# 2022 ANNUAL REPORT









### **SUPPORTERS**































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### **MISSION**

The PhRMA Foundation fosters biopharmaceutical innovation and value-driven health care by investing in the frontiers of research. The Foundation catalyzes the careers of promising researchers through competitive, peer-reviewed grants and fellowships.

### VISION

A healthier world where all people have access to innovative, life-changing medicines.

### **VALUES**



### **INTEGRITY**

We strive to be scientifically independent and evidence-based in our decision-making.



### **INNOVATION**

We invest in cutting-edge research and ideas that will improve patient health.



### **COLLABORATION**

We support collaborative research efforts that are diverse and inclusive.



### MESSAGE FROM THE PRESIDENT AND CHAIR

The PhRMA Foundation holds a unique role in the biopharmaceutical research landscape. For nearly six decades, we have funded investigator-driven academic research that serves as the foundation for industry efforts to develop groundbreaking medicines that improve human health.

Thanks to the generosity of our industry supporters, the PhRMA Foundation is fostering biopharmaceutical innovation and value-driven health care by investing in the frontiers of research. Through a peer-reviewed, competitive process, the Foundation awards grants and fellowships to researchers pursuing science that advances the fields of drug discovery, drug delivery, translational medicine, value assessment, and health outcomes research.

### **CATALYZING CAREERS**

Since our founding in 1965, the PhRMA Foundation has awarded more than \$110 million to 2,700 researchers from diverse backgrounds at more than 300 institutions. In 2022, the Foundation awarded 37 researchers a total of nearly \$2.7 million. For many of the predoctoral, postdoctoral, and early-career researchers the Foundation funds, this is the first financial award they receive in their career. Providing support at these early stages is vital for creating a pipeline of talent that will sustain and grow fields of research important to the biopharmaceutical industry. Many Foundation award recipients go on to start their own research laboratories in academia or transition into careers in industry or government.

### **EXPANDING OUR REACH**

The PhRMA Foundation continues to execute effective and impactful programs, but this year we took our efforts a step further to expand our reach. In 2022, the Foundation hired its first-ever head of communications to amplify our messages and the stories of our researchers. The Foundation is more than just a grant-making body — it is a community dedicated to advancing the frontiers of discovery. Our researchers' work has important implications for drug development and health care policymaking, directly affecting patients' lives. This research deserves attention and these scientists' stories are worth telling. Details on these efforts are available on the Foundation's blog, Twitter, and LinkedIn.

### **LOOKING AHEAD**

The PhRMA Foundation is implementing changes that will strengthen our work and provide additional funding opportunities for researchers. We launched our Value Assessment Initiative in 2017 to address challenges in assessing the value of health care interventions. The Foundation is one of the few nonprofit funders in this space and has been incredibly successful in seeding this young field. However, value assessment overlaps in many ways with health outcomes research, which we have been funding for two decades. For 2023, the Foundation is combining these activities into a joint Value Assessment and Health Outcomes Research (VA-HOR) Program, which will fund predoctoral students, postdoctoral trainees, and early- and mid-career faculty working to define and measure value to ensure health care decisions are guided by the best possible evidence. The Foundation is also unveiling a new funding mechanism in this program to support researchers conducting empirical studies to test value assessment frameworks and methods.

Also in 2023, the PhRMA Foundation will launch a new program focused on improving diversity in clinical trials through digital health technologies (DHTs). With the COVID-19 pandemic spurring even greater use of DHTs in research, the Foundation seeks to fund research that fills our gaps in knowledge of how DHTs work across diverse populations and assess their potential to improve participation and access for patient populations currently underrepresented in clinical trials.

### THANKS TO OUR SUPPORTERS

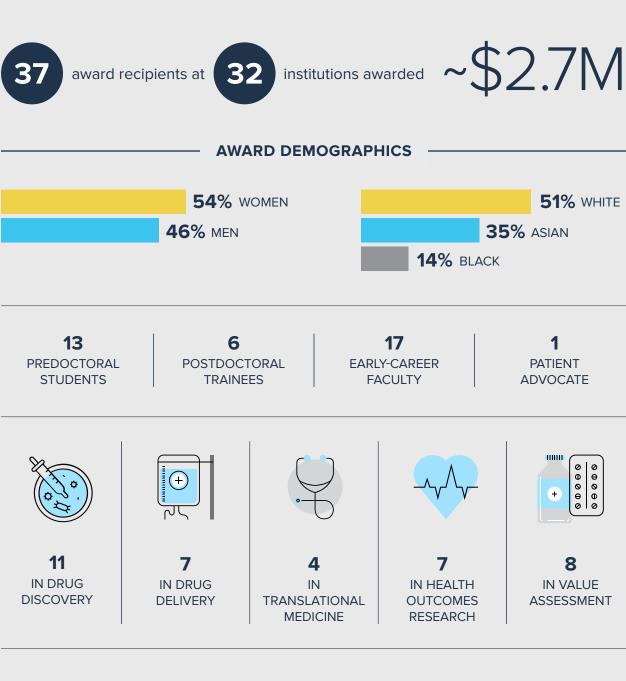
We are deeply grateful to the PhRMA Foundation's supporters — this work would not be possible without them. As the Foundation's work continues to evolve, we look forward to collaborating with the Foundation's Board of Directors, staff, partners, and researchers to create a healthier world where all people have access to innovative, lifechanging medicines.

