

NEW THERAPIES AND NEW RESEARCH BRING NEW HOPE FOR IMPROVEMENTS IN FD CARE



Researchers, doctors and experts from around the world came together to discuss FD at the 2011 International FD Research Conference in New York last October.

In October, the Dysautonomia Foundation hosted the 2011 International FD Research Conference. The event brought together forty highly-regarded scientists and doctors from the US, Europe and Israel as well as Australia and Chile. The experts shared their findings and ideas on how to advance our understanding of FD and how to improve treatment and reduce the impact of life threatening symptoms.

This was the largest-ever gathering of FD researchers and doctors. Over a three-day period, they gave presentations, participated in group discussions, and formed new connections. Many expressed how valuable it was for them to meet each other and participate in a process that fostered both formal and casual interaction, and some began plans for new collaborative research projects.

Collaboration among researchers and physicians is especially important for a rare disease like FD in which researchers, along with patients, can often feel isolated. One of the major goals of the conference was to provide researchers with a forum to freely exchange ideas and get to know others who are working on related projects.

A key goal of the conference was to encourage researchers to think about designing studies to develop and refine our ability to treat and understand FD. It was apparent that these goals were

realized as a number of researchers began developing their ideas for future FD research projects and making plans to work together on research proposals that would be submitted to the Foundation.

“People in the FD community are used to thinking of FD as an orphan disease with little interest from the research community, but at this conference you could see that the numbers of engaged researchers are growing and many new research projects are being planned,” David Brenner, Dysautonomia Foundation Executive Director, said. “We now see a new level of interest in both clinical and basic scientific FD research.” (Continued on page 8)

New clinical findings redefine FD and point the way to new treatments

Researchers from the FD Clinical Research Lab at NYU have unraveled one of the great mysteries surrounding how the FD nervous system works by exploring the function of the nerve pathways that control blood pressure.

The researchers found that in FD the brain is not getting reliable information from the rest of the body, and thus does not always make the right decisions in order to maintain stable blood pressure. Like a driver that cannot see the road ahead but still drives on, it’s easy to get into terrible difficulty by speeding up and going in the wrong direction. For the driver of the car, it will lead to disaster, and for someone with FD, it leads to an “autonomic crisis” in which blood pressure, heart rate and digestion are out of control.

“We now know that the problem with FD is very different from what we used to believe. While the nerves that carry the signals from the brain to control the different organs (blood vessels, heart, gut) work pretty well, the problem is that the nerves that carry information from the body organs to the brain do not work properly,” Dr. Horacio Kaufmann, Director of the FD Research Laboratory at NYU, said.

“The dysfunction of these blood pressure sensing nerves (known as baroreflex afferents) has terrible consequences because the brain does not know what occurs in the body but still ‘commands’ it. Sort of like trying to drive a car at high speed in complete darkness. This explains FD crises and why people with FD can find themselves to be at the mercy of their emotions,” Kaufmann added.

This is the largest study ever conducted with FD patients. The results have been published in the prestigious journal *Neurology*.

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PRESIDENT'S MESSAGE

Dear Friends,

I imagine it doesn't surprise you that I have come to consider the FD community an extended family filled with annual traditions, new additions as well as shared challenges and successes.

This year the feeling has grown as we saw old and new faces at events like our cycle tours and golf outings; as we hosted the largest-ever FD research conference; and as we welcomed new children, parents, researchers, and benefactors.

Like any growing family, there's nothing stagnant about the work we do, nor the goals we set. But one thing remains the same: The dedication we all have to making the lives of people with FD and those who love them better with every passing day.

– Faye Ginsburg



EXECUTIVE DIRECTOR'S MESSAGE

David Brenner

You have in your hands one of the most information-packed DysCourse issues to date. There's news of drug trials, advancements in research, community activities and fundraisers. Our goals of pursuing the best medical treatment and research for people with FD continue with even greater enthusiasm than ever before.

As you will discover in these pages, many changes in treatment procedures and staff have taken place at the Dysautonomia Center at NYU Langone Medical Center in the past year. This growth has proven to be positive and will serve us well in the years to come.

Promising new drug studies, an updated comprehensive treatment manual, and the addition of more bright minds from the medical community to the Dysautonomia Center and to our research efforts, are just some of the wonderful developments in the past year.

Despite the economic downturn for many, the Foundation's faithful donors continue to help us pursue our mission with their generous support. We are deeply grateful.

My optimism for the future remains at its highest that we will continue on this path of growth and success as we pursue our ultimate goal: a cure for FD.

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The lead author of the paper, Dr. Lucy Norcliffe-Kaufmann, said the results have completely changed the way FD is understood. “Now we finally have an explanation for why the blood pressure is high one minute and low the next in FD. As far as we know, FD is the only genetic disease that affects the blood pressure sensing nerves. This study shows that the protein IKAP is directly involved in the development of the blood pressure sensing pathways,” Norcliffe-Kaufmann said.

As it is now known which nerves are dysfunctional, efforts can be focused on improving the function of those specific nerves, and will have a direct impact on basic science research. Dr. Felicia Axelrod, Director of the Dysautonomia Center, added, “Because the FD Research Laboratory is part of the Dysautonomia Center, these findings have already been used to change the way we treat FD and will give rise to new treatment options for the future.”

