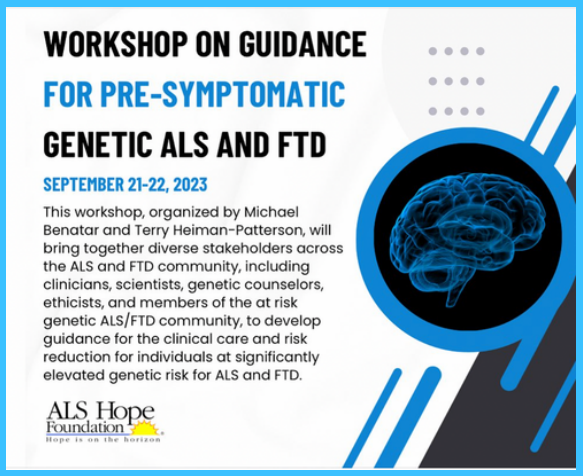
Genetic ALS & FTD: End the Legacy

July 2023 Newsletter

Julie Granning, Editor

A Note from the Chair

When our community took the first tentative steps to coalesce in 2020, we were pushing together on a purpose that felt new and scary, and which we were a bit unsure of. That was—as individuals at genetic risk of ALS and FTD, we have health concerns and needs related to that risk and those diseases prior to the emergence of the full phenotype/ classic disease symptoms. Strangely, it can feel as if medical attention is a zero-sum game, and if we get any it will be taken away from the already stretched-thin resources available to people with fully symptomatic ALS and FTD. Pushing through that, we have been making waves in one-to-one conversations and in every public venue we can.



This new request from our community, and the concurrent excitement of the success of the first genetically approved therapy for Sod1 Qalsody, has led to a groundbreaking workshop announced publicly for the first time by our allied organization, the ALS Hope Foundation! End the Legacy is one of many sponsors of the event, and myself, vice chair Cassandra, and board member Karen have been invited and all plan to attend.

The work and efforts along all our priorities continues, and is made possible by the commitment and determination of our many volunteers. Please read below and you will be as impressed as I am. - **Jean Swidler, Chair**

<u>End the Legacy Update</u>

We have had a great response from individual donors and institutional sponsors as we raise resources to execute on our mission. Our first budget has just been approved by the board members of both End the Legacy and ALS Hope!

Advocate **Support** **Educate** **Research**

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.

Follow us Instagram
Tweet us @End_The_Legacy
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Join Our Team!

You are invited to join us for our weekly team meetings! If you would like to join our strategy/update sessions held every Friday at 9am Pacific, email us at geneticalsftd@gmail.com.

SUPPORT

Group Led Support

Our peer support hour held its second gathering and again had people new and old to End the Legacy attend. Feedback on our post-meeting survey was excellent, and we look forward to sharing the results soon. Our support hour is now established on the third Wednesday of the month at 7:00 p.m. (EST), with skilled facilitation from ETL board member Linde Jacobs. Go Linde!

Sign up here to attend.

Peer Mentoring

With our group support in place we are pushing forward developing a one-to-one peer-mentoring service, as well. The team from ALS Hope, along with experienced mentoring expert (and Newsletter interviewer!) Mindy Uhrlaub, is assisting in its development.

External Support News

Light The Way: Cassandra explains LTW is a project Sano Genetic with advice from ETL team member Paul Wicks that focuses on mental health with genetic testing and gathering data. People can get tested through Sano genetics and receive information and resources (including referral to ETL). It will be up and running soon.

End The Legacy members **Karen Kornbluh, Cooper Penner, and Jean Swidler** have accepted positions on various working groups of the Foundation for the National Institutes of Health's Accelerating Medicine Partnerships for ALS or AMP ALS. We thank NIH and FNIH for including the genetic ALS community in these efforts.

"Ensuring the community of people impacted by Genetic ALS & FTD is represented when government holds discussions on our diseases is a top priority for End the Legacy. I was pleased to be included in a working group on Data for the AMP ALS run by the FNIH. When we are visible we can make a real impact." **Karen Kornbluh**

As a person with experience in the field of drug development, it was a privilege to attend the NINDS Nonprofit Forum squarely in a patient advocate role representing End the Legacy. Hearing the passion so many other non-profit organizations have for their similar efforts is an inspiration of what we hope to achieve with ETL. Having in-person chats with senior NINDS officers in the areas we care about was wonderful and I was glad to share both my personal experience and facts about our community as a whole.

