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 2024

From the Commonwealth Health Research Board

The Virginia Commonwealth Health Research Board (CHRB) has recently awarded **$1,431,173** in grants to medical and health researchers in Virginia. Of this amount, **$699,998** represents grants to seven medical and health researchers for new 2024 Grant Awards and **$731,175** represents continued second-year funding for eight grant awards initially approved in July 2023. 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, and Virginia Polytechnic Institute & State University. 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 **306** research grants totaling approximately **$26.6 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 **$78 million** in additional private and federal grant funds to further their research studies.

2024 Grant Awards: $699,998

Principal Investigator: Michel Audette, Ph.D.		**Old Dominion University Research Foundation**
Grant Title: *Intranatal Force-sensing And Patient-derived Anatomy and Kinematics Modeling For Real-time Virtual Reality Obstetrics Simulation*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$99,998	**$100,000**	**$199,998**

Project Summary: The US egregiously underperforms in obstetrics practice in relation to other developed countries. Poorer hospitals have complication rates double or worse those of richer hospitals in vaginal deliveries. Maternity health care services are limited or absent in a third of rural counties. Our long-term objective is to achieve a virtual reality (VR) simulation based on bimanual haptic gloves, anatomical models of the fetus and maternal pelvis derived from fetal MRI, and interactive biomechanics, to train obgyns, and rural physicians and midwives, to develop safe practices for difficult cases such as shoulder dystocia. Yet to eradicate deleterious practices, we must ask: what is a tolerable force in a delivery? This project consists of I) a prenatal and intranatal phase, and II) a VR simulation phase. Phase I will characterize safe practices that lead to healthy labor outcomes. Phase II will achieve VR-based simulation that also builds on anatomical modeling of the fetus and maternal pelvis, haptics-driven skeletal dynamics, and real-time soft tissue simulation. Bimanual haptics based on grounded forcerendering gloves will be developed downstream of this project. Aim 1 will establish a reference for excessive force, we will achieve a means of acquiring intranatal forces, with Pliance force-transducing gloves worn by an obstetrician (under latex gloves). Aim 2 will provide a detailed personalized anatomy will be achieved by registering an anatomist-drawn CAD model to fetal MRI datasets. This detailed anatomy will represent the neonate during birth as imaged intranatally and provide the anatomy model input to the VR simulation.

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Principal Investigator: Sol Lim, Ph.D.		**Virginia Polytechnic Institute & State University**
Grant Title: *Enhancing Parkinson's Disease Rehabilitation Through Remote Haptic Guidance*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Individuals with Parkinson's disease (PD) experience declining motor symptoms that disrupt their daily activities and quality of life. Effective physical rehabilitation can slow the progression of these symptoms. Nevertheless, it remains quite difficult to deliver such rehabilitation in an accessible and cost-effective manner, largely due to both individual-level and system barriers within healthcare services. To help overcome these barriers, there is growing interest in at-home, technology-based rehabilitation programs that can reduce therapy costs and enhance accessibility. However, critical obstacles to implementing such programs are the important challenges of remotely assessing and guiding patient movements while providing essential hands-on assistance. Our project will address these challenges by integrating a new low-cost haptic-guidance approach into an at-home rehabilitation system for PD patients. Our aims are to: 1) Evaluate the efficacy of the haptic-guided rehabilitation system in lab-based user testing; and 2) Determine the effects of the new haptic-guided remote rehabilitation system on diverse motor functions among PD patients, using a randomized controlled trial. Our team has broad expertise– in intelligent physical training systems, biomechanical performance modeling, and haptic interfaces– and we will collaborate closely with healthcare partners. This collaboration will ensure that our work helps improve the delivery of physical rehabilitation, by making it more accessible and effective for a broader spectrum of PD patients.