The insight into these blood pressure sensing nerves makes the disease attractive to a variety of researchers from different fields. The work has already made a big impact at two national meetings: the American Academy of Neurology and the American Autonomic Society. At both meetings it was one of very few studies selected for discussion in the highlights sessions.

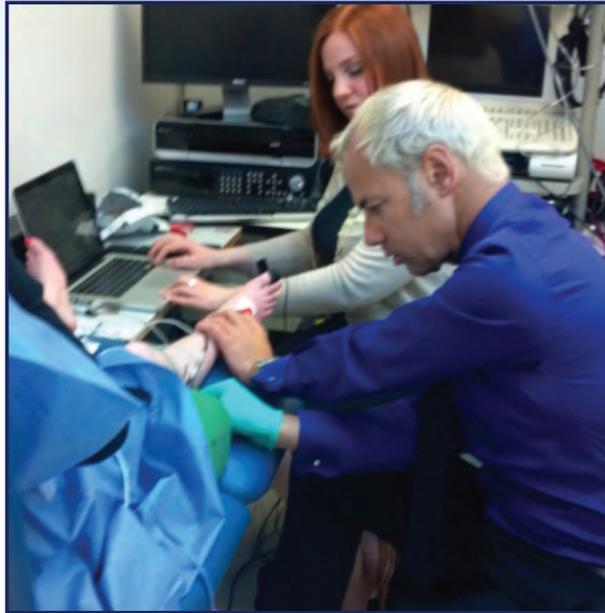
The results have completely changed the way FD is understood.

In terms of treatment, having an explanation for this aspect of FD is nearly as important as discovering the gene. It has broad implications for treatment, clinical research and basic research. It also helps us connect the genetic root cause to the physiological symptoms. While we have known for quite some time that the nervous system is dysfunctional in people with FD, we now know much more about how and where in the nervous system the communication breakdown occurs.

The Dysautonomia Foundation congratulates Lucy Norcliffe-Kaufmann, PhD, Felicia Axelrod, MD, and Horacio Kaufmann, MD for their work on this study. It demonstrates how the combination of the world’s only FD clinical research lab and the United States’ only FD treatment center can result in better understanding and improved treatment of FD. The Dysautonomia Foundation is proud to support the Dysautonomia Center its mission to help people with FD live better, healthier and longer lives.

Visiting researchers work with Dysautonomia Center to investigate and develop new approaches to FD care

The Dysautonomia Center at NYU continues to set the international standard for FD research. Enhanced therapies and treatments are helping to improve the quality of life and survival for people with FD. Part of this success is derived from collaboration with world-class experts from a variety of disciplines. These experts visit the Center to conduct clinical research on FD patients.



Vaughan Macefield, PhD, (left) from the School of Medicine at University of Western Sydney in Australia, comes to the Center to study how nerves conduct signals that affect the gait of patients with FD. Using new techniques in microneurography, he has discovered key mechanisms that determine the cause of the unsteady walk –known as ataxic gait – that FD patients develop over time. Macefield and the team at the Center found that patients with FD are missing sensory receptors in the leg muscles. The ongoing research

aims to strengthen this hypothesis and the understanding of FD from its many angles.



Carlos Mendoza-Santiesteban, MD, is a neuro-ophthalmologist at Tufts University who collaborates with the Center to study optic atrophy, a major cause of poor vision in FD patients, especially as they get older. All of the participants in the study were found to have optic nerve damage, demonstrating that people with FD have an optic neuropathy similar to other hereditary diseases. Until now, FD patients’ eyesight has not been studied extensively, and further investigation could lead to vision-saving treatments.



Joel Guterrez, MD is the director of clinical neurophysiology at the Cuban Institute of Neurology and Neurosurgery in Havana. He has been visiting the Center to learn more about basic functions, such as swallowing, breathing and blinking, in people with FD by studying the neurological mechanisms of the brainstem. Identifying specific problems people

with FD have in these areas is among the first steps to improved treatment.

New FD Research Projects Funded



Dr. Michael Brownstein

In March, the Dysautonomia Foundation awarded funding for six new research projects. With a commitment for nearly one million dollars over the next two years, this represents the largest initiative for new research projects in our history. The Chairman of the Dysautonomia Foundation Scientific Advisory Board, Michael J. Brownstein, MD, PhD, who has occupied leadership positions at the NIH and the J. Craig

Venter Institute, led the committee that solicited and reviewed proposals for FD research projects.

Susan Slangenaupt, PhD (MGH/Harvard Medical School) and **Ioannis Dragatsis, PhD** (University of Tennessee) are working together to create an improved animal model of FD. They have shown that mice without the FD gene (IKBKAP) die as embryos due to the absence of IKAP protein. However, they've also shown that mice can survive with defective IKBKAP genes that make only 10% as much IKAP as normal genes produce. These mice have many of the features of FD: postnatal failure to thrive, reduced numbers of fungiform papillae on the tongue, gastrointestinal dysfunction, poor balance, skeletal abnormalities, and impaired development of the sensory and autonomic nervous systems. They cannot be used to study FD gene splicing, however, so this project will introduce copies of the human FD gene into these mice to see how genetic therapies can be used to treat FD symptoms. These are studying how drugs like kinetin that improve splicing of human FD messenger RNA will work in the mice. This will certainly advance our knowledge of kinetin's effects and allow us to study other genetic therapies as well.

