SEPTEMBER 2024

PURA Syndrome FOUNDATION

NEWSLETTER

A letter from our Co-Presidents

Hello PURA Community!

We really enjoyed seeing many of our families at the PURA Conference in June. It was our largest gathering yet and we hope to continue to get together to learn and support one another. If you were unable to join us in person, videos of the presentations are available at our conference website, www.puraconference.org.

At the conference we talked about many of the ways the global Foundation is working to support our families, and one way is by launching our new Clinician Directory. One of the biggest questions we get from new families is how to find doctors familiar with PURA Syndrome. We've been compiling a directory of doctors known to us that see multiple PURA patients and are experts in their specialties. This serves not only to help our community connect with care, but also to help clinicians connect with each other to better care for their patients and support additional research. This directory can be found in the resources section of our website. If you have any clinicians that you think should be included, please contact us at president@pura-syndrome.org.

We are rapidly approaching the 10 year anniversary of the discovery of PURA Syndrome next month! The PURA Foundation has had a few key priorities leading up to the anniversary this year. One is to reach our goal of 100 individuals registered in our Patient Registry by the end of 2024. We are currently at 51 completed registries with 37 more started but incomplete. You can read more about this on page three.

Our second priority is our Together for PURA Fundraiser, which we are looking to raise $250,000 by the end of 2024. We haven't had a major fundraiser since 2020 and in order to continue providing our annual conference, research grant funding, family support and more, we need our PURA family's help. Host a fundraiser, participate in an athletic event, create a team and help us achieve our goal! Every person you reach out to will help us get closer to our goal as well as increase awareness for PURA Syndrome! Any questions, please contact Nancy at n.boccia@pura-syndrome.org.

Finally, we've entered into an agreement with Odylia Therapeutics, who will provide us with a neutral, third party gap analysis of current PURA Syndrome Research. This will allow us to determine what areas we should financially support in order to continue moving the research forward in the most effective and efficient way!

If you have any questions please feel free to reach out to us at president@pura-syndrome.org.

Sincerely,
Liz Astridge & Eva Tucker

The PURA Syndrome Foundation Recently Joined Epilepsies Action Network and Rare Epilepsy Network (REN)

Epilepsies Action Network brings together parents, siblings, caregivers, and advocates in partnership with doctors, nurses, researchers, and policy makers to raise awareness and increase funding for The Epilepsies to improve the lives of all persons living with this disease. The network is currently leading the effort to create a National Plan for epilepsy in the U.S. Alzheimer's, Parkinson's, Autism, ALS, and MS all have National Plans. (Epilepsy is the only common neurological disorder without one.) Learn more

The mission of **Rare Epilepsy Network (REN)** is to work with urgency to collaboratively improve outcomes of rare epilepsy patients and families by fostering patient-focused research and advocacy.

- **Signed On in Support of European Action Plan for Rare Diseases**: Foremost among the Open Letter's demands is a call for the European Commission to launch a comprehensive policy framework in the form of a European Action Plan for Rare Diseases. This framework, with clear and measurable objectives, should foster collaboration across EU Member States and other European countries to significantly improve the lives of people living with rare diseases. Learn more
- **Signed On in Support of Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative:** The BRAIN Initiative is aimed at revolutionizing our understanding of the human brain. It is a partnership between the U.S. Federal and non-Federal partners with a common goal of accelerating the development of innovative neurotechnologies. Through the application and dissemination of these scientific advancements, researchers will be able to produce a revolutionary new dynamic picture of the brain that, for the first time, shows how individual cells and complex neural circuits interact in both time and space. Through this sign-on letter, we urge Congress to prioritize funding for this important program, ensuring that researchers have the resources they need to make significant strides in neuroscience research and drug discovery.
- **Signed Letter in Support of U.S. Funding Appropriations for Epilepsy-Related Programs and Research:** Along with other organizations in the epilepsy community we signed a letter supporting continued or increased funding for epilepsy-related programs and research in FY 2025. It discusses the importance of epilepsy-related programs and research at the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Congressionally Directed Medical Research Programs (CDMRP) and the VA.
- **Signed Letter in Support of Epilepsy Research as Part of 21st Century Cures Act:** The letter thanks Representatives DeGette and Bucshon for their leadership on Cures 2.0, and expresses our strong support for this important initiative. It also urges Congress to continue to build on the 21st Century Cures Act in supporting epilepsy research and the development and coverage of epilepsy therapies. Specifically, the letter discusses the need to support issues and programs that are critical for epilepsy. It also asks Representatives DeGette and Bucshon to include a new provision in Cures 2.0 authorizing a national plan for the epilepsies. Lastly, the letter discusses the importance of Food and Drug Administration (FDA) guidance and Cures 2.0 provisions on issues such as cell and gene therapy, health literacy, diversity in clinical trials, the coverage of breakthrough medical devices, and more. These comments are in alignment with and reinforce those of other advocacy coalitions, including the National Health Council (NHC) and the American Brain Coalition (ABC).

