Summaries of **UW ICTR Funded Clinical and Type 1 Translational Research Pilot Awards, 2009**

An Arsenic-Based Platform for IGF1R Targeted PCa Imaging
PI: Weibo Cai, UW School of Medicine & Public Health (SMPH)
Collaborator: Robert Nickles, SMPH
An interdisciplinary team with expertise in radiology, chemistry, and cancer biology will develop a unique molecular imaging technique to aid in diagnosis and treatment of prostate cancer. The new method utilizes various isotopes of arsenic to bind a receptor protein (insulin-like growth factor, IGF1) present on the surface of tumor cells. Non-invasive imaging of IGF1R will allow a tailored clinical approach for the treatment of prostate cancer, as well as other cancers and diseases involving IGF1R. The UW Carbone Cancer Center is co-sponsoring the project.

The Design and Proof of Principle for a Novel Implantable Limb Lengthening and Deformity Correction Device
PI: James McCarthy, UW School of Medicine & Public Health (SMPH)
Collaborator: Heidi-Lynn Ploeg and William Murphy, UW College of Engineering
With support from the Coulter Translational Research Partnership in Biomedical Engineering, this research award will aid in the development of an implantable device to correct leg length discrepancies in children. Currently, only external devices are available, which universally lead to complications including pain, infection, and limited motion. Proof of concept may allow similar devices to be adapted to other conditions.

Polymorphisms in Cytochrome b5 and its Reductase, and Risk of Sulfonamide Hypersensitivity
PI: Lauren Trepanier, UW School of Veterinary Medicine (SVM)
Collaborator: Catherine McCarty and Steven Yale, Marshfield Clinic Research Foundation (MCRF)
ClinSulfamethoxazole (SMX) is an inexpensive and effective antimicrobial agent. Nonetheless, safe use is hindered by delayed drug hypersensitivities that can lead to severe complications, including death. Investigators from both the UW Madison and Marshfield Clinic will collaborate to determine genetic and biochemical factors contributing to SMX hypersensitivities, thereby allowing health care providers to prescribe SMX with greater confidence.

The Role of Aβ and Isoflavones in Audiogenic Seizures
PI: Cara Westmark, UW Graduate School (GS), UW School of Medicine & Public Health (SMPH)
Collaborator: James Malter, SMPH
Although seizures often occur in conjunction with neurological disorders, the causal mechanisms are not well understood. This research will examine the potential link between dietary isoflavones and rates of seizure induction and(or) neuronal cell morphology. Establishment of a link may provide a dietary intervention to decrease the rate of seizures.

Plasticity Changes in the Brain after a Stroke
PI: Vivek Prabhakaran, UW School of Medicine & Public Health (SMPH)
Collaborator: Justin Stattin, Dorothy Farrar Edwards, JoAnne Robbins, and Sterling Johnson, SMPH.
Stroke is the leading cause of long-term disability in the US. An interdisciplinary research team will examine changes in the human brain during recovery from stroke using functional Magnetic Resonance Imaging (fMRI) and both cognitive and behavioral performance measures. The overall goal is to elucidate stroke related functional changes in the brain and to develop fMRI as a tool to guide stroke recovery therapies.

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Development of a Non Human Primate Model of Heart Dysautonomia
PI: Marina Emborg, UW School of Medicine & Public Health (SMPH)
Collaborator: Timothy Kamp and James Holden, SMPH; Heather Simmons, GS.
Parkinson's disease (PD) impacts more than just movement, as neurons of the autonomic nervous system also degenerate. As a result, patients develop cardiovascular symptoms such as arrhythmias that do not respond to anti-PD treatments targeted toward muscular symptoms. The aim of this research is to develop a non-human primate model of heart dysautonomia as a means to assess neurodegeneration, as well as potential treatments. The Wisconsin National Primate Research Center is partnering with the ICTR to fund this research.

Sclerostin, the Local Regulator of Bone Mineralization in Hypophosphatemic Animal Models
PI: Baozhi Yuan, UW School of Medicine & Public Health (SMPH)
Collaborator: Marc Drezner, SMPH
Bone formation is a complex process involving numerous regulatory factors and optimum phosphorus and calcium levels. Using animal models, Dr. Yuan will examine the effects of a negative regulator of bone mineralization. Understanding the molecular basis of mineralization will likely identify key therapeutic targets for intervention in human diseases such as osteomalacia and rickets.

