



**2019 – 2020**  
**YEAR IN REVIEW**

THE LATEST IN RESEARCH IN  
FAMILIAL DYSAUTONOMIA

CENTER FOR  
**NYUDysautonomia**

## A MESSAGE FROM OUR DIRECTOR



In recent years, we have seen rare neurological disorders transform from neglected areas of research, into hotbeds of scientific innovation. As the technologies for fixing gene defects become a reality for some rare diseases, our FD scientists have been hard at work. At the Center, I am making sure we are ready to test new treatments. Twelve years ago, I made the promise to bring the best therapies to patients; meaning treatments that work and have no serious side-effects. To make sure we are on target, we are looking for treatments that improve things that matter most to FD patients and impact their lives.

I've taken a deep dive into our natural history data to pin down what we can use as biomarkers to show success. We are continuing to focus on the eye and walking abilities, but regardless of our progress, bringing new treatments to the clinic requires all patients to be involved. I have built collaborations with doctors around the world that take care of our FD patients. From Tel Aviv, Jerusalem, England and Mexico, we have experts on the ground, that know FD. With this global initiative in place, we have a platform for clinical trials so patients can safely enroll in a treatment trial, when we have a candidate ready to go.

We will need different treatments at different stages of the disease. When it comes to treatment pipeline, I continue to be impressed by the extraordinary basic science teams working on FD. These scientists are our collaborative partners. Their range of complementary expertise is staggering. This means FD is being approached from all angles, including fixing splicing, correcting the mutation, supporting the life-cycle of the neurons. We are embarking on some exciting cutting-edge research to turn these ideas into reality.

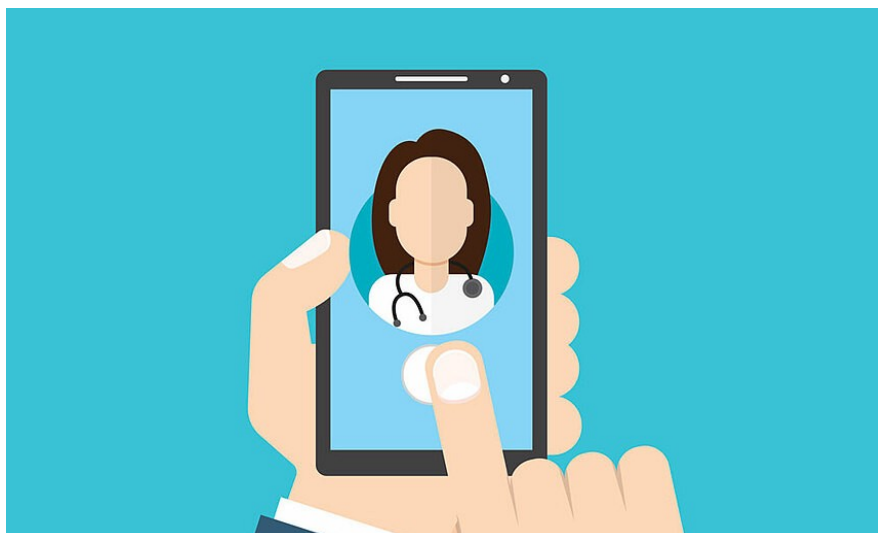
Once those potential treatments enter the clinic, we will need to answer whether they work. I've challenged our FD data scientists at the Center to go beyond the "classic thinking" when it comes to clinical trial design. I believe every patient with FD deserves the chance to try a potential new therapy, regardless of their age or where they live. For us to get therapies approved, there is no way around the issue of placebo. So, I've pushed our scientists to think outside the box when it comes to placebo. I have been creative in designing a trial so that as few people as possible will get placebo, those that do will be on it for the least amount of time possible, and eventually everyone will get the active drug, and then stay on it if they think it helps.

Finally, I couldn't do my work if it weren't for the fantastic team of neurologists, nurse practitioners, clinical trial managers, project assistants, administrators, and other specialists in the hospital. I continue to be grateful for the FD Foundation's unwavering support of the Center. Our team of nurse practitioners and doctors are available day and night for the FD families. This has never been more important than at the time of the COVID outbreak. Our team faced hurricane Sandy, now they are facing coronavirus. Their dedication and drive inspire me.

