Deater Foundation, Inc.

PO Box 255
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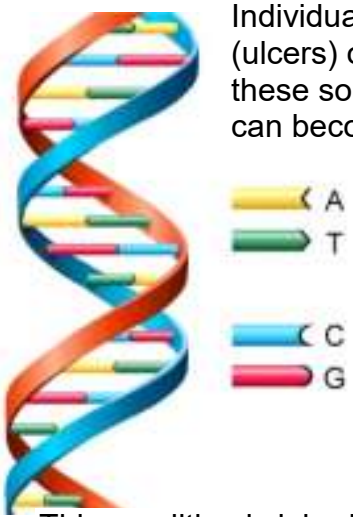
Deater Foundation Newsletter 2016

A Foundation dedicated to finding the cause and cure of HSN1

The purpose of the Deater Foundation, as stated in the bylaws, is “to provide medical research and conduct any and all activities pertaining thereto for the purpose of doing research on the disease Hereditary Sensory Neuropathy I (HSN I).. This may be done by providing technical assistance to public, private, profit, and non-profit sponsors of medical research to encourage and assist in the medical research for HSN I.”

The Foundation has provided $346,000.00 to advance research since its incorporation in 1990. The most valuable contribution of the Deater Family has been those volunteers who have given of their time, their blood, and their well-being to researchers over the past 77 years, since 1939.

Hereditary sensory neuropathy type 1, also called Hereditary sensory and autonomic neuropathy type 1 (HSAN1), is a condition characterized by nerve abnormalities in the legs and feet (peripheral neuropathy). Many people with this condition experience prickling or tingling sensations (paresthesias), numbness, and a reduced ability to feel pain and sense hot and cold. As the disorder progresses, the sensory abnormalities can affect the hands, arms, shoulders, joints, and abdomen. Affected individuals may also experience shooting pains in their legs and feet, muscle wasting and weakness and ultimately require wheelchair assistance.



Individuals with hereditary sensory neuropathy type 1 typically get open sores (ulcers) on their feet or hands. Because affected individuals cannot feel the pain of these sores, they may not seek immediate treatment. Without treatment, the ulcers can become infected and may require amputation of the surrounding area or limb.

Mutations in the *SPTLC1* gene cause hereditary sensory neuropathy type I. The *SPTLC1* gene provides instructions for making one part (subunit) of an enzyme called serine palmitoyltransferase (SPT). The SPT enzyme is involved in making certain fats called sphingolipids. Sphingolipids are important components of cell membranes and play a role in many cell functions. *SPTLC1* gene mutations result in an SPT enzyme with altered activity. This altered enzyme makes molecules called deoxysphingoid bases, which it does not normally produce. When accumulated, deoxysphingoid bases are toxic to neurons.

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Each child of a parent with the defective gene and a parent with a normal gene has a 50% chance of inheriting the disease.

Progress report on the L-serine HSAN1 Trial
by Florian Eichler, M.D. with Kailey Joan Walsh

There were 18 subjects enrolled in this two-year, double-blind, placebo-controlled trial studying the efficacy of L-serine in patients with HSAN1. The study was initially randomized to placebo versus study drug, and both the participants and the investigators were blinded as to who was on placebo and who was on the study drug. At week 48 all participants were switched over to L-serine, regardless of their randomization from the previous year.

At the last DSMB (Data and Safety Monitoring Board) meeting (May 18, 2015) it was recommended that an open-label extension be added to the protocol. This would allow the continued collection of outcomes data on the first 16 subjects from the time they complete the original study to the time that the last two subjects complete the study in February 2016. Upon the board's suggestion and after further investigation, it was decided that an extension of one year would be added to the protocol. After the original 2-year period, subjects would be given the option of being re-consented for the open label extension. All consented subjects would then be treated with L-serine (400 mg/kg/d) for an additional year. An amendment which included the updated protocol, protocol summary, and consent form was submitted and accepted by the IRB (Institutional Review Board) (7/24/2015). Due to budgetary restrictions it was decided that there would only be one additional visit added to the study via the open label extension rather than the two that were originally planned for.