**Amy M. Miller**, PhD President, PhRMA Foundation

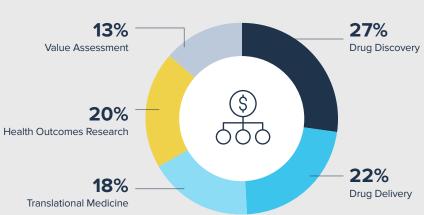
Amy M. Suller

**Andrew Plump**, MD, PhD Chair, PhRMA Foundation









## HIGHLIGHTS FROM THE YEAR



### **Networking with Awardees**

The PhRMA Foundation supports a community of dedicated researchers, and our grant and fellowship recipients value the ability to meet and make connections with fellow awardees. We were excited to be able to return to meeting awardees at in-person conferences this year as COVID-19 restrictions began to lift. The Foundation team attended ISPOR 2022, the annual meeting of the professional society for health economics and outcomes research, and PharmSci 360, the meeting of the American Association of Pharmaceutical Scientists.



Top: Past and present PhRMA Foundation awardees connected at ISPOR 2022. Bottom left: PhRMA Foundation President Dr. Amy M. Miller presents an award to Dr. Asmi Chakraborty of Harvard Medical School. Bottom right: Dr. Vakaramoko Diaby of the University of Florida poses with his award at ISPOR.



### **Honing Professional Skills**

The PhRMA Foundation seeks to provide more than just financial support to our awardees. In 2022, we hosted events aimed at helping researchers improve important career skills such as communicating their research to the public and writing strong funding applications.

### SCIENCE COMMUNICATIONS: HOW TO WRITE A LAY SUMMARY

PhRMA Foundation Head of Communications Emily Ortman trained our 2022 fellowship and grant recipients on how to write a lay summary, a research description that uses clear, plain language for non-experts. Read their research summaries in the "Grants and Fellowships" section of this report.

### TIPS FOR WRITING A WINNING GRANT APPLICATION

In a webinar, former PhRMA Foundation Scientific Advisory Committee member Peter J. Neumann, ScD, director of the Center for the Evaluation of Value and Risk in Health at Tufts Medical Center, shared his insight into writing a successful application for the Foundation's Value Assessment and Health Outcomes Research fellowships and grants.



### **Exploring Career Paths**

Through our awards, the PhRMA Foundation is building a pipeline of talented researchers for academia, industry, and government. To help our awardees explore their career options, the Foundation began a series of webinars highlighting industry opportunities.

#### **COMMUNITY-BASED CLINICAL RESEARCH**

The Foundation held an informational webinar about the Robert A. Winn Diversity in Clinical Trials Award Program, which supports early-stage investigator physicians and medical students of diverse backgrounds interested in becoming community-based clinical trialists. The program is supported by the Bristol Myers Squibb Foundation, Virginia Commonwealth University, Gilead Sciences, and the American Association for Cancer Research.

### ABBVIE'S VISITING SCIENTIST FELLOWSHIP PROGRAM

The Foundation hosted fellows from AbbVie to talk about their experiences working at a global, research-based biopharmaceutical company and share information on how to apply for the one-year program.



### VALUE ASSESSMENT



Value assessment is a multidisciplinary field focused on the evaluation of health care interventions such as pharmaceuticals, medical devices, or medical procedures to accurately define and quantify their value. The PhRMA Foundation Value Assessment Initiative launched in 2017 to fund transformative, multistakeholder-driven solutions to address challenges in assessing the value of medicines and health care services. The overarching goal of the program is to improve patient outcomes and reduce health care spending and inefficiency. The Foundation's Research Awards fund projects that aim to advance value-based care and cost-effectiveness in health care.

### **RESEARCH AWARDS**

## Understanding Differences in Value Assessment Methods for Prostate Cancer



**William Padula,** PhD University of Southern California

Value assessment in the 21st century has evolved from simple cost-effectiveness analyses based on calculations about cost relative to health gains in terms of life expectancy and quality of life. Patients and providers now see value beyond cost and quality of life and consider the importance of additional elements such as hope of a cure, health equity, improved accessibility, and even having multiple options for treatment. Together with my team, I am investigating the differences between cost-effectiveness analyses using traditional approaches and risk-adjusted cost-effectiveness models that include weights for these other value elements. We are applying these advancements in health economics to treatments for prostate cancer to develop new value propositions for this fatal condition that has been traditionally costly to treat. We plan to communicate our findings to the methodological communities that govern health economics (e.g., ISPOR) and to major public and commercial U.S. payers to illustrate value of care for prostate cancer through a more modern lens.

### Modeling Individual Preferences in Diagnostics Utilization



**Eline van den Broek Altenburg,** PhD University of Vermont

In an ideal world, everyone who is eligible for cancer screening would be screened and everyone who needs imaging would have easy access to this diagnostic service. Research has found, however, that some groups have lower utilization of key screening services, including mammography and CT imaging. Health disparities have typically been measured by observed differences between the most advantaged group in a category (income, race, etc.) and disadvantaged groups. Standard analysis of a "representative" group yields average effects and reporting across the entire population. But a subtle yet significant problem is how to model differences in unobserved preferences and knowledge — the things we do not know about the individual patient — when looking at their motivation for not getting recommended health care services. I am developing research methodology to create stepwise value assessment that better incorporates the factors we cannot directly observe, like individual emotions, perceptions, and beliefs. This methodology can subsequently be used to develop incentives and reimbursement models that better incorporate value of health care services to individual patients. We will do this with a pilot project analyzing data regarding preferences for diagnostic imaging services.



The Value Assessment Research Award is a validation of the relevance of my research on human decision-making and choice in health, and how to better model value for individuals. The Foundation award allows me to focus my research on modeling the unobserved — patients' emotions, perceptions, and beliefs.

