"Reduction of Sacsin in peripheral blood mononuclear cells as a diagnostic tool for spastic ataxia of Charlevoix- Saguenay"

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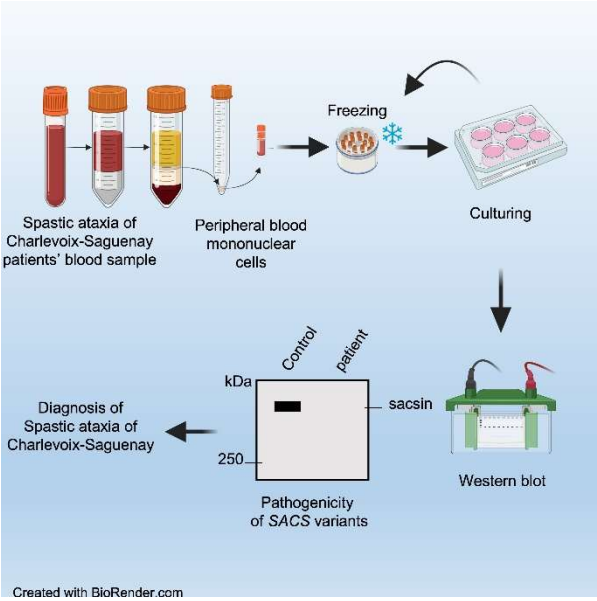

Lay summary

De Ritis *et al*. report a novel, fast and minimally invasive diagnostic method for ARSACS based on the quantification of sacsin protein levels in patients' blood cells. This study represents a follow-up of a previous paper from the Maltecca lab (Longo 2021), in which they demonstrated that sacsin carrying missense variants undergoes cotranslational degradation. In this work, De Ritis developed a protocol that allows propagation and conservation of blood cells for further functional studies and biomarkers research. They show that ARSACS patients with missense variants almost completely lacked sacsin protein in blood cells. Moreover, two healthy carriers of a *SACS* missense variant showed 50% reduction of sacsin protein levels compared to control samples. This work represents an advancement for ARSACS molecular diagnosis, as the quantitative reduction of sacsin determines the pathogenicity of *SACS* missense variants, something which can't be predicted bioinformatically with high certainty.