CELLULAR AND MOLECULAR MECHANISMS OF NEUROGENESIS DISRUPTED BY THE LOSS OF FUNCTION OF *Mnb/Dyrk1A*. IMPLICATIONS FOR MICROCEPHALY.

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The *Mnb/Dyrk1A* encodes an evolutionary conserved protein kinase that plays diverse functions in brain development and has been implicated in Down syndrome neurodevelopmental disorders. We identified its founding member in *Drosophila melanogaster* (*Dm*) and named it *minibrain (mnb)* because of the reduced brain size associated to its loss of function (LoF), suggesting key functions for Mnb/Dyrk1A in the control of neural proliferation and neurogenesis (Tejedor et al., 1995).

Previous works of our lab have shown that Mnb/Dyrk1A plays sequential functions in the regulation of the neurogenic switch, the cell cycle, and in the terminal differentiation of neuronal progenitors. The dissection of the molecular mechanism underlying these functions that we are carrying out display a complex signaling network in which Mnb/Dyrk1A acts on various cell cycle regulators, signaling cascades and several transcription factors in order to coordinate these mechanisms along the cellular processes of neurogenesis, ensuring the precise timing of neuronal production.

Remarkably, the haploinsufficiency of *MNB/DYRK1A* in humans causes microcephaly and autosomal dominant mental retardation-7 (MRD7; OMIM 614104), clearly resembling the *mnb* LoF phenotype in *Dm*.

We will present and discuss data showing how we are using the larval brain of *Dm* to find out what cellular and molecular mechanisms are particularly disrupted by the LoF of *Mnb/Dyrk1A* causing a deficient neurogenesis, which leads to neuronal deficits.

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