One of the highlights: the overwhelming support I felt for our shared vision of finding prevention strategies for asymptomatic genetic carriers. We were delighted to discover that many of the individuals we spoke with are equally passionate about this crucial aspect of ETL's mission. —Karen King

EDUCATE

Educational Webinars

Recent webinar: Genetic Modifiers in Genetic ALS & FTD

This underscored the need to have older unaffected obligate carrier relatives in research! An obligate carrier is when a family has an established, inherited ALS or FTD gene, and their child is confirmed to have an ALS- or FTD-linked mutation.

Recent webinar: Brain Function in Familial ALS

This talk from Dr. Kiernan was great, and some very interesting insights into the likely beneficial role of Riluzole pre-symptomatically was shared.

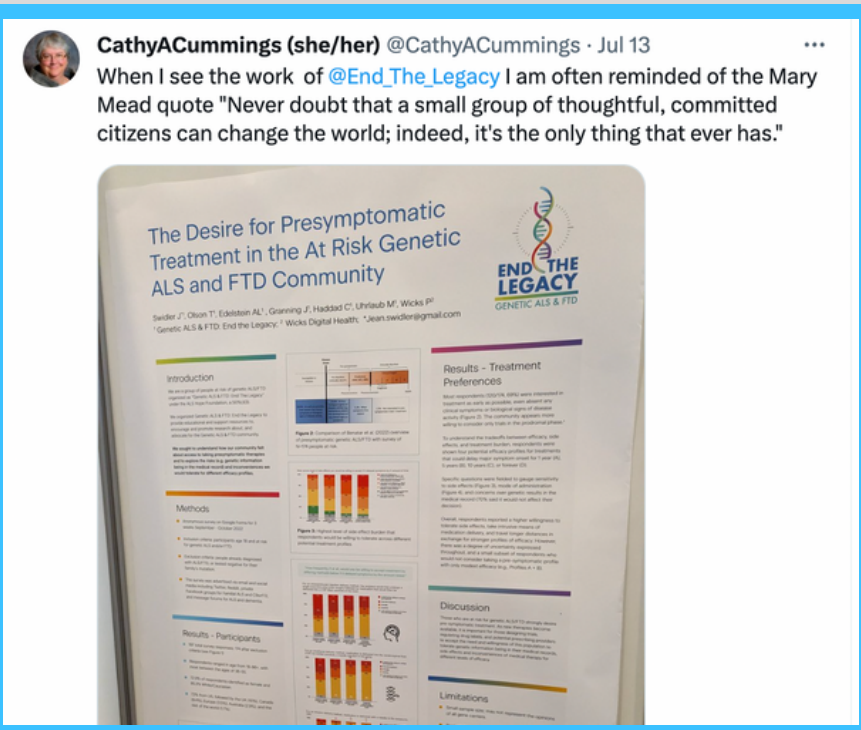
Upcoming webinar: Updates on C9orf72 Research from Dr Jeffrey Rothstein, August 22

Resources

Our first patient-facing resource guide for ALS- and FTD-linked genes is finished! We hope to have one for each major gene soon. Cheers to the authors who compiled and refined these well-cited facts and presented them in a reasonable way for impacted people to use. Link to Resource

Patient-Led Research

- Paul Wicks presented our ETL poster on the desire for presymptomatic treatment in our community at the prestigious European ALS (or MND) Research meeting ENCALS in Barcelona, Spain, in July.
- There were many positive reactions, including this one from the executive director of the International Alliance of ALS/MND Associations. Thank you, Cathy!



Member Spotlight

Paul Wicks, Interviewed by Mindy Uhrlaub

Can you please explain your connection to ALS? How does having ALS in your family affect the way you view the disease?

I got into ALS entirely by chance. I was the first in my family to go to university and studied psychology after being inspired by books like The Man Who Mistook His Wife for a Hat by the renowned neurologist Dr Oliver Sacks. Initially I was fascinated by autism, particularly the "savant" skills that some individuals have, which offered insights into the human mind. As it turned out, autism was hugely competitive and after my degree when I applied for over 50 PhD positions, I only got one interview. And it wasn't for autism; it was for a disease I'd barely heard of, called Motor Neurone Disease, that I knew Stephen Hawking had lived with for a long time. Once I started looking into it, I was apalled at how slow progress had been, but intrigued at some of the "big questions" the disease posed to the field. Over the course of three years, I read every single paper that had ever been written about clinical research in ALS, so I thought I knew a thing or two. But when my father-in-law was diagnosed a decade later, I realized all that book learning didn't amount to as much as I thought. Acting as the "chief strategy officer" for my family member with my medical knowledge and network was somewhat useful to explain and interpret what was going on, but we soon hit a ceiling of where book-smarts could take us. I've never been able to be dispassionate about ALS (or against ALS, as I think of it). Some scientists have pulled me aside and told me I was getting too close to advocacy to be a detached researcher. Now that I'm a caregiver too, I no longer have to apologize for the fire in my belly.

