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From the Commonwealth Health Research Board

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The Commonwealth Health Research Board [CHRB] has awarded **\$1,517,067** in grants to 16 medical and health researchers in Virginia for FY 2020/2021.

George Mason University

Principal Investigator: Farrokh Alemi, Ph.D.

Grant Award: \$78,382

Grant Title: *Optimizing Antidepressant Selection through Artificial Intelligence*

The goal of this project is to improve medication management for patients suffering from depression. Currently, the majority of such patients do not benefit from their antidepressant medications, as only about a third experience symptoms improvement. Dr. Alemi will tap into a dataset of over 110 million patients for information about antidepressant regimens history. By artificial intelligent methods he will extract predictive decisions for antidepressants, tailored to specific case history of individual patients. Next, he plans to engage patients from various regions in Virginia in testing the algorithm. The participants will be “interviewed” by an interactive computer using a secure platform. Their individual case history will be analyzed by the computer algorithm to produce suggestions for the most effective antidepressants regimen. This is the first study in the USA to assess effectiveness of antidepressants based on personalized mental health case history.

Virginia Polytechnic Institute and State University

Principal Investigator: Bahareh Behkam, Ph.D.

Grant Award: \$100,000

Grant Title: *Mechanobiology of Implant Infection: Effect of Surface Roughness on the Attachment Density and Phenotype of Adherent Staphylococcus aureus*

Demand for orthopedic implants in our aging society is increasing, and with it the increase in implant-associated antibiotic resistant bacterial infections. Dr. Bekham aims to mitigate medical implant infections by analyzing the nanoscale patterns of implant surfaces. Such patterns appear to determine how well bacteria can colonize on implants and surgical tools. Based on observations of natural ‘anti-fouling’ patterns of sea shells and insect wings, Dr. Bekham focuses on nano-grooves of specific sizes and spacing that force bacteria to stretch and stress the outer wall, preventing them from settling on such surfaces. This team will fabricate and study titanium surfaces of different nano-groove patterns, looking for optimal repelling of bacteria. The research team includes a brain surgeon with experience in procedures requiring skull implants.

Virginia Polytechnic Institute and State University

Principal Investigator: Matthew Buczynski, Ph.D.

Grant Award: \$100,000

Grant Title: *Evaluation of a 12/15-LM receptor as a target for Non-Opioid Pain Therapeutics*

The goal of this project is to identify new non-opioid drugs that are more effective in chronic pain management than currently available nonsteroidal anti-inflammatory drugs (e.g., ibuprofen). The Buczynski group has identified a new potential molecular target for non-opioid pain therapeutics, and intends to characterize that target and screen potential lead compounds that would block its activity and reduce pain. This drug discovery effort could identify new pain-relieving drugs that will alleviate the need for opiates thus mitigating their misuse and resulting addiction.

Virginia Commonwealth University

Principal Investigator: Paul Fisher, MPhil, Ph.D.

Grant Award: \$100,000

Grant Title: *Rational Design of Cancer Invasion and Metastasis Inhibitors*

Approximately 90% of patient deaths from solid cancers result from metastasis. Dr. Fisher has discovered an oncogene - Melanoma differentiation associated gene-9 (mda-9) – that controls invasion and metastasis in a broad range of solid cancers. The investigator plans to develop a novel mda-9 inhibitor that could suppress cancer cell invasion and be amenable to future drug development. The team has already generated a prototype inhibitor, PDZ1i, and now aims to produce the next-generation inhibitors, with more stringent requirements for specificity and efficacy. The medicinal chemistry strategies are designed to reduce potential side effects in healthy organs. This project is conducted in collaboration with the Virginia-based biotechnology company, InVaMet Therapeutics.

University of Virginia

Principal Investigator: Brent French, Ph.D.

Grant Award: \$100,000

Grant Title: *Bioengineering of Cardiac Regeneration In Situ after Myocardial Infarction*

Dr. French and his team continue to address one of the most important problems in heart health: the fact that heart muscle does not grow back or repair after damage from events like heart attack. They are employing genetic methods to reprogram heart muscle cells so that, after injury, the cells' innate programmed behavior is directed away from formation of scar tissue and toward regeneration of normal tissue.

Eastern Virginia Medical School

Principal Investigator: Aurora Esquela Kerscher, Ph.D.

Grant Award: \$100,000

Grant Title: *Molecular dissection of a microRNA cluster network of aggressiveness*

Dr. Kerscher and her team are exploring the reasons why prostate cancer (PCa) can be so hard to treat and be so lethal. The planned research stems from the observation that a class of small RNAs are abnormally regulated and work together in patients to promote cancer progression. They will focus on the miR-888 cluster, which consists of seven miRNA genes mapping close together on human chromosome X within a hereditary PCa locus.

University of Virginia

Principal Investigator: Kyle Lampe, Ph.D.

Grant Award: \$100,000

Grant Title: *Self-assembling, shear-thinning peptide hydrogels to support cell transplantation and host cell interaction after ischemic stroke*

Up to now, it has been impossible for stroke patients to regenerate their lost brain tissue in the correct amount and in the proper structure. Dr. Lampe and his team are working with injections of an engineered biogel that would transplant neural stem cells within a scaffold directly to the site of injury within the brain or spinal cord. The gel, once in place, would encourage the growth of newly implanted neural stem cells.

University of Virginia

Principal Investigator: James Landers, Ph.D.

Grant Award: \$100,000

Grant Title: *Diagnostic Assay for On-Site Detection of Bordatella pertussis*

There has recently been a world-wide resurgence of whooping cough, caused by Bordatella pertussis, especially in situations where vaccinations are not readily available or ignored. It would be a great public health benefit if there were a point-of-care device to enable rapid detection of the disease, which could replace the current time-consuming process of sending samples to be processed at a central facility and enable timely initiation of treatment to prevent transmission and reduce mortality. Dr. James Landers and associates would meet this need by using state-of-the-art approaches to develop a "lab-on-a-CD" microfluidic tool to screen for the presence of B. pertussis DNA, allowing for detection of infection within 20 minutes.