If you would like to get involved in advocacy, please contact president@pura-syndrome.org to get connected.

PURA Syndrome Awareness Day: Wednesday, October 23

PURA Syndrome Awareness day is fast approaching and this year we are celebrating our 10th Anniversary of Discovery. Need ideas on how to spread awareness? Visit our website at: https://purasyndrome.org/make-an-impact/awareness/

Have you created your team yet?

Help make our Together for PURA fundraising campaign a success! Visit our website at: https://purasyndrome.org/ and click on our Together for PURA banner to get started today!

Strategic Planning to Support Our Mission

Key Pillars and Top Level Goals

Our board spent six months having extra meetings to complete our strategic plan. We presented this at the conference but wanted to share our key pillars and top level goals.

While the registry and biobank are part of research, we decided to give them their own individual pillars. This is because we've learned how vitally fundamental they are to rare disease research, in creating clinical guidelines for doctors to understand how to care for people with PURA Syndrome, and also for us as parents to know what to expect and/or watch out for as we care for and advocate for our children.

Financial Sustainability	Family Support	Infrastructure & Process	Research	Registry	Biobank	Data	Marketing/ Communications
Ensure long term sustainability of the foundation, while funding research and community initiatives	Provide access to to as many resources as possible to assist in supporting families and caregivers impacted by PURA Syndrome	Ensure efficient management of operations and administration of the foundation to ensure long-term sustainability	Act as partners, collaborators, and drivers of research on PURA Syndrome and therapeutics for people with PURA	Ensure PURA Syndrome researchers around the world have access to patient registry and natural history data for relevant research	Ensure PURA Syndrome researchers around the world have access to patient tissue samples for relevant research	Securely and ethically maintain a database of people and organizations affiliated with PURA Syndrome. Provide due diligence and oversight in partnering with outside orgs.	Consistently create transparency, engagement, recruitment, awareness, and education about PURA Syndrome through our communication channels

RESEARCH UPDATES

Patient Registry Update

Parents and Caregivers - We Need Your Help to complete at least 100 Patient Registries! Dr. Hunt gave an update at our June Conference as to where we are at with our Global Patient Registry. We currently have 51 completed registries with 37 more started but incomplete. **We cannot stress the importance of taking the time to do this in order to offer researchers more insight into PURA Syndrome!**

This year we have added a few tools to help our families complete their registries:

- One-on-one appointments with our Research Nurse Tessy or PURA Aunt Lyn who are both available in hour increments to help you along as you fill in the Registry.
- A checklist of items that you will need to gather beforehand in order to complete the registry.

For more information and to register, please visit: www.purasyndrome.org/registry

Biobank Agreement Finalized

In July, the PURA Syndrome Foundation signed an agreement with Helmholtz Zentrum München in Germany to provide grant funding that will help finalize administrative work and prepare for the launch of the Biobank. It will serve as a global collection and distribution point for PURA research. The PURA Biobank can then act as a resource for researchers across the globe that wish to study the condition. Samples will be used for research with the long-term goal to understand and develop treatment strategies for PURA syndrome or related disorders that include genomic deletion or duplication of the PURA gene.

