees in Medical Biotechnology at the Technical University in Berlin, Germany and his Bio-Chemical Engineering at Dongseo University in Busan, Korea. Dr. Eissmann conducted his PhD studies in the field of tumor biology and received his PhD from Goethe University in Frankfurt, Germany in 2012. Dr. Eissmann then trained as a Postdoctoral Research Fellow at the Walter and Eliza Hall Institute in Australia and since 2015 at the Olivia Newton-John Cancer Research Institute (ONJCRI) in Heidelberg, Australia. Since 2021, he has been a Victorian Cancer Agency Fellow and leads his independent research group within the Cancer and Inflammation program of the ONJCRI.

ACKNOWLEDGMENT OF SUPPORT
This prestigious award will fuel my passion to conduct gastric cancer research which aims to improve patient outcomes. Importantly, this award empowers me to pursue a project, which if successful, will bring hope for better therapies for those metastatic gastric cancer patients with the worst prognosis.

AACR-GERTRUDE B. ELION CANCER RESEARCH AWARD

With generous support from GlaxoSmithKline, the AACR Gertrude B. Elion Cancer Research Award represents a joint effort to encourage and support tenure-eligible junior faculty.

Yuxuan 'Phoenix' Miao, PhD
Assistant Professor

The University of Chicago
Chicago, Illinois

Unraveling the Roots of Cancer Immune Resistance

SCIENTIFIC STATEMENT OF RESEARCH
The development of immunotherapies has revolutionized cancer treatments. However, many treated patients often experience tumor relapse, and the underlying basis is still poorly understood. Gaining insights into this process will be vital for advancing clinical outcomes. Recently, in squamous cell carcinomas of skin or head & neck, we revealed that a group of TGFb-responding tumor-initiating stem cells appear to be the root of tumor relapse after adoptive T cell transfer-based immunotherapy treatment. This key finding raised the importance of identifying the critical molecular features of these tumor-initiating stem cells in driving cancer immune resistance. In this project, we designed genetic approaches to identify the essential master regulators orchestrating the stem cell-specific intrinsic and extrinsic immune evasion program that governs head and neck cancer recurrence after immunotherapy. The information derived from this study can potentially reveal new targets for overcoming tumor relapse.

BIOGRAPHY
Dr. Miao obtained his Ph.D. from Duke University, studying the immune responses against bacterial infections. He then completed his postdoctoral training as a Jane Coffin Childs fellow at Rockefeller University, focusing on cancer immunotherapy resistance. In September 2020, Dr. Miao joined the Ben May Department of Cancer Research at the University of Chicago and The UChicago Comprehensive Cancer Center as an assistant professor. His research program aims to dissect the crosstalk between tissue stem cells and immunity, with a particular focus on immune resistance mechanisms specific to tumor-initiating stem cells.

ACKNOWLEDGMENT OF SUPPORT
It is a special honor to receive the 2022 AACR Gertrude B. Elion Cancer Research Award. This award will provide a valuable resource and critical support to establish my research program interrogating stem cell-specific immune resistance and build a solid foundation for my effort to design effective cancer immunotherapy.

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.

Shaheer Khan, DO
Assistant Professor

The Trustees of Columbia University
in the City of New York
New York, New York

A Phase I/II Study of BET and MEK inhibition in Advanced Uveal Melanoma

SCIENTIFIC STATEMENT OF RESEARCH
Uveal melanoma is a rare melanoma subtype associated with poor outcomes in the metastatic setting. Virtually all cases harbor activating mutations of GNAQ, GNA11, PLCB4 or CYSLTR2 which result in activation of the MAP kinase pathway, amongst others. In addition, epigenetic dysregulation is known to play a critical role in disease pathogenesis. Based on preclinical data showing that the combination of MEK inhibition and Bromodomain and Extra-terminal (BET) protein inhibition (an epigenetic regulator) is associated with synergistic anti-tumor activity, Dr. Khan will investigate the safety and efficacy of combined BET and MEK inhibition in a multi-center phase I/II clinical trial in patients with metastatic uveal melanoma. Translational components of this study will assess potential mechanisms of treatment response and resistance using tumor and blood samples from patients.