Of the 18 subjects enrolled, 16 have completed their 96 week visit. We are in the process of scheduling subjects for their upcoming continuation visits. At this point the investigators are still blinded. They will remain blinded until the next DSMB meeting. The meeting, which will potentially be held in June, will be scheduled once we've received all of the results. We're currently awaiting results from the deoxysphingolipid analysis which will be sent to us shortly from Zurich (Switzerland).
As of 3/22/16 there has been one serious adverse event (AE) reported. There have been 46 adverse events reported since randomization. Forty-five (45) AEs are not related to the study drug. One (1) AE is unlikely to be related to the study drug. Zero (0) AEs are possibly, probably, or definitely related to the study drug. 1 of the 46 AEs has been a SAE (Significant Adverse Event). Subject 701-007 developed esophageal cancer which was unrelated to the study drug. Dr. Eichler regularly reviews the AEs to ensure subject safety.

As we prep for the final meeting we are ensuring data accuracy. We recently had an internal audit to ensure data integrity, and protocol compliance. We also had a FDA site visit on May 10th. We reviewed the progress of the study, and plans for the coming year. Looking forward we are planning to publically release the results at one of the top neurological conferences next fall.

Personal Perspectives

Louise Adams Hess

It's hard to believe more than two years have come and gone and our L-serine drug testing is coming to a close. We are anxiously awaiting the outcomes from our efforts. My effort seems trivial... taking the serine 3 times a day was not a problem (even though I don't like the after taste and would prefer to take it in capsule form instead of the current powder that must be mixed with warm liquid to dissolve...hence the after taste!)

The 7 hour trips to Boston twice a year were sometimes hectic with traffic and storms but when we arrived we had a comfy hotel to rest ourselves prior to testing. The hotel is situated between the neurology offices and Massachusetts General Hospital (walking distance for those that could) where we had appointments for bloodwork and neurological workups. Once each year we had to stay a second day for more testing there and additional testing at the University of Massachusetts Hospital (UMASS) in Dr. Browns arena. These tests were rather unusual ...sweat testing, tilt table testing and skin biopsies (that left its little pencil point size scar each time).

The best part of each visit was the potential to connect with a family member we had never met or hadn't seen in a very long time. A connection we wouldn't soon forget as we had precious little time to compare similar symptoms, shared problems and most importantly...how each one is over coming those problems! I always wish we had more time to do just that!

Well now you would think it's over but we have been asked to continue with the study. I sincerely hope the funding is available because I think that this is working!!! I have had some positives that I think are directly related to taking the L-serine...first I had 4 fingernails grow back that I thought were gone forever and my fingers have opened up some (although still not straight) and I now have some sensation (for cold) in my hands and forearms. I thank God for the strides being made and pray the study goes forward.

I am extremely thankful to all who made this possible by funding this important study, integral to the understanding of HSAN1. From the bottom of my heart... Thank you!

Christine Deater Christensen

My L-serine saga begins with the flight from Denver to Boston. It would have been a nightmare to travel alone, but because the study paid for a travel companion to assist me, it was a joy. I also had the opportunity to visit with Larry and Rory, my brother and sister-in-law, every 6 months and that made the trip exciting. I think each of the coordinators that handled the appointment scheduling and testing did an awesome job keeping the patients and doctors happy. Not an easy task.

As for the L-Serine itself, it tasted like salt to me and was a chore to drink salt water three times a day, every day. But it must have done something because over the course of the study I got back a lot of pain sensation in my hands. I'm sure this was a good sign from a scientific point of view, but for me it just hurt. Since being off of the L-Serine, my pain has retreated to pre-medication levels and I am happier. I look forward to seeing the test results when everyone else is done. Hopefully there is some remarkable data.

The testing at UMASS and MGH was kind of fun for me. The tilt table, sweat test, nerve conduction and biopsy were interesting and did not bother me, though I know some people found them unpleasant. I absolutely loved Dr. Friedman and had lovely chats with her during her neurologic exams. I didn't spend much time with Dr. Eichler but I'm glad for his participation in the study. I know we are all hoping and praying for an end to this disease, and if our part in the study leads to that end, what could be better?

I am thankful to have been part of the test group, and am thankful to be done with it. I appreciate all of my relatives affected and not, that make being a Deater so awesome. Our family is the best support group we could have, and I have become closer to some cousins through this process than I might have otherwise. Thanks to my siblings who keep encouraging me, and all the people working on a cure. I know some day it will happen.

Jon Ellsworth

It's that time of the year again! Spring is in full swing and summer is right around the corner (writing this in early May). Of course, I live in Florida so there's no such thing as seasons – just summer.

Here's a quick update on the trial from my seat. The original 2-year trial was set to end in the Fall of 2015. At my visit last October, for the first time in forever I was actually able to feel the electrical pulses in my legs during the nerve conduction testing! How amazing is that?!? Does this mean the Serine is working? I'm not a doctor, but I'd say there is a good probability it's doing something. During that visit, I was offered an extended 1-year "add-on" to the trial which I accepted. Not sure how that's all going to play out since I have yet to be scheduled for my Spring visit, but at least the study has still provided me with Serine.

