Commonwealth Health Research Board
P.O. Box 1971, 101 N. 14th Street, 2nd Floor, Richmond, Virginia 23218-1971
804.371.7799 Telephone 804.692.0222 Fax
www.chrb.org

PRESS RELEASE Dated July 2023

From the Commonwealth Health Research Board

The Virginia Commonwealth Health Research Board (CHRB) has recently awarded **$1,541,750** in grants to medical and health researchers in Virginia. Of this amount, **$741,750** represents grants to eight medical and health researchers for new 2023 Grant Awards and **$800,000** represents continued second-year funding for eight grant awards initially approved in July 2022. Researchers may receive up to $100,000 in first year funding, with up to $100,000 in second-year funding contingent upon compliance with CHRB reporting requirements and satisfactory progress during the initial year of funding.

Investigators approved for funding in this round are affiliated with Eastern Virginia Medical School, George Mason University, Old Dominion University Research Foundation, The College of William and Mary, the University of Virginia, Virginia Commonwealth University, and Virginia Tech. Institutional matching funds supplement the amount awarded by the CHRB. Entities eligible for CHRB Grant Funding include state-supported Virginia institutions of higher education, agencies of the Commonwealth of Virginia, and nonprofit organizations located in the Commonwealth of Virginia and exempt from income taxation pursuant to §501 c (3) of the Internal Revenue Code.

The Commonwealth Health Research Board (CHRB) was created by Virginia Code §32.1-162.23 to provide financial support, in the form of grants, donations, or other assistance, for research efforts that have the potential of maximizing human health benefits for the citizens of the Commonwealth. Research efforts eligible for support by the Board include traditional medical and biomedical research relating to the causes and cures of diseases as well as research related to health services and the delivery of health care. Since its inception in 1999, the CHRB has funded **291** research grants totaling approximately **$25.2 million**.

The CHRB encourages collaborative research efforts among two or more institutions or organizations, gives priority to those research efforts where Board support can be leveraged to foster contributions from federal agencies or other entities, and supports both new research efforts and the expansion or continuation of existing research efforts. CHRB grant recipients --- for grant awards life-to-date --- have leveraged over **$38.2 million** in additional private and federal grant funds to further their research studies.

2023 Grant Awards: $741,750

Principal Investigator: Swadesh Das, Ph.D.	**Virginia Commonwealth University**	
Grant Title: ***Applications of Deep Learning to Predict Anti-Prostate Cancer Drug Synergy***		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Clinically localized prostate cancer (PC) when diagnosed early can be effectively treated, whereas advanced PC is resistant to current therapies. However, responses to standards of care are not always durable, and most patients eventually progress to a hormone-refractory stage, which emphasizes the mandate to develop innovative, more efficacious treatments. Drug combinations are a mainstay of modern cancer therapy, potentially reducing side effects associated with high doses of a single drug, presenting opportunities for more precise disease control. Our proposal embodies screening data from 1971 FDA-approved drugs, with documented biological activities, which are merged with a multidisciplinary machine learning process to predict drug-synergisms leading to the development of novel approaches to treat men with lethal PC. Beyond its primary predictions in identifying drugs that synergize with IL-24 and its modified enhanced version IL-24S, our approach will also provide potential new drugs that can be repurposed to treat PC.

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Principal Investigator: Diane Duffy, Ph.D.	Eastern Virginia Medical School	
Grant Title: *PCO or No? Healthy Androgens and Ovulation*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$65,622	**$56,137**	**$121,759**

Project Summary: Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder. Over 300,000 Virginia women live with negative health impacts of PCOS, including type 2 diabetes and failure to ovulate (infertility). Elevated androgens are implicated in PCOS, but no one understands how androgens affect ovulation. Our pilot data show that 1) androgens are needed to produce oocytes capable of fertilization, and 2) the "classical" androgen receptor (AR) and a novel androgen receptor (SLC39A9) are present in cells of primate ovulatory follicles. We hypothesize that androgens act through AR, SLC39A9, or both to promote follicle maturation and healthy oocyte release. In this CHRB-funded project, we will use single-cell RNA-sequencing to identify actions of androgens via AR and SLC39A9 in the ovulatory follicle. These studies, leveraged by pilot studies funded by EVMS and others, will likely identify one or both receptors as druggable targets to improve fertility for women, especially PCOS women.

