



Ataxia of Charlevoix-Saguenay
Foundation

ARSACS – APPENDIX TO THE 2015 FINANCING OFFER

Background

In 2006, the Ataxia of Charlevoix-Saguenay was established to reinitiated and accelerate research on autosomal recessive spastic ataxia of Charlevoix-Saguenay (“ARSACS”). At that time, little was known about cellular dysfunction on ARSACS and about the functions of the Sacsin protein. Now, ARSCAS is confirmed as the 2nd most common form of recessive ataxias in the world.

ARSACS Scientific Developments – 2015 Update

The functions of the Sacsin protein are complex. It contributes to the cytoskeleton organization and mitochondrial dynamics in neurons. The absence of Sacsin leads to cytoskeleton and mitochondrial disorganization with an accompanied respiratory defect. As of now, we do not know if such respiratory defect leads to neurons dysfunction and death.

Structural studies have been undertaken that indicate that the Sacsin protein is composed of several different functional domains, one of which the HEPN domain, helps Sacsin to dimerise.

Studies of Sacsin’s chaperon function have also been undertaken. It remains unclear which proteins are clients of Sacsin but it has been proposed that they may play roles in mitochondrial dynamics and proper neurofilament organization and maintenance.

Knockout and Knockin mice have been developed that both develop phenotypes very reminiscent of the human disease.

To support future clinical trials work on a validated clinical ARSACS severity scale, a clinical data base and a natural history study are underway.

To further accelerate basic research and clinical trials an extensive Canadian network is establishing new partnerships with North-American and European colleagues, with the objective of creating an expanded multidisciplinary International ARSACS research network.

Main focus for future funding projects

- ✓ Research related to the Sacsin protein
- ✓ Research related to proteins that are clients of Sacsin's chaperon function
- ✓ Research that would lead to accelerate pre-clinical and clinical trials in ARSACS using already available molecules
- ✓ Research focusing on pre-clinical and clinical investigations on new candidate molecules
- ✓ Research that could accelerate the identification of novel treatments for ARSACS
- ✓ Research that relies on international collaborations

Special consideration will be given to proposals that support new scientists and clinicians to join the ARSACS research community.