

## **Project:**

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### **Genetics of cortical interneuron development: modelling interneuron function in health and disease**

The neural circuitry of the cerebral cortex constitutes one of the most complex physical systems in the World. Much of this complexity arises during development through the interaction of two distinct neuronal types, glutamatergic projection neurons, which comprise the majority of cortical neurons, and GABAergic interneurons. Whereas abnormal development of projection neurons commonly leads to severe cortical malformations that are frequently incompatible with life, abnormal interneuron development may cause profound functional deficits without obvious morphological alterations of the cerebral cortex. Accordingly, recent studies suggest that abnormal interneuron function may underlie some neurological and psychiatric disorders, such as epilepsy, schizophrenia or bipolar disorder, and that interneuron dysfunction may arise during development. Thus, a detailed picture of interneuron development seems to be essential for understanding some of these important neurological diseases associated with cortical dysfunction.

The general aim of this project is to obtain a comprehensive definition of the cellular and molecular mechanisms controlling early events in the development of cortical interneurons, such as specification and migration. To reach this goal, we will take a multidisciplinary approach by combining mouse genetics, genomics, imaging techniques, and conventional cellular and molecular biology methodologies. The successful execution of this project will lead to new knowledge of the mechanisms underlying the development of cortical interneurons and to the generation of mouse models of cortical disorders resulting from interneuron deficiency.

## **Comments:**

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The understanding of the development and architecture of the human cortex is absolutely crucial to deciphering the function of the brain and to the understanding of major pathologies. This proposal will build ground-breaking insights from the candidate and is expected to clarify long lasting questions in the area of brain development and pave the way for important medical developments.

The candidate has an outstanding track record of publications in the field of brain development. Although his laboratory was set-up a year ago, he has already demonstrated his capacity to lead a group and work extremely efficiently. He has already established himself as a leader in the field of intraneural development, essential for cortical brain function, and the basis of human diseases such as epilepsy, autism and schizophrenia.

The proposal is very ambitious and coherent, and it offers the possibility to understand the development of this cell population, so important for cell function. This is a very innovative area and he will use state-of-the-art technology to approach it.

The candidate will perform this project in a new institute with strong Spanish support in this field in which Spain has long history and experience. The institute has already succeeded in recruiting first class scientists.

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**New institution:** Instituto de Neurociencias de Alicante, CSIC-UMH

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