MASTER 2 Neurosciences Fondamentales et Cliniques

Internship proposal 2021-2022

(internship from January to end of May 2022)

Host laboratory:
Institut NeuroMyoGène, CNRS UMR5310 | INSERM U1217, Université Claude Bernard Lyon 1, Faculté de Médecine, 8 Avenue Rockefeller, 69008 LYON, FRANCE.

Host team :
Genetics and Neurobiology of *C. elegans,* Team leader: Professeur Jean-Louis Bessereau, Team website: https://www.inmg.fr/bessereau/?lang=en

Internship supervisors :
Manuela D'Alessandro, Researcher, CRCN Inserm
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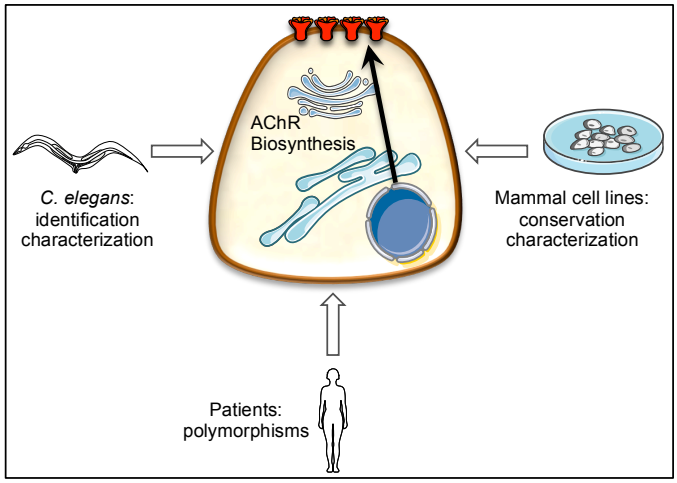
Project title :
Genetic control of acetylcholine receptor biosynthesis: from C. elegans to human pathologies.

Project summary :
Acetylcholine ionotropic receptors (AChR) are supporting neuro-transmission at the neuromuscular junction and have a neuromodulatory function in the central nervous system. Dysfunction of these receptors is linked to several pathologies, including myasthenia, schizophrenia or epilepsy. The quantity of the receptors present at the plasma membrane is thus finely tuned and results from a balance between biosynthesis, recycling and degradation.

One axis of our research aims to identify and characterize new factors involved in the biosynthesis of the AChR. Our strategy consists in:

1. identifying new factors involved in AChR biosynthesis using the model organism *Caenorhabditis elegans*,
2. characterizing the function of these factors in *C. elegans*,
3. testing the conservation of the function in human cell lines,
4. data mining for polymorphisms in the identified genes that might be associated with human diseases; if applicable, introducing the same polymorphisms in *C. elegans* genome to test the potential pathogenicity of the human mutation



Please send your proposal to emiliano.macaluso@univ-lyon1.fr and marion.richard@univ-lyon1.fr for publication on the Master of Neuroscience website.

During the internship, the student will characterize two proteins, TMED7 and TMED2, which have been identified by a genetic screen conducted in *C. elegans*. TMED7 and TMED2 are involved in endoplasmic reticulum to Golgi mediated transport. Until now, they have never been linked to AChR biosynthesis.

3-5 recent publications :

- D'Alessandro M, Richard M, Stigloher C, Gache V, Boulin T, Richmond JE, Bessereau JL. 2018. CRELD1 is an evolutionarily-conserved maturational enhancer of ionotropic acetylcholine receptors. **Elife** 7 pii: e39649.
- Abiusi E, D'Alessandro M, Dieterich K, Quevarec L, Turczynski S, Valfort AC, Mezin P, Jouk PS, Gut M, Gut I, Bessereau JL, Melki J. 2017. Biallelic mutation of UNC50, encoding a protein involved in AChR trafficking, is responsible for arthrogryposis. **Hum Mol Genet** 26:3989-3994.
- The netrin receptor UNC-40/DCC assembles a postsynaptic scaffold and sets the 2 synaptic content of GABAA receptors. Zhou X , Gueydan M , Jospin M , Ji T, Valfort A, Pinanlucarre B, Bessereau JL. **Nat Commun.** 2020