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# ARSACS NEWS

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**In this edition, we highlight a study identifying the clinical, radiological, and genetic characteristics of Japanese patients with ARSACS, as well as Dr. Maltecca's latest research report, which focused on identifying potential therapeutic compounds to address calcium dysregulation in ARSACS.**
**We also share details about our upcoming participation in the scientific conference dedicated to ARSACS, which will be held in Milan. Finally, you will discover the inspiring story of Christos Scarpinato and learn about the many ways you can support our mission.**

## RESEARCH HIGHLIGHTS

***«Six Novel SACS Mutations Expand the Autosomal Recessive Spastic Ataxia of Charlevoix–Saguenay Spectrum»***

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**Abstract**

**Background:** The clinical spectrum of autosomal recessive spastic ataxia of Charlevoix–Saguenay (ARSACS) in Asian populations remains incompletely defined. We aimed to characterize the clinical, radiological, and genetic features of Japanese patients with ARSACS and to expand the mutational and phenotypic spectrum of this disorder.

**Methods:** We conducted a retrospective case series of patients diagnosed with ARSACS in our department between January 2016 and December 2023. Five patients from four families with biallelic SACS variants were identified.

**Results:** Genetic analysis revealed seven pathogenic SACS variants, of which six were novel. Clinical heterogeneity was notable, with age at onset ARTICLE IN PRESS ranging from 1 to 27 years. Four patients showed classical ARSACS-related neuroimaging findings, whereas one patient presented with a Charcot-Marie–Tooth disease (CMT)-mimicking phenotype characterized by predominant peripheral neuropathy, mild cerebellar involvement, and absence of the classical pontocerebellar magnetic resonance imaging features.

**Conclusions**: The recognition of CMT-mimicking presentations supports considering ARSACS in the differential diagnosis of hereditary peripheral neuropathies, particularly in patients with additional cerebellar, pyramidal, or supportive neuroimaging features.

Read the full article here

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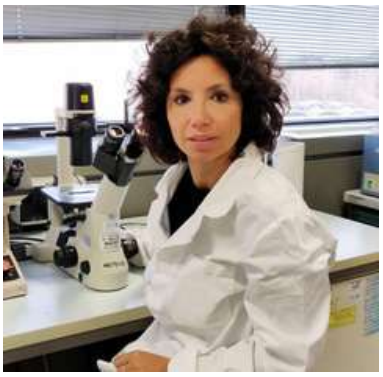
## RESEARCH HIGHLIGHTS

***"Targeting Cav2.1 to recover firing defects and degeneration of Purkinje neurons in ARSACS".***
(1st year)



Francesca Maltecca,PhD, Group Leader,
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This project aimed to identify potential therapeutic molecules to address calcium dysregulation in ARSACS, for which currently no disease-modifying therapies are available. Our previous work (Del Bondio et al., 2023) demonstrated that correcting altered calcium homeostasis can halt Purkinje cell degeneration and improve motor symptoms in a mouse model of the disease, providing strong proof of concept that calcium signaling pathways represent a promising therapeutic target in ARSACS.

Building on these findings, and on our more recent evidence that sacsin plays an important role in regulating calcium channels in Purkinje neurons, this project is exploring complementary pharmacological strategies aimed at restoring calcium homeostasis in disease models. In particular, we investigated the potential of clinically approved compounds known to modulate calcium-related pathways as candidates for drug repurposing in ARSACS.

In parallel, we established a collaboration with a specialized contract research organization to perform a large-scale screening campaign aimed at identifying novel compounds with similar or complementary mechanisms of action. This effort combined advanced computational approaches, virtual screening, and experimental validation to prioritize candidate molecules for further development.

By integrating targeted drug repurposing with broader compound discovery efforts, this project generated important tools, preliminary proof-of-concept data, and a portfolio of promising candidate molecules that we are exploring in the frame of the second year of funding.

Overall, these results provide a strong foundation for the future development of therapeutic strategies aimed at slowing or preventing Purkinje cell dysfunction and degeneration in ARSACS.

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## UPCOMING CONFERENCE FOR ARSACS

### MILAN 2026: SCIENTIFIC CONFERENCE ON ARSACS

The Foundation is pleased to participate to the scientific conference entitled "Focusing on Rare Conditions: Advances, Challenges and New Horizons in ARSACS," which will take place in Milan on September 24, 2026. Among the organisers of this unique event is ARSACS OdV, a parent-led Italian charity dedicated to advancing research and finding a treatment for this rare but globally present condition. This one-day conference will highlight the latest scientific advances, ongoing challenges, and future perspectives for ARSACS.

**TO VIEW THE PROGRAM AND TO REGISTER**

## FUNDRAISING ACTIVITY

### RUNNING IN SUPPORT OF FAMILIES AFFECTED BY ARSACS

On November 1, 2024, Christos Scarpinato lost his mother to Autosomal Recessive Spastic Ataxia of Charlevoix–Saguenay (ARSACS), a rare and degenerative neurological disease. Two years later, he is taking on a meaningful challenge: running a marathon in England in her memory and to help advance research.
On this occasion, a fundraising campaign has been launched to support efforts to better understand and treat this disease, for which there is currently no cure.

👉 Every donation and every share truly make a difference. **Read here**
💙 Support him and be part of this inspiring initiative! **Donate**

### DIFFERENT WAYS TO SUPPORT ARSACS RESEARCH

Every donation brings us one step closer to better treatments for people living with ARSACS. Thanks to the generosity of our supporters, the Foundation can continue funding innovative research projects. No matter how you choose to give, your support helps accelerate research and brings hope to families affected by ARSACS around the world.

**DONATE**

### ORGANISE A FUNDRAISING EVENT OR ACTIVITY



Get creative — host a virtual event, take on a challenge, celebrate a birthday with donations, or organize activities like bake sales or merchandise sales. Every contribution makes a difference.

**Let the Foundation know**

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