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 September 2021

From the Commonwealth Health Research Board

The Virginia Commonwealth Health Research Board (CHRB) has recently awarded approximately **$2.7 million** in grants to medical and health researchers in Virginia. Of this amount, **$1,400,000** represents grants to eight medical and health researchers for new 2021 Grant Awards and **$1,317,127** is for grants to eight investigators for 2020 Grant Awards approved in October 2020. 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, 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 **260** research grants totaling approximately **$22.2 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.

2021 Grant Awards: $1.4 million

Principal Investigator: Liheng Cai, Ph.D.		**University of Virginia**
Grant Title: ***Voxelated 3D Bioprinting of Multiscale Porous Scaffolds for Islet Transplantation***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**-**	**$100,000**

Project Summary: This project seeks to develop a novel platform encapsulation technology for islet transplantation to treat type 1 diabetes (T1D). We do so by integrating super biocompatible alginate (Z1-Y15) and our newly invented 3D bioprinting technique that enables the digital assembly of 0D spherical hydrogel voxels. Preliminary studies demonstrate that voxelated bioprinting permits the fabrication of mechanically robust 3D structures formed by interconnected yet distinguishable sub-millimeter hydrogel particles in which are encapsulated islets. We hypothesize that such a multiscale porous structure, when being made by Z1-Y15 alginate with optimized viscoelasticity, enables immunoprotection, cell viability, transport, and ease retrievability, thereby providing an ideal scaffold for islet transplantation. To test this, we assemble a team with complementary expertise in biomaterials, engineering, and islet physiology and transplantation. This project will yield new means to treat T1D and novel technologies that enable engineering highly heterogeneous yet tightly organized tissue reconstructs for basic and applied biomedicine.

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Principal Investigator: Daniel Conway, Ph.D.	**Virginia Commonwealth University**	
Grant Title: ***Inhibition of cell-cell fusion as a potential mechanism for treatment of covid19***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Limited therapies are available for COVID-19, in part due to a lack of understanding of how SARS-CoV-2 (SARS2) virus interacts with and affects host cells. This proposal is focused around developing a comprehensive understanding of the process by which SARS2 fuses host cells together, to form large, multi-nucleated cells, known as syncytia. SARS2 has increased syncytia formation, as compared to the original SARS virus, suggesting syncytia formation is a critical aspect of SARS2 pathogenicity. The PI (Conway) and co-I (Narayanan) have expertise in biophysics and live cell imaging and virology, respectively. The Narayanan group has found Maraviroc, an FDA-approved anti-viral, inhibits SARS2 viral replication. The Conway group has identified a potential mechanism of action, showing that Maraviroc inhibits the formation of syncytia. Data from this proposal will be critical for design of new targeted approaches to inhibit syncytia formation, which may have therapeutic value for treatment of COVID19 infection.

Principal Investigator: Babette Fuss, Ph.D.	**Virginia Commonwealth University**	
Grant Title: ***The role of LPA6 receptor signaling in myelin repair***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: There are currently no neuroprotective therapies for debilitating diseases, such as Multiple Sclerosis (MS), where damage to the myelin sheath, which enwraps and protects central nervous system (CNS) nerve fibers, causes chronic nerve fiber degeneration and neurological disability. An emerging concept toward the development of novel treatment options is seen in the characterization of signals that are present in the demyelinating CNS and impede the repair capabilities of CNS myelinating cells, namely oligodendrocytes (OLGs). In this context, our novel findings suggest that the lipid signaling receptor LPA6 significantly contributes to such impediments in myelin repair. Notably, while lipid signaling has been described to be dysregulated under demyelinating conditions, its precise role in the regulation of CNS remyelination is not fully understood. Thus, in the long-term, our studies are anticipated to lead to the identification of novel therapeutic targets for stimulating myelin repair under pathologic conditions such as MS.

