Dr. Scott Small, MD
Boris and Rose Katz Professor of Neurology
(in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, the Gertrude H. Sergievsky Center and in Radiology)
Director, Alzheimer's Disease Research Center

“Alzheimer’s pathophysiology: From Regional vulnerability to Retromer”

Why would a disorder target one brain region and spare its neighbors, despite shared genes and environmental risk? Answering this simple question can clarify disease mechanisms and suggest interventions. Although the question is simple, identifying patterns of regional vulnerability is challenging, particularly in progressive diseases like Alzheimer’s. We have tackled this problem by focusing on the hippocampal formation, a circuit organized into discrete regions and affected by Alzheimer’s and other disorders. First, we had to optimize variants of in vivo imaging that could pinpoint regional dysfunction within the hippocampal circuit. Once achieved, we then imaged patients and animal models, establishing patterns of regional vulnerability. Next, we set out to determine the molecular correlates of regional vulnerability, and then validated the identified molecular pathways through various techniques. This project has isolated retromer-dependent endosomal trafficking defects in Alzheimer’s, which is now a validated cytopathogenic mechanism of disease. We are currently developing pharmacological interventions designed to correct retromer-dependent endosomal trafficking defects found in Alzheimer’s.

FEBRUARY 13 AT 4:30PM HSB T-739
FACULTY HOST: JESSICA YOUNG

To request disability accommodations, contact the Disability Services Offices at least ten days in advance of the event: 206-543-6450 (voice); 206-543-6452 (TTY); 206-685-7265 (FAX); dso@u.washington.edu