Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : **UMR-1270, Inserm, Sorbonne université** **Intitulé Equipe : Stem cells and Neurodevelopment** **ED d'appartenance : ED CDV 515** **Responsable de l'Equipe : Stéphane Nedelec**	**Responsable du Stage :** **Contacts Stéphane Nedelec** Adresse : Institut du Fer à moulin, 17 rue du Fer à Moulin 75005 Paris Email : stephane.nedelec@inserm.fr Tel :+33145876159 (email de préférence)

Titre du projet: Molecular mechanisms of human nervous system development using embryonic organoid models derived from human pluripotent stem cells

Résumé du Projet de Stage

Human nervous system development relies on the formation of a neural tube along which distinct neuronal populations are generated supporting the emergence of neural circuits encoding our behaviors. The molecular mechanisms coordinating neural tube **morphogenesis** (formation of an elongated, folded, neuronal tube) with **cell fate specification** (generation of distinct neuronal identities) remain largely unknown in human despite numerous diseases affecting these processes. In the "Stem cell and Neurodevelopment" team, we are using 3D-differentiation of **human pluripotent stem cells** (hPSCs) into **organoids** or specific cell types coupled to transcriptomic, pharmacological and live imagining to tackle this question. We have recently developed a new organoid model that recapitulate human embryo caudal regions' development including the formation of a neural tube along which different neuronal populations controlling motor behaviors are specified.
The project is aiming at using this in vitro model to study how signaling molecules coordinate neural tube morphogenesis with cell fate specification to engineer new models of human nervous system disorders. In collaboration with the LOCCO lab (Institut Curie, PI: Mathieu Coppey, specialist of **optogenetic** tools to study cell biology, see second page for referenecs), we are developing genetically-modified hPSCs carrying live reporters of signaling pathway activities and light-activable versions of signaling effectors (optogenetic). The student will use these tools complemented with pharmacological approaches to record and perturb pathway activities in organoids and determine the parameters by which they control shape (neural tube formation) and cell fate (neuronal diversity). This project will provide a unique mechanistic model of cell fate and tissue morphogenesis in human. It will also help improving human cell and tissue engineering for basic and translational research.

Publications de l'équipe relatives au projet de stage (max 5)

- *Dynamic extrinsic pacing of the HOX clock in human axial progenitors control motor neuron subtype specification.* Mouilleau V*, Vaslin C* et al . **Development.**148. **2021**
- *In vitro models of spinal motor circuit's development in mammals: achievements and challenges.* **Nedelec S** and Martinez-Arias A. **Current Opinion in Neurobiology.** 66:240-249**. 2021**
- *BMP4 patterns Smad activity and generates stereotyped cell fate organization in spinal organoids*. Duval N. et al. **Development**, Jul (14);146, **2019**.
- *Combinatorial analysis of developmental cues efficiently converts human pluripotent stem cells into multiple neuronal subtypes.* Maury Y et al, **Nature Biotechnology**. 33 :89-96, **2015**
- *Optogenetic dissection of Rac1 and Cdc42 gradient shaping.* de Beco S. et al. **Nature Communication**, **2018**