BIOGRAPHY
Dr. Khan is an Assistant Professor of Medicine at the Columbia University Herbert Irving Comprehensive Cancer Center. He received his medical degree from the New York College of Osteopathic Medicine after which he completed his training in internal medicine at Medstar Georgetown University Hospital and hematology and medical oncology at Columbia University Medical Center. Dr. Khan's research is focused on the development of novel therapies for the treatment of cutaneous malignancies, including cutaneous squamous cell carcinoma and uveal melanoma

ACKNOWLEDGMENT OF SUPPORT
It is a tremendous honor to be the recipient of the 2022 AACR-Ocular Melanoma Foundation Career Development Award, in honor of Robert C. Allen, MD. This award will be critical as I develop my research career and will be an important resource to facilitate the conduct and analysis of this promising clinical trial.

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

The Breast Cancer Research Foundation-AACR Career Development Awards to Promote Diversity and Inclusion represent a focused effort to encourage and support investigators from diverse backgrounds that are underrepresented in cancer research and to foster their career advancement. This grant program also intends to build a more diverse and inclusive future for breast cancer research. Eligibility is limited to members of racial or ethnic groups that have been shown to be traditionally excluded in the cancer-related sciences workforce.

Kim Blenman, PhD, MS
Assistant Professor

Yale University
New Haven, Connecticut

Characterization of pre-existing autoantibodies in breast cancer

SCIENTIFIC STATEMENT OF RESEARCH
Dysregulated immunoglobulin production and preexisting autoantibodies may contribute to autoimmune AEs of immunotherapy (e.g., thyroid disease) and immune-mediated AEs of chemotherapy (e.g., peripheral neuropathy (CIPN)). This proposal aims to identify autoantibodies that are associated with therapy-induced immune-related AEs (irAEs) in patients with breast cancer.

Aim 1. To determine if preexisting serum autoantibodies are associated with irAEs. Serum autoantibody profiling will be performed using HuProt™. Differential antibody: protein complex expression and pathway analysis will be used to assess differences between irAEs and no irAEs patients. Aim 2. To determine if specific preexisting serum autoantibodies protein epitopes are associated with irAEs. HuScan™ serum autoantibody peptide epitope profiling will be performed. The number, distribution, and fold-change of whole proteins and individual peptides will be compared between irAEs and no irAEs patients. This study could uncover biomarkers that can be used to forecast and monitor irAEs before, during, and after therapy to help guide treatments and evaluate survivorship.

BIOGRAPHY
Dr. Kim Blenman is an immunologist and clinical chemist who uses and develops novel software tools to understand the mechanisms responsible for disparities in disease pathogenesis and therapeutic response. She earned a doctorate in immunology, a master's in clinical chemistry, and a bachelor's in chemistry from the University of Florida. Dr. Blenman also has a certificate in Drug Development and Regulatory Sciences from the University of California, San Francisco. She had the privilege of learning and working on drug discovery and clinical development at Procter & Gamble's Pharmaceutical division as a senior scientist and as a global research director for autoimmune diseases, inflammatory bowel disease, and irritable bowel syndrome. She was also a Postdoctoral Fellow at the City of Hope Comprehensive Cancer Center in Duarte, California. Dr. Blenman is currently an Assistant Professor in the Yale School of Medicine Department of Internal Medicine Section of Medical Oncology and the Yale Cancer Center as well as in the Yale School of Engineering and Applied Science Department of Computer Science.

ACKNOWLEDGMENT OF SUPPORT
The Breast Cancer Research Foundation-AACR Career Development Awards to Promote Diversity and Inclusion will be instrumental in helping me be a leader in the field and an advocate for equity in clinical research for all.

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

The Breast Cancer Research Foundation-AACR Career Development Awards to Promote Diversity and Inclusion represent a focused effort to encourage and support investigators from diverse backgrounds that are underrepresented in cancer research and to foster their career advancement. This grant program also intends to build a more diverse and inclusive future for breast cancer research. Eligibility is limited to members of racial or ethnic groups that have been shown to be traditionally excluded in the cancer-related sciences workforce.