- ELINE VAN DEN BROEK ALTENBURG

# Utilities for All: An Open-Access Database for Economic Evaluation and Preferences Research



**Zachary Ward,** MPH, PhD Harvard T.H. Chan School of Public Health

Economic evaluation is increasingly used to assess whether a treatment provides good value for the cost. However, the concept of value can be difficult to measure. A common approach is to elicit quality-of-life preferences for a given patient population. Known as "utilities," these numbers represent the preference weights for different health states and provide a way to quantify value. My research aims to develop an open-access registry of utilities to improve the quality and impact of economic evaluations. This project advances an "open science" framework, facilitating and promoting best practices for data sharing, preservation, analysis, and replication. The registry will provide a unified repository of quantitative utility estimates, which can be used to assess quality-of-life outcomes as they relate to broader concepts of value. Also, by providing a comprehensive view of current utilities research, this project can identify areas of future, more equitable health services research, as well as more personalized decision-making for patients.



I am excited for the opportunity provided by this award to develop this project, which advances an 'open science' framework for economic evaluation and preferences research. This will be a useful resource for the research community and help to improve the quality and efficiency of our work.

- ZACHARY WARD



### **Value Assessment Challenge Grants**

This year, the Foundation also awarded five individuals with Challenge Grants for responding to an essay topic posed by the Foundation related to health equity and patient-centered outcomes.



**GEOLANI W. DY, MD**Oregon Health and Science University

Paper Title: "TRANS (Transgender And Non-binary Surgery)
Registry: Building a Patient-Focused Registry for Genital Gender
Affirming Surgery"



**EGBE-ETU ETU, PHD**San Jose State University

Paper Title: "Prediction of Length of Stay in the Emergency Department for COVID-19 Patients: A Machine Learning Approach"



**JOEY MATTINGLY, PHARMD, PHD** University of Utah

Paper Title: "Mapping Domains and Levels of Influence: A Health Disparities Research Framework Adaptation for Cost-Effectiveness Analysis"



ZACHARY D. URDANG, MD, PHD

Thomas Jefferson University

Paper Title: "Electronic Health Record Big-Databases Under-Report American Indian/Alaska Natives (Al/AN) with COVID-19 – Strategies and Solutions to Address Al/AN Data Underrepresentation"



ASHLEY VALENTINE

Sick Cells

Paper Title: "Community-Based Participatory Research (CBPR) Initiative for Sickle Cell Disease"



### HEALTH OUTCOMES RESEARCH



Health outcomes research provides crucial information to doctors, patients, policymakers, and other stakeholders on the effectiveness of health care interventions and the impact of policies on patient outcomes. The PhRMA Foundation's Health Outcomes Research Program funds predoctoral students and early-career researchers working to develop and implement real-world data and tools to perform patient-based assessments, evaluate patient-centered outcomes, and ultimately improve the effectiveness of health care interventions. The Foundation has funded health outcomes research fellowships and grants since 2002.

### **PREDOCTORAL FELLOWSHIPS**

## The Impact of Vertical Integration of Oncologists on Cancer Care Delivery and Patient Outcomes



Xin (Cynthia) Hu Emory University

The share of oncology practices acquired by hospitals more than doubled in the past decade. This practice of entities at different levels of the health care supply chain combing is called vertical integration. There are growing concerns about the impact of vertical integration on cancer care and outcomes, but empirical evidence is limited. My research explores how oncology market structures, such as vertical integration, affect care quality and patient welfare. Using population-based administrative data, I will study the geographic variation in vertical integration of oncologists across the U.S. and investigate how integration between hospitals and oncologists affects cancer care delivery, dissemination of new cancer treatments, patient outcomes, and health care costs. This project will identify areas and patient populations that are disproportionately affected by vertical integration of oncology practices. Findings from this research have important implications for policymakers responsible for regulating health care market structures and defining value-based payment efforts.

## Disease Risk Prediction and Value of Polygenic Risk Scores



**Shangqing (Joyce) Jiang** University of Washington

A key goal of precision medicine is to identify patients at higher disease risk and target them with preventative treatment and screening. Polygenic risk scores (PRS) estimate an individual's genetic risk for a given disease by aggregating the effect of genome-wide common genetic variants associated with the condition. However, before clinical implementation of PRS, we need to improve their predictive accuracy and assess their clinical and economic value. Colorectal cancer is one of the leading causes of cancer death in the United States. My research aims to improve PRS predictive accuracy for colorectal cancer risk using machine-learning methods. I will also quantify the value of PRS in guiding colorectal cancer screening using health economic modeling. My work will help generate a better PRS prediction algorithm for colorectal cancer, which may be of interest for future research and clinical use. I also hope my work will inform policymakers about the value of PRS in improving health outcomes and help payers with reimbursement decisions for PRS.

## Incorporating Equity into Health Care Decision-Making Around New Cancer Treatments



**Sara Khor** University of Washington

New cancer drugs have increased longevity and quality of life of many people, but concerns have been raised that these advances do not benefit everyone equally, leading to inequities. The first part of my research examines the extent to which there is a tradeoff between racial equity, financial wellbeing, and overall health improvement when new cancer drugs are introduced. I will also explore how this tradeoff varies with drug prices. The results will provide evidence to support the inclusion of health and financial equity in cancer drug pricing and coverage policies in the United States. After a new cancer treatment becomes available, there remains the challenge of deciding who should receive the treatment. Clinical prediction algorithms can guide these oftencomplex treatment decisions. The second part of my research seeks to understand whether the explicit consideration of race/ethnicity in these clinical prediction algorithms will reduce racial health disparities. The study results will support the development of clinical prediction algorithms that ensure equitable treatment decisions for all.

