UCDAVIS
Center for Neuroscience

BHCOE Pilot Award 2021-2022
Novel roles of the intellectual disability-relevant gene *Chd8* in the adult cerebellum
PI: Diasynou Fioravante, PhD

Progress Report

Cognitive and emotional intelligence are mental faculties essential for healthy daily functioning, but our understanding of how they are regulated in the neurotypical brain and dysregulated in autism and intellectual disability (ID) is far from complete. *Chd8* is a gene that regulates early brain development by remodeling chromatin and has emerged as a top risk gene for autism and ID. We have proposed 2 aims to characterize how targeted removal of *Chd8* specifically in the adult cerebellum impacts ID-relevant social and emotional behaviors and cerebellar physiology. The significance of the proposal is two-fold: first, it focuses on a brain region -the cerebellum- whose contributions to Chd8-related pathology have been overlooked and understudied thus far, despite the cerebellum's documented roles in neurodevelopmental disorders. Second, by identifying the impacts of Chd8 specifically in the adult cerebellum, the proposal has game-changing potential of extending the time window for clinical interventions in Chd8 ID beyond early development, thus also expanding the availability of treatment options.

We have made significant progress toward both aims: **1**) we have established a *Chd8* transgenic mouse colony in our lab, which has already produced animals for behavioral testing (aim 1) and will also produce animals for physiology (aim 2); **2**) to achieve brain region- and developmental time-specificity in *chd8* deletion, we have injected viruses in the cerebella of several cohorts of adult animals, which are currently undergoing sociability and motor control testing (aim 1); **3**) we have optimized conditions for TUNEL staining in order to evaluate levels of regulated cell death in cerebellar nuclei (aim 2); **4**) in collaboration with the Nord lab, we are optimizing conditions for isolation of single nuclei and transcriptomics analysis in order to assess how *Chd8* deletion affects gene expression and physiology in the adult cerebellum (aim 2).

We anticipate that, barring unforeseen delays, we will achieve our experimental goals in the next 6 months and will be in an excellent position to submit federal grant proposals. **We are tremendously thankful to the BHCOE and its sponsors for their support.**