Novel Methods Pilot Awards ($50,000 for one year)

Evaluation of the Impact of a Problem Oriented View on Clinical Workflows
PIs: Joel Buchanan, MD; **Michael Semanik, MD MS**, School Medicine & Public Health
Collaborators: DuWayne Willet, UT-Southwestern; Adam Wright, Harvard

Summary: The Problem Oriented Medical Record (POMR) organizes crucial clinical information such as labs, imaging reports, medication lists, and clinician notes in the context of the patient's conditions or problems. Potential benefits of a POMR include enhanced provider efficiency, improved clinical thinking, and streamlined communication. Yet widespread adoption of the POMR remains elusive. Successful POMR adoption requires development of effective context dependent views of data. Thus, a critical need exists for an automatic tool that can aggregate data and create these context dependent views—a Problem-Oriented View (POV). Our specific aim in this proposal is to demonstrate the impact of POV on clinician efficiency, effectiveness, cognitive workload, and satisfaction in a simulation environment. We will accomplish our specific aim by conducting a multi-site, randomized, cross-over trial of 36 resident physician participants.

A Genetically Engineered Knockdown-Rescue Strategy to Replace Mutant with Functional Proteins
PI: Erik Dent, PhD, School of Medicine & Public Health
Collaborators: Kara Rain Vogel, SMPH

Summary: We are actively developing a novel system to carry out complete, physiologically-matched genetic replacement of proteins of interest using an inducible, modular plasmid. Our method overcomes fundamental issues intrinsic to all currently available alternatives for primary cell transfection. At its core, this technology will allow researchers to knockdown endogenous proteins and replace them with mutated proteins to study the functions of individual proteins without the interference of endogenous proteins. Importantly, this technology could translate into a way to knockdown mutant proteins in diseased cells and replace them with functional wild-type proteins. If successful, this knockdown-rescue strategy would allow for the replacement of non-functioning, constitutively active or dominant negative proteins with physiological levels of functional wild-type proteins.

Muscle Quality: a Future Target for Nutritional Intervention
PI: Adam Kuchnia, PhD, College of Agriculture & Life Sciences
Collaborators: Kenneth Lee, Scott Reeder, SMPH; Brian Anthony, MIT

Summary: Structural changes describing muscle quality may present early in hospital admission and identify as a marker for timely nutritional intervention. Although the clinical characterization of muscle quality may provide insight for optimizing nutritional therapy, clinicians currently lack valid bedside tools of assessment and the comprehensive context needed to interpret such measures. This is a major obstacle to providing meaningful nutrition therapy. Our long-term goal is to improve health outcomes in all clinical populations suffering from malnutrition. In this proposal, we plan to initiate the development of a

methodology to standardize the objective assessment of muscle quality and identify individuals to benefit from judicious nutrition intervention. The rationale is that validating objective biomarkers of disease and age-specific muscle quality will initiate a new approach that will lead to targeted nutrition intervention, and help clarify the role of nutrition in mitigating the effects of disease and aging.

Novel Method for Enhancement of Kidney Transplant Graft Survival by Transfer of iPSC-Derived MDSCs in a Rhesus Model

PsI: Igor Slukvin, MD, PhD; **Dixon Kaufman, MD, PhD,** School of Medicine & Public Health

Summary: Establishing functional immune tolerance in human solid organ transplant recipients to eliminate chronic immunosuppression, remains a significant challenge. There are, however, opportunities to utilize several immune tolerance mechanisms to overcome these challenges. One promising approach is the establishment of a stable mixed chimerism. Safe and reliable methods for mixed hematopoietic chimerism induction need to be developed to achieve a reproducible kidney allograft acceptance without chronic immunosuppression. In the current application, we propose to develop a novel precision method to enhance the rate of mixed chimerism in setting of solid organ transplantation using myeloid-derived suppressor cells (iMDSCs) generated from induced pluripotent stem cell (iPSC). The main objective of this application is to develop technology for the efficient production of MDSCs from nonhuman primate (NHP) iPSCs with the ultimate goal to establish a NHP model for the preclinical evaluation of the produced iMDSCs in a combined kidney and HSC transplant model and subsequent translation of this novel therapeutic method to the solid organ transplant clinic.