## Heart Health for Women With Breast Cancer — How Can We Do Better?



Vanessa Paul Patterson University of Colorado, Denver

Advancements in cancer treatments have dramatically improved the survivability of breast cancer, one of the most common cancers in the world. Unfortunately, while women are increasingly surviving breast cancer, survivors have an increased risk of developing heart disease due to adverse effects of their cancer treatments. Despite our understanding of these cardiovascular risks, use of protective heart medications among breast cancer patients and survivors is low. My research seeks to understand how we can better protect the heart health of women who experience breast cancer by looking at potential barriers to the prescribing of certain heart medications. These barriers include how cardiovascular risk is assessed for prescribing purposes within this population and how care is organized for these medically complex patients. I will also seek to describe the potential health impact of improving prescribing of heart medications for this population. If we can understand ways to improve delivery of cardiovascular care, there is potential to have significant impacts on the health of women who experience breast cancer.

### **RESEARCH STARTER GRANTS**

# Examining Social Determinants of Health Underlying Disparities in Heart Failure Treatment and Outcomes



**Jingchuan (Serena) Guo,** MD, PhD University of Florida

Heart failure (HF) affects more than 6.5 million individuals in the United States. A resurgence in HF mortality in the past decade has particularly affected racial and ethnic minority groups and people experiencing social disadvantages. While new treatments have emerged to reduce HF hospitalizations and mortality, existing data show disparities in use of these novel agents, with individuals from racial-ethnic minority groups and those with lower socioeconomic status receiving suboptimal treatment and care. My research will apply machine-learning approaches to a statewide database of electronic health records and claims data to evaluate the individual and aggregate effects of

different social risk factors on HF treatment and clinical outcomes. This research will also yield an aggregated social risk score that can be used for identifying unmet social needs and providing targeted support in patients with heart failure. These findings will inform the development of interventions and policy programs to address disparities in HF treatment and outcomes, which will improve health equity for millions of Americans living with heart failure.

## Aligning Value and Efficacy in Cancer Drugs



**Meng Li,** ScM, PhD University of Texas MD Anderson Cancer Center

Rebates are discounts paid by drug manufacturers to health insurers, pharmacy benefit managers, and pharmacies after a drug is dispensed. Rebates for brand-name prescription drugs in the U.S. can be nearly half of the list price. Because data on rebates and net prices (the cost after all rebates, discounts, and fees are accounted for) were not available in the public domain until recently, most research and discussions on drug pricing and value have been based on the list prices. My research explores (1) how competition may influence list prices, net prices, and rebates of cancer drugs marketed in the U.S., and (2) whether the list and net prices of cancer drugs correlate with how well the medicines work in extending patient lives. My study seeks to provide important insights on the very complex drug pricing dynamics in the U.S. to inform the design of effective policies to improve competition and align price with value for drugs.



The PhRMA Foundation's Research Starter Grant has been instrumental in launching my academic career. The support has allowed me to accelerate my research on prescription drug rebates, which will help me make significant contributions to our understanding of the drug pricing dynamics in the United States.

- MENG LI

### Under Pressure: Evaluating Strategies for the Treatment of Chronic Hypertension During Pregnancy



**Mollie Wood,** PhD University of North Carolina at Chapel Hill

About 1% of pregnancies in the United States occur in people with a pre-existing diagnosis of hypertension (high blood pressure), making it one of the most common chronic diseases complicating pregnancy. Both hypertension and the medications used to treat it have been linked to worse outcomes for the pregnant person and their infant. These outcomes may include miscarriage, birth defects, low birth weight, and others. There is uncertainty as to the best treatment strategy for pregnant people, particularly those with other comorbidities, with past poor pregnancy outcomes, or whose prepregnancy hypertension was well managed by a medication associated with increased risks to the fetus. My research will use data from electronic medical records to compare the safety and effectiveness of different antihypertensive medications during pregnancy. The highly detailed data include blood pressure measurements, clinical notes, and information on prescription fills, clinical diagnoses, and procedures. The results of this study will help people with hypertension and the clinicians who care for them make informed decisions about how to manage high blood pressure during pregnancy.



The PhRMA Foundation Starter Grant affords me the time and resources to do rigorous research on the treatment of chronic hypertension during pregnancy. The ability to create an electronic medical records database for comparative safety studies in pregnancy has been an incredible boost to my independent research portfolio and lays the groundwork for future efforts in this critical research area.

- MOLLIE WOOD

### TRANSLATIONAL MEDICINE



Translational medicine is a discipline focused on bridging discoveries in experimental and computational research to their application in clinical practice. The PhRMA Foundation's Translational Medicine Program funds postdoctoral fellows and early-career researchers working in collaboration with clinicians to address clinical needs in the diagnosis, treatment, and prevention of disease through both experimental and computational methods. The Foundation has funded translational medicine fellowships and grants since 2013.

### **POSTDOCTORAL FELLOWSHIPS**

# Understanding Mechanisms of Communication Between Cancer and Healthy Brain Cells



**Brian Andersen,** MD, PhD Brigham and Women's Hospital

Glioblastoma (GBM) is the most common and lethal type of cancer that develops in the brain. While other metastasized brain cancers frequently respond to treatments that activate the immune system, immunotherapy does little to slow GBM's growth. Currently, scientists are seeking to understand how the immune system can fight this devastating cancer. Under the microscope, GBM contains a mixture of cancer, immune, and brain cells. Researchers can now analyze gene expression — the cell's instructions — at single-cell resolution. If we can understand gene expression in single cells, we can know what hinders the immune system's fight against GBM. Initial studies show that GBM grows via interactions with surrounding noncancerous cells. My research will investigate single-cell interactions of GBM in astrocytes, a multipurpose brain cell. Astrocytes are capable of powerful immune functions that GBM researchers have largely overlooked but which might be valuable for treating GBM. I will identify interactions in recurrent GBM specimens correlated with tumor recurrence and interrupt these interactions in cell culture as a test of therapeutic value.

