Key Takeaways from the 2025 SPATA Foundation Family Conference

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1. **Symptom Management**
    a. **Cortical Visual Impairment**
    b. **Epilepsy**
    c. **Movement Disorders**
2. **Mechanism of Genes Research**
3. **Unravel Drug Repurposing Research**
4. **Future of The SPATA Foundation**
5. **Questions & Answers**

Symptom Management

Cortical Visual Impairment

- Brain-based visual impairment - the eyes see, but the brain struggles to interpret
- CVI affects 30-40% of all children with visual impairments but often goes undiagnosed
- Cortical Visual Impairment can improve because of neuroplasticity
- It's important to request visual assessments
    - CVI Assessment
    - Functional Vision Assessment (FVA)
    - Learning Media Assessment (LMA)
    - Expanded Core Curriculum (ECC) screening
    - Orientation and Mobility (O&M) Assessment
- Ensure IEP OR IFSP includes CVI-based accommodations from the assessment
- Your child's educational plan should reflect how they see, not just what they see.
- Good Resources:
    - CVI Scotland
    - CVI Now – Perkins
    - Paths to Literacy
    - Teach CVI

Epilepsy

- 40-70% of people with SPATA5/SPATA5L1 Disorder have epilepsy and are at a high risk of developing epilepsy
- Seizures typically begin in early childhood & often present as multiple seizure types that are often drug-resistant
- Many meet the criteria for Development and Epileptic Encephalopathy and/or Lennox-Gastaut Syndrome
- An EEG is the best way to monitor seizure activity
- Work with your neurology team to come up with the best treatment plan and seizure-action plan

- Look into drug, diet, natural, and surgical intervention options
    - Anti-Seizure Medications (often times may need multiple)
    - Diets: Ketogenic, Modified Atkins
    - Natural: CBD & THC
    - Surgical: VNS, RNS, DBS. etc
- Always ensure you have a seizure-action plan in place for safety
- Filling out the Patient Registry is a great way for researchers to obtain SPATA-specific data for epilepsy

Movement Disorders

- SPATA disorders are not known to cause weakness due to a disease of the muscle or nerves themselves. Most physical disabilities in patients with SPATA disorders appear to be due to movement disorders driven by brain dysfunction
- Many children with SPATA disorders may be diagnosed with cerebral palsy
- Cerebral Palsy (CP) is a neurodevelopmental disorder that affects motor function
- Making a SPATA5 or SPATA5L1 diagnosis does not “undiagnose” epilepsy or CP; instead, there can be value in dual diagnosis
    - Most people in schools or communities will be families with epilepsy or CP as developmental diagnoses but not SPATA disorders, so this can be the start of a dialogue
- Try to find the best treatment to take away the bad stuff but leave the good stuff
    - Daily Medication
    - Injection Therapies
        - Botox, Phenol
    - Surgical Interventions
        - Selective Dorsal Rhizotomy (SDR)
        - Baclofen Pump
        - Deep Brain Stimulation
- Rescue plans may be needed for severe Dystonia/Chorea cases
- Filling out the Patient Registry is a great way for researchers to obtain SPATA-specific data for movement disorders

Mechanism of Genes Research - Tapas Mukherjee

Discovery

- SPATA5 is essential for a major cellular “cleanup and recycling” system called autophagy (from the Greek meaning “self-eating”). When SPATA5 does not function properly, this recycling process breaks down.
- As a result, damaged proteins accumulate like cellular waste, and persistent “danger” signals build up inside the cell, leading to harmful overactivation of the immune system.
- SPATA5 normally works together with another key autophagy protein to maintain this recycling pathway.

Tools Used

- To better understand the range of diseases observed in patients with SPATA5/L1 mutations, we used a combination of cell culture systems, pre-clinical animal models, and patient-derived samples, along with genetic engineering, biochemical analyses, and computational research tools.