Gil Ast, PhD (Tel Aviv University) is also working on mouse models of FD. The most interesting is a so-called conditional knockout of the FD gene. In these mice, he should be able to "turn on" the defect in IKBKAP in specific tissues. This will allow him to determine the impact of FD on an organ by organ basis. Gil is also continuing his search for compounds that might mitigate the effects of FD by increasing the level of IKAP messenger RNA production. He has found some compounds that have already proven to be effective in increasing levels, including phosphatidylserine (PS). His mouse models will be used to test PS, kinetin and other potentially therapeutic compounds. Gil is also looking at the role of IKAP in neuronal development in embryos and signaling pathways involved in IKAP gene activation.



A researcher holds up an FD mouse in Gil Ast's lab.

Frances Lefcort, PhD (Montana State University) has also created FD mice. Her mice lack IKAP in the nervous system. While most die in utero, those that are born live an average of 5 months with a severe, progressive movement disorder. She wants to characterize them in more detail and to learn why there is so much animal-to-animal variability in the defects they have. She is also interested in the effects of other genes on the FD phenotype. Her work could be quite significant if she can discover a modifier gene with a major beneficial or deleterious effect. By identifying which neuronal activities are most disrupted in FD, and which genes are protective, she will enhance the development of new targets for therapeutic treatments of FD.

El Cherif Ibrahim, PhD (Aix-Marseille University) observed that up until now, efforts to understand FD have been limited by the difficulty in obtaining an abundant source of patient cells from the nervous system to model the neurodegenerative processes occurring in FD. In an effort to address this problem, he has isolated olfactory mesenchymal stem cells from the nasal cavities of FD patients, which can be thought of as immature sensory neurons. The ones from FD patients splice the FD gene poorly, and their movement in tissue culture plates is defective. He plans to use this to understand the effects of kinetin on the expression of genes that are regulated by IKAP. These stem cells provide a nice, simple--albeit incomplete--model of FD.

Adrian Krainer, PhD (Cold Spring Harbor Laboratory) is using so-called antisense oligonucleotide (ASO) technology to target specific portions of individual mRNAs to correct splicing defects. He has used these ASO short pieces of single-stranded DNA to improve the splicing of a defective gene in another disease, spinal muscular atrophy (SMA). Adrian will use a similar strategy to try to correct the splicing defect in FD. Developing this therapy, based on the use of a piece of synthetic DNA, might take a lot of time and effort, but it holds great potential for future FD genetic therapies.

Carlos Mendoza-Santiesteban, MD (Tufts University) has demonstrated that FD patients suffer from a progressive and selective type of optic neuropathy similar to other hereditary optic neuropathies which are due to the dysfunction of mitochondria. He has found that people with FD have a defect in red-green color vision and loss of cells in the macular region of the retina. This observation suggests that vision can be improved in FD patients if they are trained to use a different fixation point. In addition, he may have discovered a biomarker that is an ideal way to follow drug therapy and disease progression. Last, but not least, he may have set the stage for using gene therapy to correct the defect in FD patients' photoreceptor cells which cause reduced vision or blindness.



New Clinical Trials Underway at the NYU Dysautonomia Center

Several studies are underway to test the safety and efficacy of new compounds that have the potential to treat the degenerative and debilitating effects of FD.

Kinetin: A Potential Genetic Therapy?

Kinetin, a natural compound found in our food supply, has been shown to hold great promise in its ability to correct the FD splicing defect. A clinical trial is underway to investigate the safety and correct dosage of kinetin for people with FD.

Thanks to the work of Professor Susan Slaughaupt, we know that FD patients are deficient in the protein IKAP. And while we don't yet know exactly what IKAP does in healthy people, we do know that a deficiency in IKAP production leads to the symptoms of FD. Professor Slaughaupt also discovered that kinetin is extremely effective in laboratory tests in correcting the IKAP protein production problem in FD cell lines.

The NYU FD Research Laboratory team has conducted limited kinetin safety and dosage trials on FD carriers and patients in the past, after extensive pre-clinical investigations were completed.

Kinetin was first used in a clinical trial at the Dysautonomia Center in 2006, conducted with FD carriers, primarily parents and relatives of people with FD. In 2009, a small-scale, short-term study was conducted on FD patients.

Encouraged by the results of those trials, a new trial began in 2011, involving a larger FD adult patient population with in-depth monitoring of a wide range of biomarkers. It is set to expand to even more patients, including those as young as 16 years old. Our hope is that kinetin will increase IKAP production and that this will result in a reduction of both FD symptoms and the long-term degenerative effects of FD.

Carbidopa: Goodbye to Nausea?

The FD Research Lab is also testing the drug Carbidopa as a potential therapy for the pervasive and debilitating nausea and retching that plagues many patients with FD.