I'm also grateful to our solid clinical trial staff who work behind the scenes in making sure the research continues no matter what. Finally, the reason we come to work every day is our patients. They never give up, and neither shall we.

Horacio Kaufmann, MD, FAAN,  
Director of the Dysautonomia Center

## UPDATE



### FD in the time of COVID

**A**s the medical world battles the unfolding COVID pandemic, our FD clinicians have risen to the challenge of the global clinical crisis by keeping clinical care going at this uncertain time. With New York City becoming the epi-center of the outbreak, it was no longer safe for patients to come to the office. Annual check-up visits were put on hold and the team quickly ramped up their abilities to connect with patients over the phone.

**Telemedicine visits** quickly became the new normal. Through video-calls, the team remained connected with some of the most vulnerable patients to continue to manage their medical needs. While most patients have safely sheltered in place, a few were inevitably exposed to the virus. Similar to the general population, there appears to be a vast range of how people with FD present with COVID; some have few symptoms, other can manage at home with oxygen, and some need the ICU. It's still unfolding, we are still learning, but for now everyone with FD is trying to stay out of harms-way.

With schools shut and dayhab programs closed, many patients were starting to feel their world become smaller. To create a sense of community, mental health expert Lily Armstrong, who is supported by a grant from the FD Montreal chapter of Dysautonomia, created a **virtual "happy hour" for our patients**. Patients with FD can join the video call and share their challenges. Having the mental health program is a huge asset for the FD Community.

Projects like the natural history database migration from our outdated server into a faster, more secure server might not seem that vital, but in the time of COVID, this created a life-line for clinicians and researchers to continue their FD work. Before the global pandemic hit, the natural history scientists had spent months overhauling the database, **making remote secure access a possibility**. Sometimes it is hard to see what the most important project is. It was remarkable foresight to modernize. This means that our team can still answer questions about a possible pacemaker surgery being considered in Israel or delve deep into the historical archives to summarize cases for a new publication on brain function.

The show must go on. For the first time, **FD Day will turn virtual** and instead of coming to New York City, families with FD will join an online meeting from the safety of their own home. As the landscape surrounding COVID evolves, the team continue to put out **advice for patients with FD** on our blog ([www.dysautonomiacenter.com](http://www.dysautonomiacenter.com)) on how to reduce their risk of infection, monitor their health at home, and how to slowly restart life while protecting FD patients in the household. There is no doubt we are responsible for a group of potentially very vulnerable people. Several staff at the Center have themselves recovered from COVID. They bring first-hand experience to the job.

## NEWS



### Dr. Kaufmann given the Irwin Schatz Award in Autonomic Neurology

**O**ur Director of the Dysautonomia Center, Dr. Horacio Kaufmann was recognized with the 2020 Irwin Schatz award from the American Academy of Neurology (AAN). The award honors clinical neurologists in the field of autonomic medicine.

The AAN award is named after Dr. Irwin Schatz, who in 1964 stood up to the US Public Health Service for deliberately withholding life-saving penicillin treatment to poor, uneducated black men for 40 years to study untreated syphilis. The now infamous Tuskegee study is mandatory learning for anyone wanting to embark on an experiment with humans, and a firm reminder of the oath to *first do no harm*. Dr. Schatz, went on to have a successful career in autonomic medicine. Following his death in 2015, the **AAN created an award to recognize pioneering clinical scientists** that have made a difference to patients living with autonomic disorders.

Throughout his 35-year career, Dr. Kaufmann has helped hundreds of patients with dysautonomia, as well as taking on some of the most difficult to treat disorders, like FD. He has been instrumental in bringing new therapies to the clinic, getting drugs like midodrine and carbidopa approved for patients in the U.S. Today, Dr. Kaufmann leads our team of physicians, fellows, nurses, and scientists focused on finding treatments for familial dysautonomia.

Dr. Kaufmann said “It’s an honor to be recognized by the AAN. I knew Irv Schatz really well. He was the kind of physician I admired because he was never afraid to criticize things that were wrong in medicine. I am grateful to have been able to call him a colleague and a dear friend”. Dr. Kaufmann was selected by the AAN’s Committee. Please join us on congratulating him on this well-deserved award.

