# Genetic ALS & FTD: End the Legacy

## March 2023 Newsletter

Julie Granning, Editor

### A Note From the Chair

As the only organization dedicated solely to the needs and interests of the Genetic ALS & FTD community, we have our work cut out for us. But we are so heartened to see the advance of science and regulatory understanding at play in the Tofersen Adcom, to have the spirit of democratic education of top scientists in our webinars, and to feel the warm welcome extended to us by so many in the field. I hope these few updates inspire you as they do me and our team.

### Shared Governance

As we continue to operate under the umbrella of the ALS Hope Foundation, we are pleased to announce Cassandra Haddad in her new role as vice chair. A SOD1 carrier, she brings many skills to our group, including her expertise in the medical field. We also welcomed policy expert Karen Kornbluh onto our initial governing board, joining Cassandra, our mentor Dr. Terry Heiman-Patterson, and our chair Jean Swidler.

### Mission Statement

The Genetic ALS & FTD community is large and growing. ALS & FTD are terminal conditions, and being at a heightened risk for them can have profound impacts on people and families. We organized Genetic ALS & FTD: End the Legacy to provide educational and support resources to, encourage and promote research about, and advocate for the genetic ALS & FTD community.

# Educate

Dr. Matt Disney spoke on February 22nd regarding current drug developments for ALS and on some discoveries that have happened in his lab with regards to c9orf72. His webinar can be viewed here.

Dr. Aaron Gitler spoke with our community on March 14th. He is a pre-eminent scientist at Stanford University with groundbreaking findings on genetic ALS and FTD which have translated to clinical trials that are enrolling now. His webinar can be viewed here.

Don't miss our upcoming webinar for the Genetic ALS & FTD Community, a conversation with expert RNA biologist Professor Guillaume Hautbergue whose lab recently announced promising findings for c9orf72. You can register to attend here.

We are planning more educational events. If you are interested in presenting to the Genetic ALS and FTD community, please reach out! Email us at geneticalsftd@gmail.com.

# Support

Ensuring our community has options for support is incredibly important. We are inspired by—and picking the brains of—those who have worked in the Huntington's Disease support space for best practices. Stay tuned for future updates.

# Advocate

On March 22, 2023, the FDA held an Advisory Committee Meeting on SOD1 directed ASO, Tofersen. Twenty-three members of the ALS community, many impacted by genetic ALS and their families, and several neurologists and other subject matter experts, provided incredible testimony as to how this medication has changed their lives or the lives of their loved ones, and how if approved, will change lives. Many of the stories were heartwrenching, describing the impact of multi-generational ALS, but a theme of hope with Tofersen clearly emerged. There were three dissenting presentations. There were also over 100 written comments submitted.

***As a member of the genetic ALS community, I was so excited to be a part of this pivotal moment in ALS history. Together with many others from End the Legacy, I know our voices are being heard and recognized as we come together to take ownership of genetic ALS/FTD and to mold our future. Giving my own testimony was difficult, I felt like I was bearing the suffering heart of my family for the world to see. Listening to my friends and fellow community members give testimony was also heartbreaking. But like a phoenix rising from the ashes, hearing the FDA discussion on finally recognizing biomarkers and the likelihood of at least an accelerated approval for Tofersen, our community's hope was clearly shining. Our future is brighter than ever as we fight for not only treatment of the SOD1 community with Tofersen, but recognition of biomarkers to benefit the entire community and future treatments for other causative genes. The stress and high emotions of participating was totally made worthwhile for me by the positive outcome not only that day, but for the future this pivotal meeting will provide. I encourage everyone to participate in speaking out for all of us about testing and treatment. It is an incredibly empowering experience!***

**Cassandra Haddad**
**Vice Chair**
**Sod1 Carrier**

# Other Advocacy Updates

Despite being the largest group of people for whom any new knowledge of ALS or FTD can be utilized in, and having seen too much of ALS and or FTD as part of the care community for our relatives, the perspective of pre-symptomatic gene carriers have often been ignored when these diseases are discussed.

Starting with a pronounced push to get our chair Jean Swidler appointed to the NIH ALS Strategic Plan, we have been vigilant, ensuring our community has a voice when our care is discussed. Congrats to member Mindy who was appointed by the National Academy of Sciences to serve on their committee on ALS: Accelerating Treatments and Improving Quality of Life. Jean was appointed as a patient advisor on the steering committee for the Critical Path for Rare Neurodegenerative Diseases, a joint FDA and NIH project.

If you want to make sure the Genetic ALS &FTD community is included in any efforts you are involved in, please reach out to us!

# Research

Our website has a new research page, including a link to current, genetic-focused research that you may be interested in: End the Legacy Research. Throughout the year, so many of us travel and set aside time to take part in numerous studies. We congratulate the Neurofilament Surveillance Project for completing its enrollment of their 300th participant!

*Patient-Led Research*

We are continuing to develop analysis of our survey from fall 2022, and to work on new concepts for future submissions for the field to consider, including further estimates of the size of our Genetic ALS & FTD Community.

