APPENDIX

Version disponible en anglais seulement

ARSACS is the common name for Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay. This condition was first seen in people of the Charlevoix-Saguenay region of Quebec, Canada. Most people with ARSACS live in Quebec or have recent ancestors from Quebec. People with ARSACS have also been identified in various countries such as Japan, Turkey, Tunisia, Spain, Brazil, Poland, Italy, and Belgium. It is a progressive disease that affects the body's ability to create a protein called sacsin, normally found in the brain, skin, and muscles. Over 170 *SACS* mutations have been reported worldwide. Mutations in *SACS* may cause a loss of function of sacsin, a poorly characterized and massive (520 kDa) protein.

Research suggests that sacsin might play a role in folding newly produced proteins into the proper 3-dimensional shape because it shares similar regions with other proteins that perform this function. Mutations in the *SACS* gene cause the production of an unstable sacsin protein that does not function normally. It is still unclear how the abnormal sacsin protein affects the brain and skeletal muscles and results in the signs and symptoms of ARSACS.

In existing in vitro (cell and patient's cells) and in vivo (Sacs (-/-) mouse) models, a disruption of mitochondrial transport is observed along with abnormal accumulation of non-phosphorylated neurofilament (NF) bundles in the somatodendritic regions of vulnerable neuronal populations, a significant reduction in mitochondrial motility and elongated mitochondria. Existing data suggest that alterations in the NF cytoskeleton and lines defects in mitochondrial homoeostasis are the underlying pathophysiological basis of ARSACS.

There is currently no treatment available to cure people with ARSACS.

The present call for proposals aims to fund projects that will clearly advance the understanding of the disease and lead the way to the development of a treatment for ARSACS patients.