Dennis Jones, PhD
Assistant Professor

Trustees of Boston University
Boston, Massachusetts

Improving anti-breast cancer immunity by targeting solid stress

SCIENTIFIC STATEMENT OF RESEARCH
Lymph nodes play a critical role in the expansion of anti-cancer T cells. Yet, they are frequent sites of metastatic spread and often fail to control metastatic outgrowth. Since metastases usually leads to a lower survival rate elimination of metastatic cancer cells is necessary to improve patient outcomes. Prior work by Dr. Jones and colleagues found that compression of blood vessels by breast tumors in lymph nodes is associated with impaired T cell entry into these metastatic tumors. In this project, Dr. Jones and his group will test the hypothesis that relieving this compression will improve T cell entry into nodal metastases. They will use long-term intravital imaging to measure whether decompressing blood vessels enhances T cell entry into metastatic tumors. Further, they aim to combine decompression therapy with immune therapy to test whether this drug combination will enhance the killing ability of T cells that enter lymph node tumors.

BIOGRAPHY
Dr. Jones obtained his PhD in Immunobiology from Yale University, where he studied basic mechanisms of lymphatic vessel expansion during pathological inflammation. He completed his postdoctoral training at Massachusetts General Hospital/Harvard Medical School, where he developed mouse models of lymphatic metastasis and characterized tumor progression in lymph nodes. He is currently an assistant professor at the Boston University School of Medicine in the Department of Pathology and Laboratory Medicine. His lab studies immune suppressive mechanisms within metastatic tumors with the goal of identifying novel targetable proteins for effective therapy of advanced breast cancer.

ACKNOWLEDGMENT OF SUPPORT
I appreciate the Breast Cancer Research Foundation's and the AACR's commitment to supporting underrepresented minority investigators and I am honored to receive the 2022 Career Development Award to Promote Diversity and Inclusion. This support will be instrumental in allowing us to understand and overcome mechanisms of tumor-mediated T cell suppression.

LUSTGARTEN FOUNDATION-AACR PANCREATIC CANCER CAREER DEVELOPMENT AWARD, IN HONOR OF JOHN ROBERT LEWIS

The Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research, in Honor of John Robert Lewis, has been established to honor the life and legacy of Representative Lewis, who worked tirelessly to advance the civil rights of all Americans, even while battling pancreatic cancer. The intent of this program is to support the development and diversity of talent working in pancreatic cancer research. Eligibility is limited to members of racial or ethnic groups that have been shown to be underrepresented in the cancer related sciences workforce.

Edwin R. Manuel, PhD
Assistant Professor

Beckman Research Institute of the City of Hope
Duarte, California

Targeting Macropinocytosis as a Novel Avenue for Pancreatic Cancer Therapy

SCIENTIFIC STATEMENT OF RESEARCH
Macropinocytosis is a process by which copious amounts of extracellular materials are engulfed and utilized for tumor cell biosynthesis in pancreatic cancer (PC). Heparan sulfate proteoglycans (HSPGs) upregulated on the surface of tumor cells serve as key mediators of macropinocytosis. The pro-tumorigenic activities of HSPGs are regulated by enzymatic modification of their heparan sulfate (HS) moieties. While mammalian heparanases promote ECM remodeling, invasion, and metastasis, bacterial heparinase depolymerizes HS through a contrasting mechanism, resulting in the suppression of tumor growth. However, the inability to restrict bacterial heparinase activity to tumor tissue prohibits its use as a therapeutic agent. Using attenuated, tumor-targeting Salmonella typhimurium (ST) vectors, Dr. Manuel and his team have developed the first recombinant ST expressing functional heparinase through a tightly regulated, inducible promoter. The goal of their study is to determine the impact of this novel agent on nutrient scavenging and therapeutic resistance in models of PC.

BIOGRAPHY
Dr. Manuel is an Assistant Professor at the Beckman Research Institute of the City of Hope located in Duarte, California. He earned his bachelor's degree in Microbiology from San Diego State University and his PhD in Virology from Harvard. The overall goal of his research program is to develop microbial-based therapies for the treatment of solid and hematological malignancies, i.e., "Bugs as Drugs". His lab has been primarily focused on engineering recombinant, tumor-colonizing Salmonella to curtail processes contributing to therapeutic resistance in pancreatic cancer, namely desmoplasia and macropinocytosis.

