

Internship Proposal

Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : Neurosciences Paris Seine, INSERM U1130/CNRS CNRS UMR 8246

Research Unit Director : Hervé Chneiweiss
Research Team Director : Pascal Legendre
Team name : Development of Spinal Cord Organisation

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2. Internship project title:

Role of acetylcholine release at the onset of the first electrical activity and synaptogenesis in the embryonic mouse spinal cord

3. Internship Description :

Cholinergic signaling via nicotinic acetylcholine receptors (nAChRs) is necessary for the generation of synchronized neuronal activity (SNA) in many parts of the fetal central nervous system such as the spinal cord (SC). Cholinergic SNA begins at a time when axons are still growing and making their first synaptic connections. Previous studies suggest that SNA is necessary for the proper formation of neuronal connections in the developing network. However, its exact role and mode of action are still poorly understood, especially during the formation of spinal motor networks in the embryo. Our studies show that in the SC, SNA not only involve a recurrent loop between cholinergic motoneurons (MNs) and spinal interneurons (INs) but also interact with glial cells and neural stem cells. However it remains unknown how acetylcholine (ACh) is released from MNs and how it controls INs activity during SNA.

To address this issue MNs will be activated using optogenetic stimulation (ChAT-ChR2-EYFP mice) and holographic stimulation. To determine whether MN stimulation results in paracrine ACh release, we will use the "sniffer" technique. We will then record and dye-fill individual IN and activate groups of MNs at various locations using holographic stimulation. Based on preliminary data of the team, it will be tested whether release of ACh by MNs could trigger INs to fire by acting either on postsynaptic (orthodromic) or presynaptic (antidromic) or both nAChRs. The spatial arrangement of MN-IN cholinergic interaction will then be mapped. If MNs only act through postsynaptic nAChRs, only INs located in the same segment should be activated, since MN neurites are confined to a narrow segment. Rather, if MN act on presynaptic nAChRs located on RC axons, MNs located several segments away should evoke an antidromic action potential in INs.