Alberto Bacci

DevInDS

Development of over-inhibition of cortical circuits in Down syndrome (DevInDS)

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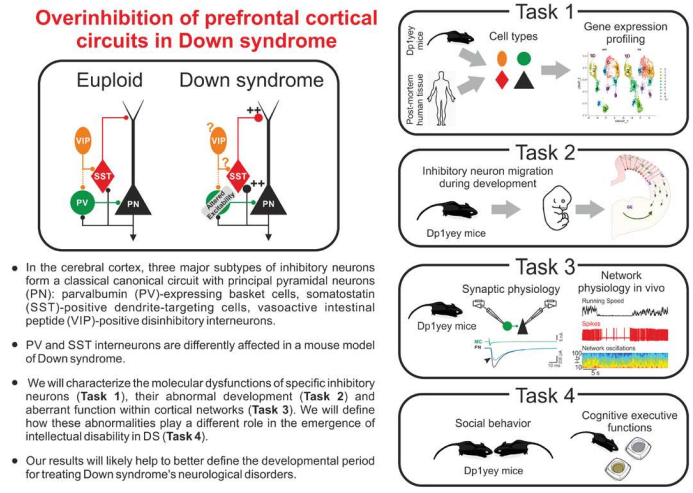
Down syndrome (DS) is a developmental disorder caused by the presence of an extra copy of human chromosome 21 (Hsa21) and is characterized by various physical and neurological features, including intellectual disability and autism spectrum disorder. Recent research, including our work, suggests that intellectual disability of DS subjects might result from an over-inhibition of cortical networks. Cortical inhibition originates from a rich diversity of inhibitory neuron subclasses, which operate a fine division of labor during brain activity responsible for cognitive functions. We hypothesize that specific developmental alterations of distinct inhibitory circuits of the prefrontal cortex underlie cognitive and sociability deficits in DS. We will characterize the molecular dysfunctions of specific inhibitory neurons, their abnormal development and aberrant function within cortical networks. We will define how these abnormalities play a different role in the emergence of intellectual disability in DS.



This consortium combines a multi-scale, interdisciplinary approach: cellular and molecular biology, neurophysiology, genetics and behavioral analyses in mouse models. Importantly, we will also use neuropathology and molecular and cell biology in human tissue. This consortium will strongly benefit from the close collaboration with Dr. Marie-Claude Potier (ICM, Paris, France) and Dr. Mara Dierssen (CNAG-CRG, Barcelona, Spain).

We expect to provide a first detailed investigation of neuronal/cellular mechanisms that may underlie cognitive abnormalities of DS, paving the way for novel therapeutic interventions, essential to help DS individuals to live an adequate independent life. Importantly, unexpected results originating from research programs like this, will also advance our knowledge on the mechanisms underlying brain function.