Therapeutic approaches for C9ORF72-Amyotrophic Lateral Sclerosis (ALS)

Acronym: DRUG- C9DPR

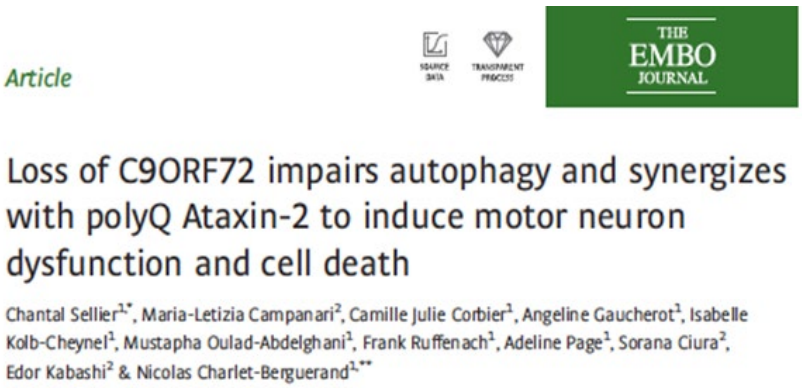
Principal Investigator: Nicolas CHARLET- BERGUERAND

Grant: 100 000€

Duration: two years

Summary of the research project

ALS is a progressive, lethal and devastating disorder that leads to progressive muscle weakness and death from respiratory failure. The most common genetic cause of ALS is an expansion of GGGGCC (G4C2) repeats located within the C9ORF72 gene. This mutation leads to expression of toxic proteins composed of dipeptide repeats (DPR) translated from the repeats, and to decreased expression of the C9ORF72 protein. Thanks to a previous (2015-2016) funding from the Thierry Latran foundation, we found that the C9ORF72 protein regulates autophagy (Sellier et al., 2016), a catabolic process essential to neurons.


Article

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Loss of C9ORF72 impairs autophagy and synergizes with polyQ Ataxin-2 to induce motor neuron dysfunction and cell death

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With this new project, they want to explore further this mechanism showing that death of motoneurons is due to a vicious cycle: GGGGCC repetitions diminish the expression of the C9ORF72 protein, which alters the ability of neurons to degrade the DPR protein aggregates, which are translated from GGGGCC repetitions. In addition, they showed in preliminary results that pharmaceutical compounds could "break up" this vicious cycle and slow the death of neurons in cell culture. The researchers therefore want to test these molecules in animal models in order to confirm these results and hope to develop a potential treatment strategy.

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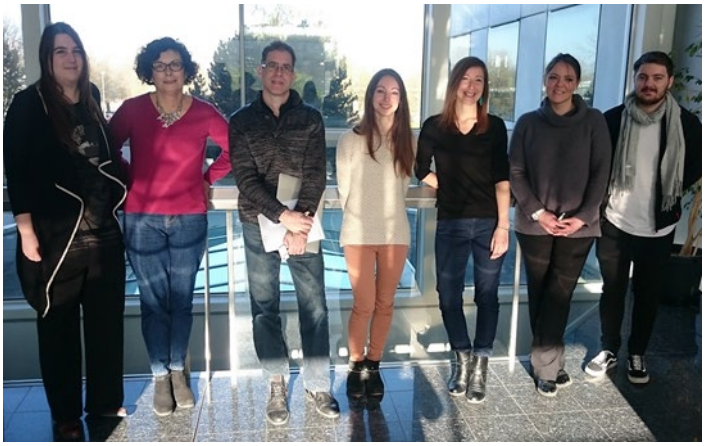
The study will be conducted by Nicolas Charlet Berguerand, team leader of the RNA diseases grop within the department of Translational Medicine and Neurogenetics at the Institute of Genetics and Molecular and Cellular Biology (IGBMC) in Strasbourg, France.



Research team from left to right:

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