**Commonwealth Health Research Board**
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**PRESS RELEASE Dated July 2, 2019**

**From the Commonwealth Health Research Board**

The Commonwealth Health Research Board [CHRB] has awarded **$1,399,997** in grants to 14 medical and health researchers in Virginia.

**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 opioid crisis has reached epidemic proportions in the United States, and in 2016 Governor McAuliffe declared opioid addiction in the Commonwealth to be a Public Health Emergency. Rural western VA repoı some of the highest per capita opioid abuse in the country. New non-opioid therapeutic alternatives to NSAIDs (Nonsteroidal Anti-inflammatory Drugs, e.g., ibuprofen) for the effective management of chronic pain are essential to limiting opioid overuse. The Buczynski group has identified a novel class of signals (12/15-lipoxygenase metabolites, 12/15-LMs) that contribute directly to (NSAID)-insensitive nociceptive behaviors in multiple pre-clinical pain models, and preliminary results revealed a novel receptor for 12/15 LMs. This project would characterize the 12/15-LM receptor, and screen potential lead compounds that block receptor activity. The ultimate goal is to enable drug discovery efforts for novel analgesics with minimal abuse potential and to mitigate risks of opiate misuse, diversion and addiction.

**Virginia Commonwealth University**
**Principal Investigator: Charles Clevenger, M.D., Ph.D.**
**Grant Award: $100,000**
**Grant Title: *HDAC6 as a Therapeutic Target in Breast Cancer***
Funding continues for Dr. Clevenger to explore a new target for drugs to treat breast cancer. Breast cancer is a major health problem in the US. Over 1000 Virginia women die of breast cancer each year. The PI and his team have identified histone deacetylase, HDAC6, and discovered that it can remove acetyl groups from proteins and thereby act as a signaling switch. The PI and his team hypothesize that HDAC6 globally controls breast cancer gene expression and growth, by functioning as an "oncogenic node". Phase I trials in myeloma patients have shown that small molecular inhibitors of HDAC6 are safe and could be therapeutically used in breast cancer patients. The team will conduct *in vitro* studies using the advance technique of immunoprecipitation sequencing (ChIP-Seq) in breast cancer lines to identify the genome-wide relationships between HDAC6/HMGN2/H1.2 on promoter/enhancer chromatin both in terms of occupancy and co-localization. Also planned are translational *in vivo* studies in a mouse model of breast cancer.

**Virginia Commonwealth University**
**Principal Investigator: Paul Dent, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Novel anti-sarcoma therapies***
Sarcomas, while relatively rare, are a heterogeneous group of tumors that are quite difficult to treat. The drug pazopanib is an approved therapeutic for sarcomas, and Dr. Dent has found that a class of drugs known as histone deacetylase inhibitors, including sodium valproate, increase the lethality of pazopanib in sarcoma cells. This CHRB project will use a mouse model of sarcoma tumors to continue studies of pazopanib and valproate, plus another FDA-approved inhibitor (crizotinib) to generate data that will ultimately support a Phase I clinical trial of the three-drug combination for treatment of this devastating type of cancer.

**University of Virginia**
**Principal Investigator: Brent French, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Bioengineering of Cardiac Regeneration In Situ after Myocardial Infarction***

Heart failure currently afflicts some 5.7 million Americans, and by 2030 this number will increase by 46%. The single most common cause of heart failure is heart attack (or myocardial infarction) which results in the irreversible loss of cardiac muscle. Current statistics show that ~790,000 people in the US have heart attacks each year. Of those, about 114,000 will ultimately die from heart failure. The overarching goal of this project is to combine recent advances in cardiology, radiology and gene therapy to demonstrate that cardiomyocytes can be genetically-reprogrammed to divide and replace the heart muscle lost during heart attack. This is important because the adult heart has essentially no capacity to repair itself after a heart attack. Instead, injured cardiomyocytes are replaced by scar tissue to prevent the heart from rupturing. If successful, this research will show that gene therapy can regenerate muscle tissue after heart attack.

