Deater Foundation, Inc. Newsletter

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Reunion Reminder!

Hope to see you at the 66th Deater Reunion on July 12, 2008 at Butler's property.

Report on HSAN1 Symposium

Submitted by: Ellen Burns, Medical Liaison

It was Wednesday, April 23, 2008, and unusually warm for Boston, with spring trees and flowers bursting into bloom. A group of scientists gathered at the Royal Sonesta Hotel for dinner the night before the first HSAN1 Symposium. Many knew one another's work. Some had met at other conferences. Still others had communicated by e-mail. This night they met to match the person with the work. This is much the same goal as the Deater Foundation has in meeting doctors and scientists and attending conferences. We want the specialists who are working with cells and test tubes and sophisticated analysis instruments to remember the people behind the disease.

Eric Newcomer and Cindy, Larry Deater and Rory, and Ellen Deater Burns were also at the dinner, which buzzed with excitement about sphingolipids and cellular biology. Donna Crowe, with the Day Laboratory at Massachusetts General Hospital (MGH) arranged a wonderful meal for the gathering, and she and Diane McKenna-Yasek, the Neuromuscular Research Coordinator, joined us and the many researchers there. Dr. Robert H. Brown, Jr. served as host, as he and Dr. Florian Eichler had invited the participants there. People were so interested in sharing ideas, the hotel staff had to move the tables out from under us to get the group to leave the room! Many people moved to the lounge area where the discussions continued.

The next morning the group re-convened, with additional members including Tami Newcomer Murphy, at the MGH research facilities at the Charlestown Navy Yard. Dr. Brown welcomed the group. Then Teresa Dunn, PhD, who has been working in cooperation with the Day Laboratory on a NIH grant for HSAN1, presented her recent work with yeast and sphingolipid metabolism.

Hereditary Sensory Neuropathy Type 1 (HSN1), sometimes called Hereditary Sensory Autonomic Neuropathy Type 1, is known to be caused in some, but not all cases, by a defect in a gene on chromosome 9. The gene is identified as SPTLC1. Genes make proteins and proteins make enzymes. SPTLC1 encodes one subunit of the enzyme serine palmitoyltransferase (SPT). In yeast, there are 3 sub-units of this enzyme. In mammals, there are thought to be only 2: LCB1 and LCB2.

Teresa Dunn, who works at the Uniformed Services University of Health Sciences, Bethesda, Maryland, has been studying the interaction of the serine sub-units. Her research shows that the structure of the enzyme is very complicated. The dynamics between the

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DFI Receives another Grant from Enterprise Rent-a-Car Foundation

Submitted By: Carol Dorward

What a surprise it was when Jon Ellsworth notified us a few months ago that he was, once again, submitting an application for a grant offered by the company that he works for (Enterprise Rent-a-Car). Last year when Jon was working for Enterprise Rent-a-Car in Chicago, IL, Jon submitted the required application which later was approved, resulting in a $2,500 grant in 2007 to Deater Foundation, Inc. from Enterprise Rent-a-Car Foundation.

Jon now works for Enterprise in Florida. Early this spring, he submitted the required application forms for another grant for Deater Foundation. In April 2008, we were notified that a grant for $2,500 had been awarded to Deater Foundation, Inc. This award was made possible due to the company's philanthropic gestures and Jon's willingness to follow application procedures.

Deater Foundation, Inc. is grateful to the Enterprise Rent-a-Car Foundation for considering DFI worthy of the grant and for the generous award. And we are equally grateful to Jon for pursuing this funding adventure again this year.

Because of this grant, Deater Foundation, Inc. is better able to fund research for a treatment/cure for the disease that has plagued our family for generations.

Perhaps others in the family will follow Jon's example and pursue the possibility of similar philanthropic opportunities in their work places. The place to start is in your company's Human Resource Department to see if your company offers a grant or has a gift matching program to non-profit organizations.

Jon Ellsworth

Perhaps others in the family will follow Jon's example and pursue similar opportunities in their own work places.

