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From the Commonwealth Health Research Board

The Commonwealth Health Research Board [CHRB] has awarded **$950,916** in grants to 10 medical and health researchers in Virginia. In addition, the CHRB in collaboration with the Virginia Biosciences Health Research Corporation [VBHRC], has contributed **$200,000** to Eastern Virginia Medical School for a jointly funded research project. A description of these grants include:

Eastern Virginia Medical School
Principal Investigator: Frank Castora, Ph.D.
Grant Award: $100,000
Grant Title: *The role of differentially expressed mitochondrial energy production genes as regulators of amyloid precursor protein processing in Alzheimer's disease*

This new grant award will enable Dr. Castora and colleagues to pursue their recent finding of abnormal expression of a number of genes in the brains of Alzheimer patients. These genes are important for energy production and are also involved in the development of protein formations known as plaques that compromise brain cell function. The goal of this research is to employ gene editing technology to identify new targets for drugs that could delay the onset of Alzheimer's Disease and/or reduce its severity.

Christopher Newport University
Principal Investigator: Kathryn Cole, Ph.D.
Grant Award: $50,921
Grant Title: *Anticancer Drug Design: Structure and Function of New HDAC8-Depsipeptide Complexes*

This new study will investigate the action of two drugs approved for the treatment of cancer. Dr. Cole and her team intend to increase the understanding of how the anti-cancer drugs, Spiruchostatin A and Xyzistatin, inhibit histone deacetylases. Histone deactylases are crucial enzymes involved in progression of many types of cancer. It is hoped that Dr. Cole's work will lead to new drugs for better cancer treatment.

Virginia Commonwealth University
Principal Investigator: Nicholas Farrell, Ph.D.
Grant Award: $100,000
Grant Title: *Targeting Triple Negative Breast Cancer*

The work supported by this new grant aims at the challenge of eliminating the mortality associated with metastatic triple negative breast cancer by developing safe and effective interventions. Key objectives are preventing spread of the cancer tumor (metastasis) and limiting the primary tumor to a relatively localized site, thereby allowing for more effective intervention at that site. Dr. Farrell and his team conceptualize new treatments based on drugs that act on multiple levels overcoming limitations of single-targeted drugs. Development of new medicines which may simultaneously attack a range of targets, and with potential for personalized medicine based on genetic profile, would represent a significant addition to therapy for triple negative breast cancer.

Virginia Commonwealth University
Principal Investigator: Babette Fuss, Ph.D.
Grant Award: $100,000
Grant Title: *Regulation of myelin repair: the role of the actin cytoskeleton*
Research supported by this new grant is aimed at stimulation of endogenous progenitor cells to develop therapies for diseases in which the central nervous system (CNS) myelin sheath is affected. The most prominent of such diseases is Multiple Sclerosis (MS), but myelin injury may also play an important role in a number of neuropsychiatric diseases. Investigations will focus on a conceptually novel molecular mechanism, namely the role of a calcium/calmodulin-dependent protein kinase IIß (CaMKIIß)-actin cytoskeleton axis, in regulating myelin repair in the CNS. Actin cytoskeleton regulatory mechanisms as part of the regulation of CNS remyelination are understudied despite known defects in such mechanisms in MS. The studies planned may lead to novel therapeutic targets for stimulating CNS repair in MS and other conditions that involve injury to the myelin sheath.

Virginia Commonwealth University Principal Investigator: Matthew Hartman
Grant Award: $100,000
Grant Title: *Development of an oxygen-independent strategy for targeted phototherapy of cancer*
This grant will continue our support for promising studies to diminish side effects of cancer therapy by methods that would activate an anticancer drug only in the vicinity of the tumor. Dr. Hartman and his colleagues are developing a technology that uses red light illumination at the site of a tumor to release into cells an anticancer drug, doxorubicin. A form red light releasable of doxorubicin, Pc4-Dox, has been synthesized. Tumor studies in animals have begun.

Virginia Polytechnic Institute and State University
Principal Investigator: Jia-Qiang He, Ph.D.
Grant Award: $99,995
Grant Title: *Biodegradable Microcapsules Containing Stem Cell Derived-Biological Pacemaker to Treat Mice with Bradycardia*
This grant will continue research on stem cell-derived beating biological pacemakers in combination with microencapsulation for the treatment of cardiac arrhythmias. The investigators to date have established mouse colonies, generated beating cardiomyocytes and aggregates from pluripotent stem cells, generated of alginate microcapsules, modified alginate through chemical reaction and gamma irradiation, and cell viability assay using fluorescent microscopy. Successful completion of the study would establish a basis for stem cell/biomaterial-based personalized regenerative medicine to treat cardiovascular diseases. Potentially, the approach could be applied to the treatment of other disorders, such as traumatic brain injury.

