INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 16 de Febrero de 2024
12:30 h. Instituto Cajal - CSIC

Dra. MURIELLE SAADE

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NEURAL ARCHITECTS: UNRAVELING THE MECHANISMS OF NEUROEPITHELIAL CELLS IN SHAPING THE CENTRAL NERVOUS SYSTEM

Abstract

Building a properly functional central nervous system relies on the precise coordination of neural progenitor cells (NPCs) proliferation and differentiation. Essential intrinsic determinants, including centrosome maturation, ciliogenesis, microtubule polymerization capacity, and polarity complex organization, interconnect to influence cell fate decisions and tissue growth. Dysregulation of these molecular processes can lead to Neurodevelopmental Disorders (NDDs), such as microcephaly.

Our investigation, utilizing the developing chick embryo neural tube as a model, has brought to light Sonic Hedgehog as a crucial instructive signalling pathway capable of overcoming the asymmetric properties of the mitotic spindle pole. This mechanism ensures the sustained proliferative capacity of NPCs, thereby contributing to tissue growth. In the context of Zika virus-induced microcephaly, we have discerned that the anomalous premature neuronal differentiation arises from the effects of the viral non-structural protein NS5, inducing ciliopathy and prompt end-feet apical constriction. Remarkably, one subcellular structure impacted by NS5 is the ciliary rootlet, the function of which remains elusive in NPCs. I will present our latest advancements in deciphering the significance of actively remodeling the ciliary rootlet during the apical end-foot constriction of NPCs and its involvement in neuronal delamination. Additionally, I will discuss the intriguing possibility that ciliary rootlet remodeling coordinates with the actin cytoskeleton and microtubule dynamics, offering novel insights into the mechanisms of neuronal delamination in both healthy and diseased conditions.

Affiliation and short bio

Murielle is a cell and neurodevelopmental biologist, born of Lebanese parents and grew up in Mali. In 2008, she obtained a PhD in Immunology from the University of Aix-Marseille II, France. During her PhD work, she studied embryonic thymus development and severe combined immunodeficiency. Her background in developmental immunology sparked an interest in neurodevelopment. Joining Pr. Elisa Marti's laboratory at CSIC as a postdoctoral scientist, she developed innovative tools to separately follow the three division modes (PP/PN/NN) of neural precursor cells (NPCs) and modeled the dynamics of motor neuron generation in the developing central nervous system (CNS). She made seminal discoveries in elucidating the impact of growth factors in coordinating growth and patterning of the developing CNS. More recently, she unraveled the crucial mechanisms by which the Zika virus induces microcephaly, providing breakthroughs on the key roles of the centrosome/ciliary axis in neurogenesis. Since 2020, she has led a research group at the IBMB-CSIC. Her fascination with how intracellular cell fate determinants evolves at the organelle scale to sustain NPC proliferation has profoundly shaped her scientific trajectory. Her current lab endeavors to understand the role of the centrosome/ciliary axis in CNS growth and associated neurodevelopmental disorders.

Related publications with the topic

1.- Murielle Saade, Diego S Ferrero, José Blanco-Ameijeiras, Elena Gonzalez-Gobartt, Marco Flores-Mendez, Victor M Ruiz-Arroyo, Elena Martínez-Sáez, Santiago Ramón y Cajal, Naiara Akizu, Nuria Verdaguer and Elisa Martí * (2020) Multimerization of Zika Virus-NS5 causes a ciliopathy and forces premature neurogenesis. Cell Stem Cell 27(6): 920-936.e8. doi:10.1016/j.stem.2020.10.002. https://pubmed.ncbi.nlm.nih.gov/33147489/

2.- Murielle Saade, Jose Blanco-Ameijeiras, Elena Gonzalez-Gobartt, and Elisa Martí (2018) A centrosomal view of CNS growth. Development 145: dev170613. doi: 10.1242/dev.170613. https://pubmed.ncbi.nlm.nih.gov/30401784/

3.- Murielle Saade, Elena Gonzalez-Gobartt, Rene Escalona, Susana Usieto and Elisa Martí (2017) Shh-mediated centrosomal recruitment of PKA promotes symmetric proliferative neuroepithelial cell division. Nature Cell Biology 19, 493–503 (2017) doi:10.1038/ncb3512. http://www.nature.com/ncb/journal/v19/n5/abs/ncb3512.html

4.- Murielle Saade, Irene Gutierrez, Gwenvael Le Dreau, M Angeles Rabadán, David G. Miguez, Javier Buceta and Elisa Martí (2013) Sonic hedgehog signaling switches the mode of division in the developing nervous system. Cell Reports 4(3):492-503. doi: 10.1016/j.celrep.2013.06.038. http://www.ncbi.nlm.nih.gov/pubmed/23891002

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