“Targeting deregulated calcium homeostasis as potential therapeutic option for ARSACS” - Dr. Francesca Maltecca

Research project 2019-2020

Summary

The group headed by F. Maltecca at Ospedale San Raffaele, Milan, Italy has discovered that the absence of sacsin impacts on calcium homeostasis in cerebellar Purkinje neurons by multiple mechanisms. They found that calcium deregulation appears very early in the Sacs-/- mice, representing a potential trigger of the ataxic phenotype. Indeed, a growing number of genetic forms of cerebellar ataxia shows alteration of calcium as pathogenetic mechanism. As a proof of concept, the researchers conducted a preclinical trial in Sacs-/-mice with an off-label drug regulating calcium homeostasis. This treatment markedly improved the motor skills of Sacs-/- - mice, at both pre- and post-symptomatic stages. Histological analysis of Sacs-/- -treated mice showed an increased Purkinje neuron density when compared with vehicle-treated Sacs-/- controls, suggesting a delayed Purkinje neuron degeneration. These results indicate that targeting calcium may represent a therapeutic option for ARSACS and encourage further optimization of protocols in this direction.

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