Hope & Future Research

- Goal: to further explain the molecular mechanisms underlying SPATA5/L1-related disease features. Through genetic interventions and pharmacological (drug) strategies, we aim to improve neurological outcomes in SPATA5-deficient pre-clinical animal models.
- Together with the SPATA Foundation, we also intend to build a patient registry and biorepository to facilitate long-term translational and clinical research.

Summary

- Overall, our findings show that SPATA5 plays a crucial role in keeping the cell’s immune alarm system in check. This work provides new insight into how SPATA5 variants lead to neurological symptoms and highlights promising avenues for future therapeutic strategies.
- Additional work is ongoing to look at the same functions within SPATA5L1 models
- Autophagy: In simple terms, Autophagy is the body's natural cellular "housekeeping" process where cells break down and recycle old, damaged, or

abnormal components to create new ones.

- Recent research suggests that the process of Autophagy is an important part of understanding many disorders, not just neurological or neurodevelopmental, such as COVID and Diabetes, as well as the natural process of aging.
- More research is needed to better understand the relevance of Autophagy to SPATA Related Disorder.

Unravel Drug Repurposing Project

Overview

Families dealing with rare diseases like SPATA5 and SPATA5L1 Disorders often face long confusing diagnostic journeys, few or no treatment options, and little research that directly reflects their individual child's biology.

Unravel Biosciences is trying to change this by building treatments starting with the patient, not with the disease label.

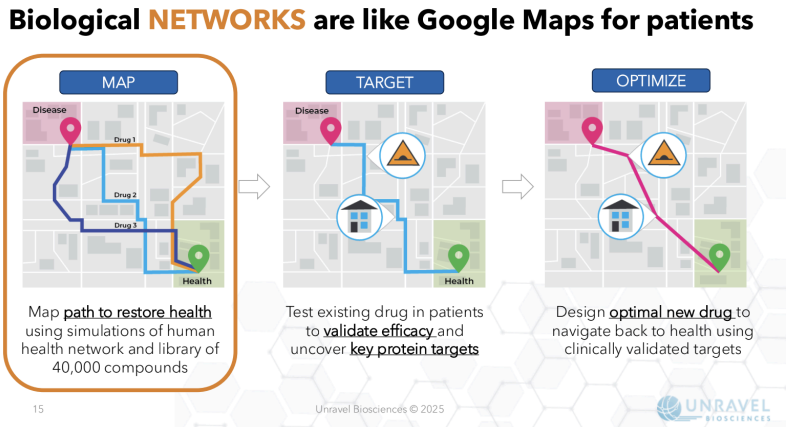
What Unravel Does (simplified)

They study RNA, not just DNA.

- DNA holds genetic information that tells you what might happen
- RNA shows what's actually happening at that moment in the body and changes day to day with things like illness, stress, diet, medication, sleep

Unravel's approach of looking at DNA and RNA gives a more accurate picture of **what's going wrong in the cells right now**.

“Google Maps for Biology” Approach



Imagine the body as a huge biological road map. A disease causes traffic jams or roadblocks. Unravel’s software (“BioNAV”) tries to:

- Detect where the roadblocks are
- Predict which drugs could clear the traffic
- Test those drugs in model organisms
- Then design new drugs if needed

Unravel Partners Directly with Patients

Using at-home nasal swabs, they collected:

- RNA data from **19 SPATA patients**
- RNA data from **18 healthy family members**

This creates a scientific “datamine” that allows them to compare patterns.

Key Findings (so far) in the SPATA Study

- There are two subgroups of SPATA patients
    - One large group
    - One smaller group
- These groups do **not** differ by their SPATA5/SPATA5L1 gene expression. Instead, they differ in:
    - **mitochondrial metabolism** (energy production)
    - **fatty acid metabolism**
    - **immune system / inflammation pathways**, especially the **IL-17 pathway**
- This suggests SPATA has **distinct biological subtypes**, which may explain why kids have different severities.
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What does this mean?

Future treatments may work better if tailored to the patient's subgroup. SO, we must figure out what the true differentiating factor is and how to determine what subgroup each child is in before treating.

SPATA Tadpole Models

Why Tadpoles?

