

Internship Proposal Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : CIRB UMR7241
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Team name : RMSS

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2. Internship project title:

Consequences of deficient long-term depression specifically in cerebellar Purkinje cells

3. Internship Description :

Complement Control Protein (CCP) modules are emerging as important evolutionarily conserved domains with roles in brain development. One example is the CCP domain containing protein LEV9 necessary for acetylcholine receptor clustering in *C. elegans*. Deletion in the gene coding Sushi domain containing protein 4 (SUSD4), a CCP domain containing protein, is associated with autism spectrum disorders or Fryns syndrome in humans. However, the role of SUSD4 in brain development is still unknown. We have shown that *Susd4* mRNA is expressed in various regions of the developing brain. Loss of SUSD4 in a constitutive mouse knockout model (*Susd4* KO) is associated with motor learning and spatial memory deficits. Using a combination of morphological, functional and biochemical analysis, we have shown that SUSD4 is essential for the fine control of AMPA receptor synaptic accumulation, synapse maturation and plasticity (Gonzalez-Calvo, Iyer et al. In preparation). This study suggests obvious links between SUSD4 deficiency and the etiology of neurodevelopmental disorders.

In order to understand the cell autonomous role of SUSD4 on network development and identify whether there is a critical period for SUSD4's control of synapse maturation and plasticity, we will generate an inducible Purkinje cell specific KO mouse. Using this model, we will perform morphological and electrophysiological analysis to identify whether there is a critical period for SUSD4 function or whether its function is the same throughout the lifespan of the animal. We will also perform behavioral analysis to determine how the modification of plasticity in Purkinje cells affect a whole range of behaviors, not only classical cerebellum-dependent ones, but also other types of behavior that have not been demonstrated yet as cerebellar dependent.