AAP China Scholarship Council - CSC 2024

PROJET DE RECHERCHE DOCTORALE (PRD)

Titre du PRD : Comparative study of peripheral nervous system formation in ascidians: ancestral condition and drift.

DIRECTION de THESE

Porteuse ou porteur du projet (***doit être titulaire de l'HDR***) :

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Ecole doctorale de rattachement : ED515 - Complexité du vivant

Nombre de doctorants actuellement encadrés : 0

CO-DIRECTION de THESE (HDR) ou CO-ENCADREMENT (Non HDR) :

NOM :

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Titre : Sélectionner ou Autre :

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Unité de recherche : Code (ex. UMR xxx) et Intitulé :

Ecole doctorale de rattachement Sorbonne Université : Sélectionner ou autre :

Nombre de doctorants actuellement encadrés :

CO-TUTELLE INTERNATIONALE envisagée : ☐ OUI ☒ NON

DESCRIPTIF du PRD :

*Ce texte sera affiché en ligne à destination des candidates et candidats chinois : il ne doit pas excéder **2 pages** doit être rédigé en **ANGLAIS***

The vertebrate peripheral nervous system (PNS) is defined as the portion of the nervous system outside of the central nervous system (CNS), the brain and the spinal cord. It arises during embryonic development from discrete ectodermal cell populations, the neural crest and the placodes, that form dorsally at the border of the neural plate. Since these cell populations also give rise to a variety of cell types and structures that make vertebrates unique, understanding their formation and identifying their evolutionary origins has been the focus of numerous studies. The different steps of PNS formation and the underlying cellular and molecular mechanisms have been described in great detail, and formalized into developmental gene regulatory networks (GRNs) that describe regulatory and differentiation genes and their interactions. Importantly, despite some differences between distantly related groups, these GRNs are globally conserved in vertebrates 1–3.

The tunicates are the vertebrate sister group. These marine invertebrates have been scrutinized to understand the emergence of the vertebrate neural crest and placodes, in particular ascidians that are well suited for functional genomics. The larval PNS of the reference ascidian species Ciona intestinalis is made of a small number of chemo- and/or mechano-sensitive neurons that are specified in two steps. First, a broad neurogenic territory is defined following induction involving signaling pathways such as FGF and BMP; second, the binary fate choice between epidermis and neuron is regulated by Notch. The GRNs downstream of these signaling pathways start being resolved with some details and bear a number of similarities with PNS GRNs in vertebrates. However, ascidians belong to a fast evolving group of animals where drift of GRNs is pervasive 4,5. For proper comparison of PNS GRNs between vertebrates and ascidians it is essential to infer the ancestral condition of the GRNs in ascidians.

The PhD project aims at achieving this goal and describing GRN drift by performing a functional and comparative study of PNS formation in different ascidian species. Having the C. intestinalis GRN as a reference, the goals will be to determine its deployement in selected species that cover ascidian lineage diversification by:

- describing the PNS and the expression of orthologous genes

- evaluating the role of key signaling pathways (FGF, BMP, and Notch) in the formation of neurogenic territories and neurons

- studying gene expression regulation at the level of cis-regulatory DNA using in vivo and cross-species assays

- determining the function of key nodes of the GRNs by gene inactivation using CRISPR/Cas9

1. Patthey, C., Schlosser, G. & Shimeld, S. M. The evolutionary history of vertebrate cranial placodes – I: Cell type evolution. Developmental Biology 389, 82–97 (2014).

2. Schlosser, G., Patthey, C. & Shimeld, S. M. The evolutionary history of vertebrate cranial placodes II. Evolution of ectodermal patterning. Developmental Biology 389, 98–119 (2014).

3. Martik, M. L. & Bronner, M. E. Riding the crest to get a head: neural crest evolution in vertebrates. Nat Rev Neurosci 1–11 (2021) doi:10.1038/s41583-021-00503-2.

4. Chowdhury, R. et al. Highly distinct genetic programs for peripheral nervous system formation in chordates. BMC Biol 20, 1–25 (2022).

5. Coulcher, J. F. et al. Conservation of peripheral nervous system formation mechanisms in divergent ascidian embryos. eLife 9, e59157 (2020).

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