

## Seattle Institute for Biomedical and Clinical Research

April - June 2019

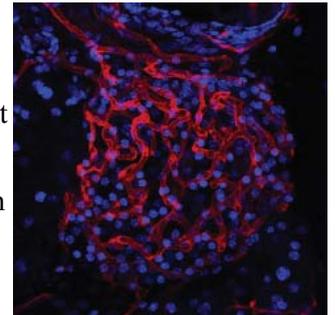
### Spotlight Feature

#### REBECCA HULL-MEICHLE, PHD



Rebecca Hull-Meichle, PhD is a Research Biologist at VA Puget Sound Health Care System and a Research Associate Professor in the Division of Metabolism, Endocrinology and Nutrition at the University of Washington. Rebecca's research focuses broadly on how novel aspects of the islet milieu contribute to dysfunction and death of the islet  $\beta$ -cell that are a critical component of diabetes pathogenesis. Her current research interests aim to answer three main questions: **1. How does the islet endothelial cell contribute to  $\beta$  cell failure in type 2 diabetes?** Rebecca's lab has shown that islet endothelial cells develop an inflammatory and proadhesive phenotype in multiple models of diabetes. This is associated with altered composition and remodeling of the islet extracellular matrix. This altered endothelial phenotype results in decreased insulin release from islets, suggesting it is a novel modulator of the beta cell in diabetic conditions and thus a potential therapeutic target. She is using novel in vitro approaches, along with animal models to understand how and why the islet

endothelial cell becomes dysfunctional and how this affects  $\beta$  cell function in diabetes. **2. What are the mechanisms underlying islet amyloid-mediated toxicity?** Rebecca's recent data suggests that islet endothelial cells are a novel target of islet amyloid toxicity (a pathological feature that occurs in almost all individuals with type 2 diabetes). Further, her work shows that islet amyloid-induced inflammation in islet endothelial cells has numerous downstream effects that impact the  $\beta$  cell. Specifically, these include further stimulation of islet amyloid formation, recruitment and activation of macrophages and direct effects to impair  $\beta$  cell function and/or survival. **3. What causes islet failure in cystic fibrosis-related diabetes?** Diabetes affects up to 50% of patients with cystic fibrosis, but islet pathology and the mechanisms by which islet dysfunction occur in CFRD are still poorly understood. Rebecca recently found that islet inflammation is a widespread feature of CFRD, occurring even in young children with the disease; we are following up on those observations in the lab. Islet amyloid is also a common feature of CFRD, but it occurs decades earlier in this disease than it is typically seen in type 2 diabetes, suggesting a different etiology. Her group is studying a novel mouse model that expresses the most common human CF mutation along with amyloidogenic (human) islet amyloid polypeptide in order to better understand the role of islet amyloid in the development of CFRD.



#### ANNUAL MEMBERS' MEETING

SIBCR's Annual Members' Meeting is scheduled for April 30, 2019 in building 1 room 240 at noon. The agenda is available on our website.

#### UPCOMING R&D SEMINARS

Research Seminars are held in building 1 room 240 at noon.

**Jerry Jarvik, MD, MPH**, Professor of Radiology, Neuroradiology, Health Services and Neurological Surgery, and Adjunct Professor of Orthopedics & Sports Medicine and Pharmacy at the UW, "Making It CLEAR- the UW Clinical Learning, Evidence and Research Center for Musculoskeletal Disorders", **April 22, 2019**.

**Konrad Talbot, PhD**, Associate Professor, Loma Linda University Medical Center, Departments of Human Anatomy, Pathology, and Neurosurgery; Associate Researcher, UCLA Department of Neurology; and PI in Research and Development, Loma Linda and West LA VA, "A New Hope for Treating Alzheimer's Disease with Novel Antidiabetics", **May 20, 2019**.

**William DePaolo, PhD**, Associate Professor of Medicine at the UW | Director of the Center for Microbiome Sciences & Therapeutics (CMiST), "Hacking the Human Microbiome", **July 16, 2019**.