From:	Coughlin Lab
To:	Coughlin Lab
Subject:	Coughlin Lab December 2025 newsletter
Date:	Tuesday, December 30, 2025 3:23:51 PM
Attachments:	2025_vanKarnebeek_New tx for PDE due to aldh7a1 deficiency. first proof of principle of upstream enzymes inhibition in the mouse.pdf

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[External Email - Use Caution]

Dear Families,

Thank you for subscribing to the Coughlin Lab PDE newsletter. We are grateful to have you as part of our community.

We hope everyone had a wonderful holiday spent with family and friends.

NEWS:
We are thrilled to share that the CurePDE fundraiser for the siRNA study raised an incredible **$107,090**. A heartfelt thank you to everyone who donated, shared the fundraiser, and cheered on the effort. Your support and belief in this work mean more than we can say. We would also like to extend a special thank you to Anastasia and CurePDE for the generous $50,000 matching contribution, which made this milestone possible.

We are also excited to announce an upcoming webinar in Spanish for our Spanish-speaking families, hosted by our PhD student Nicole, on June 2 at 10:00 AM MST. Nicole will provide a brief introduction to the Coughlin Lab and the projects currently underway, followed by a live Q&A where parents are welcome to ask any questions they may have. The webinar will be recorded and shared on the CurePDE YouTube channel, where it can be viewed with English subtitles.

UPDATES ON RESEARCH:
This recent paper by **van Karnebeek et al.**, describes the development of an Aass/Aldh7a1 double knockout (DKO) mouse model. In this study, metabolite levels in the brain and liver were compared across wild-type mice, Aass knockout mice, Aldh7a1 knockout mice, and the double knockout model.

The enzyme AASS was chosen as a treatment target because people who lack this naturally do not develop serious symptoms. When AASS was inactivated in the mouse model with PDE, levels of the disease-related metabolites, 6-oxo-pipecolate (6-oxo-PIP) and 2-OPP, returned to normal in both the brain and liver. In addition, levels of P6C and pipecolic acid were reduced to amounts similar to those seen in mice lacking only AASS, representing about a two-fold decrease compared to mice with PDE alone.

Together, these findings provide strong evidence that inhibiting AASS can reduce neurotoxic metabolites in PDE-ALDH7A1 mice, supporting the promise of upstream therapeutic strategies. A PDF of the article is attached for those interested in reading more. Email me if you have any questions.

LAB UPDATES:
In parallel with these encouraging findings, progress in the lab continues across several fronts. Mice for the siRNA study are breeding well, and we have successfully generated new offspring from our aging PDE knockout mice. These animals are now being bred to establish

the specific mouse line that will be used to test the siRNA therapy. At the same time, we are developing laboratory tests that enable us to measure the same disease-related metabolites in animals receiving siRNA treatment compared to those that do not.

We are also looking ahead to the January CurePDE webinar, where Curtis will share updates on these efforts as well as several other ongoing projects in the lab.

OPPORTUNITIES FOR INVOLVEMENT:
We have added a couple of new faces to our *Our Little Legends* wall. We are always happy to receive photos to highlight your amazing kids, so if you haven't sent yours in yet, we'd love to see them.

UPCOMING EVENTS:
CurePDE Webinar: January 6, 2026 | 8:00 PM EST

Topic: Conversation with updates from Curtis and information about the 2026 Family Retreat

- **CurePDE Webinar Link: CurePDE webinar link**
- **Past recorded webinars:** Available on the CurePDE YouTube channel

As always, feel free to reach out to us with any questions or suggestions on anything you are curious about.

Sincerely,

--The Coughlin Lab

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