I wanted to also take a moment to talk about money. For the past many years, I've worked with my employer to apply for a grant from its foundation. This year the Enterprise Holdings Foundation has once again awarded a grant of $5000 to the Deater Foundation. I am humbled by their unwavering support for over 10 years now!

Many organizations have grant programs or employer match programs to direct funds to non-profit organizations. The Deater Foundation needs financial resources to continue helping fund research. Please consider discussing this with your company's HR department and consider donating yourself!

Foundation Donation

The Enterprise Holdings Foundation has again made a donation to the Deater Foundation, Inc. for the 10th year in a row! The **$5,000.00** grant received this spring equals the record amount provided last year. The Deater Foundation is grateful to Jon Ellsworth and Enterprise Holdings, the largest car rental service provider in the world (Enterprise, Alamo, and National). Because of Jon's efforts through his employer, Enterprise Rent-A-Car, and the generosity of the Enterprise Holdings Foundation, **Enterprise has provided the Deater Foundation with a total of over $22,500.00.**

"The Enterprise Holdings Foundation gives back and strengthens through charitable support the thousands of communities where our employees and their customers work and live."

Deater Family Reunion July 16, 2016 at 12 Noon

Deater Foundation Meeting at 10:30 AM

A gathering of the descendants of Alvin and Ellen Wilson Deater and their extended family will be held at the Butler property near Noxen, Pennsylvania. It will be preceded by a Deater Foundation meeting.

Everyone is invited and welcome to attend!

Alvin and Ellen Deater with the first 3 of their 12 children, Isabelle, Ethel, and Harvey

Gratitude

I touch a hot pan and my hand jerks back in response, avoiding a burn. I shovel snow in winter and my fingers make me aware of the cold and the need for warming before frostbite sets in. I walk across a field of uneven ground and my feet employ proprioception to maintain my sense of balance. I recognize these everyday miracles with gratitude. Others in my large extended family do not have these protective mechanisms. The hereditary disease HSAN1 has robbed them of these sensations. The results are injury, infections, and amputations.

We can make a difference in the lives of our brothers, sisters, aunts and uncles, cousins and friends! A donation to the Deater Foundation propels research forward. Great strides have been made but there is much left to do to alleviate the pain and suffering of a disease present at birth. The next time you feel a frosty glass in your hand or warm water on your toes, do so with gratitude. And make a donation to the Deater Foundation! Ellen Deater Burns

Update on the Genetic Research at the University of Massachusetts

By Robert H. Brown, Jr., D.Phil., M.D.

Activity Report – Day Lab – U Mass Medical School

The Day Lab at UMMS has had another strong year of HSAN1 research. First, we have enjoyed collaborating with Florian Eichler at the Mass General Hospital to see the serine trial move toward completion. Second, we have continued to work on the use of small DNA molecules (oligonucleotides) to silence the HSAN1 gene. This work represents the efforts of a graduate student, Ms. Havisha Karnam, with an outstanding faculty member, Dr. Anastasia Khvorova. Dr. Khvorova has patented several new types of DNA molecules to silence genes and has made three of these available for our work on HSAN1.

Third, in a parallel project, we are working on an entirely different approach to silencing the mutant SPT (the enzyme serine palmitoyltransferase) gene using non-toxic, adeno-associated viruses to deliver a different type of silencing element into the spinal cord and dorsal root ganglia.

Finally, starting in August we will have a new post-doctoral fellow on our team who has prior experience studying the HSAN1 gene (the SPT gene). She will participate in these experiments as one component of her overall fellowship program. So, in summary, we are very excited that the next year will see substantial new progress in the efforts to silence the HSAN1 gene. As well, we look forward to working closely with the Deater Foundation to plan the next HSAN1 conference.

Anne Louise Oaklander, MD, PhD,
is the Director of the Nerve Unit at Massachusetts General Hospital. She is an Associate Professor of Neurology at Harvard Medical School as well as an Associate in Neurology and Assistant in Pathology (Neuropathology) at Massachusetts General Hospital. Dr. Oaklander writes, “I am a neurologist/ neuroscientist working in patient care, research, and education. I direct a laboratory that studies causes of neuropathic pain. My goal is to help bring these syndromes into the medical mainstream to improve diagnosis, and thus treatment.”