Principal Investigator: Robert Hinkle, Ph.D.	The College of William and Mary	
Grant Title: *Synthesis and Biological Assessment of a Polyyne Library via Glaser-Hay Reactions*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$76,900	**$75,400**	**$152,300**

Project Summary: The polyyne (multiple C≡C bonds) core of linear, electron-rich, highly conjugated alkynes has been demonstrated to be selectively potent in a wide range of biological systems; however, its true potential has yet to be realized due to challenges with their synthetic preparation. As a result, the polyyne scaffold represents a prime opportunity for the fusion of organic synthesis and biochemical application. This collaborative, symbiotic approach integrates the expertise of the co-PIs to facilitate rapid preparation of diverse, targeted, polyynes for systematic biological screening to identify how structural alterations impact biological potential and molecular stability. Additionally, the rapid and efficient nature of the project is optimal for utilization with undergraduate researchers as a training platform. Ultimately, this research aims to develop novel, simple polyynes that have been thoughtfully designed to maximize their potential biological activity and exploit the unexplored potential of the polyyne core.

Principal Investigator: Andrew Lowell, Ph.D.	Virginia Polytechnic Institute & State University	
Grant Title: *Pioneering new routes for antibiotic development: Using computational modeling and medicinal chemistry to reconfigure cytotoxins as selective antibiotics*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Our work develops treatments for antimicrobial resistant (AMR) pathogens by creating new antibiotics from existing, potent drugs. To achieve this goal, we use a combination of cutting-edge molecular modeling and medicinal chemistry techniques to convert broadly cytotoxic agents into bacteria-specific antibiotics. Comparisons of general cytotoxicity to antibacterial activity were used previously to identify antibiotic candidates, but no attempts were made using medicinal chemistry to perturb this continuum. Aiding in the development of this novel area is our innovative application of large-scale biochemical modeling to the ribosome, providing atom-level binding and interaction details not previously achievable for this target. Our work will result in new classes of potent antibiotics and first-in-field software applications for the analysis of large organelles, both being commercialize for ribosome drug targeting and computational analysis of other complex biological systems. Comprehensively, this work will mitigate the growing impact of AMR infections in the Commonwealth and nationwide.

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Principal Investigator: Michael McVoy, Ph.D.	**Virginia Commonwealth University**	
Grant Title: *Substitution-inert charged coordination complexes: a novel class of broad spectrum antivirals*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: The majority of pathogenic viruses initiate infection by binding to cell surface glycosaminoglycans (GAGs). Inhibitors that disrupt virion-GAG interactions are therefore anticipated to have broad spectrum antiviral activity. This proposal seeks to develop a novel class of broad-spectrum antivirals based on substitution-inert charged coordination complexes (CCCs) that target GAGs to inhibit viral attachment and entry. The proposed studies, focused on SARS-CoV-2, are designed to establish proof-of-concept that CCCs can serve as bona fide antivirals worthy of further development. Two Specific Aims will (1) use in vitro cell culture models to identify CCCs with minimal toxicity and maximal antiviral activity against SARS-CoV-2; and (2) use in vivo (mouse) models to define toxicity, pharmacokinetics, and antiviral therapeutic efficacy of lead CCCs for treatment of SARSCoV-2 infection. Completion of these studies will establish CCCs as a novel class of antivirals and will leverage support for future preclinical and clinical development of lead candidates.

Principal Investigator: Peter Pidcoe, PT, DPT, Ph.D.	**Virginia Commonwealth University**	
Grant Title: *iTREAT – Improved Treatment using Advanced Technologies*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$99,228	**$99,638**	**$198,866**

Project Summary: The purpose of this proposal is to implement a non-intrusive, easily deployed, scalable system that uses wireless sensing to produce an accurate measure of therapeutic rehabilitation dose for patients who have suffered a Cerebrovascular Accident (CVA or stroke). Since structured intensity plays a key role in recovery, the accurate assessment of rehabilitation dose is needed to infer its relationship to outcome and drive future practice patterns. This system will be deployed in three Richmond clinical sites to assess efficacy and validity.

Principal Investigator: Michael Schulz, Ph.D.	**Virginia Polytechnic Institute & State University**	
Grant Title: *Developing Enhanced Sealants for Neurosurgery*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Dural tears are one of the most challenging complications during neurosurgery, resulting in cerebral spinal fluid leakage and increased risk of infections and complications. To mitigate these issues, numerous dural sealants have been developed, but their efficacy is limited. Consequently, a highly effective dural sealant remains an unmet medical need. Partnering with practicing neurosurgeons, the goal of this work is to design and synthesize improved materials for sealing dural tears. By tuning the molecular structure of polyester/polyurethane adhesives, we will produce materials that balance resistance to cerebral spinal fluid leakage with strong adhesion to dura, while maintaining ease of use, biocompatibility, and biodegradability. Candidate materials will be evaluated to determine water uptake (swelling), tensile strength, modulus, curing kinetics, and degradability, as well as their adhesive properties (adhesion strength and mode of failure) and biocompatibility. Ultimately, this project will produce enhanced surgical sealants for neurosurgery applications.

