



## Decrypting Cadherin-13 function in cortico-cerebellar circuitry underlying neurodevelopmental disorders! (DECODE!)

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Autism spectrum disorders (ASD) are a group of neurodevelopmental disorders characterized by deficits in social skills and communication, stereotyped and repetitive behavior, and a range of alterations in cognitive function. ASD shows high heritability and comorbidity with other disorders such as intellectual disability and attention-deficit/hyperactivity disorder.

The recent progress in human genetics have led to the identification of hundreds of genes associated with autistic-like behaviors, including a growing number of genes encoding synaptic proteins. Recently, rare de novo and inherited deletions at the CDH13 locus have been linked to ASD1,2, indicating the clinical relevance for loss-of-function mutations in CDH13. Although CDH13 has been characterized as an adhesion protein in non-neuronal cells, surprisingly little is known about its function in the brain.

In DECODE! we will develop mouse models to study the cell- and circuit-specific effects of CDH13 deficiency. In particular, we will focus on the cortico-cerebellar circuitry, which recently has been implicated in ASD. In addition we will harness the potential of human induced pluripotent stem cells (iPSC) to characterize CDH13 dysfunction in patient iPSC-derived cultured inhibitory neurons at the molecular and cellular level. Understanding circuit-specific alterations caused by CDH13 deficiency in mouse and human models may ultimately help us designing targeted treatment of specific ASD symptoms.