**University of Virginia**
**Principal Investigator: Li Jin, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Could we treat acute back/leg pain with nanoparticle fullerene instead of steroid?***

Funding continues for Dr. Jin to explore new molecules/drugs for treating low back pain. Intervertebral disc herniation is the most common cause of low back pain which, in turn, is a leading source of disability in adults. Fullerenes are forms of carbon having a large spheroidal molecule consisting of a hollow cage of atoms, of which buckminsterfullerene was the first known example. Some fullerenes, including C60, C70 and C80 have been shown to be antioxidants due to delocalization of the π-electrons over the carbon cage, which can readily react with free radicals and subsequently deliver a cascade of downstream properties for numerous biomedical applications. The proposed research would characterize the anti-inflammatory effects of C80, a fullerene that the PI and his team has shown to have strong radical scavenging capability, anti-inflammatory effects and anti-oxidative effects. They plan to do in vitro and in vivo studies using C80 nanoparticles. If this approach is successful, it would point to fullerenes as possible new bases for anti-inflammatory drugs to treat low back pain and other chronic pain conditions.

**University of Virginia**
**Principal Investigator: Peter Kasson, M.D., Ph.D.**
**Grant Award: $100,000**
**Grant Title: R*apid identification of entry inhibitors and neutralizing antibodies for emerging viruses***

Zika virus infection is a critical public health problem. This proposal is for further development of a new microfluidic flow cell approach to discover antibodies and drugs that can inhibit the entry of Zika virus into cells (thus preventing infection); the improved technology should be adaptable to other viruses as well.

**University of Virginia**
**Principal Investigator: James Landers, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Diagnostic Assay for On-Site Detection of Bordatella pertussis***

*Bordetella pertussis*, the causative agent of whooping cough, infects millions of individuals worldwide each year and continues to be the world's leading cause of vaccine-preventable deaths. In recent decades, there has been an alarming resurgence of reported pertussis cases. A major contribution to addressing this problem would be an ability to rapidly detect *B. pertussis* during a suspected outbreak, enabling initiation of treatment, limitation of transmission and reduction in mortality. However, current methods require patient samples to be sent to centralized laboratories for analysis, and results are typically not available in time to support epidemiologic intervention. Instead, physicians and healthcare officials use presumptive antibiotic treatment until diagnostic results are available, thereby putting many individuals at risk unnecessarily. To address this challenge, this project would develop a portable "lab-on-a CD" microfluidic device to screen for the presence of *B. pertussis* DNA and allow for robust identification of infection in 20 min or less.

**Eastern Virginia Medical School**
**Principal Investigator: Albert Musto, M.D., Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Role of CD40L in Limbic Epilegtogenesis***
Funding continues for Dr. Musto to pursue his hypotheses that certain inflammatory processes are central in the cause and development of temporal lobe epilepsy. There is no cure for temporal lobe epilepsy, also termed, limbic epilepsy. Temporal lobe epilepsy is the most common form of epilepsy in adults. Between 4 and 10 cases occur in every 1,000 people. Available medical treatments are not effective in controlling some limbic seizures. Early mortality and numerous related medical problems make temporal lobe epilepsy a major medical problem in the US. Numerous studies, including those of the Dr. Musto, suggest that inflammation via immune system activity contributes to LE. This proposal is based on the idea that temporal lobe epilepsy develops because immune processes alter neuronal connectivity in a region of the brain called the hippocampus. Evidence of modification of neuronal dendritic spines will be sought with special focus on the protein, CD40L, which is primarily expressed on activated immune cells, known as T cells. If successful, this project would move epilepsy research into considerations of inflammatory and immune processes and point to new therapeutic approaches.

**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 (ALI). Although mechanical ventilation remains the last resort of treatment, it carries risks of lung cell injury, high mortality, and morbidities. *Pseudomonas aeruginosa* is an opportunistic pathogen causing a wide range of acute and chronic infections and is a major cause for Ventilator-Associated Pneumonia (VAP). The ineffectiveness of conventional antibiotics therapy among severe pneumonia-induced lung injury patients appeals for novel options of treatment. One such candidate is Cannabinoid receptor-2 (CB2R) that is predominantly expressed in immune cells. Synthetic agonists like endocannabinoids (that do not generate undesired psychotic effects) can be used to activate these CB2Rs leading to the display of anti-inflammatory functions. Considering the unique stance of CB2R as a potential novel therapy for bacterial pneumonia, the hypothesis that CB2R activation can ameliorates bacterial pneumonia induced lung inflammatory/injury (using a well-validated mouse model) will be tested in this project.