We are excited to keep moving this key part of our research pillar forward and will let our PURA Community know when it will be ready to accept samples. Please note - in order to submit samples to the Biobank you will need to have completed the PURA Patient Registry. For more information, visit our website at: https://purasyndrome.org/research/biobank/

Published PURA Research

PURA Syndrome-causing mutations impair PUR-domain integrity and affect P-body association

Marcel Proske, Robert Janowski, Sabrina Bacher, Hyun-Seo Kang, Thomas Monecke, Tony Köhler, Saskia Hutten, Jana Tretter, Anna Crois ... Dierk Niessing ... show 7 more

At our PURA Syndrome conference, Dr. Robert Janowski presented about this new publication in the eLife journal. To summarize the paper:

- Knowing only the genetic variation does not really tell you which function is lost in a patient. This study investigated 6 different genetic variants and asked if they all cause the same defects on a molecular and cellular level.
- To date, it is unclear why so many different genetic variations all result in the full disease spectrum. In other disorders such as Rett syndrome, many more patients with milder symptoms are known. Dr. Janowski found a likely answer to this PURA riddle
- One of the highlights of this study is the first snapshot of human PURA at atomic resolution.

To read the full publication, go to:
https://elifesciences.org/reviewed-preprints/93561

Inherited *PURA* Pathogenic Variant Associated With a Mild Neurodevelopmental Disorder

Michael S. Hildebrand, PhD, Ruth O. Braden, PhD, Mariana L. Lauretta, MSP, Antony Kaspi, PhD, Richard J. Leventer, MBBS, PhD, Melinda Anderson, Himanshu Goel, MBBS, MD, ... SHOW ALL ..., and Angela T. Morgan, PhD | AUTHORS INFO & AFFILIATIONS

Another scientific article has been published in the journal of Neurology Genetics showing evidence of the first identified inherited case of PURA syndrome.

- This publication describes a mother-daughter pair who have a mild case of PURA syndrome, where the primary symptoms are dysarthria (slurred speech), and borderline intellectual disability.
- Other symptoms are discussed given a thorough evaluation of the patients, and the study may open screening and genetic counseling to patients who exhibit these symptoms.

To read the full publication, go to:
https://www.neurology.org/doi/10.1212/NXG.0000000000200181

Differences in manifestations of epilepsy and developmental delay in PURA syndrome and 5q31 microdeletions

Andreas W. S. Kofoed[1] | Silvia S. Kristiansen[1] | Maria J. Miranda[2,3] | Guido Rubboli[4,5] | Katrine M. Johannesen[3,6]

There's a new scientific review paper published in the journal Clinical Genetics which takes a close look at patients with different genetic changes that affect the PURA gene, located at chromosome 5q31. To summarize the paper:

- The publication illustrates three specific groups: 1) patients with a mutation in the PURA gene (called PURA-SNP in the paper, or single nucleotide polymorphisms/variants); 2) patients with a deletion at chromosome location 5q31 where the PURA gene is also affected or deleted (called 5q31+PURA); and 3) patients with a deletion on the chromosome at location 5q31 where the PURA gene is not part of the chromosomal deletion (5q31-PURA, where the PURA gene is intact and thus is not technically defined as PURA Syndrome).
- The review found that all three groups had symptoms that include hypotonia, feeding difficulties, and physical features that are commonly seen in PURA Syndrome patients.
- The primary difference is that patents in the 5q31-PURA were not as affected by epilepsy, and were able to reach certain developmental milestones more than those without the PURA gene.
- These results show that among these three groups, PURA is a significant contributor to developmental delay and epilepsy in the PURA population.