Eastern Virginia Medical School**Principal Investigator: Nagaraja Nagre, Ph.D.****Grant Award: \$100,000****Grant Title: *Exploring the potential role of cannabinoid receptor type-2 activation in protection against bacterial pneumonia-induced lung injury***

Bacterial pneumonia is a major risk factor for developing acute lung injury. Ventilator-associated pneumonia carries even higher risks of bacterial infections, lung cell injury and mortality. Conventional antibiotics therapy is not always effective due to antibiotic-resistant strains. Dr. Nagre proposes to study an option for pneumonia treatment, by enhancing immune capabilities via the cannabinoid receptor-2 (CB2R). This receptor is predominantly expressed on immune cells, and can be activated by synthetic CB2R agonists, that effectively enhance macrophages and neutrophils activity without the undesired psychoactive effects. In pilot studies, the investigator showed that treatment with such CB2R agonist reduced bacterial-induced lung injury in mice. His goal is to obtain in-depth information on the most effective course of treatment, and to identify the immune cellular compartments that regulate this protective scenario.

Virginia Commonwealth University**Principal Investigator: Swati Palit Deb, Ph.D.****Grant Award: \$99,940****Grant Title: *Targeting mutant p53-dependent checkpoints of genome duplication in lung cancer***

Dr. Deb and her team continue to address lung cancer which is one common causes of death in Virginia. They have found that Gain-of-Function mutations alter the tumor suppressor P53 which promotes cancer growth by inhibiting immune checkpoints. These are the inbuilt control mechanisms of the immune system that maintain self-tolerance and help to avoid collateral damage during a physiological immune response. Tumors can create microenvironments to evade immune surveillance and attack, particularly by modulating certain immune-checkpoint pathways. This project explores the anti-cancer potential of GOFp53-induced checkpoint signaling inhibitors.

McGuire Research Institute**Principal Investigator: Bhaumik Patel, M.D.****Grant Award: \$100,000****Grant Title: *Development of a Selective Non-Saccharide Glycosaminoglycan Mimetic for Colon Cancer***

Despite current knowledge and treatments, some cancers, such as colorectal cancer, are never completely cured. Dr. Patel and his colleagues continue their work on cancer stem cells. These cells are not eradicated after treatment and function as seeds for recurrence of tumor. The team is focusing on a newly synthesized, inexpensive short sequence of a heparin look alike molecule that shows therapeutic promise.

Virginia Polytechnic Institute and State University**Principal Investigator: Alicia Pickrell, Ph.D.****Grant Award: \$100,000****Grant Title: *STING-Dependent Type 1 Interferon Response in TBI***

This project involves a search for a way to mitigate the consequences of traumatic brain injury (TBI). Dr. Pickrell will use a mouse model of TBI to pursue an observation that brain neurodegeneration following a mechanical insult involves a novel immune response that includes abnormal upregulation of Type I interferons. The plan is to characterize the pathway whereby these interferons are generated to see whether targeting interferon signaling therapeutically reduces long-term sequelae, including inflammation, following TBI.

Virginia Commonwealth University

Principal Investigator: Jason Reed, Ph.D.

Grant Award: \$100,000

Grant Title: *A new approach for detecting IGH translocations in hematologic malignancies*

Blood cancers comprise about 10% of all cancers diagnosed in the United States. Treatment of such cancers can be complicated, and there is a need for methods to detect them in less specialized medical settings such as community hospitals. Thus it is planned to use an approach dubbed “DNA barcoding” that will allow detection of chromosome rearrangements that are characteristic of these cancers. The outcome will be a tool that is as rapid and accurate as existing alternatives, but that has a considerably lower cost, thus potentially improving outcomes for patients in underserved populations.

University of Virginia’s College at Wise

Principal Investigator: Steven Shell, Ph.D.

Grant Award: \$38,745

Grant Title: *Mass Spectrometry Analysis of the Human XPA-XPC Complex*

Numerous anti-cancer drugs act by damaging DNA, a process that is presumably more harmful to rapidly dividing cancer cells than to normal cells. There are several natural DNA repair processes that can thwart the effects of such drugs. This project, from Dr. Steven Shell at UVa-Wise, involves a basic biochemical characterization of the “nucleotide excision repair (NER)” pathway. Modern techniques will be used to construct models of the molecular complexes involved in human NER, which will provide a basis for future functional studies in human cells and potentially underpin the design of therapeutics to counteract the deleterious effects of DNA repair in cancer treatment.

University of Virginia

Principal Investigator: Martin Wu, Ph.D.

Grant Award: \$100,000

Grant Title: *Are persister cells culprits of recurrent Clostridium difficile infections?*

Dr. Wu and his team continue their promising studies on treatment failures in *Clostridium difficile* infection. Their focus is on the genetic basis of *C. difficile* cells that linger in the body (persister cells) and potentiate recurrence of infection.

University of Virginia

Principal Investigator: Chongzhi Zang, Ph.D.

Grant Award: \$100,000

Grant Title: *Aberrant CTCF binding as an epigenetic signature of cancer*

CTCF (CCCTC-binding factor) is a multiple zinc finger protein that exerts diversified functions under different genomic contexts. The team’s preliminary work indicates that abnormal CTCF binding is correlated with clinical outcome. Dr. Zang and his team are beginning to test the hypothesis that aberrant CTCF binding is an epigenetic signature of cancer that indicates altered gene regulation and cancer progression.

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 **246** research grants totaling approximately **\$20.7 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.