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Principal Investigator: Zhaomin Yang, Ph.D.		Virginia Polytechnic Institute & State University
Grant Title: *Antivirulence--new weapon against old foe: targeting type IV pilus of antibiotic resistant bacteria*		
FY 2023/2024	**Planned FY 2024/2025**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Antivirulence is a promising new strategy for fighting the global antibiotic resistance pandemic. Bacterial pathogens have armors and weapons that allow them to defeat our immune system and do harm. Antivirulence is to strip them of their menacing arsenals. Once disarmed, they are no more than the normal human microflora that generally provides health benefits. Unlike antibiotics, antivirulence measures do not apply a life-death selection on bacteria. As such, their resistance is not expected to develop and spread, making antivirulence an attractive approach for combating antibiotic resistance. In this proposal, we focus on developing small molecules targeting the bacterial type IV pilus, one of the most potent weapons of bacterial pathogens. The success of our work will lead to novel therapeutics that will impact not only the citizens of Virginia, but also human health worldwide.

Continued Second-Year Funding for 2022 Grant Awards: $800,000

Principal Investigator: Michael Brown, Ph.D.		University of Virginia
Grant Title: *Risky Variants in Human Cardiovascular Disease*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Cardiovascular disease (CVD) is the leading cause of death globally.1 A primary contributor to CVD is atherosclerosis with coronary artery disease (CAD) being the main cause of heart attack and death. Known CVD risk factors poorly predict acute events in asymptomatic individuals.2 Clinical studies of anti-inflammatory agents establish that atherosclerosis is a chronic inflammatory disease.3,4 Arterial wall lipid deposition and immune infiltration contribute to large, unstable lesions.3 Immune checkpoint proteins (ICP) regulate immune interactions. The murine glucocorticoid-induced TNFR-related (GITR) ICP drives atherosclerosis, and human GITR+ cells have been identified in unstable atherosclerotic plaques.5 Herein, we found CD56bright NK cells associated with CAD severity, and GITR variation may regulate NK responses. Our multidisciplinary team with expertise in NK cells, CVD and bioinformatics will test the novel hypothesis that variant GITR expression corresponds with human CAD and alters GITR cytoplasmic tail signaling domain expression and function in NK cells (see Figure 3).

Principal Investigator: Todd Fox, Ph.D.		University of Virginia
Grant Title: *Nervonic Acid and Obesity*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Obesity in Virginian adults is currently 32% of the population. As higher fat mass is associated with dramatically increased morbidity and mortality, such as in response to COVID-19, there is an urgent need for new strategies to help people control body weight. The premise of this proposal is based on our recently published work demonstrating; 1) the fatty acid, nervonic acid, is dramatically reduced in models of obesity, and 2) dietary nervonic acid diminished weight gain with improved glucose and insulin parameters. The central hypothesis is that reduced nervonic acid plays a critical role in the development of obesity and related complications. This proposal will elucidate the underlying mechanism for reduced nervonic acid in obesity and assess nervonic acid specificity and the need to be acylated into sphingolipids for a therapeutic effect. These results will facilitate the design of new strategies to address the current need for improved weight control.

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Principal Investigator: Bryan Hsu, Ph.D.	**Virginia Polytechnic Institute & State University**	
Grant Title: *Self-assembling biomaterials for improved menstrual health and hygiene*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: We propose to use nondescript self-assembling biomaterials to coagulate menstrual fluid into a semi-solid, mitigating many challenges associated with traditional liquid absorption or collection strategies. We will test the efficacy of these hydrogels using in vitro models that simulate various menstrual conditions including light to heavy bleeding, frequent to infrequent hydrogel replacement, and mechanical deformation due to physical activities. In addition to coagulating menstrual fluid, these biocompatible and biodegradable hydrogels will be loaded with compounds that reduce pain, and inhibit bacterial growth, each with unique release kinetics that maximize their efficacy.

Principal Investigator: Timothy Jarome, Ph.D.	**Virginia Polytechnic Institute & State University**	
Grant Title: *The role of DNA 5-hydroxymethylation in the development of obesity*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Obesity affects 40% of the U.S. population and is responsible for an estimate 300,000 deaths per year. In Virginia alone, the obesity rate in adults is around 30%, with an annual cost of over $4 billion. However, therapeutic interventions which can reverse the progression of obesity remain equivocal. The goal of this project is to identify the role of a robust, highly persistent genetic-molecular mechanism in the brain to the development of obesity. Specifically, we will test if blocking the weight gain-induced reductions in DNA 5-hydroxymethylation (5-hmC) in the hypothalamus in a cell-type specific manner prevents the development of obesity over time. Additionally, we will determine if increasing DNA 5-hmC at the major satiety gene, Pomc, in the hypothalamus can prevent obesity development. Results from this study could provide critical information needed for the development of therapeutic strategies to treat the underlying pathophysiology of obesity.