### Harnessing Tumor-Neuron Interactions to Identify Treatment Targets



**Andy G. S. Daniel,** PhD University of California, San Francisco

Gliomas are cancerous brain tumors with dismal prognoses despite the best available treatments. Therapeutic development is extremely challenging due to tumor heterogeneity, the blood-brain barrier (a network of cells that protects the brain from harmful substances), and the tumor immune microenvironment (the cells, molecules, and blood vessels that surround tumor cells). To add to this complexity, recent studies have shown that glioma cells can communicate with neurons through direct and indirect connections and that these interactions promote cancer progression and spread. At present, the effects of these interactions on the tumor immune microenvironment are poorly understood. Using primary patient-derived glioma cells, in vitro co-culture models, and mouse models, my research aims to elucidate the mechanisms through which glioma-neuron interactions are influenced by neuroimmune factors. A deeper understanding of these relationships may identify novel treatment targets and support the development of desperately needed immunotherapies for glioma.

### **RESEARCH STARTER GRANTS**

### Building New 3D Models to Study Neuromuscular Disease



**Ritu Raman,** PhD Massachusetts Institute of Technology

Recent advances in biomedical science have enabled the development of living mimics of the tissues in our bodies by patterning cells into 3D architectures. These systems help researchers study complex tissues in a lab setting and can serve as platforms to test new therapies prior to clinical trials. By giving scientists the ability to rapidly test and optimize new ways to combat disease and to understand toxicities, these model systems could play a significant role in bringing safe and effective therapies to patients. My research focuses on developing 3D models of the neuromuscular system, which is powered by skeletal muscle and controlled by nerves. The neuromuscular system generates all voluntary movement in our bodies, and damage or diseases that affect muscle or nerves can severely limit health, mobility, and quality of life. My team anticipates that our platform will be useful

for studying a range of neuromuscular diseases. Specifically, we are designing and testing therapeutic strategies that can help regenerate tissue after nerve injuries, with an emphasis on techniques that can be translated to the clinic to help patients suffering from mobility loss.

### Using Machine Learning to Develop Better Detection and Treatment Methods for Rheumatoid Arthritis-Associated Lung Disease



**Fan Zhang,** PhD University of Colorado, Denver

Although interstitial lung disease (ILD), a common manifestation of rheumatoid arthritis (RA), is detected in up to 60% of patients with RA, it is a complex condition to diagnose. By the time ILD is visible in a CT scan, it is often in an advanced state and difficult to treat. My research seeks to identify molecular phenotypes and biomarkers that could serve as diagnostic markers and potential treatment targets. Using machine learning — computer systems that use algorithms and statistical models to analyze and draw inferences from patterns in data — I plan to analyze millions of single-cell profiles from the joint and lung tissue of patients with RA and ILD to see whether there are common connections that could help predict development of ILD. Ultimately, completing this work will provide needed multi-disease and cross-tissue integrative machine-learning strategies that delineate promising targets for the joint-lung axis, which can be generalized to study the many manifestations of RA.



The PhRMA Foundation Research Starter Grant has tremendously boosted the establishment of my independent research programs in translational medicine. This award has encouraged me to strive for excellence in developing powerful computational tools for precision solutions to inflammatory conditions.

- FAN ZHANG



### DRUG DISCOVERY



Modern drug therapies rely on a wide range of cutting-edge technologies and a variety of novel therapeutic approaches. The PhRMA Foundation's Drug Discovery Program funds predoctoral students, postdoctoral trainees, and early-career researchers exploring the innovative application and integration of multiple scientific disciplines to create efficacious, safe, and differentiated treatment options for patients. The Foundation has funded fellowships and grants in drug discovery (formerly known as pharmacology and toxicology) since 1978.

### PREDOCTORAL FELLOWSHIPS

## Testing a New Approach to Curing Type 1 Diabetes



Joshua Centore Case Western Reserve University School of Medicine

Type 1 diabetes is an incurable autoimmune disease in which a patient's immune cells destroy their body's own insulin-producing pancreatic cells, resulting in high blood sugar (hyperglycemia). My team discovered that hyperglycemia increases the level of a sugar attached to a particular protein involved in controlling immune cell function. When our protein of interest is aberrantly modified in hyperglycemia, healthy levels of selected genes are pushed out of balance and immune cells become increasingly destructive. We believe that blocking the function of only the modified form of our protein of interest will restore the balance of these genes disrupted by hyperglycemia and re-establish proper immune cell function. Hence, we aim to develop a drug that specifically binds only to the sugar-modified protein to block its function. This research will study how this approach works to restore immune cell functions in diabetic mouse models and in patient cells.

### Developing a Platform for the Systematic Discovery of Plant-Derived Compounds for Drug Development



**Desnor Nicole Chigumba** University of Michigan, Ann Arbor

Plants are an important source of medicines for a broad range of diseases. Traditionally, plant-derived medicines have been discovered through a process known as bioactivity-guided fractionation, which screens for bioactive chemicals in natural sources. However, this approach has several limitations including the potential need for large amounts of source material and largely nonspecific chemical discovery. My research focus is on building a platform to enable the systematic discovery of a specific class of plant-derived compounds known as cyclic peptides. Plant cyclic peptides have gained increasing attention due to their diverse functions including anticancer, antibacterial, and antiviral properties. My research uses a combination of plant genome mining and mass spectrometry analysis of plant extracts to discover new cyclic peptides. Subsequently, I test these peptides against human disease models to characterize their mechanism of action. This approach overcomes the bottlenecks of bioactivity-guided fractionation that have inhibited plant peptide discovery for drug development.



The PhRMA Foundation fellowship has enabled me to advance my research thesis and network with talented researchers. As an international student, there are very few fellowships I am eligible for. Being selected as an awardee is an incredible honor.

