BRADLEY-HERZFELD CATALYST AWARDS – SUMMER 2015

Diagnosing Early Stage Intervertebral Disc Degeneration ($41,000)

Naira Campbell-Kyureghyan, Ph.D., Associate Professor and Chair for the Department of Industrial and Manufacturing Engineering, Mechanical Engineering

Dr. Naira Campbell-Kyureghyan applies her expertise in biomechanics of the spine and hand to developing ergonomic tools that can reduce job-related injuries. Snap-on Incorporated recently licensed a wrench designed by her lab members which is now in production for thousands of pre-orders by gas utility companies. She created the Consortium for Advanced Research in Gas Industries (CARGI) to improve safety in the gas industry through ergonomics, for which membership has grown to 200 industry partners. She has led multiple industrial service and research programs over the last five years and has been a contractor on several small business innovative research (SBIR) grants.

Better Diagnosis of Lower Back Pain. It is estimated that approximately 50 million people in the U.S. suffer from back pain. The growth of the spinal surgery products is driven by growing numbers of people with degenerative disc disease. The disease is caused by gradual disc damage and often results in disc herniation and chronic, debilitating lower back pain. It is most common in otherwise healthy people in their 30s to 40s and affects about half of the US population age 40 and older. Unfortunately current diagnostic methods do not allow for early detection when preventative measures might be effective. Recent research has developed MRI techniques that correlate well with detection of late stage disc degeneration, but these methods are not suitable to detect early stage disease. It is known that 80% of lower back pain is misdiagnosed. One of the possible explanations is that the diagnostic imaging is not well correlated with the back pain or with early stages of intervertebral disc (IVD) degeneration.

Understanding Fundamental Causes. Over the past several decades, researchers have developed two theories regarding the causes of disc degenerations. One hypothesizes that scar tissue builds up in the endplates due to micro fractures. The second describes an increase in porosity and permeability at late stages of degeneration. This project aims to determine characteristics of the discs during degeneration. The ultimate goal is to use this information to develop novel diagnostic methodologies and tools to improve low back pain diagnosis and prevention.

Improved Diagnosis and Treatment. The U.S. market for back pain drug treatment is predicted to rise to almost $23B in 2018 while the global MRI market was estimated to be about $7.5B by 2015. The most common procedures were for brain, head, and neck with spine and extremity scans running a close second in 2010. The goal of this research is to provide new methods for early detection of intervertebral disc disease and license this new approach to a company that produces MRI contrast agents. The American Academy of Physical Medicine and Rehabilitation reports that procrastination is not the best avenue to take when experiencing back pain. It is extremely important to treat low back pain at the onset in order to avoid aggravation and compounding the problem.

UWM Innovation Accelerator. The UWM Innovation Accelerator building in Wauwatosa houses her primary research activities, including a micro X-ray CT scanner which will be used to support these studies.

New Drugs to Enhance Memory Formation ($50,000)

Karyn Frick, Ph.D., Professor, Department of Psychology

Dr. Karyn Frick's research program studies how aging, sex-steroid hormones, and environmental factors affect hippocampal function and hippocampal-dependent memory. Her goal is to identify how these factors affect the cellular and molecular mechanisms underlying memory formation. Memory deficits are common to aging and neurodegenerative diseases like Alzheimer's disease. Because the U.S. population is rapidly aging, the incidence of memory dysfunction will increase exponentially. A promising avenue for treatment of memory impairment is the use of histone deacetylase inhibitor drugs (HDACis). Histone deacetylase enzymes are intimately involved in the organization of DNA structure and in reducing the activity of many genes. HDACis would thus lead to the increased activity of numerous genes. Dr. Frick and others have found that HDACis enhance learning and memory in mouse models of Alzheimer's disease.

Novel HDACis May Overcome Solubility and Toxicity Problems. Small molecule HDACis have previously been approved for the treatment of certain cancers, but their effectiveness is limited by unwanted toxicity and/or poor solubility – key aspects to making a drug work in humans. Dr. Frick's colleague on this project is Dr. Mahmun Hossain, Associate Professor, Department of Chemistry and Biochemistry. Dr. Hossain and his colleagues at UWM have synthesized a small library of potent HDACi molecules that show good solubility and low toxicity in animal models. The goal of this catalyst grant study is to test lead compounds to determine their ability to enhance the formation of two types of memory using a well-established mouse model of memory formation – studies that will point toward treatment for memory loss.

