2017 IGBMC Summer Internship

Role of CEP41 during cortical development: implication in neurodevelopmental disorder

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The cerebral cortex develops from the most anterior part of the neural tube and contains neurons that are distributed within layers and are regionally organized into specialized areas that underlie sophisticated motor, cognitive and perceptual abilities. Cortical lamination follows an «inside-out» sequence of neuronal placement and maturation that arises from the sequential birth and orderly migration of the two major classes of cortical neurons, the pyramidal projection neurons and the GABAergic interneurons The development of the cortex progresses through several stages including, neural proliferation, neuroblast migration and neuronal differentiation. Disrupting the completion of one or several of these steps often cause cortical malformations that lead to severe learning disabilities, mental retardation and epilepsy.

The centrosome is the major microtubule organizer in animal cells, playing critical roles in cellular functions including cell division, cell migration and cell proliferation. Remarkably, mutations in proteins associated with the centrosome have been linked to several diseases of brain development. Those neurodevelopmental disorders are thought to involve abnormal neuronal proliferation, migration, differentiation and/or maturation, suggesting crucial roles of the centrosome at those different neuronal developmental stages. The major goal of the current proposal is to better characterize the centrosome-regulated cellular and molecular pathways that contribute to the cortical embryonic neurogenesis in heath and disease.

We will adopt a candidate-based approach and fully characterize the function of CEP41, a centrosomal protein mutated in several neurodevelopmental disorders. We will use CEP41 constitutive and conditional knockout models to evaluate the function of CEP41 at the sequential developmental steps taken by cortical progenitors in order to mature into fully functional neurons: i) proliferation; ii) specification and iii) migration. During the summer internship, the student will participate to the characterization of the knockout models using histological approaches both at the macroscopic level (brain dissection, analysis of brain organisation, layering and cyto-architecture at different developmental stages) and at the cellular level (analysis of cell survival, cell proliferation, cell migration).