## NEW FACES

Being at the front-line when it comes to FD requires a special set of skills. You have to be prepared for the unpredictability and uncertainty of what FD can throw at you. One minute a patient is fine, the next minute they can be facing a lung infection that can turn overwhelming in a short space of time. It requires a talented team of people and to invest in their training to manage this. This year, thanks to the continued support of the Foundation we have found two nurse practitioners to take on the challenges of FD. We have also taken on bright new scientists and project assistants to run our operations.

### Specialist nurses



**Zenith Khan, FNP-BC, MSN, RN, CPN, PHN.** A board-certified Family Nurse Practitioner with her Master's degree in Nursing from UCLA. She has over 8 years of clinical training with expertise in pediatrics, organ transplant, gastroenterology, pulmonology, immunology, and allergy. Zenith loves working at the FD center because of its mission to integrate the latest medical advances with the oldest principles of medicine rooted in compassion, healing, and touch. She will be starting her doctoral program at NYU School of Nursing with a clinical focus on chronic autonomic diseases.



**Kaia Dalamo, DNP, FNP-BC.** A board-certified Family Nurse Practitioner with her Doctor of Nurse Practice degree from the University of Arizona. Nurse Practitioner Dr. Dalamo has over 11-years of clinical training with expertise in inpatient and outpatient practice. She has been a charge nurse overseeing 50 inpatient beds and was an adjunct faculty professor at Northern Arizona University where she taught nursing students. She joined the Center in September 2019 and she has really enjoyed learning all about FD and about developments in care, and is honored to know and provide that care to people who inspire her every day.

### Doctors in training



**Patricio Millar, MD.** A fully trained neurologist from the leading neurological institute FLENI in Argentina, Dr. Millar joined the Center in July 2019 as a post-doctoral researcher. Within the FD program he is responsible for measuring the blood pressure during a clinical visit while learning about rare disease research. He has experience in statistical analysis and is now learning about the management of blood pressure issues. He hopes to join the clinical fellowship training.

### Research Assistants



**Barr Morgenstein Hillyer, MS.** Originally from Israel, Barr works as our biomedical research coordinator. She processes and analyzes data gathered in the center for statistical modelling. Focusing on the assessment of optical coherence tomography (OCT) measurements, she looks to find correlations between neurodegenerative disease progression and the thickness of the retinal layers. Barr completed her Master's degree in Electrical Engineering from NYU this May.



**Siobhan Bhirangi.** Siobhan has been working as a project assistant at the Center since June 2019. She really enjoys the job and has gained insight into the complexity of FD and the research efforts to improve patient care. She helps organize patient visits and assists with the collection of data. Siobhan received her bachelor's degree in psychology at NYU and is currently a Master's student at NYU's School of Global Public Health. During her graduate program, she will be doing research on substance use disorders among people with co-occurring mental health conditions.



## UPDATE



*Learn how our collaborative effort is forging a path forward for familial dysautonomia.*

### A clinical development plan for FD

Children born with FD have symptoms from birth. Their sensory neurons fail to develop due to a lack of a protein called ELP1 (or IKAP). By the time they leave the nursery, it's usually apparent that they have swallowing problems and then lung issues. By the time most of the children reach their teens, the neurodegenerative aspects of the disease strike and they struggle with walking and seeing. It's a hard disease to treat, as there is no cure, but that doesn't stop us from trying, explained our Director Dr. Horacio Kaufmann, who cares for the largest number of FD patients worldwide.

#### Partners in progress

In a neighboring state, Harvard geneticist and endowed professor **Dr. Sue Slaugenhaupt** leads a team of scientists at her lab where they have been studying the genetic underpinnings of FD for over 2 decades. Dr. Slaugenhaupt's early work showed that although the ELP-1/IKAP gene was mutated, patients were still capable of producing some normal (wild-type) protein. In other words, the gene was misread, but not completely defective, this opening the possibility of being able to fix the message and restore the protein. Fast forwards today, and we have great candidate molecules that cause a potent increase in protein levels and we are also working on other strategies. What we need now is to do our due diligence to check these molecules are safe for humans and then effective for FD.