To read the full publication, go to:
https://onlinelibrary.wiley.com/doi/abs/10.1111/cge.14581

PURA and GLUT1: Sweet partners for brain health

Rocío B Colombo [1], Clarisa Maxit [2], Diego Martinelli [3], Mel Anderson [4], Diego Masone [5], Lía Mayorga [6]

A study published in the journal Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease illustrates a potential link between PURA syndrome, and a condition called hypoglycorrhachia, which occurs when a patient has low levels of glucose in their cerebrospinal fluid.

- The study found a potential link between the PURA protein, and GLUT1 which regulates glucose movement across the blood-brain barrier, where GLUT1 deficiency syndrome has several symptoms similar to PURA syndrome and includes hypoglycorrhachia.
- The cell-based experiments in this paper demonstrated that PURA protein enhanced glucose uptake in cells, PURA and GLUT1 co-localize within the cells both visually and physically, providing a molecular lead to further explore PURA's role in glucose regulation in the body. To read the full publication, go to: https://www.sciencedirect.com/science/article/abs/pii/S0925443924002503?via%3Dihub

PURA Siblings Update

Hello Sibs & Parents!

I'm going to be hosting very relaxed zoom chats for all sibling age groups starting at the end of September so we can start to get to know each other! For some of the younger age groups, we would like to invite parents to join us. Please keep an eye our your email for zoom links and if you aren't yet signed up for our email list, visit purasyndrome.org/siblings to do so. Since I only speak English, if there is anyone in need of translating, or is able to translate, please contact me at siblings@pura-syndrome.org. Looking forward to meeting you all!

- Chrissie Brock, Siblings Ambassador

Mark Your Calendars! PURA Siblings Meet-ups

Adults: Sunday, September 29, 4:00 pm UTC+0 (London Time)

Siblings Ages 13-17: Sunday, October 6, 4:00 pm UTC+0 (London Time)

Siblings Ages 9-12: Sunday, October 13, 4:00 pm UTC+0 (London Time)

Siblings Ages 4-8: Sunday, November 3, 4:00 pm UTC+0 (London Time)

Arrivals & Departures

Welcome, Nancy Boccia

We welcomed Nancy Boccia to the board earlier this year! She is a familiar face as she has helped organize our PURA Conferences since 2021. We are so grateful to have her insight and contributions to the PURA Community so far. Enjoy reading her bio below and welcome, Nancy!

Nancy Boccia has had a long career in food and beverage and event planning. She is the former Director of Food & Beverage at The Metropolitan Museum of Art and Lincoln Center in New York City and assisted in the food & beverage management of major sporting events including the U.S. Open. In 2001 she moved to Boston to join Harvard Business School as the Director of Special Events. She officially retired in 2014 but continues to do projects for Harvard and private clients. Nancy now lives on Cape Cod with her husband Carlo, and Jasper, her beloved bloodhound. In addition to her projects, Nancy loves to garden and being part of the PURA Community.

Thank you Mel and Carolyn

We are so grateful to Mel Wardhaugh and Caroline Thorpe for their time and dedication to the PURA Syndrome Board. Mel served on the board but as our UK Ambassador and helped organize our conferences. Caroline had many different key roles however was instrumental to forming our Ambassador program and family outreach. We thank you both for your time and dedication, you are missed!

2024 PURA SYNDROME FOUNDATION CONFERENCE

We spent a wonderful three days in Chicago, Illinois, USA for our 2024 PURA Syndrome Conference. It was our largest gathering yet, with over 150 people attending including almost 30 PURA Perfect individuals!

If you are interested in planning our 2025 conference, please contact Nancy at n.boccia@pura-syndrome.org.

The PURA Syndrome Foundation is a volunteer based organization. With that comes the need to recruit many hands to accomplish our mission and the goals we set forth as an organization. Please consider helping out if you are able to do so, or if there is someone in your life you think may be able to help ask them to fill out the form on our website or reach out to volunteer@pura-syndrome.org.