Principal Investigator: Alessandra Luchini, Ph.D.		**George Mason University**
Grant Title: *Host response mechanisms of neuroborreliosis*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Purpose: In Virginia, an estimated 192,000 individuals grapple with Lyme disease, and new cases are on the rise. Neuroborreliosis, the neurological impact of Lyme disease on the brain and nerves, causes significant suffering, yet its underlying causes are still unknown. Our goal is to investigate previously unexplored cellular and molecular mechanisms contributing to brain damage in Lyme disease patients. We hypothesize that bacterial extracellular vesicles (BEVs), released by the Lyme disease-causing Borrelia, trigger the activation of microglia, the immune cells in the central nervous system, leading to long-term brain dysfunction. Using a direct test developed through a multi-year clinical study, we identified Borrelia-derived proteins in the urine of over 400 Lyme disease patients. These proteins, originating from the spirochete's functional machinery, may play a role in the damage inflicted on patients. Methods. We will generate and characterize BEVs produced by Borrelia, studying their direct effects on human microglia cells, and confirming the presence of Borrelia BEV markers in urine samples from Lyme disease patients. Populations: We will study banked urine collected from 50 Lyme disease patients who previously participated in our clinical study. Expected outcomes: Insights gained from this study will pave the way for innovative therapeutic strategies to alleviate the neurological suffering caused by Lyme disease including inhibitors of bacterial vesicle production and neuroinflammation suppression compounds. Additionally, the research may contribute to the development of new diagnostic tests for early identification and prompt antibiotic treatment.

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Principal Investigator: Amanda Morris, Ph.D.		**Virginia Polytechnic Institute & State University**
Grant Title: *Metal Organic Framework Smart Drug Delivery Vehicles for the Next Generation of Personalize Patient Care*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Drug discovery over the past several decades has led to the development of numerous therapeutic agents for a wide variety of diseases. However, the clinical application of many of these drugs is limited by unwanted side effects, off-target accumulation, and poor pharmacokinetics. *To fully realize the potential of this immense amount of work, there is a critical need to develop tools to control the localization and delivery of therapeutics*. We have developed a one-of-a-kind, metal-organic framework (MOF) drug delivery vehicle (DDV) for the photo-controlled release of therapeutics with simultaneous breakdown of the carrier into small molecules, Fig. 1. 1–5 In contrast to other known DDVs, such as inorganic nanoparticles, liposomes, and polymeric micelles, our MOF DDV is comprised of components with *low toxicity*, exhibits *high drug loading capacities*, demonstrates *favorable pharmacokinetics*, delivers drug in a controllable fashion in response to an *external stimulus*, and has an *easily modifiable surface for advanced targeting*. The proposed work aims to optimize our proof-of concept MOF for clinical translation with light absorption properties, drug loading (including cocktails), and drug release rates amenable for patient care through a combined and iterative computational and experimental approach. Our proposed work holds the potential to provide a unique platform to deliver therapeutics in line with the "holy grail" of personalized medicine, i.e., the duration of treatment, therapeutic dose, and therapeutic cocktail (one drug or multi-drug administration) can be tuned to match each patient's determined treatment plan.

Principal Investigator: Sharon Swanger, Ph.D.		**Virginia Polytechnic Institute & State University**
Grant Title: *Serotonin modulation of thalamocortical dysfunction in Dravet syndrome*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: In 2020, fenfluramine became the first serotonin-based therapy approved for epilepsy. Fenfluramine enhances serotonin signaling in the brain and is approved only for Dravet syndrome (DS), an infantile-onset epilepsy. This was a major advance for DS treatment, but decades of preclinical research suggest a wider patient population may benefit from enhanced serotonin signaling. Approximately 1% of the U.S. population has active epilepsy, including ~85,000 people in Virginia, but less than 0.5% of epilepsy patients have DS. Our long-term goal is to determine how modulating serotonin signaling can be broadly applied to improve human health. Epilepsy has diverse causes, but similar disease pathology occurs in seizure-prone brain areas. Therapies targeting these areas could be applied broadly for epilepsy. To predict which patient populations will benefit from serotonin therapies, we need to understand the neurobiological mechanisms by which serotonin suppresses seizures. We will utilize a DS mouse model to define how fenfluramine and enhanced serotonin release affect neuronal activity in the thalamus, a brain area that generates seizures. We hypothesize that enhanced serotonin signaling will correct vital aspects of thalamus physiology disrupted in DS and many other epilepsies. The project outcomes will support long-term funding proposals aimed at broadly advancing serotonin-based therapies for epilepsy.