- They share many genes with humans
- You can test drugs on them quickly
- They show behaviors similar to neurological symptoms

Tadpoles were genetically engineered to mimic SPATA5 and SPATA5L1 Disorders. The tadpoles showed:

- Developmental delay, Smaller brains, Lower survival, Seizures, Balance issues, Abnormal swimming

These match symptoms seen in children with SPATA-related disorders.

****Please do not be alarmed by "lower survival." Please keep in mind that, while tadpoles are good models of humans, they are not humans. These tadpoles are also what we call "knockout" models meaning they are completely missing one copy of the gene. Our children do not have total copies missing, so some of the symptoms shown in the tadpoles are exaggerated.*

Drug Testing Results (Early But Promising)

- High-ranked predicted drugs (from the RNA analysis): improved tadpole survival and behavior
- Low-ranked drugs: made symptoms worse
- This gives early confirmation that their prediction system (BioNAV) is working properly.

What's Next?

Unravel is now:

- Narrowing down the best drug candidates for each SPATA subgroup
- Testing them in the tadpole models
- Preparing to move forward toward potential clinical use

Long-term plan:

- Validate the best drug candidates in tadpoles
- Move the safest, strongest ones into **patient testing**
- Use subgroup biomarkers to match patients to the right treatment

Why This Matters

For the first time, SPATA5 and SPATA5L1 have:

- A biological explanation for different severities
- Potential treatment targets identified
- Live disease models
- Early drug candidates showing benefit

This is a major step toward **real, personalized treatments** for SPATA disorders.

Disclaimer: *Please understand The SPATA Foundation cannot legally or ethically release the drugs being tested in tadpoles. We will, however, release information when it becomes relevant. When we find a drug or drugs that show valid data, we will then work with Unravel to release information.*

Future of The SPATA Foundation

Current Projects & Research

- Mouse Models | Jax Labs | SPATA5 & SPATA5L1
- Drug Repurposing | Unravel Biosciences | SPATA5 & SPATA5L1
- Mechanism Research | Tapas Mukherjee | SPATA5 & SPATA5L1
- Natural History Study | Barbara Vona | SPATA5 & SPATA5L1
- Mechanism Research | Michael Kruer & Michael Buszczak | SPATA5 & SPATA5L1

Current Known Researchers

- Dr. Michael Kruer, MD & Team
    - Barrow Neurological Institute Phoenix Children's Hospital
- Dr. Michael Buszczak, PhD & Team
    - Dept. of Molecular Biology UT Southwestern
- Dr. Tapas Mukherjee, PhD
    - Dept. of Immunology University of Toronto
- Dr. Barbara Vona, PhD & Team
    - Institute of Human Genetics Neuroscience University Medical Center Göttingen
- Dr. Roger Greenberg, MD, PhD, FRCP, FRCPath & Team
    - The Perelman School of Medicine at the University of Pennsylvania
- Dr. Henry Houlden, MD, PhD & Team
    - Professor of Neurology and Neurogenetics at UCL (London)
- Dr. Mark Hester, PhD
    - Institute for Genomic Medicine at Nationwide Children’s Hospital
- Ruby Gupta
    - Neuroscience PhD Student | University of Tartu

Long-Term Goals

- Treatment options for ALL those affected:
    - Drug Repurposing
        - Short-term more available treatment option
        - Treat symptoms NOW to improve quality of life
    - Gene Therapy
        - Long term “cure”
    - Other therapeutic options
        - ERT, ASO, mRNA

Gene Therapy

- Is it feasible? YES
    - Both SPATA5 and SPATA5L1 are within the size limits of AAV packaging, making them realistic and practical targets for gene therapy.
- Is it coming?
    - Currently in close discussion with three universities regarding potential collaboration for Gene Therapy
- What stands in our way?
    - Time
        - Time in General
        - Unexpected setbacks
        - Protocols
        - Change of Direction
    - Money
        - The NIH National Budget only sets aside 0.1% of funds for rare disease research

How can Families help?