Report on HSAN1 Symposium

—Submitted by Ellen Burns, Medical Liaison *(Continued from Page 1)*

two subunits are affected by the mutation. This affects their stability and the ability of the sub-units to regulate the production of glycosyl ceramide, a fatty substance in the body.

Dominic Cappopiano, PhD Chemist from the University of Edinburgh, Scotland demonstrated the crystalline structure of the enzyme serine palmitoyltransferase. Chemists have been working to discern this structure for 20 years. He postulates that because of a loss of flexibility, there is a deficit in serine binding that leads to the enzyme's malfunction.

Christopher Haynes, a graduate student in the School of Biology at the Georgia Institute of Technology, Atlanta, presented impressive mass spectrometry imaging of the structure of sphingolipids.

Garth Nicholson, PhD, the University of Sidney, Australia, whose team was first to discover the location of the genetic mutation, raised many questions still to be answered. He does not believe there is truly an autonomic dimension to the disease, but does believe there is a motor component. He proposed that an alteration in the enzyme activity may damage the nerve axons. This brings to question: where are lipids (like glycosyl ceramide) synthesized? It is believed that the

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Garth Nicholson, PhD

Photo Credit: http://www.anzac.edu.au/files/imagemanagermodule/@random41940634b401d/DSC_0632a.jpg

DFI

Pictures from Last Year's 65th Deater Reunion

July 14, 2007 Submitted by: Carol Dorward

It's so nice to get a group photograph of the sisters (and a sister-in-law who is like a sister to the others) as shown here at last year's reunion:

Standing (L-R) : Aunt June, Aunt Laura Mae, Aunt Boot, and Aunt Mickey. Seated (L-R) Aunt Helen, and Aunt Mona.

How possible is it that you can identify everyone in each of the other photos? Even if the photos were larger and the images clearer, I'm afraid that there are more than one or two members of the family pictured that I would not be able to identify by name. Perhaps you'll do better than me. Enjoy!

Without a doubt, I'll have my camera with me again this year. I sure hope that you have marked the date on your calendar for this year's reunion: July 12, 2008. Once again, we will be meeting at Butler's property.

Hope to see you there.

Report on HSAN1 Symposium

—Submitted by Ellen Burns, Medical Liaison

((Continued from Page 2)

enzyme is in the cell body; then what is the mechanism of the enzyme to go from the cell body to the axon?

Thorsten Hornemann, PhD, at the Institute for Clinical Chemistry, University Hospital, Zurich, Switzerland, presented what seemed to be the most radical proposition. He demonstrated the presence of a third sub-unit in the enzyme serine palmitoyltransferase. He suggests that there is a toxic side product that builds up in cells and causes the disease. He proposes that the presence of a third sub-unit may present a method of treatment for the disease.

Alex McCampbell, PhD, with Merck Research Laboratories, West Point, Pennsylvania, but formerly with the Day Lab, presented on his experience with developing the mouse model of HSAN1. He underscored the question of whether the disease is caused by a toxic property or a rate-limiting step in the synthesis of ceramide. Research currently supports both hypotheses.

Florian Eichler, PhD, Department of Neurology, Massachusetts General Hospital, updated the group on the newest findings from the mouse model of HSN1. The observations seem to demonstrate that decreased SPT activity causes the disease although there are differences in the ways the disease is expressed in humans and mice.

Ann Moser, BA, Research Associate in Neurology at the Kennedy

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Dr. Alex McCampbell questions whether the disease is caused by a toxic property or a rate-limiting step in the synthesis of ceramide.

DFI

In Honor of Helen Deater Wilson

Submitted by: Grandsons Charles and Gary Paul Wilson

Our grandmother is very special to us. I (Gary Paul) only remember my grandmother in her wheelchair, but I know she walked at some point because she went with my brother (Charles) to Disney. *[I've seen the pictures]*. I've heard stories of her driving— I think mostly to remind me how *not* to drive. I've seen pictures of her standing outside their farmhouse and of her back before she was married. I even remember seeing her stand once at the kitchen counter cooking something for us.