#### Community action

For new drugs to be given to humans, they require the oversight of the U.S. Food and Drug Administration (FDA). But first, we need the FDA to see what our unmet needs are. The Familial Dysautonomia Foundation is taking on this challenge, by hosting a **Patient Focused Drug Development Meeting** for FDA officials (to be held in Washington D.C. on October 19th, 2020). We have kids that can still walk and see, but one day they might not, we are in a rush. The goal would be to get candidate drugs to as many patients as possible. We are in it to help all patients, not just those that we can most easily measure an endpoint in when they come to the office. Every person with FD deserves a chance to see if these therapies work for them. The afternoon for the FDA officials will be a real opportunity for the FD community to speak up.

## Being clinical trial ready

When it comes to testing the success of new drugs, we need good endpoints, which are features of the disease that matter most to patients and worsen predictably overtime. When you give a new potential disease-modifying therapy, the hope is that you stop or at least halt the progression. Learn about how **retinal scans** are helping us test new therapies (page 11).

There are only 700 cases of FD known worldwide. But that doesn't stop us from being well organized. We have a **natural history study with 2 additional sites in Israel** so that we can follow patients with FD and learn what we can improve. It's always been a strength to our program. Our team has been able to put together a clinical development plan that tells us how many patients we need to enroll to show a measurable difference. The clinical development plan will need patients from all over the world to participate. This means more patients will have the opportunity to try potential treatments. Working closely with the Familial Dysautonomia Foundation's scientific advisory board is a key part of our strategy (page 8). Recently, the Foundation reshuffled the members bringing in top FD basic-scientist Dr. Frances Lefcort and drug development expert Dr. Adrian Gilbert as co-chairs.

We have a successful track record in guiding patients through **clinical trials** (page 13). We have always tested new treatments introduced to the clinic with the highest scientific rigor. Within the treatment Center, we carefully think through each new intervention medication and consider the evidence for that choice in each patient. We want to know when drugs are effective and when they are not. If they are not effective, it means we need to refocus our efforts and try something new. At the Center we question, we discuss, and we decide based on the available facts. Then, we monitor and continue to learn.

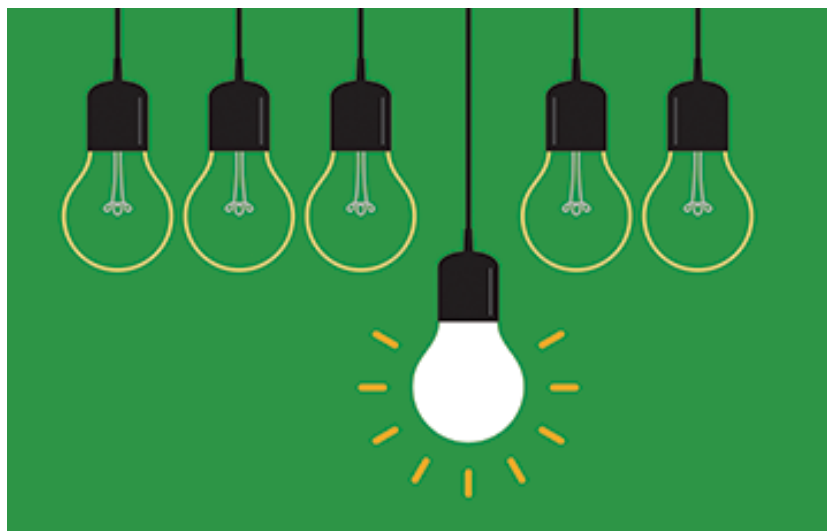
## Supporting research

We know we have a responsibility to our patients to help them be a part of a research program that works for them. We give patients the opportunity to share their samples with leading research teams throughout the world, so they can advance the science of FD. We have a busy collaboration to study the microbiome with **Dr. Frances Lefcort at Montana State University** (page 8). We recently arranged for the shipment of over 60 blood samples to Israeli investigator Dr. Miguel Weil, so his basic science research could go forward. We support the careers of residents and fellows who spent their elective research time at the Center, working on projects. The Center is considered the backbone of academic research when it comes to FD. Our collaborating scientific family continues to grow, thanks to the patients and their families that trust us with their care.

