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SPF SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support

2015 ANNUAL REPORT

STEPPING FORWARD TODAY TOWARD A CURE TOMORROW

President's Letter

Dear Friends,

2015 was a huge step forward in our quest for a cure for HSP and PLS and we owe it all to you. Our sincere and heartfelt thanks go out to the community at large and to all our generous supporters for making this possible.

There are currently 79 known genetic causes of HSP and most were discovered in just the last few years. These great discoveries were the starting points to the transformative progress that is taking place now. We are constantly breaking exciting new ground! Let me tell you about just some of the highlights of the progress that is taking place with the research we are sponsoring.

Dr. Teepu Siddique, PhD at Northwestern University's Feinberg School of Medicine in Chicago has increased the size of his PLS Registry which began in 1998 to 201 PLS patients. The goals of this registry are to establish clinical trial feasibility and to characterize clinical and EMG characteristics for PLS patients. He is seeking to have better biomarkers for PLS in order to more quickly diagnose and understand the progression of PLS. Work on the function of Alsin, a protein involved in juvenile onset PLS, has shown that it is involved in neuronal transport in PLS patients.

We have sponsored Dr. Holger Sondermann PhD with Cornell University in his study of HSP SPG3A in a 3 generation Amish family in Lancaster County PA.. Dr Sondermann has made considerable progress in his study of the structure and malformation of the protein Atlastin.

Our research with Dr. Andrew Grierson PhD, Dr. Kurt De Vos PhD and Dr. Mimoun Azzouz PhD at Sheffield University in Sheffield UK has been momentous. Dr. Mimoun Azzouz has made remarkable strides on actual SPAST gene replacement therapy for HSP patients. Dr. Grierson and Dr. De Vos are identifying the molecular mechanisms underlying regulation of mitochondrial axonal transport in HSP patients. They are developing and characterizing novel vertebrate models of HSP in zebrafish and mice and are learning about the biology of the contacts between the endoplasmic reticulum and mitochondria in HSP patients. A preclinical assessment of histone deacetylase 6 (HDAC6) inhibition as a therapy for HSP is being initiated along with tests of several novel drugs aimed at restoring identified malfunctions of HSP axonal transport.

Our research with Evan A.L. Reid PhD at the University of Cambridge, UK has led to remarkable discoveries regarding where the cortico spinal tract axons degenerate in HSP patients. His research has evolved from gene mapping & i.d. studies to concentrate more on cell biological studies, particularly in the area of the role of HSP proteins in membrane traffic. His overall aim is to understand the normal function of selected HSP proteins, to determine how the abnormality of these proteins leads to the disease and to use this knowledge to design new therapeutic strategies for HSP.

Many of you are aware of the project we are working on, hand-in-hand, with the Australian HSP Research Foundation and Dr. Alan Mackay-Sim, PhD. SPG4 HSP patients have a mutation in SPAST, a gene that encodes Spastin, a microtubule severing protein. Patients with SPG4 HSP have 50% of the spastin, 50% of the acetylated atubulin and 150% of the stathmin, a microtubule destabilizing enzyme compared to people without HSP (control). Dr. Mackay-Sim, PhD hypothesizes that SPG4 HSP patients probably compensate for reduced spastin with stathmin but this makes the microtubules less stable and alters organelle trafficking. Fortunately, they have discovered that the microtubule binding drugs, paclitaxel and vnblastine, increase acetylated atubulin levels in patient cells to normal. These two promising drugs are currently being screened with both neuronal stem cells and mice to determine their efficacy before human clinical trials can begin. When this study is complete, hopefully in early 2017, we will need to be ready for Clinical Trials on people.

To this end, we are also supporting Dr. Rebecca Schule, PhD from Germany who is developing a Hereditary Spastic Paraplegia Patient Registry in several countries. A Patient Registry is critical for Stage 2 FDA Clinical Trials because scientists need to have a sufficient number of confirmed SPG4 patients and they need to know what is "normal" for HSP progression to judge these drugs against. Paclitaxel and vnblastine have already been shown safe for people as cancer drugs so we will be able to skip FDA Stage 1 requirements for Clinical Trials.

Leaders of HSP foundations from many countries of the world met for the first time in Madrid Spain last June. I represented The Spastic Paraplegia Foundation. This group vowed to work together to promote awareness of HSP worldwide and demonstrate to pharmaceutical companies, FDA and EMEA that we are united and organized so as to be recognized and accepted for funding and pharmaceutical research. An international HSP logo has been designed and approved by a vote of HSP patients worldwide.

Thanks so much to everyone who has helped fund this research that will lead to treatment and eventually to a cure for HSP and PLS.

Sincerely,

Frank Davis

SPF President

HEREDITARY SPASTIC PARAPLEGIA
Taking Steps Toward a Cure

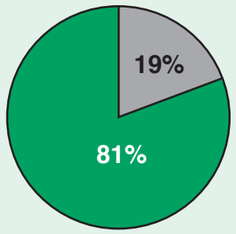
Would you like more information about us?

The Spastic Paraplegia Foundation, Inc. ("SPF") is a not-for-profit corporation that is a United States & Canada, volunteer-run, health organization dedicated to funding cutting-edge scientific research to discover the causes and cures for Hereditary Spastic Paraplegia and Primary Lateral Sclerosis, and to diminishing suffering by education and support.

The SPF home corporate office is located at 1605 Goulart Place, Fremont, CA 94539-7241. A copy of our latest annual report or financial statement may be obtained by writing to this same address or calling 877-773-4483.

Financial Activities

Where your dollars go



81% Mission
19% Management and Administration

REVENUE	2015	2014	2013
Donations	$464,936	$569,276	$443,304
Team*W*alk	30,739	44,716	53,436
Special Events	27,743	40,568	59,584
Program Fees & Products	17,009	14,386	12,021
Investment Income	202	167	90
Total Support and Revenue	**$540,629**	**$669,113**	**$568,435**
DIRECT EXPENSES			
Management and Administration	64,593	40,028	41,704
Program Expense	42,002	22,278	28,225
Total Expenses	**$106,595**	**$86,053**	**$100,665**
GRANTS PLEDGED	**$600,000**	**$280,000**	**$800,000**
NET ASSETS	**$1,536,685**	**$1,309,341**	**$1,041,869**
(as of December 31)			

The Board of Directors continues to maximize your donations as 81% of each dollar raised supports the foundations mission of research, information and support. Donations in 2014 included one $100,000 donation that was not reoccurring. Management and Administration expenses went up due to increased issues of our *Synapse Newsletter.* Program Expense went up due to the increased cost of our Annual Conference in Seattle which, though higher cost, was profitable. Other major costs include the annual audit fee, license filings in multiple states and bank credit card fees.

Professional fees which are valuable and necessary foundation expenses are services which are donated to the foundation. Legal, accounting, income tax preparation and medical grant review services are all provided at zero cost.

We are pleased to report that a total of $400,000 has been approved for research funding for 2016. This is made possible by the continued support of our generous donors. 2015 was highlighted by the Match My Gift program. Over $310,000 was raised as the result of anonymous donor matches. Our heartfelt Thank You goes out to them.

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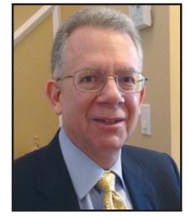

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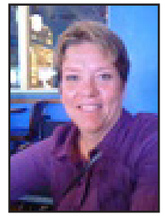

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