Summaries of UW ICTR Basic & Clinical Pilot Awards, 2013

PI: Nathan Artz, PhD, UW School of Medicine & Public Health  
Collaborators: Richard Kijowski, UW SMPH; Kevin Koch, GE Healthcare  
Title: Advanced Magnetic Resonance Methods for Imaging Near Metallic Implants  
Summary  
Magnetic Resonance Imaging (MRI) is widely regarded as the best non-invasive imaging method to evaluate a large number of musculoskeletal disorders; unfortunately, the ability of conventional MRI to detect these abnormalities is limited in the presence of metal due to magnetic field inhomogeneities. With the growing number of knee and hip replacement surgeries, the need to improve diagnostic imaging near metallic implants to evaluate prosthesis-related complications is increasing rapidly. This overall goal of the research is to develop novel methods for distortion-free MRI.

PI: Joshua Lang, MD, UW School of Medicine & Public Health  
Collaborator: David Beebe, UW College of Engineering  
Co-Funding: UW Carbone Cancer Center  
Title: Genomic Studies of Circulating Tumor Cells: Novel Metastatic Biomarkers  
Summary  
Easy access to tumor samples, without the need for painful and expensive tumor biopsies, would allow repeated interrogation of patient samples to identify mechanisms of therapeutic resistance and personalize treatments. Circulating tumor cells (CTCs), although occurring rarely in blood, represent a potential source for a “fluid biopsy”. The team is utilizing a novel platform to capture these CTCs from blood and isolate nucleic acids for assay. Such fluid biopsies could be used as personal biomarkers to identify and predict therapeutic response and resistance to anti-cancer therapies.

PI: Vivek Prabhakaran, MD, PhD, UW School of Medicine & Public Health  
Collaborators: Justin Williams, Mitchell Tyler, UW College of Engineering; Justin Stattin, Veena Nair, UW SMPH; Dorothy Farrar Edwards, UW School of Education  
Title: A Closed-loop Neural Activity-triggered Stroke Rehabilitation Device  
Summary  
A majority of individuals who have survived a stroke suffer from some degree of persistent motor deficits and behavioral dysfunction. This proposal investigates a new method that adopts a multi-modal approach, is non-invasive, and aims to restore brain function while improving corresponding motor function. By combining multiple modes of functional neural stimulation, and monitoring brain reorganization changes using fMRI, we hope to identify stroke patients who can successfully use the integrated system for improving motor function and activities of daily living.

PI: Ryan Herringa, MD, PhD, UW School of Medicine & Public Health  
Collaborators: Ned Kalin, Marilyn Essex, UW SMPH; Richard Davidson, UW Letters & Science  
Title: Neural Basis and Treatment of Youth Post-traumatic Stress Disorder  
Summary  
In contrast to adult PTSD, very little is known about the neural correlates of emotion regulation in pediatric PTSD, and no reported studies have examined treatment effects on this circuitry. This pilot study aims to address these knowledge gaps by examining baseline differences in emotion regulation circuitry in pediatric PTSD compared to healthy youth, and examining feasibility of detecting longitudinal, treatment-associated changes in this population.
The project involves collaboration with a school-based trauma screening and treatment program, thereby leveraging community and academic resources together.

**PI: David McCulley, MD, UW School of Medicine & Public Health**  
Collaborators: Xin Sun, Marlowe Eldridge, Peiman Hematti, UW SMPH  
Co-Funding: UW Stem Cell & Regenerative Medicine Center  
**Title:** Congenital Diaphragmatic Hernia: Genetic Basis and Stem Cell Therapy  
**Summary**  
Infants born with congenital diaphragmatic hernia (CDH) often die early in life due to severe pulmonary hypoplasia and pulmonary hypertension. Given the lack of targeted therapies to address pulmonary hypoplasia and pulmonary vascular disease in patients with CDH, the researchers propose to use a mouse model to investigate the role of genetic mutations on lung development and pulmonary vasculature. Understanding how mutations impact lung development can lead to new therapies, such as treatment with mesenchymal stem cells.

