Our lab studies Spinocerebellar Ataxia Recessive 20 (SCAR20), a fatal, early-onset neurodegenerative disorder characterized by cerebellar ataxia, Purkinje cell loss, coarse facial features, and severe intellectual disability. Biallelic loss-of-function mutations in the ubiquitously expressed Sorting Nexin 14 (SNX14) protein have been reported in more than 45 patients with SCAR20 to date. We and others have uncovered that SNX14 regulates cerebellar lipid homeostasis and interacts with its paralog, SNX13, in neurons. We recently found SNX13 mutations in three children with a cerebellar disorder like the one caused by the loss of SNX14. Like SNX14, SNX13 is also an endoplasmic reticulum (ER) resident protein that has been shown to regulate lysosomal cholesterol homeostasis.

Taken together, we hypothesize that the interaction between SNX13 and SNX14 functions to regulate neuronal lipid homeostasis. To date, we are currently dissecting the molecular topology of this interaction, as well as determining the importance of this interaction for neuronal homeostasis through biochemical and cellular studies. Our work will provide critical insights into our understanding how two sorting nexins are important for cerebellar lipid homeostasis. Like many ataxias, there are no effective treatment options for SCAR20 and patients with SNX13 mutations. With this study, we hope to further understand disease mechanisms and identify novel targets for treatment of associated neurodegenerative disorders of the cerebellum.