



Summaries of **UW ICTR Funded Clinical and Type 1 Translational Research Pilot Awards, 2010**

Co-Funded Clinical and Type 1 Translational Research Pilot Awards

Treatment of painful Chemotherapy-Induced Peripheral Neuropathy with the MC-5A pain therapy medical device, a randomized, double-blind, sham-controlled clinical trial

PI: [Toby C Campbell](#), UW School of Medicine & Public Health

Collaborators: Miroslav Backonja and Kyungmann Kim, UW SMPH; Thomas Yen, UW COE

Co-funders: The UW Carbone Cancer Center; UW ICTR

Chemotherapy-induced peripheral neuropathy (CIPN) is an often disabling, toxic outcome that impacts 30-40% of patients undergoing chemotherapy, with no effective treatment. A novel pain therapy device, MC-5A, acts to replace pain signals with “no pain” signals. The interdisciplinary team will conduct a blinded clinical trial to determine effectiveness of the MC-5A to decrease pain symptoms in conjunction with detailed psychological, emotional, and biological data.

Estrogen receptor beta in Triple Negative Breast Cancer

PI: [Kari Wisinski](#), UW School of Medicine & Public Health

Collaborators: Howard Bailey, Andreas Friedl, and Adin-Cristian Andrei, UW SMPH; Adedayo Onitilo, Marshfield Clinic Research Foundation

Co-funders: UW Carbone Cancer Center; Marshfield Clinic Research Foundation; UW ICTR

Triple negative breast cancers (TNBC) are characterized by the lack of three major cellular receptors, including the estrogen receptor (ER α). TNBC has a worse prognosis than other breast cancer subsets, and is associated with a higher rate of 5-year recurrence; identification of patients with a lower risk of recurrence could require less toxic systemic therapy. Estrogen receptor beta (ER β) is recently identified and may be expressed in at least 50% of TNBC and associated with an improved prognosis. A joint collaboration between the UW and Marshfield Clinic, the study will examine whether expression of ER β in tumor samples correlates with improved 5-year disease free survival.

iNs from neurodevelopment and neurodegenerative diseases

PI: [Qiang Chang](#), UW School of Medicine & Public Health

Collaborators: Su-Chun Zhang and Hrissanthi Ikonomidou, UW SMPH

Co-funders: UW Waisman Center; UW ICTR

Utilizing iPSC technology, the research aims to generate disease specific (Rett syndrome, RTT, and juvenile neuronal ceroid lipofuscinosis, JNCL) neurons with defined mutations from patient skin cells as a means to model these diseases. The induced neurons will be examined to ensure the cells exhibit the expected pathological characteristics; namely, RTT neurons are neurodevelopmental (they do not die), whereas JNCL neurons are neurodegenerative (they die). The successful development of disease model systems will lead to a powerful drug-screening platform to identify potential therapeutic options for RTT and JNCL, where none exist presently.

Human RPE cell electrophysiology to model eye disease,

PI: [Bikash Pattnaik](#), UW School of Medicine & Public Health

Collaborators: De-Ann M Pillers and David Gamm, UW SMPH

Co-funders: The Stem Cell and Regenerative Medicine Center; UW ICTR

Human induced pluripotent stem cells (iPS) are a useful tool to study disease mechanisms and potentially to serve as a therapeutic gene delivery system. Two progressive eye diseases in children, Snowflake Vitreoretinal Degeneration (a form of juvenile macular degeneration) and Best’s disease, involve hereditary defects in ion channels. Initial work



will focus on validating the ion channel function of cells differentiated from fetal and human iPS origin. These cells will then be used to study alterations in ion channel function suspected of causing vision disorders.

Modeling genetic skin diseases using patient-specific iPS cells

PI: Joyce Teng, UW School of Medicine & Public Health

Collaborators: Vijay Setaluri, UW SMPH; Sean Palecek, UW COE

Co-funders: The Stem Cell and Regenerative Medicine Center; UW ICTR

The use of patient specific human induced pluripotent stem cells (iPS) to treat disease avoids potential ethical objections and may minimize the risk of rejection. This project will develop iPS cell lines from inherited dermatologic disease tissues as a means to establish unique in vitro disease models. Such models are useful in the development of new therapeutic treatments.

The Common Marmoset model of pediatric obesity and MetS

PI: [Toni Ziegler](#), UW Graduate School

Collaborators: Ricki Colman, UW Graduate School

Co-funders: The Wisconsin National Primate Research Center; UW ICTR

Obese children are at greater risk for developing cardiovascular disease and metabolic syndrome (MetS) than nonobese children. The complete and detailed characterization of a nonhuman primate model of pediatric obesity and MetS allows a unique opportunity to translate previous findings to a genetically close human relative, and ensures access to tissues unavailable in a human clinical trial.

