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: Institut de la Vision, Sorbonne Université, INSERM, CNRS
Research Unit Director: Pr JA SAHEL
Research Team Director: Dr O GOUREAU
Team name: Retinal development and repair

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Supervisor of the Research Intern for this project: Dr G. ORIEUX
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2. Internship project title:

Assessment of the therapeutic potential of retinal ganglion cells derived from human induced pluripotent stem cells

3. Internship Description:

Retinal ganglion cells (RGCs) whose axons form the optic nerve are the unique output from the retina to the central visual areas. RGCs degeneration, causing permanent loss of vision, is observed in different optic neuropathies such as glaucoma which is the second cause of blindness in the world. New alternative therapeutic approaches are under development for these patients with no treatment available. Our project aims to develop new stem-cell based therapy to replace lost RGCs by using RGCs derived from human induced-pluripotent stem cells (iPSCs). Our recent studies have shown that, following simple manipulations, iPSCs can be differentiated into retinal organoids. These mini 3D retinas contain all the retinal cell types, particularly the RGCs, and we have developed a magnetic cell sorting system allowing the selection of RGCs by targeting the CD90 protein, specifically expressed on the cell surface of RGCs.

Based on these preliminary results, one objective of the project presented here is to inject purified human iPSCs-derived RGCs in the vitreous of immunodeficient mice to evaluate the survival and the spatial distribution of transplanted cells, essentially by immunostaining with specific human and RGC markers. After this initial phase, the same approach will be performed in mice with an optic nerve lesion (degeneration of RGCs). The survival, differentiation and integration of transplanted cells in the host retina will be follow-up on longer term (up to 3 months) using histological approaches and immunostaining (markers of RGCs, neuronal maturation and synaptic compartments). Cell death will be also assessed using TUNEL labelling or immunostaining of specific markers of apoptosis. The ultimate goal (beyond a M2 project) will be to evaluate and validate the functionality of RGCs as well as their ability to regenerate the optic nerve in this mice model of optic neuropathy.