JPND research
EU Joint Programme – Neurodegenerative Disease Research

Fly-SMALS

Common RNA-dependent pathways for motor neuron degeneration in spinocerebellar muscular atrophy and amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA) are characterized by degeneration of motor neurons. Both diseases are characterized by non-functional ribonucleic acid (RNA)/protein complexes and impaired neuronal RNA homeostasis, which might however be triggered by distinct mutations in the three conserved RNA-associated proteins TDP-43, FUS and SMN, respectively.

We will test the hypothesis that neurodegeneration in ALS and SMA share common molecular pathways triggered by distinct mutations through a combination of genetic, biochemical and functional studies using transcriptomic/ proteomic and computational approaches.

First we will assess which genes and splicing isoforms differ in ALS compared to SMA using drosophila fly models. We seek to determine the neuronal-specific RNA-protein and protein-protein interactions established by the drosophila homologues of the disease-causing proteins Fus, TDP-43 and SMN. We thereby aim to identify common neuronal gene networks or pathways and their contribution to disease progression.

The findings will be translated to the human situation by verifying if the identified candidate genes are also mis-regulated in tissue derived from affected patients, with the goal of developing clinically relevant markers and therapeutic targets. This shall allow for reliable monitoring of ALS and SMA disease progression and the eventual development of biomarkers for early therapeutic intervention.

Total Funding: To Be Finalised *

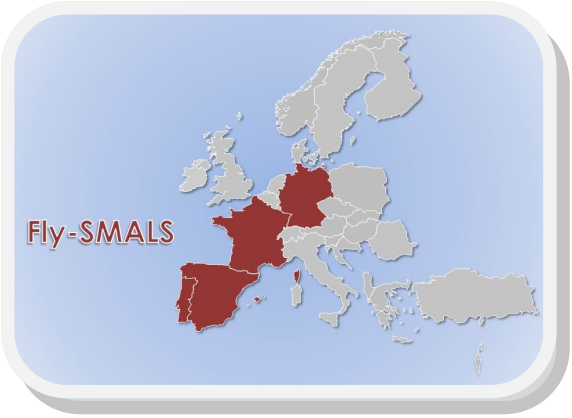
Start Date: May 2015

Duration: 3 years

Coordinator: Jörg B. Schulz

T: + 49 241 808 9600

E: jschulz@ukaachen.de



Project Partners:

COORDINATOR I JORG B. SCHULZ

- **Jörg B. Schulz**, University Medical Center, RWTH Aachen, Germany
- **Aaron Voigt**, University Medical Center, RWTH Aachen, Germany
- **Florence Besse**, University of Nice Sophia-Antipolis, Nice, France
- **Margarida Gama-Carvalho**, University of Lisbon, Lisboa, Portugal
- **Javier De Las Rivas**, University of Salamanca, Salamanca, Spain
- **Joachim Weis**, University Medical Center, RWTH Aachen, Germany

* Contributions from participating JPND Member Countries are currently being finalised for this project