Carbidopa is already used to counteract the side effects of other powerful drugs used to treat Parkinson's disease. Encouraged by Carbidopa's anti-nausea capabilities, Dr. Horacio Kaufmann at the FD Research Lab has found it to be a promising alternative to the traditional medications FD patients take when they experience an FD "crisis" marked by extreme nausea and retching. Traditional crisis medications were often effective, but they also had a harmful impact on the patient's blood pressure, respiration and alertness. "The traditional treatment of the FD crisis is potentially as dangerous as the crises themselves," Dr. Kaufmann said.

"Carbidopa is potentially a much more effective therapy with fewer long-term risks."

Carbidopa has an advantage over other drugs used by FD patients, such as clonidine and benzodiazepine, in that it does not modify respiration, it does not sedate and it does not lower the blood pressure of those who take it – it simply blocks the hormone (dopamine) that is responsible for the vomiting and retching experienced by FD patients.

Most patients participating in the trial showed dramatic reductions in the intensity and frequency of their nausea. Doctors are optimistic that Carbidopa might be an innovative and simplified approach to dealing with some of the enduring problems brought on by FD.

The trial is about to wrap up a phase of the trial in which some patients are taking Carbidopa and others are taking a placebo. "If the trial goes really well it will be a new paradigm," Dr. Kaufmann said. "This could become standard therapeutic treatment for many patients."

The researchers also discovered that blood pressure variability seems to decrease in people taking Carbidopa, meaning that while the blood pressure highs and lows were still extreme, it was more often within the normal range. This could have a significant effect on reducing organ damage, especially renal failure, which correlates closely to variability in blood pressure. This very positive and unexpected discovery has warranted further investigation of Carbidopa, which could turn out to be a new FD "wonder drug."

These trials could lead to significant new therapies for FD.

Phosphatidylserine: Increased IKAP from an over-the-counter supplement?

Professor Gil Ast and his team of researchers in Israel found that the nutritional supplement phosphatidylserine (PS) increases IKAP protein levels in FD mice as well as in cells derived from FD patients. Increased IKAP levels could help slow or reverse the symptoms of FD. The effect of PS on IKAP levels is especially encouraging because PS has been used extensively and safely by people around the world for many years.

While PS does not have as dramatic an effect on IKAP production as kinetin, its ubiquitous availability and established safety record make it an extremely attractive alternative.

PS's ability to increase IKAP levels has been shown in experimental models, but not in people. Doctors at the NYU Dysautonomia Center are preparing a study to see if the same effect on IKAP levels occurs in people with FD. "We are encouraged because this compound has been around for many years and appears to be very safe," Dr. Kaufmann said of the potential for PS as a therapy for FD patients in the US and abroad. A trial involving FD patients taking PS is scheduled to begin in the second half of 2012.

New Treatment Initiatives

Every day, the doctors at the Dysautonomia Center combine research with new treatment options, always looking for better ways to make FD patients healthier. Here are a few recent developments that have had a positive impact on treatment.

Hypertension vs Hypotension

Drs. Kaufmann, Axelrod and Norcliffe-Kaufmann have changed the way they look at blood pressure in patients with FD. After discovering that reducing hypertension (high blood pressure) could be beneficial to the kidney health of those with FD, there is less emphasis on raising low blood pressure and more concern with lowering high blood pressure and reducing blood pressure variability. The three published their findings in the *Journal of Human Hypertension* in 2011.



The staff of the NYU Dysautonomia Center. Front Row: Dusan Roncevic, MD, Felicia B. Axelrod, MD (Co-Director), Horacio Kaufmann, MD (Co-Director) Back Row: Niamh Goulding, PhD, Jocelyn Acosta, Lauren Stok, RN, Lucy Norcliffe-Kaufmann, PhD. Not pictured: Jose Martinez, MS, and Deborah Dore, MSW.

Reducing dosages of Florinef and Valium

In a comprehensive retrospective study, the Center's researchers found that patients who were taking higher doses of glucocorticoids, such as Florinef, used to control blood pressure, had a faster progression of renal disease and higher blood pressure. "By reducing the amount of Florinef the FD patients were taking, we have been able to reduce the average blood pressure," Dr. Kaufmann explained. "As a result, we hope to slow the progression of renal disease in FD patients."

The doctors at the Center also found that patients taking Valium had a significant deterioration of pulmonary function which negatively affected respiration, causing hyperventilation. By reducing the amount of Valium taken to mitigate an FD crisis and manage blood pressure, there has been a marked improvement in carbon dioxide levels in blood.

Assisted Breathing

The increased use of noninvasive assisted ventilation machines, BiPAP and CPAP, is helping reduce carbon dioxide levels in the blood of FD patients. Using assisted ventilation for at least a few hours during the night reduces the level of carbon dioxide in the blood during the day. The reduction has made patients more alert and has reduced their hypertension and headaches. As a result, people with FD can enjoy better quality of life and reduce the severity of long-term threats to their life span.

New Faces

Nurse Lauren Stok, RN joined the team at the Dysautonomia Center in November 2011. Many patients might recognize Lauren from her years of volunteer work at Camp Simcha Special and Kids of Courage. Lauren said that both she and the patients value the fun times they have had together, especially now that she is at the Center. "Going for an exam is very clinical and it helps to have a familiar person there you associate with doing things like pottery," she said of her role change from camp to the Center. After earning her nursing degree from NYU she went into homecare, always knowing that she wanted to find her way to the FD community.