## Going global

Having all of these initiatives in place, both in the clinic and the research fronts, has made the Center think about ways in which all patients can get involved regardless of where they live. With this in mind, we recently implemented a "remote" consent option, for those patients who are unable to come to the clinic but would still like to participate in the Natural History study. We are also making it easier for all the patients and caregivers to complete the questionnaire for their yearly clinical visits: patients will now receive the questionnaires electronically and, thanks to its app-like design, with auto-fillable boxes and user friendly screens, the questionnaire will easily adapt to whichever mobile device they use. Last, in times of COVID-19, opportunity strikes: we have adapted our clinic annual visit to a remote format. This allows the Center to maximize the care we provide to our FD patients, to continue collecting very valuable information to find a cure for FD, and to give access to our clinic and research projects to those patients who, due to distance or illness, do not have the capability to come in person to their annual visits.

## VISITORS



### The Foundation's new Scientific Advisory Board forms at NYU

**T**he FD Scientific Advisory Board are tasked with evaluating the science of FD and crafting a path to advance treatments. The full board had not met in over 3-years, and the forum to talk about new findings was silent. When it comes to discovering new medicines, progress doesn't happen in a vacuum. the sequence of events is more than one person observing cell behaviors under a microscope, and rushing to the patient with a new treatment in hand. It takes giant steps to translate that idea to the clinic. Often, this involves extracting funding from federal grants and staffing laboratories with bright scientists. Then, ideas start to unravel and new treatments emerge. In order to go from the bench to the bedside, basic science and clinical research have to come together.

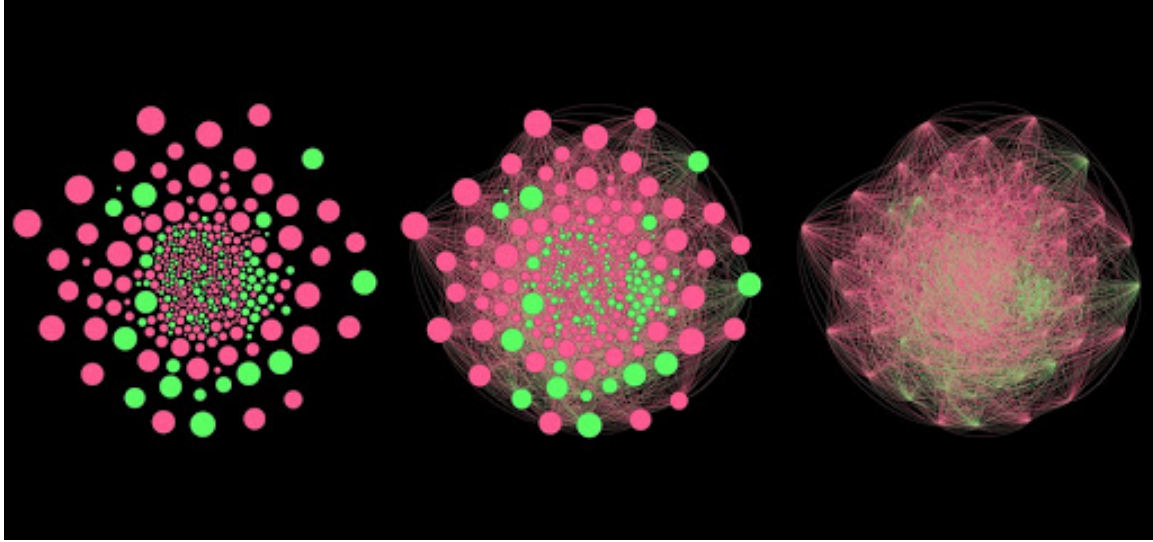
At the Center, one hears stories every day from people facing FD. Our patients know what they want to fix, but their specific problem needs to be in the hands of the basic scientists. Only they can take potential promising strategies forward by experiments in cells or genetically engineered mice. When basic science and clinical medicine don't interact, the science can move in opposite directions, rather than in unison. We know what features of FD progress over time and which specific cells we need to save and support. If you want to save vision, you need a way to target the cells of the retina, you don't need a drug that is going to stay concentrated in the GI tract and not reach the eye. The key to making this happen is communication.