# Member Spotlight

## Julie Granning, Interviewed by Mindy Uhrlaub

### 1. Where are you from, what is your connection to ALS, and why is the fight against familial ALS so important to you?

I *am from the midwest, living in Minneapolis currently. My mother passed from ALS in January 2014. She had two doctors—an older doctor who believed it was everything but ALS and put her through rigorous testing, surgeries, delaying her diagnosis. Her younger doctor believed it to be ALS from the start and wanted her to be gene tested despite no family history. My parents trusted the older doctor, and she was eventually diagnosed with sporadic ALS just 18 months before passing. Her decline was rapid, and they couldn't keep up with braces, wheelchairs, or other assistive devices. After a giant battle with insurance and some epic crowdfunding, we got to bring her home for hospice care where she was able to spend her last months in her own house, with her dog Dexter, visiting with loved ones and choosing to go when she was ready, by turning off her ventilator.*

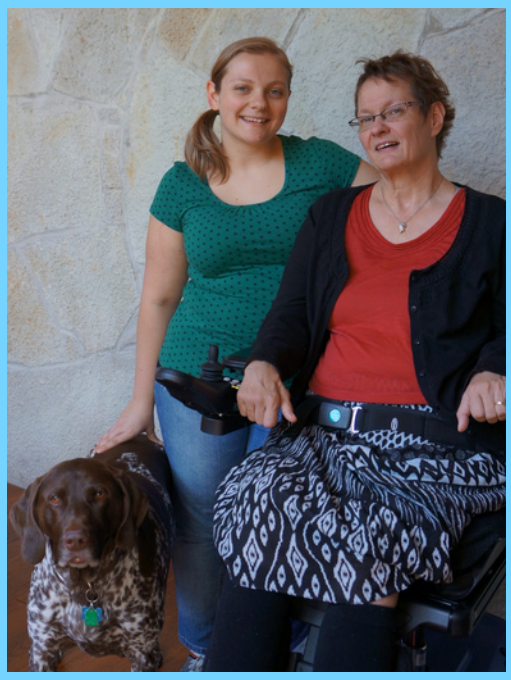
*Several years later, I did an Ancestry DNA kit for fun, out of curiosity. I was expecting to be about a quarter Italian, as my grandfather was Italian. I came back 0% Italian and 33% Polish. I had many DNA matches with people I had never met or heard of. My mother's nephew showed up as a second cousin instead of a first cousin. My lineage was incorrect. My mother had a different father than the rest of her family. I wanted to know more about this side of the family and this new biological grandfather, so I started piecing together a family tree and reaching out to DNA matches for information.*

*I had some health problems, all related to inflammatory disease. A doctor suggested I may want to explore this further, as it could point to something bigger. I began to worry about my unknown biological family and renewed efforts to connect with DNA matches. This is when a distant cousin contacted me to tell me about the family's history with ALS.*

*I went into testing blind, as no one in this branch of the family had been tested to find the genetic mutation, and I came back with a pathogenic variant of SOD1. Had my mother been tested, we could have known this at the time, and I could have made more informed choices about family planning. As it is, I found out about the genetic testing after having my two children and I fear* every day that I may have passed this cursed legacy onto them.

## 2. What do you want people to know about your family's ALS/FTD that might be different from what folks know about ALS/FTD already?

*My mother's ALS hit her at age 61, but she had been fatigued and had increasing health problems for years before. In other family members, I've found it begins anywhere between age 45 and 70 and causes their death in anywhere from eighteen months to eleven years. I am currently 38 and worried that I may only have seven good years left with my family and children. The unpredictability of this disease is so difficult. SOD1 ALS has a 90% expression rate, so I consider it a near-certainty that I will develop ALS. SOD1 ALS is also theorized to be easier than other genes to "turn on" the mutation. This can happen through illness, injury, or other environmental factors.*



## 3. Short of a cure, if you could wish for one thing regarding ALS/FTD, what would it be?

*I wish being gene-positive for ALS were treated as being in a pre-disease state. I wish we were all taken seriously and monitored for biological and clinical changes. It may surprise people to know this is not already the standard of care available to people. Right now, if people at risk wish to be monitored for ALS, they have to go through one of a few observational research studies, and spend their own time and money on travel and time off to do so. This is not feasible for very many people.*

*Also, diagnostic criteria for the genetic ALS are currently the same as for sporadic ALS. This means a gene-positive person can be experiencing many clinical and biological signs of ALS, and still have to go through rigorous rule-out style ALS testing and meet outdated criteria before they can receive any ALS-targeted care. This needs to change, and it needs to change now.*

## 4. What is a fun fact about you that we, as your Familial ALS community, don't already know?

*I grew up listening to the Beatles because my mom was a huge fan. I know nearly every word to every Beatles song and can identify them all in just one or two second clips.*

# A Final Word

Let's keep our growing community strong and informed.
Email us geneticalsftd@gmail.com
Tweet us @End_The_Legacy
Visit Us at https://www.alshf.org/end-the-legacy

Some Links :
Cassandra in Bloomberg
New member Linde Interviewed