Licensed Social Worker **Deborah Dore** joined the Center at the end of August, bringing with her 30 years of professional experience with families and children. She earned her undergraduate degree in health and human services at the University of New York, Buffalo and then went on to earn her masters in social work at Hunter College in New York City. Families can call on her for support in applying for and obtaining necessary equipment, services and other entitlements.



Dysautonomia Fellow **Dusan Roncevic, MD**, joined the Center after completing his post doctorate degree at the University of Santa Barbara and McGill University and his neurology residency at the University of Belgrade in Serbia. During his residency he rotated through the Sackler School of Medicine in Israel where he gained experience with Jewish genetic disorders and deepened his interest in neurodegenerative diseases. "I am fascinated by autonomic medicine because it is where neurology meets other somatic medicine, and where the mind meets the body. The research of interactions between nervous and cardiovascular system is very interesting, and hopefully it will provide us with advances in treatment for both systems' ailments in the years ahead," Roncevic said of his work with FD patients.



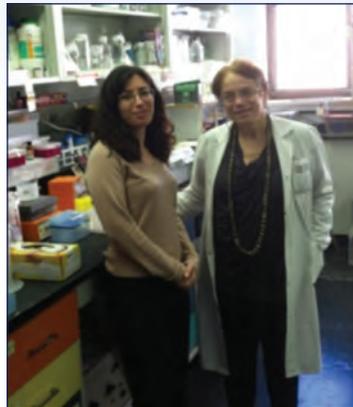
Niamh Goulding, PhD has joined the Center from Cork in the south of Ireland, bringing an interest and expertise in kidneys to the FD population. She earned a PhD in physiology at University College Cork under Professor Edward J. Johns, a world renowned renal expert. Niamh is completing research on renal failure and the neural control of the kidney. Her work placed particular emphasis on the baroreflex control of blood pressure and how dysregulation of this system leads to renal failure.





The Israeli FD Center

For over 30 years, the Israeli FD Center has been the hub for FD care throughout Israel and Europe. Israel has the largest concentration of FD patients outside of the United States, and Hadassah Hospital in Jerusalem has been the only place that offers Israeli FD patients dedicated FD medical and paramedical expertise.



Funded through grants from the Dysautonomia Foundation, the Center is under the direction of Dr. Channa Maayan.

Nearly 120 FD patients are registered with the Center, and Dr. Maayan and her staff are on call 24 hours a day to help with any emergencies that arise.

Dr. Maayan not only provides excellent medical care at the center, she also travels with FD patients on their annual group trips to make sure they receive the best available medical care at all times.

Above: A researcher and Dr. Maayan in the lab. Right: FD adults at one of their monthly gatherings. Below: the Treatment Center staff gets together for a breakfast meeting.



Israeli Labs work on FD Research

Two teams of scientists in Israel are working on FD research and the identification of new FD therapies. Both teams operate out of Tel Aviv University and were proud to demonstrate and discuss their work during a site visit by the Foundation's Executive Director.

The Dysautonomia Foundation has funded the work of Miguel Weil's and Gil Ast's labs for several years through our involvement in the FD Research Consortium. The Foundation is the largest source of funding for the consortium.

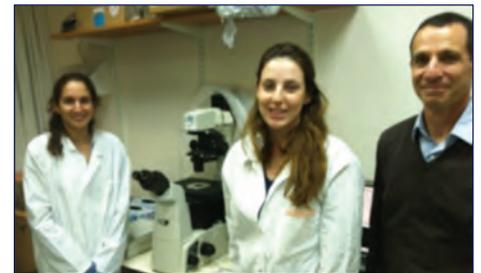
Professor Miguel Weil's lab investigates the role of the protein IKAP in peripheral nervous system neurons using in vivo and in vitro models based on chick embryos.



Miguel Weil, PhD (second from right) with members of his lab and Dysautonomia Foundation Executive Director David Brenner (center).

Weil's work on neurons contributes to understanding of the FD phenotype and the role IKAP plays in the development of the nervous system. His lab is also using high-throughput screening techniques to look for compounds that will help correct the FD splicing defect. Miguel has a special interest in helping to develop new FD therapies; his son Nir, 21 years old, has FD.

Professor Gil Ast's lab has developed innovative FD mouse models that can be used to test and understand FD therapies, and he discovered the potential therapeutic effects of phosphatidylserine (PS) on the FD splicing defect.



Gil Ast, PhD (right) and members of his lab, Hadas Keren and Shiran Naftelberg

The lab also works on projects to better understand how IKAP functions in an effort to find new approaches to genetic therapies. Work in this area includes identifying the location of IKAP expression in human and mouse cells, the development of IKAP in mouse peripheral nervous system and the mechanisms by which IKAP operates in cells.

NIH awards funding for development of FD drug



Susan Slaughaupt, PhD, was recently awarded a grant from the NIH Blueprint for Neuroscience Research Neurotherapeutics Network. The NIH Blueprint is a collaborative framework that includes the Office of the Director and all NIH Institutes and Centers that support research on the nervous system. The Neurotherapeutics Network is helping small labs develop new drugs for

nervous system disorders like FD. The Network provides research funding, plus access to millions of dollars worth of services and expertise to assist in every step of the drug development process, from laboratory studies to preparation for clinical trials.