ACKNOWLEDGMENT OF SUPPORT
The Lustgarten Foundation-AACR Pancreatic Cancer Career Development Award, In Honor of John Robert Lewis, will allow me and my team to delve into key aspects of our microbial-based therapy. This is an important endorsement of our work and will ultimately have a significant impact on patients with advanced pancreatic cancer.

LUSTGARTEN FOUNDATION-AACR PANCREATIC CANCER CAREER DEVELOPMENT AWARD, IN HONOR OF RUTH BADER GINSBURG

The Lustgarten Foundation-AACR Career Development Award for Pancreatic Cancer Research, in Honor of Ruth Bader Ginsburg, has been established to honor the life and legacy of Justice Ginsburg, who worked tirelessly to advance gender equality, even while battling pancreatic cancer. The intent of this program is to support the development and diversity of talent working in pancreatic cancer research. This Award represents a joint effort to support the career advancement of a female scientist engaged in pancreatic cancer research relevant to the goals and mission of the Lustgarten Foundation.
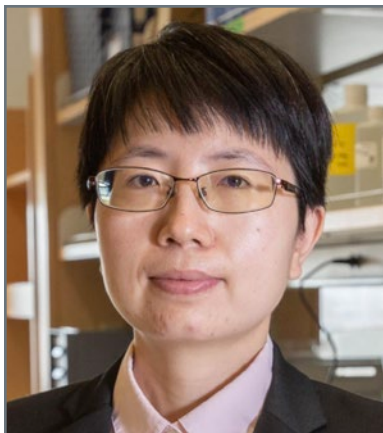
Pingping Hou, PhD
Assistant Professor

Rutgers, The State University
Newark, New Jersey

Anti-KRAS therapy resistance and pancreatic tumor immune microenvironment

SCIENTIFIC STATEMENTS OF RESEARCH
Pancreatic ductal adenocarcinoma (PDAC) is deadly with limited therapeutic options. Oncogenic KRAS (KRAS*) is the key driver of PDAC and maintains tumor growth, making it an ideal therapeutic target. However, both pre-clinical and clinical studies reveal adaptive resistance mechanisms in cancer to the treatment of KRAS* inhibitors (KRASi), an understanding of which is critical for achieving durable disease control. Dr. Hou recently discovered that tumor-associated macrophages (TAMs) drive the KRAS* bypass by nourishing PDAC cells. In the project, Dr. Pingping Hou will explore the TAM subpopulation that promotes KRASi resistance in spontaneous PDAC mouse models and dissect the crosstalk of "pro-resistance" TAMs with tumor cells and cytotoxic T cells by various single-cell assays. The mechanism insight will facilitate the development of novel combinatorial approaches with KRASi to provoke a tumoricidal immune response, further impair tumor growth, and prevent tumor recurrence for PDAC patients.

BIOGRAPHY
Dr. Pingping Hou is a tenure-track Assistant Professor at Rutgers New Jersey Medical School. She obtained her undergraduate degree in molecular biology in 2007 from China Agricultural University. Dr. Hou received her PhD in cell biology from Peking University in 2014 under the supervision of Professor Hongkui Deng. After training in cancer biology as a postdoctoral fellow mentored by Dr. Ronald A. DePinho at the University of Texas MD Anderson Cancer Center from 2014 to 2021, she joined the Center for Cell Signaling and the Department of Microbiology, Biochemistry and Molecular Genetics at Rutgers New Jersey Medical School in 2021.

ACKNOWLEDGMENT OF SUPPORT
With the support from the 2022 Lustgarten Foundation-AACR Pancreatic Cancer Career Development Award, In Honor of Ruth Bader Ginsburg, I am able to employ state-of-the-art single-cell technologies to comprehensively characterize the remodeling of tumor-associated macrophages and delineate the intercellular interactions that regulate pancreatic tumor response to KRAS inhibitors.

2022 INDEPENDENT RESEARCH GRANTS

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 a senior investigator.

