Investigating the role of exosomal RNA in C9orf72 astrocyte toxicity, moving towards gene therapy approaches

Acronym : Astrocyte secretome

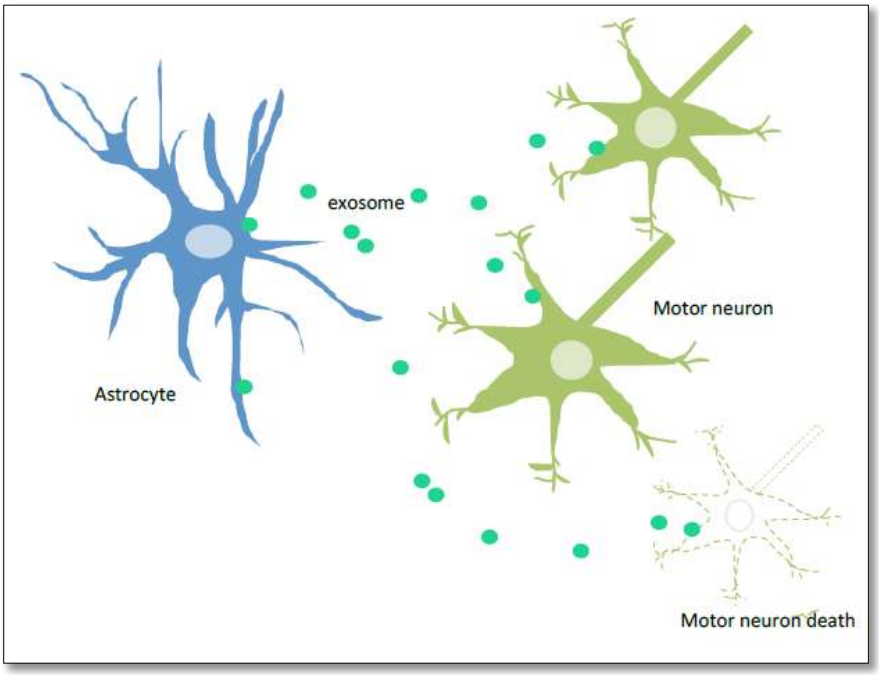
Principal Investigator: Laura Ferraiuolo

Grant : 73 600€

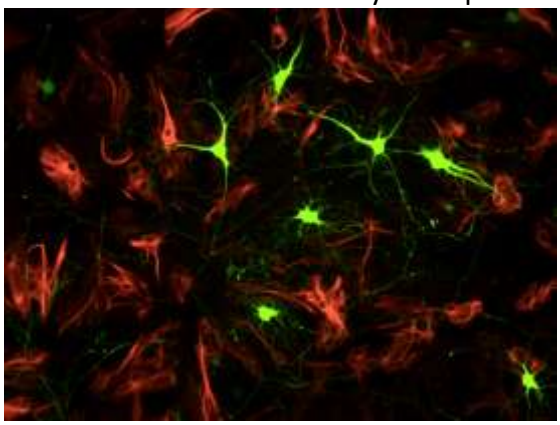
Duration : two years

Summary of the research project

Introduction: Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative condition that affects the nerves responsible for muscle movement. Patients experience initially muscle weakness that progresses inexorably to paralysis and eventually death by respiratory failure. One of the most intriguing characteristics of ALS is the recent discovery that the cells normally supporting neurons, the glial cells, are "going rogue" during disease progression and become actively toxic to motor neurons. Interestingly, this toxicity can be transferred through soluble factors that are secreted by astrocytes, a specific kind of glial cells, and are then picked up by motor neurons, like a sort of Trojan horse.



The research tools: SITraN is one of the few research centres in the world that has access to a new, fast and very reliable method to produce motor nerves and other cells involved in ALS directly from patient skin cells. In particular, this project will focus on the cells surrounding the neurons in the spinal cord, i.e. the astrocytes. Astrocytes make up for about 80% of glial cells in the central nervous system. It has been discovered that astrocytes from ALS patients are able to kill neurons when they are cultured together in a dish. We will use **human astrocytes** derived **from ALS patients and non-affected individuals** to identify the factors that these cells secrete and might be responsible not only for neuronal death, but also disease spreading.



Human **Astrocytes** in red and Neurons in green

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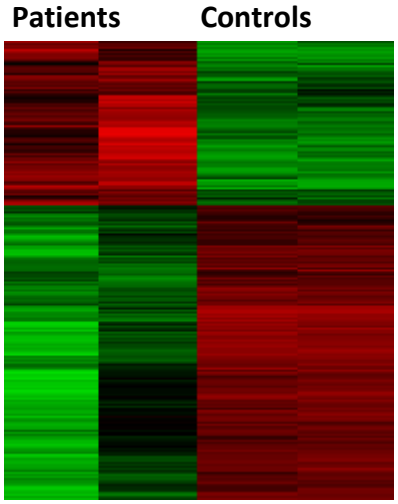

Analysis of the transcripts secreted by patients and controls.

Outcome: We have the unique opportunity to study human astrocytes from several ALS patients and identify the factors that are secreted by this cell type. We believe that this approach will reveal the identity of toxic factors. This will provide new therapeutic targets for gene therapy or drug approaches to halt disease progression.

This project is conducted at SITraN, Sheffield Institute for Translational Neuroscience by Dr Laura Ferraiuolo.

Team working on the project

from left to right:

Miss Monika Myszczynska (technician)

Dr Matthew Stopford (Post-doc)

Dr Laura Ferraiuolo

Dr Guillaume Hautbergue (co-Applicant)