DATE : SPRING 2025 NUMBER 3

# ARSACS NEWS

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**In this edition, we bring you the latest updates on ARSACS, including key research highlights and an overview of a project funded by the Foundation. We are also excited to share details about our upcoming ARSACS charity events, new funding opportunities, and important conferences dedicated to ARSACS. Stay informed and engaged as we continue advancing research and fostering collaboration in the rare disease community.**

## RESEARCH HIGHLIGHT

''*Whole Blood DNA Methylation Analysis Reveals Epigenetic Changes Associated with ARSACS*'', by Dr. Daniele Galatolo and his team published in The Cerebelllum.

Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a rare inherited condition described worldwide and characterized by a wide spectrum of heterogeneity in terms of genotype and phenotype. How sacsin loss leads to neurodegeneration is still unclear, and current knowledge indicates that sacsin is involved in multiple functional mechanisms. We hence hypothesized the existence of epigenetic factors, in particular alterations in methylation patterns, that could contribute to ARSACS pathogenesis and explain the pleiotropic effects of SACS further than pathogenic mutations. To investigate this issue, we recruited eight patients affected by ARSACS, four characterized by early onset of the disease and four with late onset. We performed Whole Genome Bisulfite Sequencing using DNA from peripheral blood to define the methylome of patients and compared them with a control group. Our analysis showed that patients with ARSACS exhibit an altered methylation pattern and that the observed differences exist also among affected individuals with different age of onset. Our study provides valuable insights for employing epigenetic biomarkers to assess the severity and progression of this disorder and propels further investigations into the role of epigenetic processes in ARSACS pathogenesis.

Read the full article here:
https://arsacs.com/wp-content/uploads/2025/01/arsacs-clinical-features-pathophysiology-and-i-ps-derived-models.pdf

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# PROJET SUMMARY - RESEARCH FINANCED BY ATAXIA CHARLEVOIX-SAGUENAY FOUNDATION



*"Charting the neurodevelopmental stage of ARSACS (NeurodevARSACS): A cross-species longitudinal characterization of the early molecular changes in the brain, CSF and blood"* by Drs Matthis Synofzik, David Mengel (University of Tübingen, Germany) and Justin Wolter (University of Wisconsin-Madison, USA).

The project aims to define the early molecular and cellular changes in ARSACS, hypothesizing a neurodevelopmental disease phase preceding neurodegeneration. Using a cross-species approach, the study characterizes cerebellar deficits in an ARSACS mouse model alongside fluid biomarkers in both mice and human patients, establishing a mechanistic link between early brain pathology and accessible biomarkers. This work aims to provide critical insights for developing preemptive therapeutic strategies and identifying biomarkers that can serve as clinical trial endpoints, thereby accelerating future interventions for ARSACS.

Over the past two years this team has successfully generated single-nucleus RNA-seq data from the ARSACS mouse at four key time points along disease progression (n=60 animals, ~200k cells). These experiments revealed age dependent alterations in specific cell types, reflecting a cascade of cellular events that define distinct stages. We were able to molecularly dissect Purkinje neuron subtypes, revealing the pathways that distinguish susceptible and resilient neurons. Future studies aim to leverage this information to define pathways which could be targeted to promote Purkinje survival. We also found stage specific involvement of non-neuronal cell types, highlighting the complex interplay of neuronal dysfunction, systemic responses, and time.

To connect this molecular data to patient data, this project collected cerebrospinal fluid and plasma from ARSACS mice and human patients, and analyzed the protein biomarker landscape with both label free mass-spectrometry and targeted assays of promising biomarker candidates. Again, this data highlighted stage dependent proteomic signatures, which reflect both underlying disease mechanisms and systemic response to neuronal dysfunction. Importantly, the Synofzik lab also identified and validated candidate biomarkers that clearly distinguish cases from controls.

The team aims to submit this data for publication in 2025, alongside the public release of these comprehensive dataset to be used by the broader ARSACS research community.

Reference:
https://arsacs.com/wp-content/uploads/2025/04/ARSCAS-Project-Summary-WolterSynofzik-v2.pdf

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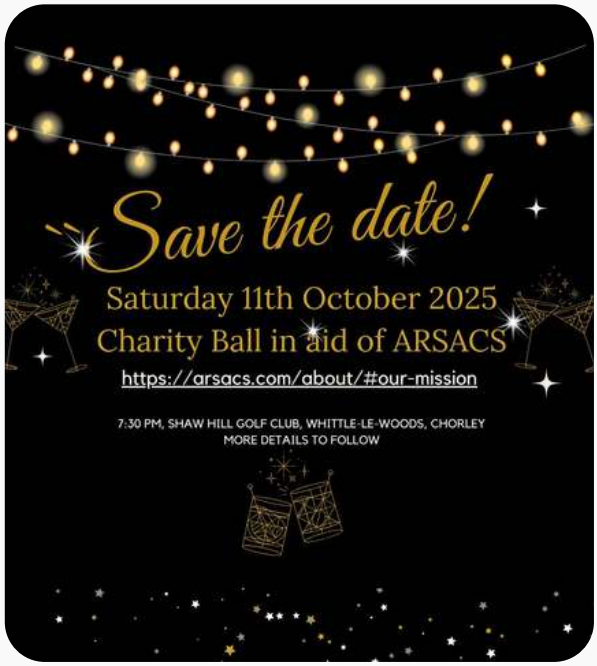
## UPCOMING ARSACS CHARITY EVENTS

A Charity Ball will be held on **October 11, 2025**, in the **UK**, in support to ARSACS research. Stay tuned for more details! For inquiries, contact Maxine Monks: max1436@googlemail.com





Join us on **November 27, 2025**, for the 18th edition of *Le Dîner des Producteurs*, a must-attend annual fundraising event in **Montrea**l dedicated to advancing ARSACS research.

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## SUBMIT YOUR RESEARCH PROJECT BY MAY 23, 2025


The call for proposals has been launched!
The Ataxia Charlevoix-Saguenay Foundation is inviting researchers to apply for funding to support 2025-2026 research projects on ARSACS. This annual funding opportunity aims to advance scientific discoveries and potential treatments for the disease.

Apply now : https://arsacs.com/research/

## UPCOMING CONFERENCES FOR ARSACS

The World Orphan Drug Congress (WODC) 2025 is fast approaching, and the Ataxia of Charlevoix-Saguenay Foundation will be there! From **April 22-24** in **Boston**, we will be participating in discussions and presentations focused on ARSACS research and rare disease advocacy:

- **April 22nd, 4:00 PM**
  Development of a Gene Therapy for Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay; Challenges and Success – Presented by Alexandre Paré (McGill PhD student).

- **April 23rd, 2:30 PM**
  Fireside Chat: ARSACS (Ataxia of Charlevoix-Saguenay): Finding Solutions for Rare Disease Patients – Presented by Sonia Gobeil (cofounder of the Foundation), Betsy Trainor (ARSACS board member), and Dr. Jeremy Schmahmann (Harvard Medical School).

If you're a patient advocate, healthcare professional, or part of a patient group organization, you may qualify for a complimentary pass to attend. Don't miss this opportunity to connect with experts, engage in critical conversations, and support the rare disease community.

WORLD OrphanDrug Congress USA 2025

For more information about the 2025 World Orphan Drug Congress and to register, please visit:
https://www.terrapinn.com/bookwodc_arsacs
50% OFF PROMO CODE : **ARSACS50**

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