- Patience & Hope
- Advocate
    - Stay informed about laws/initiatives that could benefit research and write your state representatives to encourage them to support these bills
- Be SOCIAL
    - Tag The SPATA Foundation in relevant posts
    - Invite Friends list to LIKE the page
- Fundraise
    - Share others fundraising efforts
    - Host your own fundraiser
    - Write to local fraternity organizations/orders (ie: Free Masons, Knights of Columbus, Elks)
    - Sign up for RaiseRight (gift cards that give back)
    - See if anyone you know works at a job that uses Benevity or Charity Choice
- Use your voice!
    - One of our biggest assets is our VOICE.
    - Personal stories resonate with people and pull on the heart strings
    - Share your story on social media. Reach out to news outlets.
    - Let The Foundation use your photos/videos
    - You don’t have to put on a big production, you just have to tell your story.

2026 Goals

- Fund additional research initiatives
- Move into the next step of Drug Repurposing
- Begin creating tools for Gene Therapy (vector models, proof of concept)
- Database of all patients
    - Patient Count
    - Worldwide Patient Map

Questions & Answers from The Conference

More to come

Q: As our child's abilities to do stuff changes, should we go back into the Patient Registry and change an answer?

A: Yes! The point of the Patient Registry is to track the disorder over time. Please feel free to update answers and upload new tests and results over time. For example, if you get a new MRI next year feel free to upload it. The Patient Registry does not have to be completed in one sitting. You can log in and update at any time.

Any and all data is helpful.

Q: We have a lot of researchers doing their own research, how do we bring them together?

A: This is a question I've been asking myself! The SPATA Foundation is hoping to facilitate a Scientific Roundtable discussion in 2026 with all known SPATA5 and SPATA5L1 researchers to figure out what our gaps are in research and how they can all collaborate towards the same goal of helping our kids.

It isn't as simple as it may seem when there are various institutions/universities/facilities at play with NDAs, protocols, etc. With that being said, these researchers are aware of each other and it's actually a good thing they're all working on different components.

Q: It's been said that Gene Therapy will cost millions of dollars, but as it's becoming more common has that changed?

A: The short answer is no. In the end, developing all the tools needed to create gene therapy, getting it pre-clinical ready, proving it works, then running a clinical trial will result in millions of dollars.

While we are seeing more and more gene therapies, it's still not "common."

Gene therapy development will happen in stages with the first few stages being less money and most likely funded by us. As we get further in the process towards trials, that's where the multi-million dollar funding will come to play. We can worry about that when we get there!

Q: Will gene therapy happen?

A: Eventually, yes. Gene therapy is possible. The genes are small enough to fit in the viruses they use to deliver the therapies. However, it won't happen tomorrow. There are a lot of building blocks prior to developing gene therapy.

The good news? I think we're almost there. I'm in discussion with three different groups about developing gene therapy. We're working on finalizing details, getting quotes, and timeline options before determining who will help us do this.

Q: I see gene therapy for hearing loss, can we use this gene therapy?

A: Current gene therapies on the market have been developed for other genetic hearing loss disorders. Gene therapy has to be specifically made for each individual gene, so no, gene therapies currently on the market for hearing loss will not work for our children.

The science, however, would work. We just have to develop it for our specific genes. Also please keep in mind that gene therapy for hearing loss cannot be used on patients who have cochlear implants.

Another component to gene therapy for SPATA5 and SPATA5L1 is the neurological aspect. Gene therapy for hearing loss is MUCH different than gene therapy targeting the brain, which is where we'd have to target. We have to make the gene therapy cross the blood-brain-barrier or figure out where we can inject it to affect the brain (like cerebral spinal fluid or directly to the brain).

Q: What age can kids have gene therapy?

A: Gene therapies are currently being given to people of all ages. However, each gene therapy is different and each clinical team is different. We don't know who may or may not be eligible. Gene therapies targeting neurological disorders are best when given as early as possible (birth or prior to birth) to avoid any damage before it occurs, but gene therapy is actively being given in children and adults. Our goal is to treat as many as possible.