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

Internship Proposal
Academic Year 2019-2020

1. **Host team :**

Research Unit (e.g. Department or Institute): Institut du Cerveau et de la Moelle
Research Unit Director: Dr Alexis Brice
Research Team Director: Lubetzki, Stankoff
Team name: Repair in Multiple Sclerosis: From biology to translation

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Supervisor of the Research Intern for this project: Dr Bernard Zalc
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2. Internship project title: ***Contribution of microglia in Myelin repair***

3. **Internship Description :**

In Multiple Sclerosis (MS), in order to prevent irreversible axonal damage, there is a crucial need to develop strategies aimed at repairing myelin loss. Several therapeutic targets have been identified. Oligodendrocytes and oligodendrocyte precursor cells (OPCs) are obvious candidates, but microglial cells may also have a beneficial role to play. Based on recent preliminary results, our working hypothesis is that the interaction of microglial subtypes with OPCs and axonal domains plays a significant role in inducing and favoring remyelination. Understanding the fine-tuning of these interactions will help to define novel therapeutic targets.
The identification of targets on microglia that can be manipulated for improved outcome will be essential to the development of therapies for progressive MS. It is therefore of great relevance that we have previously identified that the **TAM family of receptor tyrosine kinases (RTKs)** are important regulators of innate immunity and that they are attractive candidates for therapeutic targeting in MS.
Taking advantage of transparency of tadpoles we have developed a **transgenic Xenopus laevis,** that expresses GFP and a conditional suicide gene in oligodendrocytes (Kaya etal., 2012) and a different fluorescent reporter in microglial cells (tdTomato). This transgenic allows conditional ablation of myelin-forming oligodendrocyte and demyelination together with good accessibility for **live imaging**.
Preliminary results have shown that activation of MERTK (member of the TAM family) improves remyelination, whereas antagonists of MERTK inhibits remyelination.
Specific aim 1: Establishing that Mertk expression by microglia enhances their reparative capacity, leading to improved outcome in central demyelinating disease
Specific aim 2: Screening candidate molecules against receptor tyrosine kinases (RTKs) acting on Mertk using our double transgenic lines for live imaging of oligodendrocyte (green) and microglia (red) during conditional demyelination/remyelination in the Xenopus tadpole