Poster Presentation

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Structural and functional studies of Sacsin

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Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is an early-onset neurodegenerative disorder caused by mutations in the SACS gene. It was first described in the French-Canadian population in 1978 by JP Bouchard, but ARSACS cases have since been found worldwide. The SACS gene codes for Sacsin, a 520kDa protein, which localizes in the cytoplasm, close to the mitochondria. Sacsin is composed of an N-terminal ubiquitin-like domain, which binds the proteasome, followed by three Sacsin repeat regions (SRR), a DnaJ domain, and at the C-terminus a nucleotide-binding HEPN domain, which mediates dimerization. While over 120 mutations in Sacsin are known to cause disease, the cellular function of the protein remains unclear. We recently crystallized the ATPase-like fragment of the first SRR domain from human Sacsin. The crystals diffract to better than 2A resolution and the structure determination is in progress. Future studies will focus on larger fragments of Sacsin as well as biochemical studies to investigate the cellular function of the protein.

Keywords: ARSACS, Sacsin, SRR domain