June 2022

The TREAT-ARCA Project

The **TREAT-ARCA** project, which began in June 2021, is a preclinical research project focused on two rare ataxias: Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (**ARSACS**) and **COQ8A-ataxia** (also known as Autosomal Recessive Cerebellar Ataxia type 2 ARCA2). This 3-year project received funding from the EU's Horizon 2020 research and innovation programme.

The Project

Recessive ataxias, of which ARSACS and COQ8A-ataxia are two examples, are those which are passed on when a person receives a faulty copy of the gene from both parents (the parents will not have symptoms). Symptoms such as problems with balance, coordination and slurred speech are caused by progressive degeneration of the cerebellum, which is involved in coordinated movement. There are currently no disease-modifying treatments available for any of the ataxias.

The TREAT-ARCA project has four objectives.

(1) Test two promising repurposed drugs in mouse models of ARSACS and COQ8A-ataxia. Repurposed drugs are those which are already approved for another condition, thus potentially decreasing the development time as clinical trials have already been conducted and the drug is already in use.

(2) Test novel drugs for ARSACS in a mouse model. Novel potential treatments for ARSACS have already been identified in previous work.

(3) Test gene therapy for COQ8A-ataxia in a mouse model. COQ8A-ataxia is caused by a mutation in the gene which codes for the COQ8A protein, which could potentially be corrected by introducing the non-mutated version of the gene to the central nervous system.

(4) Identify and validate biomarkers. When preparing for ataxia clinical trials in the future, it is vitally important that neurologists have a way of measuring whether the treatment is working. This is achieved by identifying biomarkers. Failure to identify a good biomarker can even be the cause of a failed clinical trial.

Why is this research important?

The preclinical work planned in this project could help to identify potential treatments for ARSACS and COQ8A-ataxia, which could then go on to be tested in clinical trials in the future. The researchers involved in this work are carrying out parallel projects aimed at clinical trial-readiness for recessive ataxias (known as PREPARE, PROSPAX and through the Ataxia Global Initiative). By complementing the clinical trial-readiness work with this preclinical project, the researchers aim to identify treatments for ARSACS and COQ8A-ataxia, and to be in a strong position to conduct meaningful clinical trials when treatments have been identified.

Focusing this important work on ARSACS and COQ8A-ataxia will pave the way for similar work in a multitude of other recessive ataxias.

Patient engagement

Research must be informed by the voice of the patient, as the perspective of those living with the condition is key to making sure research projects aim to answer the important questions. To this end, the TREAT-ARCA project includes patient advocacy organisations at every stage of the research.

The patient groups involved in TREAT-ARCA will lead a programme of patient engagement activities, including a regular blog and a webinar series. Updates will be shared via the patient group publications and websites, and on the ARSACS and COQ8A-ataxia RareConnect forums.

The Partners

The TREAT-ARCA project is a global effort, being led by Dr Hélène Puccio from Université de Lyon, and involves research partners from Germany (Prof. Matthis Synofzik), Canada (Dr Bernard Brais), and Italy (Dr Francesca Maltecca). German patient group DHAG, Euro-ataxia (with support from Ataxia UK), and the Ataxia Charlevoix-Saguenay Foundation (based in Montréal) are representing patients on this project.