- DESNOR NICOLE CHIGUMBA

### Determining the Impacts of Age on Genetic Instability



**Alexandra D'Amico** University of Texas at Austin

Aging is one of the most important risk factors for cancer development, with over half of new cancer cases occurring in individuals 65 years or older. With the aging population increasing, it is imperative that we better understand the relationship between aging and cancer development. A hallmark of both aging and cancer is genetic instability, a term for events that cause mutations or changes to our DNA and the resulting biological processes. Alternative structures in our DNA can cause genetic instability and are commonly associated with cancers such as leukemia and lymphomas. Using animal models, my research focuses on understanding how aging affects the genetic instability caused by one of these alternative DNA structures, H-DNA. Additionally, I will investigate how aging can influence the DNA repair processes responsible for maintaining genome integrity. The results from this study will provide insight into how aging impacts genetic instability and contributes to increased cancer risk, aiding in the development of novel therapeutic strategies for cancer treatment.

### Leveraging Synthetic DNA to Address Immune Enzymes Gone Awry



Adam Hedger University of Massachusetts Medical School

The APOBEC3 family of enzymes form part of our immune system and help protect us from DNA-based viruses by mutating their genetic code. However, these same enzymes can sometimes "misbehave" and lead to drug resistance, such as in HIV patients. They can also begin to mutate our own DNA, leading to cancers including lung, cervical, bladder, and head and neck cancer. Currently, no drugs exist for inactivating APOBEC3 enzymes gone awry, despite attempts using traditional inhibitor design methods. My research focuses on developing APOBEC3 inhibitors using a new approach. I plan to make short pieces of synthetic DNA, termed oligonucleotides, that mimic the preferred DNA targets of APOBEC3 enzymes. These oligonucleotide inhibitors will be specifically designed and tailored to each APOBEC3 enzyme. Ultimately, this work will allow us to better study and understand these enzymes, and hopefully help to design a new class of drugs for the clinic.

### Testing a New Approach for Regulating Lipid Metabolism, a Driver of Prostate Cancer



**Dallin Lowder**Baylor College of Medicine

Prostate cancer is the most common and second most lethal cancer in American men. Multiple studies show men with more aggressive prostate cancer have increased dysregulation of lipid metabolism, which plays an essential role in tumor development and progression. Yet there are currently no FDA-approved medicines targeting dysregulated lipid metabolism in men with prostate cancer. Sterol regulatory element binding proteins (SREBPs) are a driver of lipid metabolism in prostate cancer. I propose that we can treat aggressive prostate cancer by shutting down SREBPs. My project will increase our understanding of how genetic and pharmacologic targeting of SREBPs affects lipid metabolism and prostate cancer development. My research will characterize the effects of our novel SREBP inhibitor using cutting-edge cell models and mouse models of prostate cancer. These preclinical studies of our SREBP inhibitor pave the way for future clinical trials and ultimately a first-in-class lipid metabolism inhibitor that can improve outcomes for patients with lethal prostate cancer.

### Testing a New Therapeutic Approach for Treating Stimulant Dependence



**Ryan Murphy** University of Texas Medical Branch at Galveston

Misuse and abuse of stimulants such as cocaine and amphetamines is a pervasive health concern affecting over 10 million Americans. Chronic stimulant use disrupts normal circuitry in the brain, impairing daily life and commonly leading to physical and psychological dependence. Unfortunately, there are no existing drug therapies to treat stimulant dependence or abuse. My project features a new potential drug target, a receptor protein called GPR52, which acts oppositely to stimulants in the brain circuitry that controls the sensations of reward and motivation. My lab recently discovered a unique molecule that activates GPR52 and may reverse stimulant-induced brain dysfunctions. Using a combination of techniques in human cell lines and computational models, I will profile the activity of newly designed variations of this molecule on several GPR52 cellular signaling pathways. With

these data, I will select the most effective and drug-like GPR52 activator, which will then be tested for reducing cocaine-taking and cocaine-seeking behaviors in rodent models. My goal is to advance our basic understanding of the GPR52 receptor protein and validate GPR52 as a therapeutic target for treating stimulant abuse and dependence.

### **POSTDOCTORAL FELLOWSHIPS**

## Treating COVID-19 With a Therapeutic Approach From Cancer Research



**Feng Gao,** PhD University of Arizona

By the end of 2022, COVID-19 had infected over 650 million people and led to nearly 6.7 million deaths worldwide. There remains an urgent need for new, effective therapeutics to treat the disease as it mutates. My research looks at the viability of a therapeutic approach pioneered in cancer for treating COVID-19. Proteolysis-targeting chimeras (PROTACs) are small molecules that can target and degrade mutant proteins linked to diseases, helping to overcome mutation-caused drug resistance and promote an adaptive immune response. My research seeks to discover novel PROTACs that can target an important enzyme in the coronavirus replication cycle for the treatment of COVID-19. My study evaluates the antiviral activity of PROTACs on cellular and animal models and explores the capability of PROTACs to induce the human immune response. If successful, this study will not only lead to the discovery of novel PROTACs to combat COVID-19, but may also provide insight into the detailed mechanisms of PROTACs in the development of an immune response, which can be useful in other therapeutic areas.



The PhRMA Foundation Postdoctoral Fellowship has provided me a great opportunity to pursue a branch of my research aimed at COVID-19. This award will have a fundamental impact on my academic career and help me develop the experience needed to be an independent researcher.