I remember she watched a few of our little league baseball games from the comfort of Pop's truck when we played in Mifflin. I remember how she taught me how to bake cakes. We didn't use a written recipe; it was all in her head. I would just dump in ingredients until she would say that's enough and our cakes would always turn out just right. *[The same technique however almost caused me to fail HS Home Economics.]*

I remember playing cards; she usually ended up being my partner and as my grandfather always says, "she always wins." I remember when Charles decided to get married on the farm to ensure she could attend. I remember when she offered me her wedding band to give to my wife before I even mentioned the thought of engagement. I remember how she came to my outdoor wedding in Aunt Verna's van. Pop drove it up a steep logging road instead of letting us move her to the 4x4 vehicle we had ready for them.

But most of all, I remember my grandmother with my grandfather. They were always together, 62 years *(exactly twice my entire life)*. What I remember most, is them

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This issue of the Deater Foundation Newsletter is

in Honor of

Helen Deater Wilson

Born January 13, 1927
Daughter of
Alvin and Ellen Deater
Married Thomas Eugene Wilson
2 Sons: Gary and Cork
4 Grandchildren
4 Great Grandchildren
1 Great-Great Grandchild

Helen Deater Wilson

Report on HSAN1 Symposium

Submitted by Ellen Burns, Medical Liaison—(Continued from Page 3)

Krieger Institute in Baltimore, was able to use new state of the art equipment to conduct a lipid analysis of the mouse model of HSAN1.

Robert Brown, Jr., MD, PhD, Director of the Day Laboratory for Neuromuscular Research, Massachusetts General Hospital, discussed potential strategies of intervention in HSAN1, taking into consideration both the loss of function model and the gain of function (toxic properties) model. Other questions were raised, including what is the basis for cellular specificity: why are sensory nerves the target for the alteration in the enzyme?

Kurt Fishbeck, PhD, Chief of the Neurogenetics Branch of the National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, led the discussion to close the conference. He especially engaged the participants who are currently working in industry. These included Alex McCampbell, Gilmore O'Neil, MD, PhD (formerly with the Day Lab), and Bob Anderson. A lively discussion followed, much of which focused on the need for further study to confirm the mechanism of action of

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Deater Foundation, Inc.

Kurt Fishbeck, PhD

DFI

April 2008 Symposium Participants

Submitted by: Ellen Deater Burns and Rory Robb-Deater

Photo: Courtesy of Rory Robb-Deater

Pictured left to right in the photo are: **Larry Deater**; **Ann Moser** *(Research Associate in Neurology, Kennedy Krieger Institute, Baltimore, MD);* **Christopher Haynes**, *(Biology Graduate Student, Doctoral Program, Georgia Institute of Technology, Atlanta, GA);* **Florian Eichler**, **MD**, *Dept. of Neurology and Day Laboratory, MGH, Boston MA);* **Gilmore O'Neil, MD, PhD**, *(Gentech Laboratories (formerly with the Day Lab);* **Xian-Cheng Jiang**, **MD**, **PhD**, *(SUNY Downstate Medical Center, Brooklyn, NY);* **Alex McCampbell, PhD,** *(Neuroscience Drug Discovery, Merck Research Laboratories, West Point, PA (formerly with the Day Lab)***; Bob Anderson,** *(Research and Development, Eli Lilly and Co., Indianapolis, IN);* **Ellen Deater Burns; Garth Nicholson, PhD,** *(Concord Clinical School, The University of Sydney, Sydney, Australia);* **Kurt Fischbeck, PhD,** *(Neurogenetics Branch, National Institute of Neurological Disorders and Stroke, Bethesda, MD);* **Robert H. Brown, Jr., MD, PhD,** *(Day Laboratory, MGH and Harvard University, Boston, MA);* **Tami Newcomer Murphy; Dominic Campopiano, PhD,** *(School of Chemistry, University of Edinburgh, Edinburgh, Scotland);* **Jeffrey Harmon, PhD**, (Chair of the Department of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, MD); **Eric Newcomer; Teresa Dunn, PhD,** *(Dept. of Biochemistry and Molecular Biology, Uniformed Services University of the Health Sciences, Bethesda, MD);* **Marina Raman,** *(Doctoral Program with Dominic Campopiano, University of Edinburgh, Edinburgh, Scotland;* **Anka Penno,** *(Doctoral Program with Thorsten Hornemann, Institute for Clinical Chemistry, University Hospital Zurich, Zurich, Switzerland)***; Thorsten Hornemann, PhD,** *(Institute for Clinical Chemistry, University Hospital Zurich, Zurich, Switzerland).*

Editor's note: What an awesome experience and privilege to have such renowned scientists meet and collaborate on the topic of HSAN1!