**PI: Paul Sondel, MD, UW School of Medicine & Public Health**  
Collaborators: Amy Erbe-Gurel, KyungMann Kim, Eneida Mendonca, UW SMPH  
**Title:** In Depth Delineation of FcγRIIc and FcγRIIIa Genotypes and Potential Clinical Implications  
**Summary**  
Unlike most cancer therapies that direct toxic agents toward the tumor, most cancer immunotherapies rely on certain host components to recognize and destroy the tumor. This study addresses important questions concerning intrinsic patient genotype that predict response to immunotherapeutics. The team will develop new methodology to accurately determine differences in patient genotypes and correlate these genetic differences with the patient’s innate immune system to effectively mediate clinical benefit.

**PI: Kris Penniston, PhD, UW School of Medicine & Public Health**  
Collaborators: Thomas Crenshaw, UW College of Agricultural and Life Sciences; Stephen Nakada, UW SMPH  
**Title:** A porcine model to study calcium oxalate urolithiasis: from the barn to the bedside  
**Summary**  
Patients who form kidney stones have reduced quality of life due to pain, anxiety and depression, loss of work and family time, medical costs, and side effects from medications and/or surgeries. Despite a lack of supporting evidence, dietary oxalate restriction is commonly recommended for these patients. Using a pig model system, the interdisciplinary group of researchers will address the question of whether oxalate restriction does indeed decrease urinary oxalate excretion and calcium oxalate stone risk, while generating evidence regarding nutrition therapy for calcium oxalate stone prevention.

**PI: Nathan Sherer, PhD, UW School of Medicine & Public Health**  
Collaborator: Ann Palmenberg, UW SMPH  
**Title:** Characterization of a Novel Block to HIV-1 Replication  
**Summary**  
The lack of an HIV-1 vaccine, issues of multi-drug resistance and complications from current therapies emphasize the need to identify new virus-host interfaces to inform the development of novel antiretroviral strategies. This study aims to elucidate new details of HIV viral replication and potentially inform the development of antiviral strategies capable of disrupting the virus. Moreover, the focus of these investigations, CRM1, is an emerging target for anticancer therapeutics and plays important roles in the life cycles of many additional pathogenic human viruses, including influenza.
**PI: Thaddeus Golos, PhD, UW School of Veterinary Medicine**  
**Collaborator: Marina Emborg, UW SMPH**  
**Title: Transgenic marmosets for translational research**  
**Summary**  
Nonhuman primates offer the most appropriate experimental model for many areas of human biomedical research, particularly in reproductive biology, immunology and transplantation, and perhaps most prominently, neurological disease. The long term goal of this work will provide investigators with transgenic and genetically modified common marmosets as platforms for translational research, particularly in the treatment of diseases for which nonprimate species are less suitable models.

**PI: K Craig Kent, MD, UW School of Medicine & Public Health**  
**Collaborator: Michael Hoffman, UW SMPH**  
**Title: HTS on Smooth Muscle vs. Endothelial Cells for Anti-Restenosis Drugs**  
**Summary**  
In current clinical practice, drug-eluting stents with inhibitors of smooth muscle cell (SMC) proliferation have been somewhat effective in reducing restenosis in the coronary circulation. Unfortunately, these drugs also inhibit reestablishment of the vessel’s protective endothelial cell (EC) lining. This work will use a high throughput screening strategy to discover drugs that selectively and potently inhibit SMC proliferation, while leaving growth of the ECs unaffected.

**PI: Michael Kim, MD, UW School of Medicine & Public Health**  
**Collaborator: James Svenson, Umberto Tachinardi, Eneida Mendonca, UW SMPH; Jocelyn DeWitt, Sandra Clark, UW Health**  
**Title: Development and Evaluation of Point of Care Clinical Trial Alert Application**  
**Summary**  
The collaborative team will develop and implement a 'Proof of concept Point of Care - Clinical Trial Alert Application' (POC-CTAA) using Health-Link and evaluate its efficacy by measuring patient recruitment efficiency of existing clinical trials in the Emergency Department. The system will create an alert in real time based on triggers that include demographic information, orders placed, and abnormal lab results. After implementation, post-recruitment data will be gathered, including numbers of eligible patients, identified patients, patients approached, and participants enrolled in clinical studies.