

Internship Proposal

Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute) : Centre Interdisciplinaire de Recherche en Biologie/Collège de France

Research Unit Director : Marie-Hélène Verlhac

Research Team Director : Martine Cohen-Salmon

Team name : Physiology and physiopathology of the gliovascular unit

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2. Internship project title:

Characterization of the gliovascular unit development

3. Internship Description :

Astrocytes are the most numerous neuroglial cells in the brain (CNS) and constitute a predominant influence for the cerebrovascular system. They control perivascular homeostasis, blood-brain barrier (BBB) integrity, crosstalk with the peripheral immune system, endothelial transport, or vessel contractility in response to neuronal activity ^{1 2}. Astroglial regulation toward the cerebrovascular system is set at the level of the gliovascular unit (GVU), a specialized interface composed by astrocyte perivascular processes (PvAP) terminated by endfeet that fully sheath the brain vessels ³. Such morphological and functional polarity is of critical importance for the brain physiology and pathophysiology as it is altered in several pathological contexts ². Nevertheless, how this specific astrocyte/vessel interface is formed during brain development and progressively influences vascular functions in the brain is a question that has never been clearly addressed. The present project aims at characterizing the gliovascular interface development and deciphering the mutual astrocyte/vascular system influences in this process. We will focus our study on two main questions:

1) The development of the PvAPs: We have set in collaboration with the group of Karine Loulier (IBM, Montpellier) state-of-the art transgenic tools, multicolor high resolution and large

volume imaging techniques to track individual astrocytes and precisely describe the GUV development ⁴.

2) The molecular mechanisms related to PvAP development: We recently demonstrated that local translation, a molecular mechanism crucial to the acquisition of cell functional morphological polarity, occurs in PvAPs. Local translation was also found in radial glia processes, the neuron and astrocyte progenitors, suggesting that this mechanism is involved in the cortical development ⁵. Our recent results demonstrate that local translation occurs in maturing PvAPs. Using already set and validated experimental approaches ^{6, 7}, we propose to characterize local translation in PvAPs during cortical development.

The developmental trajectory and organization of the GUV has never been fully characterized. Astrocytes entirely cover brain vessels at adult stages. However, how this coverage is established during development is still poorly understood. Here, using a combination of high resolution imaging techniques and dedicated molecular approaches, we will describe for the first time the GUV development. This project is based on solid preliminary data and previously validated experimental approaches and is expected to highlight fundamental neurodevelopmental processes that have remained unexplored.

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3. Mathiisen TM, et al. *Glia.* 2010 Jul;58(9):1094-103.
4. Loulier K, et al. *Neuron.* 2014 Feb 5;81(3):505-20.
5. Pilaz LJ, et al. *Curr Biol.* 2016 Dec 19;26(24):3383-92.
6. Boulay AC, et al. *Cell Discovery.* 2017;3:17005.
7. Boulay AC, et al. *Methods Mol Biol.* 2019;1938:105-16.