**Virginia Commonwealth University**
**Principal Investigator: Swati Palit Deb, Ph.D.**
**Grant Award: $99,997**
**Grant Title: *Targeting mutant p53-dependent checkpoints of genome duplication in lung cancer***
The American Cancer Society estimated that the number of new lung cancer cases for this year alone is 234,030 in the US, and 5,860 in Virginia. Over 60% of these patients will not survive, underscoring the extremely poor efficacy of current lung cancer treatment. Gain-of-function (GOF) mutations of tumor suppressor p53 are very frequent (up to 70%) in lung cancer and establish resistance to chemo- or radiotherapy and are essential for oncogenesis. Accordingly, the tumorigenic ability of human lung cancer cells lines is drastically reduced or eliminated when endogenous mutant p53 is disabled. In a recently published study (highlighted by the Journal of Clinical Investigation), we demonstrated that GOFp53 activates checkpoint signaling to establish its oncogenic activities**.** Here we propose to determine the mechanism by which GOFp53 activates checkpoint signaling to establish dependency in lung cancer cells and evaluate the therapeutic efficacy of GOFp53-induced checkpoint signaling inhibitors, which has not been explored.

**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***
Complete cure of cancer is never achieved for most advanced colorectal cancer in part because of the inability of the standard chemotherapy and other targeted drugs to eradicate the 'seeds of cancer', also called cancer stem cells (CSCs). We have demonstrated, for the first time that specific short sequence of heparin (HSO6) selectively eliminates CSCs. But, HSO6 cannot be a candidate drug as it is very difficult and expensive to purify it. However, we have succeeded in synthesizing a non-sugar mimetic of HSO6 – G2.2 which is easy to make, homogenous, and rather inexpensive. Using primary human CSCs, innovative animal models, and advanced in vitro methods to study stem cells, we will determine the efficacy and toxicity of G2.2 as well as its potent analogs against colon CSCs in conjunction with FDA approved colon cancer therapies. This, in our opinion, is a major step towards achieving complete cancer cure.

**Virginia Commonwealth University**
**Principal Investigator: Liya Qiao, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Role of TrkB.T1 in Bowel and Urinary Bladder Comorbidity***
This grant award will allow the investigator to explore a new neurological mechanism in the spinal cord which is, potentially, the cause for the sensation of bladder pain in patients suffering from irritable bowel syndrome. The association between bladder hypersensitivity and irritable bowel is observed in millions of patients, although the bladder is actually normal. The investigator will test whether specialized cells in the spinal cord (glial cells) are stimulated in episodes of irritable bowel and subsequently transmit pain signals to neighboring nerves, which culminates in registering them as bladder pain. The experiments will utilize sophisticated neurological and biochemical approaches. They may reveal new therapeutic targets for relieving patients from this comorbidity.

**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 are a large group of different malignancies and account for roughly 10% of all cancers diagnosed in the United States each year. The complexities of blood cancer diagnosis and treatment create a critical need for molecular methods that can be applied in less specialized medical settings such as community hospitals. To address this need, it is planned to use a very simple "DNA barcoding" approach to detect chromosome rearrangements in blood cancers. This method will be as accurate as all existing alternatives, but much quicker and substantially less costly. The technology can significantly improve outcomes for patients in underserved populations.

**University of Virginia**
**Principal Investigator: Martin Wu, Ph.D.**
**Grant Award: $100,000**
**Grant Title: *Are persister cells culprits of recurrent Clostridium difficile infections?***
*Clostridium difficile* infection (CDI) causes mild to life-threatening diarrhea. It poses a major healthcare burden to the global population primarily affecting individuals treated with antibiotics. The biggest challenge facing CDI is the high rate of treatment failure or recurrence, which has increased remarkably in the past two decades. Persister cells (dormant or slow-growing bacteria) are known to survive antibiotic treatment. However, whether they are a major cause of recurrent CDI remains unclear. We hypothesize that persister cells play an important role in recurrent CDI. Specifically, we aim to 1) determine whether the presence and abundance of persister cells are significant risk factors for CDI recurrence, 2) determine the genetic basis of persistence by sequencing genomes of the persister cells. This study will be the first to quantitatively determine whether persister cells are significant risk factors for recurrent CDI and therefore has the potential to shift the paradigm in therapeutic strategies.

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 **230** research grants totaling approximately **$19.2 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 **$35 million** in additional private and federal grant funds to further their research studies.