Research Design for Memory Tasks. Dr. Frick will employ an animal model using mice to test the effects of the new drugs on memory tasks. Mice will receive training in two memory tasks. Regions of the mouse brain important in these memory types will be examined to determine the correlation with HDACi activity.

Significant Market for Memory Enhancing Drugs. The Alzheimer's disease market is currently estimated at $5B annually and the global economic impact of Alzheimer's disease is shown by the worldwide cost of $640B. The global sales of drugs to treat progressive dementia with other neurological abnormalities are expected to reach $900M by 2017. Currently there are only a handful of memory-enhancing drugs on the market and there are no drugs that can cure Alzheimer's disease.

Development of New HDAC Inhibitors as Anticancer Agents ($35,000)

M. Mahmun Hossein, Ph.D., Associate Professor, Department of Chemistry and Biochemistry

Dr. Mahmun Hossain's group is interested in developing novel organic reactions that will simplify the synthesis of existing biologically active compounds and also enable the generation of a new class of therapeutics for human diseases. Over the past two years he has been collaborating with Dr. Eric Cheng to synthesize novel HDAC inhibitor compounds derived from natural HDAC inhibitor compounds discovered by Dr. Cheng's laboratory. Dr. Cheng's original compounds TDPA and TDPB, while effective at killing cancer cells in the lab, were much too toxic to healthy cells to be utilized as a drug. Hossain and his colleagues are building on that experience to develop new compounds that overcome these problems.

Promising Preliminary Results for Potential Cancer Drugs. Dr. Hossain and his team have synthesized new compounds, and tested for their activity as inhibitors of several forms of HDACs *in vitro* (performed in cell culture assays). The new inhibitors demonstrated strong anti-growth effects against tumor cell lines. Some lead compounds show great promise based on their low toxicity.

Project Objective – Obtain Key Data in Mouse Tumor Model. Initial studies of lead compounds show great promise in prohibiting growth in cancer cell lines, and the compounds do not appear to be toxic to mice at high doses. The next experiments will be crucial in determining the specificity of the drugs in cells, determining the metabolic stability of these compounds as potential drugs, and assaying whether the compounds can lead to tumor regression in a mouse model for colon cancer. In order to attract attention from pharmaceutical companies for potential licensing, mouse tumor data will be of great importance.

Market and Commercialization Opportunities. The global market for histone deacetylase inhibitors is expected to grow to $950 million by 2018. Promising therapeutics have already shown potential for oncology and current candidates are also being tested in diseases including neurological ailments, heart disease, HIV infections, and more.

Intelligent Algorithms to Manage Green Buildings with Smart Grid Technologies
($55,000)

Lingfeng Wang, Ph.D., Associate Professor, Electrical Engineering & Computer Science

Dr. Lingfeng Wang's major research interests include power system reliability and cybersecurity, renewable energy integration, intelligent and energy-efficient buildings, electric vehicles integration, microgrid analysis, cyber-physical systems, and industrial automation and manufacturing. He also directs the Cyber-Physical Energy Systems Laboratory at UWM. In a previous position he was an Associate Transmission Planner at the California Independent System Operator.

New Opportunities for Energy Efficient Buildings. Buildings consume a large portion of the world's energy. This project builds on a convergence of new systems and technologies available in powering and controlling buildings – these include different energy resources (i.e., conventional and renewable), new operating modes and advanced sensors. Building on these resources, Dr. Wang is developing a new class of cyber-physical systems which can take advantage of these technologies and adapt to achieve high energy efficiency while maintaining comfort for the buildings occupants.

Project Goals – Smart Building Controls. A smart building can be regarded as a complex adaptive system, and its control and optimization are particularly challenging. This project combines two important areas, smart buildings and microgrids, to advance buildings of the future. The project includes consideration of building occupants through comfort factors. One of the goals of this project is a building control system that operates in a dynamic environment.

Market Overview. There is a growing emphasis on reducing the carbon footprint and energy conservation and therefore there is a need for new infrastructure design to help support this urbanization. The "smart city" market is expected to have a larger demand in the near future. This market includes smart homes, intelligent building automations, energy management systems, citizen services, smart transportation systems, and security systems. Technologies involved in smart cities would be electric vehicles, traffic management, smart grids, smart metering, and use of renewable energy. The market is expected to grow to $1.1B by 2019.