Principal Investigator: Masahiro Sakagami, Ph.D.	**Virginia Commonwealth University**	
Grant Title: *Local dual-action treatment of lung fibrosis: inhibiting fibroblast activation and modulating collagenolytic activity*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Lung fibrosis causes thickened, scarred fibrotic airspaces due to aberrant extracellular matrix (ECM; collagen) accumulation. It is progressive and idiopathic, but irreversible and incurable with any drugs, resulting in respiratory failure and death in 2-5 years. AM24 is our proprietary curcumin-like derivative of melatonin. As excessive ECM accumulation in fibrotic lungs can be recognized as a net result of induced synthesis and insufficient removal of collagen, we hypothesize that AM24 uniquely possesses dual-actions of inhibiting collagen-generating fibroblast activation; and modulating collagenase and anti-collagenase imbalance, via multi-hybrid mechanisms originating from its structure origins. Hence, this 2-year project will examine AM24 for potent, mechanistically-hybrid, dual-action anti-fibrotic activities using in vitro cell-based systems (Aim 1) and an in vivo rat model of lung fibrosis (Aim 2). Successful completion will prove this dual-action strategy against “collagen dysregulation” in fibrotic lungs and offer AM24 as a novel inhaled drug for lung fibrosis treatment.

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Principal Investigator: Julia Sharp, Ph.D.	**Eastern Virginia Medical School**	
Grant Title*: Pathogenic Determinant Analysis of Community Associated Staphylococcus aureus in South Eastern Virginia*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: *Staphylococcus aureus* is a major cause of community and healthcare-associated infections resulting in significant illness and death worldwide. With increasing antibiotic resistance and no effective vaccine, novel anti-staphylococcal therapies are critically needed. To address this need, we propose an innovative, multifaceted approach to determine *S. aureus* pathogenic (disease-causing) characteristics using community associated *S. aureus* isolates from patients who reside in South Eastern Virginia. We will assess the potential of isolates to cause harm (virulence-factor potential) by examining bacterial DNA (genetic content) and activity (expression) of several clinically relevant virulence factors. Additionally, to further examine the host-pathogen relationship, the capacity of *S. aureus* isolates to bind human serum proteins (both quantity and complexity) will be evaluated. These data will permit the generation of pathogenicity profiles, cross referenced with infection type (skin/soft-tissue or blood infection) and patient locale, to benefit direct therapy interventions and highlight potential therapeutic targets.

Principal Investigator: Lisa Shollenberger, Ph.D.	**Old Dominion University Research Foundation**	
Grant Title: *Proof-of-concept study for the development of next-generation vaccines for tick-borne intracellular diseases*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Tick-borne diseases (TBD) are a worldwide threat to human and animal health. In the USA, Lyme disease is the most common, not the only, TBD. Other tick-borne pathogens (TBP) include Rickettsia, Ehrlichia, Anaplasma, and Francisella; Babesia, and viruses. Virginia had 8,895 reportable TBD cases from 2015-2019, one of the highest statewide incidences in the country, and tick-borne viral infection are not reportable. Development of effective vaccines for TBP is crucial, as there are currently no licensed human vaccines with most, if not all, being a humoral (antibody-based) response. Since many TBP are intracellular pathogens, a cell-mediated immunity (CMI) seems more appropriate. We hypothesize intracellular proteins, which may be conserved between multiple organisms, are appropriate candidate vaccine antigens for intracellular pathogens. Using rickettsial antigens as proof-of-concept, we will test this hypothesis through successful completion of the following aims: (1) development of the necessary immunological tools and (2) evaluation of CMI.

Principal Investigator: Amy Tang, Ph.D.	**Eastern Virginia Medical School**	
Grant Title: *Developing a prognostic companion molecular test to quantify and guide immune-oncology (IO) therapy for triple-negative breast cancer*		
FY 2022/2023	**FY 2023/2024**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Triple-negative breast cancer (TNBC) is an aggressive subtype with high relapse rate. Recently, the FDA approved immune checkpoint blockade (ICB) therapy for high-risk early-stage; and PD-L1- positive locally recurrent, unresectable, or metastatic TNBC. The challenge is how to predict the treatment benefit of immuno-oncology (IO) therapy. To address this unmet need, we propose to evaluate SIAH as a predictive biomarker to augment PD-L1 status and pathologic response to optimize the use of IO-therapy for TNBC. • SIAHHigh/ON in TNBC tumors reflects that the EGFR/K-RAS/SIAH pathway is ON and may indicate immuno-suppression, ICB-resistance, and/or the need for additional therapies to control TNBC malignancy. • SIAHLow/OFF in TNBC tumors reflects that the EGFR/K-RAS/SIAH pathway is OFF and may indicate immuno-responsiveness, ICB-sensitivity, and good prognosis after surgery. We aim to demonstrate the clinical utility of SIAHON/OFF expression as a new prognostic biomarker to stratify patients, predict the need for and/or efficacy of neoadjuvant and/or adjuvant immunotherapy.