Dr. Slaughaupt was awarded this grant for her work on kinetin, and she will co-chair the Lead Development Team, a group of experts that will focus on optimizing drugs for the treatment of FD. This grant will allow access to millions of dollars of drug development funds and it underscores the NIH's commitment to combating neurologic disease.

“The funding from the NIH is the best news we have had in a long time,” Dr. Slaughaupt said.

Dr. Slaughaupt, who is based at MGH / Harvard Medical School, has worked on FD research for over 20 years, including her work with MGH's Dr. James Gusella on the discovery of the FD gene and her work on the identification of kinetin as a potential therapy for FD treatment. Her lab continues to work closely with physicians at the Dysautonomia Center on the clinical trial of kinetin. This May, she visited Israel to meet FD families and deliver scientific talks in both Jerusalem and Tel Aviv.

Oxygen program helps FD families travel

Thanks to generous support from the State of New York and donor families, the Foundation has piloted an oxygen concentrator loaner program for our FD patients. Whether they fly for medical purposes or for pleasure – to visit the doctor or to visit grandma – FD patients require supplemental oxygen when traveling by plane, and they can turn to the Foundation for an easy and low-cost (often free) source of the necessary equipment.

Under normal circumstances, a healthy person can automatically compensate for atmospheric changes in a pressurized airplane environment, but people with FD don't always compensate properly. As a result, they need a supplemental supply of oxygen when traveling in an airplane.

Airlines used to routinely provide such oxygen, but with changes in federal regulations over the last few years, airlines have reduced or eliminated their oxygen programs.

The Foundation loans POC (portable oxygen concentrator) units to FD families for free. Families only pay shipping charges, and many families from the NYC metropolitan area can avoid those charges by picking up the unit in our NYC office.

In the first half of 2012, the Foundation's POC units went to over a dozen families for a total of 185 days of usage.

Some airlines still provide oxygen for a fee, and some FD families have access to oxygen through their insurance benefits, but the Foundation's program provides a low-cost, convenient alternative to the airlines high prices and the insurance companies' bureaucracy.

The Foundation has four SeQual Eclipse POCs available. Forms for arranging the loaner unit and for medical authorization from a doctor can be found on the Foundation's web site.

Research Conference (continued from page 1)

Many of the researchers in attendance were current or past recipients of grants from the Foundation, but some had never been involved directly with the Dysautonomia Foundation. Among the newcomers, some had already received funding from the NIH for FD projects, while others had never worked on FD, but had worked extensively in other closely-related areas of autonomic disorders. Thanks to the rising profile of FD in prestigious medical and scientific journals, more experts are becoming interested in FD research. As a result, the Foundation has received some of the highest quality research proposals ever submitted, and six outstanding projects were selected for funding.

The Dysautonomia Foundation sponsors an FD research conference every two or three years with the generous help of the Goldberger family, who show the researchers how much their work is appreciated through some genuinely unmatched New York hospitality. This year, they hosted two dinners and treated the attendees to a Broadway show.

During the conference, attendees reviewed, discussed and proposed new directions for FD-related research and treatment. There were 20 presentations spanning complex topics and innovative research including:

- Latest findings on autonomic clinical investigations
- Progress reports on clinical trials of new therapies
- Development of biomarkers with potential to measure disease progression and severity
- Updates on development of FD animal models
- Identification of new therapeutic compounds
- Updates on IKBKAP gene/ELP1 protein research.



Bowl-A-Thon

For seven years, the FD Bowl-A-Thon in Long Island, NY has kicked off our annual fundraising calendar with a bang and a rumble. This year's 7th Annual Bowl-A-Thon took place on March 18, 2012 and was organized by Lexi Sirota and Ally Kaplan, two of the foundation's youngest and most dedicated advocates.



Jared Sirota, chairman of past bowl-a-thons, with co-chairs Lexi Sirota and Ally Kaplan.

The event was founded in honor of their cousin Scott Fass, whose friendly but persistent fundraising appeals have made him one of our best all-time fundraisers, bringing in tens of thousands of dollars in sponsorships every year.

Path to the Cure



The second annual Path to the Cure FD Bike / Walk Tour and Family Fun Day was held in Abington, PA on April 15th. Attracting over 300 participants and raising \$80,000, this event does it all: spreading the word about FD, encouraging people to get tested for the FD gene, and giving everyone involved a great day of biking, walking, fun and food.

The event is organized by the Philadelphia Chapter of the Dysautonomia Foundation with tremendous support from the Abington Police Department and the Township of Abington. Event co-chairs Cindy Singer and Rabbi Lawrence Sernovitz do a fantastic job getting the entire community involved.

Golf Outings

Volunteers from Long Island and Chicago organize wildly popular golf outings every year which raise over \$350,000 for FD treatment and research.