Report on HSAN1 Symposium

—Submitted by Ellen Burns, Medical Liaison ***(Continued from Page 4)***

the altered enzyme.

The participants representing the Deater family proposed another study to provide blood samples to the scientists representing the various views. Dr. Brown proposed to initiate the study and it is hoped that many- if not all- affected members of the family will volunteer to participate.

Gilmore O'Neil MD, PhD

The scientists at the symposium all expressed enthusiasm and dedication for the work they are doing. They shared research information with candor. They were hopeful of being "on the brink" of new discoveries in HSAN1. And they all expressed great appreciation to the Deater Foundation for the opportunity to share their views in this forum. Eric, Tami, Larry, Rory, and I were encouraged by the process and the people who are leading the way to a treatment and potential cure.

As I was listening to the researchers talk about the complexity and intricacy of the structure and process of this single enzyme, I was in awe of the power of God's design. I recalled the verses from **Psalm 139:13-14** *"For you yourself created my inmost parts; you knit me together in my mother's womb. I will thank you because I am marvelously made; your works are wonderful, and I know it well."*

Ellen Deater Burns

DFI

A Picture of the Biochemical Process

Submitted by: Ellen Deater Burns, Medical Liaison

"*The following is excerpted from the website of Jeffrey Harmon, PhD, Professor and Chair of the Department of Pharmacology, Uniformed Services University of the Health Sciences.* ***[http://www.usuhs.mil/pha/jharmon.html] I thought it was a fairly clear picture of the biochemical process.*** **" —Ellen Deater Burns**

Dr. Jeffrey Harmon

Sphingolipids are a type of lipid, or fat, found in living cells, usually in the membrane surrounding cells. Sphingolipids are involved in maintaining the structural integrity of cell membranes, serve as ***intra***cellular and ***inter***-cellular signaling molecules, and are highly enriched in lipid rafts (specialized membrane domains in cell walls enriched in certain lipids, cholesterol, and proteins) which are implicated in protein trafficking. The rate limiting step in sphingolipid biosynthesis is catalyzed by the enzyme serine palmitoyltransferase found in the endoplasmic reticulum (a network of tubules, vesicles and sacs that are interconnected and may serve specialized functions within the cell). Mutations in the gene encoding a sub-unit of this enzyme are responsible for the neurologic disorder Hereditary Sensory Neuropathy Type I (HSAN1), a disease selectively affecting peripheral sensory neurons.

Mutations in the gene encoding a sub-unit of this enzyme are responsible for the neurologic disorder Hereditary Sensory Neuropathy Type I (HSAN1), a disease selectively affecting peripheral sensory neurons.

DFI Treasurer's Report (May 31, 2007, to May 31, 2008)

Submitted by: Nancy Newcomer, Treasurer

DFI Statement of Account

Balance as of 6/1/07	**$51,200.89**
Income:	
Contributions 6/1/07 to 12/31/07	**10,927.50**
Interest 6/1/07 to 12/31/07	**139.58**
Contributions 1/1/08 to 5/31/08	**3,316.23**
Interest 1/1/08 to 5/31/08	**112.53**
Expense:	
June 2007 Mass General Donation	**10,000.00**
March 2008 Mass General Donation	**10,000.00**
Postage Stamps	**21.50**
PayPal Service Charges	**2.93**
Balance as of 5/31/08	**$45,672.30**

Nancy J. Newcomer
Treasurer

DFI

HSN1/ HSAN1 Symposium
Technical Report on Website

Tami Newcomer Murphy has prepared an in-depth, technical report about the April 24 HSN1/ HSAN1 Symposium which was held at the Massachusetts General Hospital MIND Institute in Charlestown, MA.