Amanda W. Lund, PhD
Associate Professor

New York University School of Medicine
New York, New York

Targeting lymphatic transport to boost immune memory and reduce recurrence

SCIENTIFIC STATEMENT OF RESEARCH
The sentinel lymph node sits at the crossroads of metastasis and immune surveillance. While lymphatic transport primes lymph nodes for immune activation, it also progressively installs multiple mechanisms of immune suppression that enable tumor progression. In this project, Dr. Lund and her group will dissect the relationship between the primary tumor, lymphatic transport, and the emergence and maintenance of protective lymph node resident memory T cell populations. She will aim to 1) define the anatomic origin and developmental trajectory of sentinel lymph node resident T cell populations, and 2) determine the impact of lymph node metastasis on their maintenance and function. Finally, she will explore their clinical association with recurrence in sentinel lymph nodes of stage III melanoma patients. A basic understanding of sentinel lymph node biology, paired with an evaluation of interpatient heterogeneity, is expected to reveal new determinants of patient outcome that may inform clinical care.

BIOGRAPHY
Dr. Lund received her PhD from Rensselaer Polytechnic Institute in Troy, New York, and completed postdoctoral training at the Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland. She is currently an Associate Professor in the Ronald O. Perelman Department of Dermatology at NYU Grossman School of Medicine in New York. Dr. Lund and colleagues established the paradigm that tumor-associated lymphatic vessel remodeling regulates anti-tumor immune surveillance. Her group aims to understand the basic mechanisms that govern lymphatic/immune interactions to identify translational strategies to tune lymphatic transport and reinvigorate anti-tumor immunity.

ACKNOWLEDGMENT OF SUPPORT
The AACR-Bristol Myers Squibb Midcareer Female Investigator Grant will accelerate and expand our efforts to understand how lymphatic transport governs immunity and determines risk for progression in melanoma. I am honored to receive this award and continue to support a diverse team of early career researchers towards their own independence.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grants represent a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. 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.

Wafik El-Deiry, MD, PhD, FACP

Associate Dean for Oncologic Sciences;
Director, Cancer Center

Brown University
Providence, Rhode Island

Integrated Stress Response induction by TTF + ONC201 in cancer treatment

SCIENTIFIC STATEMENT OF RESEARCH

The goal of the AACR-Novocure Award to Dr. Wafik El-Deiry at Brown University's Legorreta Cancer Center is to develop novel therapy combinations that exploit pro-apoptotic pathways due to cell stress responses engaged by imipridones and TTFields. The team will evaluate alterations in signaling involving the integrated stress response, the p53 pathway, the extent of DNA damage and role of DDR defects in tumor cell sensitivity to combination of TTFields and imipridone drugs using cultured tumor cells. Experiments will prioritize and conduct in vivo studies with TTFields plus imipridones against GBM -/+ TMZ/RT and TTFields plus imipridones against various solid tumors. Immune cell infiltration, impact on cancer stem cells, cytokines, RNA-seq and correlates of the ISR will be assessed. Valuable mechanistic insights and combinatorial cancer therapeutics using TTFields and imipridones can be used in innovative clinical research protocols for patients with GBM and other deadly solid tumors.

BIOGRAPHY

Wafik S. El-Deiry, MD, PhD, FACP is an ACS Research Professor, Director, Legorreta Cancer Center, Brown University, Associate Dean, Alpert Medical School, Director, Joint Program in Cancer Biology, Brown/Lifespan, Professor of Pathology/Laboratory Medicine, and Mencoff Family University Professor of Medical Science at Brown. Dr. El-Deiry discovered p21(WAF1) as p53-target and cell cycle inhibitor explaining the mammalian DNA-damage response. He discovered TRAIL receptor DR5 and ONC201/TIC10 as cancer therapeutic. Dr. El-Deiry has >400 publications, H-index=121 and >89,000 citations (Google-Scholar). He treats patients with advanced cancer and focuses on cancer drug resistance and drug discovery/development. El-Deiry founded Oncoceutics (acquired by Chimerix), p53-Therapeutics, and SMURF-Therapeutics.

ACKNOWLEDGMENT OF SUPPORT

The 2022 AACR-Novocure Grant will allow our team of researchers to explore novel combination therapies with TTF that involve therapeutic cell stress pathways for brain and other solid tumors. The award facilitates discovery science, mechanistic insights, and translational directions to evaluate biomarkers that can be incorporated into early-phase clinical trials.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grants represent a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. 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.