The 16th Annual FD Golf Classic will take place on July 30, 2012. For the second year in a row, it will be held at Glen Oaks Club in Old Westbury, NY. Participants will play 18 holes and then gather for dinner and a combination silent and live auction, featuring great prizes including foursomes at exclusive golf courses, sports tickets, travel packages, electronics and memorabilia. Last year's event was marked by intermittent clouds and rain, but that did not deter the more than 150 participants from golfing and generously donating. The event's dedicated co-chairs, Paul Wexler, Steve Fass, Adam Posnack and Paul Sunderland, never fail to make this a spectacular event. Last year's event brought in more than \$275,000.



In the Chicago area, the 9th Annual FD Classic will be held at Briarwood Country Club in Deerfield, IL. Like the event in NY, it also takes place on Monday July 30th. The event features golf, dinner and auctions as well as card games. A fantastic group of volunteers and players make this event a truly enjoyable experience. Details and signup are available on our web site. Gregg Myers does a great job of organizing the event every year in honor of his daughter, Sophie. Last year the event raised over \$70,000.

Cycle Tour



The 8th Annual Tour de Foliage FD Cycle Tour raised \$175,000.

On Sunday, September 18, 2011, about 100 riders participated in the Dysautonomia Foundation's 8th Annual Tour de Foliage FD Cycle Tour at Pace University in Pleasantville, NY.

Event co-chairs Melissa Slive, Lisa Rudley and Lisa and Jeff Newman organized what is annually one of our most successful events, raising \$175,000 for FD treatment and research. Riders cycle along the rolling hills of Westchester, NY and enjoy magnificent scenery and foliage. The 2012 event will be held on September 23rd. Visit our facebook page and web site for updates.

Keep up to date with the Dysautonomia Foundation on our web site, www.famdys.org. Get all the latest news on research, events, and fundraisers. See pictures and videos from our events. Sign up for our email newsletter by sending your email address to info@famdys.org.

FD Awareness Day



NY State Senator Toby Stavisky is thanked by Executive Director David Brenner for her support of the FD Awareness Day proclamation.

February 28, 2011 was proclaimed FD Awareness Day by the New York State Assembly and Senate, and April 10th, 2011 was declared FD Awareness Day in Pennsylvania. We are grateful for the support of NY Assembly Member Linda Rosenthal, NY State Senator Toby Stavisky and PA Representatives Josh Shapiro and Thomas Caltagirone.

The proclamations help raise awareness among legislators and the general public, and they help

FD families realize they are neither alone nor ignored by state governments. The proclamations specifically detail the background and description of familial dysautonomia and highlight the incredible progress made in FD treatment as well as the need for carrier screening for the FD gene.

This year, New York State FD Awareness Day will be June 10th – the same day as our annual FD Day Conference. Assemblymember Rosenthal will present the proclamation during the proceedings of the 2012 FD Day conference.

Florida Chapter's long tradition of FD support

The South Florida Chapter of the Dysautonomia Foundation was founded in 1979 by Fay Lager when she learned that her granddaughter was born with FD. Since that time, the chapter has worked diligently to help raise funds and awareness for the treatment of FD. Through a variety of events, including their annual luncheon gala, they have never missed a year of contributions to the Dysautonomia Foundation. Since its inception, the chapter has contributed approximately \$500,000 to the Foundation's treatment and research funds.



Hortense Feldman, Nanette Bernstein, Beth Grossman, Sylvia Segarnick are long-time members of the Florida Chapter.

2012 FD Day Conference brings together families and experts

The 27th Annual FD Day Conference will be held on Sunday, June 10, 2012 from 10am to 3pm at NYU School of Medicine. We will continue our tradition of bringing together FD families, researchers, doctors and experts from near and far for a day of information on new directions in FD research and treatment as well as an update on the progress that has been made and the lessons that have been learned in the past year.

It's a day filled with fun activities for children too, making it an educational event that also builds a sense of community and hope. Younger children get to know each other while enjoying an animal show, magician balloon artist and other fun activities. FD Adults spend time together during the afternoon at our FD Casino and during the evening at our FD dinner party.



This year's conference will feature presentations by Dr. Michael Brownstein, Chairman of our Scientific Advisory Board, who will speak about our upcoming research projects, and Dr. Carlos Mendoza-Santiesteban, an expert in ophthalmologic treatment and research, who will speak about insights into FD vision problems and the possibility of using sophisticated measurements of the retina and optic nerve as biomarkers for FD clinical research.



In addition, Dr. Horacio Kaufmann and Dr. Felicia B. Axelrod, co-directors of the NYU Dysautonomia Center, will present updates on FD treatment, clinical research and demographics. The day will also include

an FD adult panel, Q&A panels with FD experts in research, treatment and social services, as well as a variety of fun activities including our FD casino. The day concludes with a dinner party for FD adults.

Last year's event, on June 12, 2011 had a hundred and twenty-five attendees. Details on the speakers and panelists, as well as abstracts of the scientific and medical presentations, can be found on our web site. This year's event is expected to draw an even larger crowd. Abstracts of this year's presentations will be available on our web site in July.



Generous Contributions help doctors and researchers focus on vision and eye disorders

For nearly 10 years, the Dorothy B. Hersh Foundation has provided grants totaling \$600,000 to the Dysautonomia Foundation for the purchase of medical diagnostic and research equipment. Their generosity, along with grants from the State of New York, has made it possible for us to provide a wide variety of state-of-the-art medical devices to the Dysautonomia Treatment Center and the FD Research Laboratory.