She introduces the report by saying that "the purpose of the symposium was to bring together leading scientists from around the world who are involved in research pertaining to the understanding and characterization of HSN1. The symposium provided a chance for these researchers to become updated on work relevant to their own through an open exchange of information, ideas, and questions. The primary goal of this conference was to move closer to determining the mechanism of HSN1 pathology for future use in developing successful therapies for treating this disease."

The full technical report is now on the Deater Foundation website for those who are interested either in reading it for their own understanding or for affected family members to recommend as a reference to their physicians. You will find it at:

deaterfoundation.org

Not on our Mailing List?
New Address?
Notify
Carol Dorward
at
cdorward@deaterfoundation.org
of your current home address and/or email address

Gift Certificate Idea

—Submitted by Rory Robb Deater

For Your Consideration:

A gift to Deater Foundation, Inc. may be the perfect gift for someone, to honor someone, to remember someone.

Give a donation:

* *To celebrate a birthday*
* *In honor of Mother's Day or Father's Day, for the parent with HSN-1 (or without)*
* *In appreciation*
* *For Christmas, for the hard-to buy-for-person*
* *In memoriam*

You may request a certificate, suitable for gift giving, to present to the recipient. To do so, contact Nancy Newcomer, Treasurer, P. O. Box 255, White Deer, PA 17887 or email her at: njnewcomer@yahoo.com

In Honor of Helen Deater Wilson

(Continued from Page 4)

both together. I remember them at mealtime and for card playing around the kitchen table. Our meals started with a prayer of thanksgiving, and our card games would sometimes end with swearing; but the love they had for others and us was unbreakable. No matter what the situation, no matter what was going on, there was always room for another at the table. People always felt welcome and there was always company at their home. Often grandma would let me play her hand and she would disappear to the living room. I always thought she did it so my brother or I could have the thrill of playing cards but later realized it was so she could help and support the people who needed her guidance in the living room. It wasn't until I got to experience it for myself that I was on to her. Our grandmother always puts others first and her own needs last. She prays for people continually and can always find the brighter side of a situation. Our grandmother, like her sisters, is simply irreplaceable.

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Deater Foundation, Inc.
P. O. Box 255
White Deer, PA 17887

DFI

We're on the Web!
deaterfoundation.org

Remember that your contributions to DFI are tax deductible.

Mail contributions to:
Deater Foundation, Inc.
c/o Mrs. Nancy Newcomer
P. O. Box 255
White Deer, PA 17887

Late Breaking News!!!

Dr. Florian Eichler and medical liaison Ellen Deater Burns are trying to arrange an opportunity for collecting blood samples from family members at the reunion. Dr. Eichler is committed to a symposium in Buffalo on the day of the reunion, but arrangements may be made for Diane McKenna-Yasek, RN, BSN, Neuromuscular Research Coordinator for the Day Lab to attend the reunion. This new blood sample collection would be used to set up cell lines to validate a possible biomarker, as Dr. Eichler collaborates with Dr. Hornemann whose research has presented a potential new approach to HSN-1. We hope many family members will want to participate in this exciting new research opportunity!

Comments from Two of the Symposium Participants

Submitted by: Ellen Deater Burns, Medical Liaison

Ann Moser states: *"The Symposium was a great success in getting the scientists and Deater family members together to discuss the latest research findings for HSN1."*

Jeffrey Harmon, PhD. said: *"Dr. Dunn and I thought the meeting was extremely useful, scientifically, as it helped us focus our thinking for future lines of experimentation. We also both found meeting members of the family affected by the disease personally rewarding. Our collaboration with Dr. Brown has been very successful; his insights and enthusiasm have energized us all. We, too, are hopeful that the coming year will bring significant new progress."*

"We, too, are hopeful that the coming year will bring significant new progress."
—Dr. Jeffrey Harmon

DFI