Recognizing the need to talk, the Foundation brought in scientists from key laboratories in the U.S. together with FD parents to NYU. The labs were each given 30 minutes to talk about their work. As different approaches were debated and ideas bounced back and forth, action items started emerging. The voices of the scientists brought new concepts to the FD program and scientific rigor. At any given time, 2 people with FD are usually hospitalized with serious medical problems. It seemed fitting that the meeting was held at NYU's Medical Center, where the patients with FD are often admitted. It brought home the urgent need to move the science along to change the lives of patients with FD.

To align the research, a close network of advisory board members is a key strategy. Following the meeting, the Foundation began re-shuffling its scientific advisory board, bringing in top basic scientist **Dr. Frances Lefcort** and drug development expert **Dr. Adrian Gilbert**, who both have personal connections to FD. Since then, the scientific progress has shifted up a notch. With the renewed energy, the scientists are talking again on a regular basis with video calls and face-to-face meetings. The scientific advisory board has again become a resource for scientists looking for input into their work on FD and collaboration.



## RESEARCH PROJECT



### The gut, the nerves, and the microbiome

**T**he human body has around 100 trillion microorganisms. The microbes living within our gut usually live in harmony and help with a variety of important biological functions. Research shows our genes influence our microbes. Our microbes support our neurons, and when imbalanced we might develop certain diseases.

Our microbes used to be thought of as opportunistic invading pathogens, now we are starting to see them in a new light. Animal models engineered to have the brain disease autism have microbes missing from their gut. The mice also behave better when their missing microbes are put back. To test the idea that probiotic bacteria could potentially improve brain function, in 2018 the *National Institutes of Health* awarded **Dr. Frances Lefcort \$2.9 million dollar grant award** to study the microbiome in FD.

We also know that the gastrointestinal tract doesn't function the way it should in FD. Patients suffer from an array of problems like constipation, diarrhea, reflux and bloating. If the 100 million neurons living in the gut could be influenced by the microbiome, this raises the prospect of making sure the microbiome is optimized to the nerve cells survive and function.

While the sophisticated analytics to profile the microbiome requires cutting edge technologies, getting patients to participate fell into the hands of one scientist at the Center. For the last year, **Dr. Maria Cotrina** has been sending patients stool collection kits and asking their relatives to be controls. At the clinic, patients and relatives give a blood sample to examine their metabolomics. For many patients, the highlight of their visit is seeing their family members also participating in the research.

Dr. Cotrina, who has an interest in metabolic diseases, was the perfect person to run the project. She sits in on all the yearly check-up visits, notes down any gastrointestinal issues the patients speak about, and goes over with each family what they eat and when. Her attention to detail means that when it comes to interpreting the microbiome data, it will be possible to connect the findings back to that specific patient at that moment in time. We know that the microbiome is influenced by your environment, your genes, your diet, when you last took antibiotics, which is why she collects this crucial information.

For many years, the diets of FD patients have been something that staff at the Center have been grappling with. There are patients that tell us they avoid certain foods hoping they'll feel better, but this is not always without risk.

A few years ago, specialists in FD around the world began seeing patients with extreme malnutrition caused by eating only very restricted diets. The idea came from avoiding foods with high tyramine, which you can do by skipping things like fermented cheese or Chianti wine. Unfortunately, instead, patients were led into restricting tyrosine, which is a vital amino-acid. The first oath of medicine is to do no harm. Before telling people with FD what they should or should not eat, we first need to understand what patients do eat, if this changes the balance of gut flora, and whether this has a downstream effect on the millions of tiny enteric neurons that are responsible for the functioning of the gut and beyond that.

For Dr. Cotrina and staff at the Center, the NIH-funded microbiome project has become a chance to dive deeper into understanding the gut in FD. Finding the right diet can be a long process involving nutritionists, gastroenterologists, and a lot of trial and error. Finding potential ways to restore the function of the nerves by tweaking the microbiome is an exciting avenue to explore.