These devices not only help doctors provide the best possible care for people with FD; they also make it easy for FD patients to get all their tests done in one visit to one location. Without this equipment, patients would have to visit a number of specialists and then have to wait as their results are sent to the Dysautonomia Center for interpretation.



This year, a grant from the Dorothy B. Hersh Foundation has enabled us to purchase an optical coherence tomography (OCT) device for the examination of the retinas and optic nerves of FD patients. The OCT provides a non-invasive method to examine the nerves of the eye in great detail. Doctors and researchers will use the OCT for both diagnostic and clinical research purposes in an effort to help patients avoid the progression of severe vision impairment.

The Hersh and New York State grants typically only provide funding for equipment, so we must seek other sources of funding for software, warranty and supplies required to operate medical devices. This year, we are grateful to the Steiner family for their donations that have supplemented our grants for medical equipment.

FD TREATMENT MANUAL

“Familial Dysautonomia -- A Manual of Comprehensive Care” provides an overview of nearly all aspects of FD care. A great resource for patients, families, caregivers and medical professionals, this handbook was authored by the FD experts at our NYU Dysautonomia Center.

One copy of the book is provided free of charge to each family registered with the Foundation and the Dysautonomia Center. Additional copies can be purchased from the Dysautonomia Foundation. Call or email us for details.

Please note: This manual is a reference only and is not intended to be a guide for clinical care. Treatment decisions should only be made in conjunction with a qualified medical professional.

Songs of Love

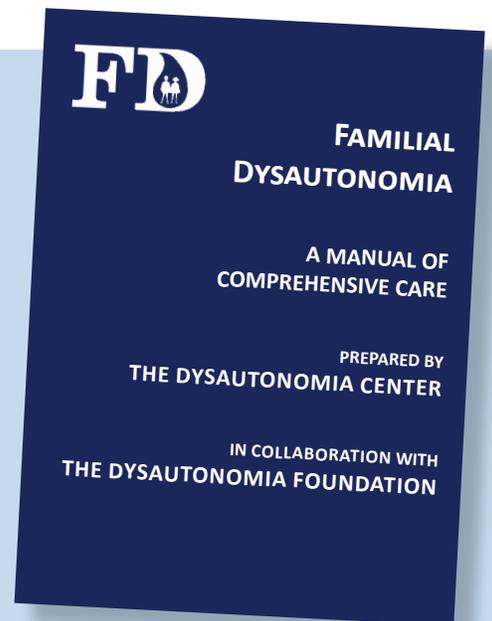
Steven Wexler was the guest of honor at a very special tribute on March 15, 2012 when a large crowd gathered to sing a song in his honor. Eric Diton, a member of the band Six Degrees North and longtime supporter of the Foundation, wrote and produced the song, “Steven’s My Friend.”

Diton performed the song to a full house at The Nutty Irishman in Farmingdale, NY. He directed the crowd to join in and help him record the choruses, and the final result was a beautiful recorded version. Visit our web site to hear it and view more pictures from the event.



Songs of Love Founder, John Beltzer, Steven Wexler, and Eric Diton are all smiles after recording Steven’s song.

The event was sponsored by Songs of Love, an organization that produces original songs for people living with life threatening and chronic illnesses. Diton said the song’s refrain, “To be brave. And do the best you can ... It’s all about trying. Never say you can’t” were taken directly from encouraging words Steven uses.



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UPCOMING EVENTS:

New York Golf Outing July 30
 Chicago Golf Outing..... July 30
 FD Concert Fall, Date TBD

Blue Genes Gala..... Oct 7
 FD Cycle Tour Sept 23
 FD Journal Campaign November

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FD RESEARCH PUBLICATIONS

Each of the publications below was co-authored by at least one researcher who has been funded by the Dysautonomia Foundation. Your contributions help make this work possible – thank you!

Afferent baroreflex failure in familial dysautonomia. Norcliffe-Kaufmann L, Axelrod F, Kaufmann; H. *Neurology*. 2010 Nov 23;75(21):1904-11.

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Developmental abnormalities, blood pressure variability and renal disease in Riley Day syndrome L Norcliffe-Kaufmann, FB Axelrod and H Kaufmann; *Journal of Human Hypertension* (2011) 1 -- 5

Phosphatidylserine increases IKBKAP levels in familial dysautonomia cells. Keren H, Donyo M, Zeevi D, Maayan C, Pupko T, Ast G.; *PLoS One*. 2010 Dec 29;5(12):e15884.

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Kinetin Improves IKBKAP mRNA Splicing in Patients With Familial Dysautonomia Felicia B. Axelrod, Leonard Liebes, Gabrielle Gold-Von Simson, Sandra Mendoza, James Mull, Maire Leyne, Lucy Norcliffe-Kaufmann, Horacio Kaufmann, And Susan A. Slaugenhaupt; *Pediatric Research Vol. 70, No. 5, 2011*

Neuroimaging supports central pathology in familial dysautonomia Felicia B. Axelrod, Max J. Hilz, Dena Berlin, Po Lai Yau, David Javier, Victoria Sweat, Hannah Bruehl, Antonio Convit; *J Neurol DOI 10.1007/s00415-009-5293-1*

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