Immunogenicity of Nanoparticles used in Drug Delivery
PI: Sandro Mecozzi, UW School of Pharmacy (SOP).
Collaborator: Rebecca Johnson, SVM; Ralph Albrecht, UW College of Agriculture & Life Sciences.
Nanoparticles are increasingly being used in drug delivery and therapeutics, despite limited knowledge of their toxicological and environmental safety. Researchers from Pharmacy, Veterinary Medicine, and Animal Sciences will characterize the immunogenicity of nanoparticle-based drug delivery platforms in both cell-free and canine systems. The extreme immunosensitivity of dogs makes them particularly valuable for identifying potential adverse responses in humans. Understanding the mechanism of nanoparticle immunogenicity is urgent because of their increasing presence in the environment.

High-throughput Screening of Potential Prognostic and Protein Biomarkers in Mantle Cell Lymphoma
PI: David Yang, UW School of Medicine & Public Health (SMPH)
Collaborator: Brad Kahl, Catherine Leith, Jens Eickhoff, SMPH; Gene Shaw, MCRF.
Clinical outcomes of mantle cell lymphoma vary widely. Differentiating patient disease risk profiles is crucial for designing appropriate therapies. The aim of this research is to develop rapid prognostic screening assays using data from gene expression profiles. The UW Carbone Cancer Center is providing matching funds for the research team of UW Madison and Marshfield Clinic investigators.

Inner Ear Hair Cell Generation using Directed Differentiation of Human Embryonic Stem Cells
PI: Samuel Gubbels, UW School of Medicine & Public Health (SMPH)
Collaborator: Clive Svendsen, SMPH; Richard Smith, University of Iowa.
Most cases of hearing loss in humans result from loss of inner ear hair cells; once lost, these cells do not regenerate, leading to permanent deafness. This research will focus on a novel approach using human embryonic stem cells to generate sufficient new hair cells for subsequent transplantation. Initial work will focus on methodology to induce stem cell differentiation, and characterization of resultant hair cells. The Waisman Center is funding the research in conjunction with the ICTR.

Cerebrospinal fluid (CSF) Biomarkers in Alexander Disease
PI: Lingjun Li, School of Pharmacy (SOP)
Collaborator: Albee Messing, SVM, GS.
Alexander disease is a fatal neurodegenerative disease caused by mutations in the astrocyte protein GFAP. Generally present at only low levels in cerebrospinal fluid (CSF), preliminary data suggest GFAP may be elevated in CSF from patients with Alexander disease. The long-term goal of the research is to identify easily quantified CSF biomarkers indicative of disease progression and severity, to aid development of therapeutic options.

Neuroanatomy of Anticipation in Anxiety Disorders
PI: Jack Nitschke, UW School of Medicine & Public Health (SMPH)
Collaborator: Alexander Andrew, SMPH; Daniel McFarlin, GS.
The overall aim of the research is to provide a better understanding of posttraumatic stress disorder (PTSD) pathology and treatment in soldiers with recent combat exposure. Using various neuroimaging techniques, soldiers with and without PTSD will perform two activities to assess function in key brain areas that process emotional stimuli. Those with PTSD will undergo a 3-month treatment regimen; both groups will then repeat the scans to determine whether treatment for PTSD results in normalization of brain function.

Investigating the Role of Biofilm in Staphylococcal Bloodstream Infections
PI: Warren Rose, School of Pharmacy, (SOP)
Collaborators: Dennis Maki, SMPH; Sanjay Shukla, MCRF; Steven Ebert, SOP.
A collaboration among researchers from Pharmacy, Medicine, and the Marshfield Clinic will investigate factors affecting optimal therapeutic response of Staphylococcus aureus to antimicrobial agents. Specifically, the team will determine whether S. aureus patient isolates capable of forming biofilms are genetically distinct and less susceptible to antibiotics than isolates that do not form biofilms. The ability to form biofilms may limit antibiotic penetration; thus, understanding the mechanisms involved in biofilm formation will focus development of alternate therapies.

Tau and Myelin Integrity in Alzheimer's Disease
PI: Barbara Bendlin, UW School of Medicine & Public Health (SMPH)
Collaborator: Alexander Andrew, Sterling Johnson, Luigi Puglielli, Howard Rowley, Mark Sager, SMPH; Cynthia Carlsson, SMPH, WSM Veterans Hospital.
Identifying early indicators of Alzheimer's disease (AD) in asymptomatic at-risk individuals could allow for treatment with subsequent disease delay or prevention. This research will examine a cohort of middle aged volunteers who are either at high or low risk of developing AD, given the presence or absence of a family history of AD. The basic premise is that an altered brain protein, tau, directly affects myelin integrity and this precedes the neuronal damage characteristic of AD. Volunteers will undergo neuroimaging to detect changes in myelin integrity; in addition, for high risk volunteers, the degree of myelin integrity will be correlated with levels of tau in cerebrospinal fluid.