# 200th WPI-IIIS Seminar

Proximity Proteomics to Reveal Synapse Function from Molecules to Memory & Disease

The interplay between protein signaling and cognitive processes is crucial for understanding neurological disorders and cognitive functions. In this talk, I will cover two unpublished proximity proteomics studies: the role of Rac1 signaling in cognitive processes and the proteomic landscape of autism risk genes. In the first study, we investigate how Rac1, a small GTPase involved in actin and phosphorylation signaling, influences hippocampal-dependent working memory and longer-term learning. We show that inhibiting Rac1 at presynaptic terminals impairs spatial working memory in mice, while postsynaptic inhibition affects long-term cognitive processes. Using mass spectrometry, we identify key phosphorylated proteins and kinases involved in Rac1 signaling, revealing its presynaptic regulatory mechanisms. The second study focuses on autism spectrum disorder (ASD), examining how risk alleles within numerous genes interact within protein complexes. By employing genome-editing-mediated proximity-based proteomics, we identify spatial proteomes of 14 high-confidence autism risk genes in the mouse brain. These proteomes are enriched for genes dysregulated in autistic individuals and highlight interactions between high-confidence and lower-confidence risk genes. Functional assays in autism models demonstrate how these interactions influence cellular mechanisms underlying ASD.
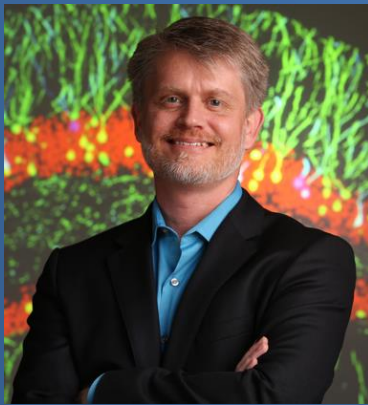
Dr. Scott Soderling

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Date: **Monday, July 29, 2024**

Time: **11:00 – 12:00**

Venue: **1F Auditorium**, IIIS Building

＊On-site participation only

INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

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