What are some of the projects you're working on specifically for the Familial ALS/FTD community?

My PhD used neuropsychological tests and brain scans to answer a question that turned out to be prescient: "Is the cognitive and behavioral change that we see in some ALS patients more or less common in those with genetic subtypes? And specifically, how do people with a SOD1 mutation differ?" It took me three years to find seven genetic ALS patients with a SOD1 mutation (and ten without) from the UK, which was far too slow. As it turns out, the European SOD1 mutations we saw in my study did not appear to have cognitive dysfunction, but it was much higher in genetic ALS cases without a SOD1 mutation (paper here). accepted now, but I spent years...

...arguing hotly with some neurologists that cognitive dysfunction was real and that we should acknowledge it (e.g. this polemic in the main field journal Neurology, which I hope puts the issue to bed). After my PhD I spent thirteen years at PatientsLikeMe, which was founded by a family affected by ALS, and we shared the data from over 14,000 patients to support a variety of projects, trials, and initiatives, like ALS Untangled. Since 2005, I've been one of the main editors on the Wikipedia article on ALS and I've recently done work to upgrade it and improve the quality of information around the risks of genetic ALS. I was lightly involved in the Ionis FUS trial as a site trainer on some of the cognitive and clinical assessments used, which gave me some insights on to how trials are executed. Recently I've been the architect of a multi-national, multi-lingual genetic education, counseling, and testing program for people at risk of genetic ALS called "Light the Way," with my colleagues at Sano Genetics. As I type this, I'm at the ENCALS meeting in Barcelona, about to present the design to the community as a poster, and I'm also presenting a poster on behalf of End the Legacy describing the survey on presymptomatic willingness to be treated that was conducted in late 2022. Any time I'm flagging, it only takes the intros at our regular Friday meeting to reinspire me.

What is ENCALS, and what is/was your experience with it?

ENCALS is the European Network for the Cure of ALS, and it's one of the two major meetings in the field (in addition to the International ALS/MND Symposium run by the MND Association). Clearly, the bulk of research, funding, and pharma investment is in the United States, but over the past decade, some of the major centers in Europe, such as Dublin, London, Oxford, Sheffield, Amsterdam, Utrecht, Milan, Paris, and beyond have been pooling their resources, standardizing their data collection mechanisms, and organizing themselves as a coordinated group. For instance, their TRICALS initiative allows pharma companies to access a network of ALS centers for clinical trials in ways that allow them to contract and set up much faster, similar in spirit to the NEALS consortium on the US side of the pond. They also have access to significant EU Horizon funding and expertise in genetics such as Project MINE ,which aims to genetically sequence over 15,000 people with ALS and 7,500 controls. Although European countries are small (often smaller than some US states!) it is possible for an ALS specialist center to see nearly every diagnosed patient in the country, and the more centralized health systems don't have some of the unique issues of cost and insurance that the US faces. I've been to the meeting half a dozen times over the past 20 years, and this one has been the best organized, with the most commercial sponsors, and I think the greatest sense of hope that we are making progress.

What gives you the most hope for the future of genetic ALS/FTD?

There's nothing like an approved therapy to spur interest and momentum in the field, and the recent approval of Tofersen's drug, Qalsody, for SOD1 ALS in the US by the FDA has been an important signal. A signal to clinicians that patients and family members need access to genetic testing, a signal to industry that there's a return to be made in this disease (they have a range of diseases to invest in from their portfolios and we need to be "investable" to get their attention and resources), and a signal to the non-profits that those at risk of genetic ALS/FTD are an important constituency. At one of the first sessions yesterday, there was a question from the audience (not me!) about a new therapy intended for those with the sporadic form of the disease. The question was one we wouldn't have heard even five years ago. They asked whether the new approach might work preventatively in those who carry ALS genes, and the professor on stage thought about it for a second and replied, "I don't see why not. Good idea!"

Let's keep our growing community strong and informed!

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Advocate **Support** **Educate** **Research**