Dr. Oaklander has worked with patients with HSAN1. The Nerve Unit website, *http://neuropathycommons.org* lists the **Deater Foundation** among its resources.

New Hope for Eliminating Hereditary Diseases

CRISPR is a new genome editing tool that allows scientists to change and correct specific genes with unprecedented precision,

efficiency, and flexibility. It is far better than older techniques for gene splicing and editing. A genome is the total amount of genetic information in the chromosomes of an organism, including its genes and DNA sequences. In humans, a copy of the entire genome is contained in all cells that have a nucleus.

CRISPR is a naturally occurring process that scientists observed beginning in the 1980's. It is an ancient defense mechanism found in a wide range of bacteria. Scientists noticed a strange pattern in some bacterial genomes. One DNA sequence would be repeated over and over again, with unique sequences in between the repeats. They called this odd configuration "**c**lustered **r**egularly **i**nterspaced **s**hort **p**alindromic **r**epeats", or CRISPR.

Scientists realized the unique sequences in between the repeats matched the DNA of viruses that attack bacteria. CRISPR is one part of the bacteria's immune system, which keeps bits of dangerous viruses around so it can recognize and defend against those viruses the next time they attack.

The second part of the defense mechanism is a set of enzymes called "Cas"(**C**RISPR **as**sociated proteins) which can precisely snip DNA. There are a number of Cas enzymes, but the best known is called Cas9. Together they form the CRISPR/Cas9 system. Cas9 is an enzyme that snips DNA and CRISPR is a collection of DNA sequences that tells Cas9 exactly where to snip. Scientists can give Cas9 the right sequence, called an RNA guide, and they can cut and paste bits of DNA sequence into the genome.

DNA is a very long string of four different bases: A, C, T, and G. Cas9 can recognize a sequence about 20 bases long, so it can be tailored to a specific gene. Scientists can repair a faulty gene by cutting it out with CRISPR/Cas9 and injecting a normal copy of it which replicates in each cell. The modified, corrected gene, can then be passed on to any offspring. CRISPR could one day hold the cure to any number of genetic diseases.

https://ghr.nim.gov Zhang, Sarah, www.gizmodo.com

Larry Deater's Legacy

When Larry Deater died of esophageal cancer on February 19, 2015 at the age of 59, he left instructions that his body be used to further the research on HSAN1, the disease he had lived with for most of his life,

On March 11, 2016 at the Neurological imaging/ Department of Radiology's weekly "Neuropathology/ Brain cutting conference", Larry's case was presented. The target audience for this activity was "trainees (medical students and residents) and faculty in clinical and experimental neurosciences (neurology, neurosurgery, neuro-radiology, neuropathology, neuro-oncology, psychiatry) and pathology."

Larry participated in neurology seminars at MGH several times during his lifetime. He would be happy to know that he was still teaching medical students a year after his death.

Message from the President, Eric Newcomer

This is an exciting time for the Deater Family as well as the Deater Foundation with the conclusion of the L-Serene trial and in anticipation of the results. I would personally like to thank everyone that sacrificed of themselves and their families for this study over the past few years. From the doctor's that devised the trial to the monetary donations and those that physically gave themselves, we couldn't have done it without you! As a Foundation we pride ourselves in using nearly 100% of the funds you donate for research (PayPal takes a small portion to cover the convenience of their service) and we have a hard working group of board members that are committed to getting the best "return" with the funds that you so graciously donate. Remember that the yearly meeting of the Deater Foundation is held right before the reunion and it is open to everyone so you are welcome to come see what we are working on next. Thanks again for all of your support!

Deater Foundation Inc. Treasurer's Report:

Balance as of 6/1/15	$28,536.42		
Income:		Expense:	
Contributions 6/1/15-12/31/15	9,025.00	PayPal Service Charges	- .85
Interest 6/1/15-12/31/15	8.77		
Contributions 1/1/16-5/31/16	6,880.00		
Interest 1/1/16-5/31/16	3.77	Balance as of 5/31/16	$44,453.11

Amazon Smile Program

Do you frequently shop on Amazon? Did you know you can get the same exact shopping experience through AmazonSmile and your purchases will help support Deater Foundation?! To get started, simply go to **smile.amazon.com** from the web browser on your computer or mobile device, then make sure to select Deater Foundation Inc. as your charity of choice, and Amazon will donate 0.5% of your eligible AmazonSmile purchases to DFI! Easy to do, and a great way to support Deater Foundation Inc!

----------The Deater Foundation is committed to supporting a fourth international Conference in October, 2016 to further the understanding of HSAN1---------