Virginia Commonwealth University
Principal Investigator: Masahiro Sakagami, Ph.D.
Grant Award: $100,000
Grant Title: *A salvianolic acid B derivative: HIF1a/STAT3-directed VEGF stimulation for lung repair in emphysema*
Emphysema progressively destroys lung's alveolar structures, leading to death, yet remains incurable, as no drug can repair its damaged lungs. This grant will continue studies on SMND309-ME, a novel drug candidate for stimulating vascular endothelial growth factor (VEGF). Data to date indicate that SMND309-ME induces lung cell proliferative and migratory promotion and inhibition against induced cell death. The team plans to complete all the proposed in vitro studies in 2017 including demonstration of concentration-dependent activities, mechanistic clarification using pharmacologic inhibitors of HIF1a, STAT3 and VEGF signaling, and promotion of progenitor cell migration and differentiation.

University of Virginia
Principal Investigator: Weibin Shi, Ph.D.
Grant Award: $100,000
Grant Title: *Characterization of reticulocalbin 2 as a major gene contributing to atherosclerosis*
Atherosclerosis is the primary cause of heart attack and stroke and inflammatory responses initiated by oxidation of bad cholesterol (LDL) trapped in the arterial wall are a central feature of atherosclerosis. No effective medicines are available to stop the inflammatory process. Research supported by this new grant will use mouse strains in which Dr. Shi and colleagues have identified a major locus, Ath29, on chromosome 9 for atherosclerosis. The hypothesis to be tested is that reticulocalbin 2 (Rcn2) is a gene that may contribute significantly to atherosclerosis. The investigators will make and characterize arterial cell-specific knockout mice to define the role of Rcn2 in atherosclerosis and arterial inflammatory responses. Successful completion of the project may derive a novel therapeutic target for treatment of atherosclerosis.

Virginia Commonwealth University
Principal Investigator: Erdem Topsakal, Ph.D.
Grant Award: $100,000
Grant Title: *Implantable Biosensors for Long-Term Continuous Glucose Monitoring*
This grant will continue the design and implementation of subcutaneous, ultra-sensitive, miniature ZnO-based sensors for long-term continuous glucose monitoring. Initial studies indicated that there is little to no degradation of the sensor using in vitro simulated body fluid. In vivo studies of both degradation and cytotoxicity are underway in rats. In vivo studies revealed that insulation designed and applied to biodegrade in stages can be used to activate multiple sensors on an implantable-chip platform. Once completed, the team will move on to multiple sensor development and growing nanowires and functionalizing the sensors for glucose sensing. In parallel, the team is working on an antenna and telemetry circuitry that will provide data transmission from the implant to a receiver outside.

Virginia Polytechnic Institute and State University
Principal Investigator: Bin Xu, Ph.D.
Grant Award: $100,000
Grant Title: *Molecular mechanisms of amylin as a novel contributor to Alzheimer's disease*
This grant will continue studies aimed at the close link between obesity-related type 2 diabetes and the risk for Alzheimer's disease. The investigators have focused on amylin peptides, typically formed in the pancreas, which can possibly travel to the brain where they can form aggregates termed amylin amyloids. The studies employ interdisciplinary, mechanistic studies of amylin amyloid-induced toxicity towards human neurons and toxicity inhibition by rationally designed small molecule inhibitors in cells and in an animal model. It is hoped that results will serve as basis for a major research program to elucidate molecular connections between diabetes and Alzheimer's disease as well as to devise potential treatment strategies.

The CHRB is also pleased to announce joint funding for a **collaborative project** with the Virginia Biosciences Health Research Corporation [VBHRC]:

Eastern Virginia Medical School and George Mason University
Principal Investigator: Jerry Nadler, Ph.D., Eastern Virginia Medical School
Grant Award – Funding from CHRB: $200,000
Grant Title: *Characterization of GUT Microbiome and Liver Cell Populations to Accelerate Commercialization of the Diamond Mouse Model*
This new grant will support Dr. Jerry Nadler's research on nonalcoholic fatty liver disease (NAFLD) and its serious progression to non-alcoholic Steatohepatitis (NASH), which constitute a major public health problem. There are no approved therapies. An impediment to research progress is the lack of an animal model that develops a disease resembling human NAFLD and NASH. Dr. Nadler and his team will conduct studies on a promising animal model, the DIAMONDTM mouse, which exhibits key components of NAFLD and NASH in humans including being triggered by the high-fat, high-sugar "Western" diet. The research to be funded will detail molecular and cellular changes in live liver cells and map disease progression in the gut microbiome and metabolome. It is hoped that results will further validate this disease model and permit testing of new therapies.

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 202 research grants totaling almost **$16.5 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 **$32 million** in additional private and federal grant funds to further their research studies.