Principal Investigator: Daeha Joung, Ph.D.	**Virginia Commonwealth University**	
Grant Title: ***3D Printing Living Platform for Spinal Cord Regeneration***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Spinal Cord Injury currently has no effective therapies that enable the restoration of disrupted signals in the impaired sites to re-establish function due to architectural and functional complexity. This project aims to develop an advanced biomanufacturing process for constructing living scaffolds using 3D printing and origami-inspired assembly that permit the use of multi-materials. The objectives of this research include: (1) develop origami-inspired folding processes to transform 3D printed plane structures into a three-dimensional scaffold, overcoming the limitations of the compatibility with a broad spectrum of biomaterials; and (2) embedded electrodes within the scaffold to deliver targeted electrical stimulation for cell growth. The integrated technology will bridge the gap between advanced biomanufacturing science and neural regeneration, ultimately promoting interdisciplinary efforts to develop life-altering clinical treatments for patients who sustain Spinal Cord Injuries in Virginia and beyond.

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Principal Investigator: Jeffrey Moran, Ph.D.	**George Mason University**	
Grant Title: ***Patient-Derived Hydrogel-Based In Vitro Models of Idiopathic Pulmonary Fibrosis for Assessment of Targeted Nanoparticle Therapies***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Idiopathic pulmonary fibrosis (IPF) is a lung disorder that kills more Americans per year than breast cancer. Its cause is poorly understood and the typical survival time is less than 5 years. IPF progression is known to depend on interactions between cells and their surrounding environment. Here, we will synthesize biomaterials that match the protein composition of real fibrotic lung tissue and use them as platforms to test new nanoparticle-based strategies to halt and possibly reverse IPF progression. Our aims are (1) synthesize decellularized hydrogels and quantify effects of changes in stiffness and pore size on disease progression in vitro; (2) test efficacy of nanoparticles, propelled by magnetic fields or ultrasound, to penetrate tissue and deliver medication to targeted locations. This work will yield insight into the effects of tissue mechanics on IPF progression and could enable lower required doses for IPF medication, reduced side effects and improved patient outcomes.

Principal Investigator: Yuchin Albert Pan, Ph.D.	**Virginia Polytechnic Institute and State University**	
Grant Title: ***Identification of novel molecular factors underlying cellular resilience to early-life stress***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**-**	**$100,000**

Project Summary: In modern society, stress is a common occurrence in everyday life. The brain's stress-response system (the hypothalamic-pituitary-adrenal axis) helps us adapt to stress, but it is vulnerable to severe or chronic stress, especially during early-life periods. Malfunction of the stress system contributes to severe mental illnesses (e.g., PTSD and major depressive disorders), which is a growing public health issue in Virginia. Novel mechanistic understanding of how the stress system responds to early-life stress is critical to developing novel therapeutic interventions. Using animal models, we will perform an unbiased gene expression analysis to identify molecular factors capable of enhancing the resilience of neurons to early-life stress. The findings from the proposed study could be applied to future therapeutic interventions to prevent or remedy the adverse effects of early-life stress.

Principal Investigator: Lee Solomon, Ph.D.	**George Mason University**	
Grant Title: ***An environmentally responsive peptide material capable of oxygen delivery***		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Despite an urgent need and years of study, there are no suitable blood substitutes that can be routinely used. Relying on donations is also troublesome as the blood can be contaminated with undiagnosed illnesses and is difficult to store. We propose to develop a blood substitute made from a novel peptide material, which binds heme B, the same cofactor found in human hemoglobin. For this stage of the work, we will optimize the material by changing the peptide sequence to promote stronger oxygen binding and tuning the environmental responses to be more aligned with physiological conditions. These peptides are highly modifiable and can be designed so they do not stimulate the immune system and be more stable than standard blood for long term storage. This work will serve as pilot studies for developing a next generation blood substitute that will help all Virginians suffering from hemorrhage inducing injuries.

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Principal Investigator: Zequan Yang, M.D., Ph.D.	**University of Virginia**	
Grant Title: *Topical Neck Cooling Attenuates Acute Myocardial Infarction*		
FY 2021/2022	**FY 2022/2023**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Myocardial infarction (MI, heart attack) accounts for the vast majority of death associated with ischemic heart disease. The key to salvage the dying heart muscle is to shorten the transportation time to the hospital. However, the prehospital management to protect the heart is sadly lacking. Mild systemic hypothermia is found to be protective against MI. However, the protection is observed only when hypothermia is achieved early during the heart attack. Induction of systemic hypothermia is resource intensive and difficult to start outside hospital. The delay in initiating the hypothermia is unlikely to be solved. A therapy, that is portable and easy to apply at the onset of heart attack, may provide better heart protection. We found that topical neck cooling could attenuate MI similar as systemic hypothermia. This application will further define the mechanisms underlying the topical neck cooling and modify the device for use in big animal model.