- FENG GAO

### Developing a New Type of Gene Therapy With Broad Application Potential



**Michael Mohsen,** PhD Yale University

Gene therapy aims to treat or prevent disease by fixing the underlying genetic problem. My research aims to develop a new type of gene therapy that could be implemented to treat a broad range of diseases, including cancers and genetic disorders. First, I will evaluate small-molecule drugs and drug-like compounds as candidates for this strategy by considering their safety in humans and bioavailability, or the extent to which they enter circulation and reach their target destination in the body. Next, I will generate novel receptors made of RNA (molecules essential in regulating genes) that selectively recognize the target compounds. These receptors will then be employed in the construction of "designer riboswitches," RNA sensors that determine which genes to turn "on" and "off" in human cells via administration of a drug-like compound. Designer riboswitches represent a new modality in gene therapy that could be applied widely and with great therapeutic outlook.

### Searching for New Treatments for Chemotherapy-Induced Peripheral Neuropathy



**Veselina Petrova,** PhD Harvard Medical School

Cancer patients worldwide rely daily on chemotherapy as a curative treatment. However, many patients undergoing chemotherapy suffer from chemotherapy-induced peripheral neuropathy (CIPN), a condition marked by numbness, burning sensations, and chronic pain. CIPN arises from the toxicity of anticancer agents to peripheral nerves. In a subset of patients, the onset of severe symptoms results in premature termination of their anticancer treatment, worsening their outcomes. My research seeks to discover new compounds or repurpose existing therapeutics for the treatment of CIPN without compromising chemotherapy's effect on cancer. To do this, I have developed a human-derived nerve cell model, which I will use as a platform to screen hundreds of new or FDA-approved compounds for their neuroprotective properties against chemotherapy. In parallel, our team will assess the effects of the most promising compounds in cancer cells. Our research could impact the quality of life for patients currently undergoing chemotherapy and those living with the long-term consequences of chemotherapy.

### **RESEARCH STARTER GRANTS**

# Unlocking the Potential of Targeted Protein Degradation in Neurological Disorders



**Fleur Ferguson,** PhD University of California, San Diego

Targeted protein degradation (TPD) is an exciting new therapeutic modality that has expanded the druggable target space. Targeted protein degraders hijack cells' natural "trash disposal" mechanisms for protein turnover and redirect cells to dispose of disease-causing proteins. Recently, numerous new anticancer drugs that act via a targeted protein degradation mechanism have entered clinical trials. However, TPD has not been applied broadly to targets in neuro-oncology because it is challenging to develop TPD drugs that can cross the blood-brain barrier (a network of cells meant to protect the brain from harmful substances). My research will investigate generalizable approaches to improving TPD pharmacokinetics (how the drugs move through the body) to enable application of this transformative technology to neurological disorders.

### Searching for Novel Antibiotics Capable of Inhibiting Cancer Stem Cells



**Jill Shirokawa,** PhD University of Cincinnati, Clermont College

Many cancer survivors fear cancer recurrence. Currently, cancer stem cells (CSCs) are thought to be the main cause of cancer recurrence and metastasis. CSCs perpetuate tumors because they are resistant to conventional therapies and initiate new tumor growth. Conquering CSCs will require the development of a new generation of anticancer drugs. Recent evidence shows that some classes of antibiotics are effective CSC inhibitors. My research team is developing a multidisciplinary screening approach aimed at discovering novel antibiotics capable of inhibiting CSCs. This project coordinates ongoing research performed by undergraduate students isolating soil microbes that produce antibiotics. Antibiotic extracts obtained from soil microbes will be housed and delivered by nanocarriers to test their ability to inhibit CSCs.



# **DRUG DELIVERY**



New medicines are increasingly complex and achieving successful delivery of these drugs to their targets in the human body requires implementing innovative technologies and formulation approaches. The PhRMA Foundation's Drug Delivery Program funds predoctoral students, postdoctoral trainees, and early-career researchers working to optimize drug formulation and delivery modalities to enable more favorable transport of drugs. The Foundation has funded fellowships and grants in drug delivery (formerly known as pharmaceutics) since 1972.

#### **PREDOCTORAL FELLOWSHIPS**

# Development of a Novel Nanoparticle Cocktail for HER2+ Breast Cancer Treatment



**Victor Ejigah, MS** Howard University

Cancers are generally difficult to treat, but the treatment of HER2+ breast cancer is particularly challenging. This cancer type grows and spreads quickly to other parts of the body, including the brain. Treatment requires a cocktail of medications; however, these medicines can cause serious side effects on healthy tissues. My research is focused on designing a medication delivery system that carries a combination of three drugs to the cancer site. Two of the three drugs will be embedded in nanoparticles to prevent contact with healthy tissues, thereby improving the medicine's safety profile. The third drug (a monoclonal antibody) will be used to "decorate" the surface of the nanoparticles. The expected outcome of this delivery system is to improve the efficacy, safety, and compliance in HER2+ breast cancer treatment.

## Bacteria-Inspired Drug Delivery for the Lungs



**Christopher Ruben** University of lowa

Lung infections are one of the leading causes of death worldwide. Treating lung infections can be difficult because the body's natural defenses can remove drugs from the body before they can have their intended effect. Bacteria and viruses have evolved to overcome the human immune system by limiting interactions with protein-rich fluids, like mucus, and hijacking cell systems. Our research focuses on designing bacteria-mimicking polymers — chemical compounds of molecules bonded together in long, repeating chains — that can avoid the body's defenses and deliver drugs to infected areas. We will explore and quantify the interactions between the polymers and bodily fluids such as mucus and lung fluid. We will also investigate the interactions between the polymers and lung cells to determine what cellular machinery the polymers are using and how it might be harmful. Additionally, we will probe the interactions between the polymers and cellular systems using computer simulations to continually alter and improve our polymer designs. Using biology as the inspiration for my project will speed up development time, and the results will help improve the delivery of drugs to the lungs.

