

Internship Proposal Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : Institut des Neurosciences Paris-Saclay (Neuro-PSI)

Research Unit Director : Dr Philippe Vernier

Research Team Director : Muriel Perron

Team name : SCANR / CERTO

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2. Internship project title:

Investigate the role of GSK3 kinases in retinal cell death under degenerative conditions.

3. Internship Description :

Glycogen Synthase Kinase 3 (GSK) proteins are key mediators of multiple signaling pathways, with crucial roles in coordinating fundamental biological processes during neuronal development. GSK3 alpha (GSK3a) and beta (GSK3b) are encoded by two different genes that control the balance between neural progenitor proliferation and differentiation in the central nervous system. Deregulation of GSK3 kinases have also a key role in neurodegenerative diseases (i.e. Alzheimer's, Parkinson's disease). Drugs targeting GSK3s hold a lot of promises to treat such diseases. Whether these kinases are also important during retinal neurodegenerative diseases remains an open question.

Our preliminary data suggest that partial loss of either Gsk3a or Gsk3b has a beneficial effect on retinal neuron survival. In this context, the goal of this internship is thus to determine whether GSK3 kinases are relevant targets for retinal degenerative diseases. The student will investigate the role of GSK3 kinases in retinal cell survival under different degenerative conditions using mouse lines allowing conditional deletion (CKO) of either one or both genes (Gsk3a and/or GSK3b). We will use different models of retinal degeneration, including *ex vivo* culture of retinal explants, optic nerve crush, light exposure and MNU or NMDA injections. The student will perform series of immunolabeling, qRT-PCR, immunoblot and TUNEL assay to decipher the role of GSK3 during retinal cell death. Depending on the results, whole transcriptome sequencing experiments will be performed to identify the molecular mechanisms underlying protective effects.