2020 Grant Awards: $1,317,127

Principal Investigator: Farrokh Alemi, Ph.D.	**George Mason University**	
Grant Title: *Optimizing Antidepressant Selection through Artificial Intelligence*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$78,382	**-**	**$78,382**

Project Summary: The long term goal of this study is to improve management of depressed patients in primary care. Robert Wood Johnson Foundation has funded the principal investigator to analyze outcomes for depressed patients taking antidepressant. The foundation has funded the analysis of data on 115 million lives, at QualLabs, under the supervision of Alemi. No funds are available for activities at the university. The current request will supplement the existing foundation-funded effort and enable the creation of the first Artificial Intelligence decision aid for prescription of antidepressants. The aid is composed of two parts: (1) an emphatic, conversational interview to assess the patient's medical history and (2) a report to the patient and the patient's clinician of the antidepressant most likely to benefit the patient.

Principal Investigator: Bahareh Behkam, Ph.D.	**Virginia Polytechnic Institute and State University**	
Grant Title: *Mechanobiology of Implant Infection: Effect of Surface Roughness on the Attachment Density and Phenotype of Adherent Staphylococcus aureaus*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: The increasing demand for orthopedic implants in our aging society, coupled with a dramatic increase in the emergence of antibiotic-resistant bacterial strains has made implant infection control progressively challenging and costly. Bacterial adhesion and biofilm formation on implants play important roles in infection and treatment resistance. It has been demonstrated by us and others that nanoscale surface features significantly affect microbial adhesion and viability; however, the physical and biological underpinnings of microbe-nanostructure interactions remain largely unknown. We propose to nanofabricate topographical features of well-defined sizes and spacing on titanium implants and investigate the effect of the nanostructures on the attachment density and biological activity of *Staphylococcus aureus*, the most common etiological agent for orthopedic infections. Through understanding the mechanisms by which the physical properties of engineered surfaces regulate adherent bacteria behavior, this proposal has the potential to uncover novel non-toxic antimicrobial strategies for mitigating medical implant infection.

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Principal Investigator: Paul Fisher, MPhil, Ph.D.	**Virginia Commonwealth University**	
Grant Title: *Rational Design of Cancer Invasion and Metastasis Inhibitors*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Approximately 90% of patient deaths from solid cancers result from metastasis. Melanoma differentiation associated gene-9 (*mda-9*) is a key genomic element in diverse cancers that controls invasion and metastasis. We developed a first generation novel pharmacological inhibitor of MDA-9, PDZ1i that profoundly suppresses cancer cell spread, invasion and metastasis in a broad-spectrum of human cancers in preclinical animal models. Our central goal, is to develop effective pharmacological *in vivo* inhibitors of cancer migration/invasion/metastasis. We will apply rationally-designed medicinal chemistry approaches to produce the next generation PDZ1i (NG-PDZ1i) and PDZ2i with further enhanced anti-metastatic properties. To ensure achieving this endpoint we will use two innovative strategies we have developed, i.e., semi-high throughput screening assays in zebrafish and invasion assays using cultured mammalian tumor cells. Developing NG-PDZ1i and PDZ2i will provide significant societal health benefits and enhance the economy of VA through growth of a biotechnology company, InVaMet Therapeutics.

Principal Investigator: Aurora Esquela Kerscher, Ph.D.	**Eastern Virginia Medical School**	
Grant Title: *Molecular dissection of a microRNA cluster network of aggressiveness*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Prostate cancer (PCa) is the most prevalent form of cancer in Virginian males. Our state's PCa mortality rate is ranked 8th in the nation. This proposal will develop more effective theranostic tools for this disease, focusing on the microRNA (miRNA) class of small noncoding RNAs. MiRNA dysregulation is a common feature of PCa but little is known how they functionally interact as a cancer network to promote disease progression. We will investigate this problem by studying the miR-888 cluster, which consists of seven miRNA genes mapping close together on human chromosome X within a hereditary PCa locus. We found that the miR-888 cluster is elevated in patients with aggressive PCa and induces proliferation, invasion, and tumor formation. Our integrated translational research team (EVMS, University of Virginia) will use high throughput CRISPR gene editing, proteomics, nanostring technology and antimiR reagents to molecularly dissect the miR-888 cluster and validate its clinical potential.

