Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : **IBPS, CNRS UMR 8246 – INSERM U1130**
Research Unit Director : **Hervé Chneiweiss**
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Team name : DSCO (development of the spinal cord organization)

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2. Internship project title:

Probing radial glia-astrocyte lineage activity in gliogenesis in developing spinal cord

3. Internship Description :

Summary: Astrocytes play key roles in regulating the function, therefore the health, of the central nervous system (CNS). So far, a pivotal challenge in neuroscience is to understand their initial integration in neural circuits. Yet, the activity feature of the astrocyte lineage at the onset of gliogenesis remains unresolved. Using embryonic spinal cord as a model for CNS development, this short-term project aims at observing the intrinsic activity in the radial glia precursors and the newly derived astrocytes during gliogenesis, using either or both dynamic imaging and electrophysiology. The expected results will provide novel clues on the activity profile of radial glia-astrocyte lineage.

The mammalian central nervous system (CNS) comprises a comparable number of glial cells and neurons[1]. Astrocytes are a major type of glial cell, and strategically position by surrounding neuronal synapses and brain blood vessels[2]. They play essential roles in CNS homeostasis, such as buffering synaptically released potassium and glutamate to prevent excitotoxicity[3,4], supplying metabolic fuels (e.g., lactate) to sustain neuronal activity[5], and recycling building blocks (e.g., glutamine converted from glutamate) for neurontransmitter synthesis[6]. Notably, astrocytes show multiple forms of rises in intracellular Ca^{2+} concentrations in response to the stimulation of a variety of transmitters or occurring spontaneously[7,8]. As shown by studies in the mammalian brain, astrocyte Ca^{2+} signaling is implicated in regulating gliotransmitter release[9], K^+ and glutamate uptake[10], neurovascular coupling and perisynaptic structural remodeling [8], whereby representing a dynamic signal in astrocyte-neuron interactions.

In spinal cord, astrocytes are similarly involved in sustaining neural network physiology[11-13]. Ca^{2+} signals have been observed in astrocyte network in spinal cord using diverse techniques[14,15]. Meanwhile, accumulating evidence highlights the indispensable involvement of astrocytes in the pathogenesis of spinal cord diseases such as amyotrophic lateral sclerosis[16], spinal muscular atrophy[17], and spinal cord injury[18], in which a prominent feature is the dysregulated astrocytic functional integration.

The functional integration of astrocytes is initiated upon their generation from radial glia precursors, during the gliogenesis phase of CNS development[19]. Radial glia are multipotent precursors evolving from early neuroepithelium cells in spinal cord development, recognized by the displaying of astrocytic properties such as the expression of the glutamate uptake transporters[12,20,21]. Regionally distributed radial glia have been proposed to give rise to astrocytes of different molecular and functional features, resulting in the regional astrocyte heterogeneity[19,22]. In this context, to understand the intrinsic activity in the

transition of radial glia to astrocytes during gliogenesis will provide key insights into initial astrocytic functional integration in spinal cord, and would also offer clues on its potential dysregulation seen in neurological disorders. Similar to astrocytes, Ca^{2+} signal represents one prominent activity in radial glia[23-25 26]. However, the dynamic feature of the Ca^{2+} signal in radial glia-astrocyte lineage during spinal cord gliogenesis remains unresolved. Gaining insights into this issue will help understand the role of radial glia/astrocyte Ca^{2+} signaling in initial astrocytic integration in developing central nervous system.

Here, we propose to use embryonic spinal cord taken from mouse models, to directly image the Ca^{2+} activities in radial glia-astrocyte lineage during the phase of gliogenesis (astrogenesis). Whole spinal cord will be isolated by surgical dissection from embryos at defined embryonic age (E), following the standard procedure established in the host lab[27]. Radial glia and astrocytes will be recognized either by cell specific chemical approaches, or by immunostaining using antibodies recognizing proteins specifically expressed by astrocytes. Confocal microscope will be used to image the spatial distribution of astrocytes and astrogenic radial glia. Dynamic imaging will be performed to study the Ca2+ activities in living embryonic spinal cords, either globally in the whole population of radial glia/astroctyes, or locally in specifically defined subpopulations of cells which will be aided by electrophysiology technique.

Carrying out a portion of these experiments, will enable the student to learn about the general picture of the central nervous system development via the angle of glial signaling, and further the neuron-glia interaction. This also enables the student to practice fundamental methods used in current neuroscience research. The potential results will certainly provide a fresh hint on the radial glia-astrocyte lineage activity in spinal cord gliogenesis, which will help to design and pursue further studies in understanding the role of glial intrinsic activity in astrocytic functional integration.

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