# Leveraging Nanoparticle Therapy to Treat Sepsis and Immune Dysregulation



**Nhu Truong** University of Maryland, Baltimore

Sepsis is a life-threatening condition where the immune system overreacts to an infection. It is most often seen along with pneumonia or urinary infections. The body reacts by activating an inflammatory response where immune cells produce signaling molecules that combat the infection. Inflammation is a natural defense mechanism, but in sepsis, this response is extreme and can result in organ damage and death. There are currently no drugs that improve the mortality rate for patients with sepsis. Nanoparticles made with poly(lactic acid) polymers, which are anti-inflammatory compounds that can be naturally absorbed, offer the potential to help deliver treatments for sepsis. Anti-inflammatory drugs like histone deacetylase inhibitors (HDACis) can reduce the levels

of inflammatory signaling molecules. I plan to insert HDACis into nanoparticles that will carry the drugs to specific immune cells to reduce overactive immune responses in sepsis patients. I aim to conduct experiments using immune cells and mice to study the effect of different nanoparticle designs and drug selectivity. Ultimately, I hope to develop a breakthrough therapeutic that will benefit patients with sepsis.

#### **POSTDOCTORAL FELLOWSHIP**

# Optimizing Chemical Designs for Effective Delivery of Cancer Immunotherapies



**Blaise Kimmel,** PhD Vanderbilt University

Traditional treatments for cancer patients often have damaging effects to patient health and outcomes. To combat this challenge, a new class of therapies — termed immunotherapies — offers selective targeting of cancerous tissue. However, more than 25% of cancer patients have tumors that evade the immune system, making it challenging for this treatment platform to identify the tumor and limiting universalization of this therapy. An area of opportunity exists to build a therapy that enables immune cells to recognize hidden tumors. My research focuses on the development of a cancer immunotherapy platform that trains immune cells to recognize and destroy cancer cells, without damaging healthy tissue. This is achieved by integrating elements from engineering design into the biological space to build nanocarriers that can selectively activate within a tumor, recruiting immune cells to the tumor site. This project will explore how to improve outcomes for patients by minimizing the dose required, optimizing the amount of time that the immunotherapy remains in the body, and teaching immune cells to regain surveillance of cancerous cells before metastasis may occur.

#### **RESEARCH STARTER GRANTS**

# Improving Our Understanding of Drug Absorption with Colloid Drug Particles



**Na Li,** PhD University of Connecticut

Most oral drugs and drug candidates suffer from poor water solubility. Drugs must be soluble to permeate the intestinal wall and get absorbed into the body. Colloid drug particles (nanosized drug-containing particles) can promote absorption and therefore offer an attractive formulation strategy to enhance drugs' oral bioavailability, or the extent and rate at which drugs enter circulation and reach their target destination in the body. However, the mechanisms and extent of enhanced absorption of colloid-containing formulations remain poorly understood. The goal of this project is to better understand factors affecting the permeation and absorption of colloid formulations. First, we will investigate the impact of drug and colloidal properties on passive permeation in vitro (outside a living organism). Next, we will use rats as an animal model to examine the absorption of model formulations in vivo (in a living organism) and establish in vitro-in vivo relationships. Finally, we will explore materials to envelop the particles to facilitate active transport of drugs and promote permeability. Results from this project are expected to lead to improved bioavailability prediction and design of colloid-containing formulations, and ultimately help improve drug absorption and patient health outcomes.



I am very grateful to receive the PhRMA Foundation grant, which allowed me to dive deep into the fundamental science behind the phenomenon of enhanced absorption by drug particles. The work I have done with this grant has already resulted in several conference abstracts, a research manuscript in preparation, and a graduate student award.

- NA LI

# A New Nanotherapeutic Platform for Improving Response Rates to Immune Checkpoint Blockade Therapy in Colorectal Cancer



**Jianqin Lu,** PhD University of Arizona

Immune checkpoints (IC) serve as a "brake" on immune systems to prevent immune responses from being too strong and thus detrimental to healthy cells. However, in tumors, blocking ICs unleashes antitumor immunity that can help eliminate cancer cells. While IC blockade (ICB) approaches have worked well for diverse cancers, response rates in colorectal cancer are only around 4%. Potent chemodrug Camptothecin (CPT) can enhance the effects of ICB therapy, but the drug's poor solubility, short half-life, and systemic toxicities impede its clinical potential. I developed an innovative delivery platform by modifying CPT to form a nanotherapeutic that can address the drawbacks associated with CPT and fortify the responses of colorectal cancer tumors to ICB to prevent tumor recurrence. This project seeks to improve CPT nanotherapeutic systems via optimally codelivering an indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor that overcomes tumor immune suppression for synergistic combination immunochemotherapy, which can further boost the clinical efficacy of ICB against colorectal cancer.

# Hitching a Ride for Effective Drug Delivery



**Eden Tanner,** PhD University of Mississippi

Can you imagine if only 1% of your text messages got sent to the right person? Almost all nanoparticles used for drug delivery, especially those used for treating cancer, do not reach their intended target. In our lab, we use ionic liquids — essentially salts that are liquid at room temperature — like a GPS to make sure our nanoparticle drug compounds reach their intended targets within the body. The ionic liquids are selectively attracted to different kinds of blood components like red blood cells, white blood cells, and platelets. Because of this natural attraction, the nanoparticles can hitch a ride on the blood cells, letting the cells do all the hard work and helping more of the nanoparticles reach their targets. For example, with this method we can deliver about half of the nanoparticles we inject into the brain. This new drug delivery approach could revolutionize medicine by allowing us to effectively and selectively deliver drugs to treat brain cancer, Alzheimer's disease, depression, and many other diseases.

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