2015 Call for Projects

Novel animal models for ALS

Acronym : Model- ALS

Principal Investigator: Nicolas Charlet Berguerand

Grant : 50 000€

Duration : one year

Summary of the research project

ALS is a progressive, lethal and devastating disorder that leads to progressive weakness and death from respiratory failure. Recently, the most common genetic cause of ALS-FTD was identified as a non-coding expansion of CGGGGC repeats located within the first intron of the C9ORF72 gene. This mutation leads to expression of an RNA containing expanded CCGGGG repeats, expression of dipeptide translated from the GGGGCC repeats, and to decreased expression of the C9ORF72 gene. Currently, it is unclear which one of these mechanisms is the leading cause of motor neuron degeneration and death. Also, while mutation in the C9ORF72 gene is the most common cause of ALS-FTD, there is little, yet, known on the function of C9ORF72. Thus, we propose to determine the consequences of C9orf72 loss in a rat knock-out model.

Although many progresses have been accomplished to understand the mechanisms of ALS-FTD pathogenesis, several points remain obscure. Thus, analysis of C9ORF72 function and development of animal models are instrumental to pinpoint the leading mechanisms of neuronal degeneration in ALS-FTD, as well as to identify relevant biomarkers and to develop appropriate therapy strategies (i.e. targeting the GGGGCC repeats, the DPR or the decreased expression of C9ORF72).

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Relevant research articles for this project is :

❖ Modeling key pathological features of frontotemporal dementia with C9ORF72 repeat expansion in iPSC-derived human neurons. *Almeida S, Gascon E, Tran H, Chou HJ, Gendron TF, Degroot S, Tapper AR, Sellier C, Charlet-Berguerand N, Karydas A, Seeley WW, Boxer AL, Petrucelli L, Miller BL, Gao FB*. Acta Neuropathol. 2013 Sep;126(3):385-99.