Principal Investigator: Kyle Lampe, Ph.D.	**University of Virginia**	
Grant Title: *Self-assembling, shear-thinning peptide hydrogels to support cell transplantation and host cell interaction after ischemic stroke*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Stroke is the third leading cause of death in the US and 20% of stroke survivors are so significantly disabled that they cannot walk without help. Despite broad research, stroke and other disorders of the brain and spinal cord continue to be the leading cause of disability nationwide. No treatment exists to rebuild neural tissue destroyed by ischemic stroke and the subsequent cell death. We propose a new engineered biogel to transplant neural stem cells (NSCs), and encourage growth of host NSCs and vascular cells into the infarct site. These materials are designed to be injectable and cell compatible, and thus may improve NSC transplantation survival. Establishing this collaboration will support future development, especially early insight to biogel interventions in a rat model of ischemic stroke. The aims will provide important materials development and characterization and pre-clinical data toward supporting cell growth and decreasing or reversing stroke-induced brain damage.

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Principal Investigator: Alicia Pickrell, Ph.D.	**Virginia Polytechnic Institute and State University**	
Grant Title: *STING-dependent Type I Interferon Response in TBI*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: Traumatic brain injury (TBI) is the most commonly acquired central nervous system (CNS) injury affecting both civilian and military populations in the United States. This highly complex, heterogeneous epidemic results in excessive morbidity and long-term disability for an estimated 5.3 million Americans with an annual economic cost of $37.8 billion. In Virginia (VA), over 2% of the population suffer from disabilities related to TBI, and an estimated 28,000 Virginians sustain a TBI annually. Inflammation in the brain after the mechanical insult contributes to neurodegeneration affecting functional outcomes for patients. In our published and preliminary data, we profiled a novel immune response in a preclinical mouse model of TBI. TBI-injured mice showed an abnormal upregulation of Type I interferons. In this proposal, we plan to characterize this novel interferon pathway after TBI to decipher whether targeting interferon signaling therapeutically reduces inflammation and neurodegeneration in the brain after injury.

Principal Investigator: Steven Shell, Ph.D.	**University of Virginia's College at Wise**	
Grant Title*: Mass Spectrometry Analysis of the Human XPA-XPC Complex*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$38,745	**-**	**$38,745**

Project Summary: Many chemotherapeutics work by inducing DNA damage in cancer cells. Therefore, understanding the molecular mechanisms of DNA repair is vital to pharmaceutical development. One such process is the Nucleotide Excision Repair pathway. NER relies on a series of protein-protein complexes to repair DNA. Two proteins, XPC and XPA, act early in the human NER pathway. We hypothesize that XPA forms a direct physical complex with XPC necessary for establishing an efficient NER response. We propose using mass spectrometry footprinting to identify the molecular surfaces on each protein responsible for mediating the interaction. Chemical labeling will be used to identify all surface-exposed lysine residues on each protein and the protein complex. Residues protected from modification in the complex will be mapped onto structural models for each protein. Computational docking will be used to create a model of the complex. These results will provide targets for future functional studies in human cells.

Principal Investigator: Chongzhi Zang Ph.D.	**University of Virginia**	
Grant Title: *Aberrant CTCF binding as an epigenetic signature of cancer*		
FY 2020/2021	**FY 2021/2022**	**Total Grant Funds**
$100,000	**$100,000**	**$200,000**

Project Summary: CTCF is a protein that can function as a chromatin insulator and facilitates chromatin looping. Disruption of individual CTCF binding sites in the human genome have been reported in several cancers that associate with altered chromatin structure and dysregulation of genes in the chromatin domains. Our preliminary studies show that cancer-specific CTCF binding events are common in many cancers, and the level of aberrant CTCF binding in each cancer type is correlated with clinical outcome. We hypothesize that CTCF binding aberration is an epigenetic signature of cancer. In this project, we propose to use novel integrative computational genomics approaches to systematically characterize aberrant CTCF binding events in the genome in several human cancer systems and their function in gene regulation.