Matthew R. Sarkisian, PhD

Associate Professor

University of Florida
Gainesville, Florida

Improving TTFields Efficacy by Altering Ciliogenesis

SCIENTIFIC STATEMENT OF RESEARCH

How glioblastoma cells are targeted by or escape Tumor Treating Fields (TTFields) therapy is unclear. A significant percentage of glioblastoma cells assemble and disassemble a primary cilium, so that the centrioles can be repurposed for mitosis. Primary cilia are microtubule-based organelles often likened to cellular 'antenna'. They can mediate signaling that promote glioblastoma growth and resistance to chemotherapy. Dr. Sarkisian's group is exploring how TTFields affect cilia and vice versa. They have found that glioma cilia appear more sensitive than normal neural cell types to the effects of TTFields and may play a role in tumor cell recurrence when TTFields treatment is turned off. In this AACR-Novocure project, they will use genetic tools and small molecule inhibitors to determine whether (1) altering ciliogenesis before or after TTFields improves TTFields cell killing and prevent tumor cell recurrence, and (2) altering ciliogenesis in patient tumors ex vivo enhances TTFields-induced cytotoxicity.

BIOGRAPHY

Dr. Sarkisian obtained his BS in Biological Sciences at Clemson University. He completed his PhD in Physiology and Neurobiology at the University of Connecticut, Storrs. He did postdoctoral training at Yale University in Neurobiology and was recruited to the University of Florida Department of Neuroscience where he is currently an Associate Professor. He is also a member of the Preston A. Wells Jr. Center for Brain Tumor Therapy and the UF Health Cancer Center. His laboratory is interested in the biology of primary cilia during brain development and cancer.

ACKNOWLEDGMENT OF SUPPORT

I am honored and grateful to receive the 2022 AACR-Novocure Tumor Treating Fields Research Grant. Without this support, our efforts to unravel the underlying cell biology disrupted by TTFields and develop new ways to predict and/or enhance sensitivity to TTFields, would not be possible.

AACR-NOVOCURE TUMOR TREATING FIELDS RESEARCH GRANT

The AACR-Novocure Tumor Treating Fields Research Grants represent a joint effort to promote and support independent investigators who are conducting innovative research focused on Tumor Treating Fields. 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.

Stuart Smith, BM, BCh, PhD
Clinical Associate Professor Neurosurgery

University of Nottingham
Nottingham, United Kingdom

Combining Tumor Treating Fields with Ion Channel Blockade

SCIENTIFIC STATEMENT OF RESEARCH

Glioblastoma (GBM) is a leading cause of cancer-related death in children and adults under 40. Ion channels play a crucial role in the development and progression of brain tumors. The SCNN1 sodium channel family has been previously identified as a potential therapeutic target in combination with Tumor Treating Fields (TTFields).

Biostatistical analysis in GBM using in-house datasets and publicly available datasets will be conducted. Validation of expression levels will be undertaken on banked tumor specimens for all age groups. SCNN channels will be assessed in GBM cell lines, especially low passage patient-derived cells, including effects on membrane potential. siRNA knockdown and pharmacological inhibition will be undertaken in synergy with TTFields. The effects on cell migration will be assessed by a trans-well collagen barrier assay.

This project will give a comprehensive assessment of the SCCN1 channels as therapeutic targets in GBM, with a specific focus on combinatorial therapy with TTFields.

BIOGRAPHY

Stuart Smith is a clinical associate professor of neurosurgery at Nottingham University Hospitals in the UK, with a specialist interest clinically and academically in brain tumors, particularly gliomas. He was awarded his medical degree at the University of Oxford, followed by Neurosurgical training in Oxford, Bristol, and Nottingham. He undertook his PhD in pediatric GBM in Nottingham at the Children's Brain Tumour Research Centre. His current research includes projects examining electrotherapy in intrinsic brain tumors in children and young adults, as well as studies examining surgical drug delivery to brain tumors and targeted surgical sampling to examine glioma heterogeneity.

ACKNOWLEDGMENT OF SUPPORT

This award is hugely important to allow the investigation of promising therapeutic targets we have previously identified as synergistic with TTFields. The ion channels we are focused on are highly druggable targets and this grant will catalyze translation towards clinical evaluation, and we are extremely grateful for this opportunity.

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