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Generation of induced pluripotent stem cell to study autism

PI: [Anita Bhattacharyya](#), UW Graduate School

Collaborators: Leonard Abbeduto, UW School of Medicine & Public Health

Induced pluripotent stem cell (iPSC) technology provides a unique opportunity to address the challenge of defining neurodevelopment errors in autism. With such technology, the hypothesized cellular and molecular differences that distinguish autism iPSC-derived neurons from their unaffected counterparts can be elucidated. Nonetheless, the complexity of autism makes it difficult to identify candidate processes that go awry in autism iPSC-derived neurons. To circumvent this problem, comparisons will be made between iPSC-derived neurons from individuals with Fragile X with and without co-morbid autism to identify differences.

Development of MRI for early detection of BOS in lung transplants

PI: [Scott Nagle](#), UW School of Medicine & Public Health

Collaborators: Sean Fain, UW SMPH

Bronchiolitis obliterans (BO) is a late complication of lung transplantation, and the most common cause of lung allograft dysfunction. Early detection of BO would greatly facilitate characterization of disease pathophysiology, as well as development of therapeutic options. To this end, the project will test the hypothesis that oxygen-enhanced MRI is a robust, reproducible method for early detection of BO.

ATase 1 inhibitors in Alzheimer's disease,

PI: [Luigi Puglielli](#), UW School of Medicine & Public Health

The enzyme β -site APP cleaving enzyme (BACE1) generates the amyloid β -peptide leading to the neuropathology associated with Alzheimer's disease (AD). This focal role of BACE1 in AD nominates BACE1 as an effective target for



AD therapeutics. The interdisciplinary research team will characterize the mode of action of small molecules that decrease BACE1 activity by inhibiting an enzyme, ATase1, which activates BACE1. The team will then examine whether a decrease in BACE1 activity can delay or block the AD neuropathology in select animal models.

Novel melanoma antigen targets for cellular immunotherapy

PI: Jonah Sacha, UW School of Medicine & Public Health

Collaborators: Mark Albertini, UW SMPH

The incidence of malignant melanoma is rising and is responsible for the majority of skin cancer deaths. With few effective therapeutic options, designing new treatment strategies is tantamount. In contrast to healthy melanocytes, metastatic melanomas express human endogenous retroviral proteins and mRNA. This research will examine whether these retroviral proteins may serve as a target for immunotherapy. The team will compare the immune response of samples collected from melanoma patients with those from healthy volunteers.

T Regulatory cells and childhood asthma

PI: [Chris Seroogy](#), UW School of Medicine & Public Health

Collaborators: James Gern, UW SMPH

The incidence of allergic diseases has been increasing, consequently decreasing the quality of life for children and increasing societal burden. Gaining a better understanding of the mechanism of allergic sensitization and the impact of environmental exposures on the developing immune system is imperative. The working hypothesis is that immune T regulatory cells are modulated by early environmental exposures and these exposures are important in determining the development of allergic sensitization.

Tumor microenvironment and disease-free survival after a diagnosis of ductal carcinoma In Situ

PI: [Amy Trentham-Dietz](#), UW School of Medicine & Public Health

Collaborators: Patricia Keely, Andreas Friedl, and Brian Sprague, UW SMPH; Kevin Eliceiri, UW Graduate School
Little is known about the factors affecting the progression from Ductal Carcinoma In Situ (DCIS) to invasive breast cancer. The overall aim of the pilot project is to characterize changes in the alignment of the extracellular matrix in stromal cells surrounding malignant breast cancer cells. Specifically, research will examine the collagen alignment patterns and syndecan-1 expression in tumor samples, and the relationships of these stromal features with tumor and patient factors, and disease-free survival. Findings may aid in the development of prognostic markers to identify those DCIS tumors most likely to progress to invasive breast cancer.

Detection of liver metastases with Gd-EOB-DTPA enhanced MRI

PI: [Emily Winslow](#), UW School of Medicine & Public Health

Collaborators: Scott Reeder and Agnes Loeffler, UW SMPH

Optimal clinical outcomes for patients with hepatic metastatic colorectal cancer depend upon detection of all metastatic lesions and subsequent removal of these lesions by surgical resection. Detection of small lesions suspicious for metastases is possible by using Gd-EOB-DTPA-enhanced MRI. Nonetheless, without pathological verification of the metastases, patients may be unnecessarily subjected to surgical risk. Investigators will develop methodology to correlate radiographic and histologic findings to determine the utility of Gd-EOB-DTPA enhanced MRI.