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):
INSERM, UMR_S968
CNRS, UMR_7210
Sorbonne University
Institut de la Vision

Research Unit Director :
José-Alain SAHEL
Research Team Director :
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Team name :
Team S6, A-Z

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2. Internship project title:

Decipher retinal signaling using transcriptomic data

3. Internship Description :

Photoreceptors transform light into a biochemical signal, which gets processed through the retina via the bipolar, amacrine, ganglion cells and the optic nerve to the brain, allowing us to see. The initial steps in the phototransduction cascade are well understood, while the further signalling remains to be dissected in more detail. Rods synapse with rod ON-bipolar cells and cones synapse with cone ON- and OFF-bipolar cells. Knowledge about the phototransduction cascade was gained by genetic studies on progressive retinal diseases, in which molecules of this cascade are mutated. Particularly, knowledge about the signaling from photoreceptors to bipolar cells was gained by genetic studies on congenital stationary night blindness (CSNB), in which molecules of this cascade are mutated. Mutations in *NYX*, *GRM6*, *TRPM1*, *GPR179* and *LRIT3* lead to complete (c)CSNB, which implies ON-bipolar cell dysfunction, which is confirmed by the respective protein localization in rod and cone ON-bipolar cells. Patients with cCSNB

often have high myopia and nystagmus, in addition to night blindness. Promising preliminary data have shown that the night blindness phenotype might be rescued by gene therapy. Although genetics helped to add molecules to this signaling cascade, both their function and further signalling via amacrine and ganglion cells are not well understood. Other molecules need to be identified to elucidate this cascade in more detail, which may also help in understanding associated phenotypes. Here we will perform a comprehensive transcriptomic approach to identify novel molecules essential in this cascade by comparing available RNAseq transcriptomic data from 3 different mouse models lacking functional GRM6, GPR179 and LRIT3. Identified molecules will be validated in silico, by RT-PCR experiments and ex in vivo on retinal sections. Promising candidates will be tested for mutations in patients. These findings will identify key players missing from our understanding of retina signalling; unravel novel diagnostic targets as well as therapeutic approaches to benefit patients.