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Principal Investigator: Lifang Yang, M.D., Ph.D.	**Eastern Virginia Medical School**	
Grant Title: *Detection of Minimal Residual Disease in Early-stage Triple-negative Breast Cancer through Extracellular Vesicle-based Liquid Biopsies*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Tumor relapse from minimal residual disease (MRD) is a major clinical challenge that accounts for more than 1,000 breast cancer-related deaths annually in Virginia, particularly in women with aggressive triple-negative breast cancer (TNBC). Therefore, the ability to predict and monitor MRD after primary treatment is a key determinant of survival outcomes for patients with early-stage TNBC. Currently there are no robust tests in the clinic to accurately and reproducibly identify TNBC patients with MRD following curative-intent therapy, leading to relatively uniform treatment algorithms that cannot trade off efficacy and toxicity well. To address this gap, we have developed innovative approaches for isolation and molecular analysis of tumor-shed small extracellular vesicles (sEV) derived from human biofluids, which harbor tumor state-specific information in their cargo molecules. In this project, we will use prospectively collected TNBC blood samples and our developed tools to identify sEV-based molecular (proteogenomic) signatures for reliable prediction and timely detection of residual TNBC noninvasively. If successful, the findings of our project will advance fine-tuning of personalized medicine in the management of TNBC which ultimately improve patient-centric outcomes and quality of life.

Principal Investigator: Wei Zhou, Ph.D.	**Virginia Polytechnic Institute & State University**	
Grant Title: *Wearable Bio-Nanophotonics Technology for Wound Biofilm Infection Management*		
FY 2024/2025	**Planned FY 2025/2026**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: The project is an innovative venture to revolutionize the detection and treatment of chronic wound infections. Chronic wounds, often seen in diabetic, elderly, and immobile patients, are prone to biofilm formation, leading to increased infection risks and slower healing. The core of this technology is a wearable nanoplasmonic bio-mesh designed for combined molecular Raman fingerprinting detection and photothermal/acoustics-enhanced treatment of wound biofilm conditions. It employs spatiotemporal plasmon-enhanced Raman spectroscopy (PERS) to detect biofilm presence at the wound site without requiring invasive procedures. In parallel, the technology leverages bio-mesh surface plasmon-induced photothermal/acoustics effects to generate localized heat and micro- /nanocavitation in combination with standard antimicrobial therapies, effectively disrupting and eradicating biofilms. This project leverages our team's multidisciplinary expertise in nanotechnology, biophotonics, and wound care, aiming to significantly improve clinical outcomes for patients with chronic wounds. By enabling early detection and efficient treatment of biofilm-associated infections, the project promises to reduce treatment costs, lower the risk of severe complications, and enhance the overall quality of life for affected individuals. The project's success will testify to the collaboration between advanced bio-nanotechnology and healthcare, marking a significant stride in personalized medical care. Supported by the College of Engineering and Virginia-Maryland College of Veterinary Medicine at Virginia Tech, this endeavor stands at the forefront of innovative healthcare solutions, aligning with the CHRB's commitment to advancing medical research and patient care.

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Continued Second-Year Funding for 2023 Grant Awards: $731,175

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	**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.

Principal Investigator: Diane Duffy, Ph.D.	Eastern Virginia Medical School	
Grant Title: *PCO or No? Healthy Androgens and Ovulation*		
FY 2023/2024	**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	**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.

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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	**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.

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	**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	**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.

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Principal Investigator: Michael Schulz, Ph.D.		**Virginia Polytechnic Institute & State University**
Grant Title: ***Developing Enhanced Sealants for Neurosurgery***		
FY 2023/2024	**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.

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	**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.