**Funding:**

National Institutes of Health (R 01)  
PTC Therapeutics



*Dr. Maria Cotrina, research scientist.*

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## RESEARCH PROJECT

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### The retina and a collaborative vision forward

**T**he loss of vision is one of the hardest things to witness in the clinic. Children with FD can see, but as they enter their teens, their vision starts to deteriorate, and by early adulthood many patients are legally blind.

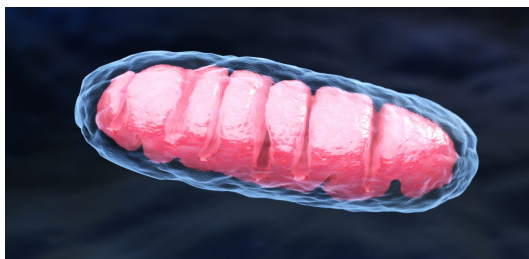
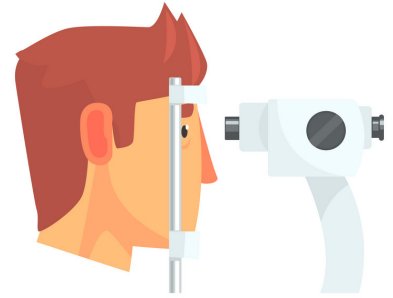
The eye is a very complicated organ. We used to blame the blindness on scarring of the corneas, but over the years, we have discovered that patients with FD are actually losing the cells at the back part of the eye, an area known as the retina. The retina is a bundle of light sensing neurons that eventually come together to form the optic nerve and travel towards the brain's visual cortex. The brain puts together this incoming information to interpret contrasts, colors, depths, textures and create our visual world. As the neuropathy advances and the retina starts to become damaged, visual perception becomes impacted. For patients with FD this starts with, perhaps, having more difficulty at night when the light is low, progressing to the point where they need large print, or in some cases can no longer see beyond a few meters and can only read by pressing their eye up to the page.

For years, scientist at the Center have been scanning the retina of patients with FD. Within minutes of entering the clinic, patients have the back of their eye imaged down to almost the cellular level. Hundreds of patients have been scanned year after year. To really understand what is happening in the eye, the Center has partnered with top neuro-ophthalmologist **Dr. Gadi Wollstein**, who recently joined NYU and works on eye diseases. Dr. Wollstein and his team began mining the data to look for patterns. After several meetings, the eye started to look like a real target for testing new therapies. When it comes to FD, there are certain static neurological characteristics of the disease that are developmental, meaning the nerves fail to survive development and the problem is there from birth. Then there are other characteristics that are neurodegenerative, meaning the cells start off functioning but progressively die overtime. This was the story that began to emerge for the eye.

With statistical analysis there was a very clear pattern. The youngest patients with FD to undergo retinal imaging were 5 years old. Already their retinas were thinner, but the cells were there, which meant that they had survived development.

But as the patients came back each year, their retinas began to thin. By their early 20s, most patients had reached a point where they had already lost a substantial amount of retina neurons and plateaued.

The rapid rate of decline by early adulthood resembles patient stories about the impact of the loss of vision. For the team it presented an important endpoint to consider for the clinical development plan. The retina has what is known as a “window of opportunity,” a time to intervene to save the existing cells from dying, and slow neurodegeneration. When it comes to finding disease-modifying strategies, what are needed are endpoints like this that can reliably and quickly track whether a treatment is working. Now we know the natural history of the progression, we can start to direct ways to try and slow the trajectory of the nerve cell loss. It is possible we will need another approach to replace the nerves in adults. This is why we are lucky to have a diverse scientific advisory board with different ideas for different stages of the disease. We have to be open to different ideas and potentially combining treatments.



Right now, the retina has become an active area of research in FD. The work led by **Dr. Frances Lefcort** linking the defective elongator protein to developmental and neurodegenerative functions was published in *Nature*. It showed the retinal cells survive, but their mitochondrial machinery is disrupted, and the cells begin to degenerate. Together with **Dr. Elisabetta Morini** in the laboratory of Sue Slaugenhaupt they were awarded a highly competitive grant to create models of FD to test potential treatments. The grant award to Dr. Lefcort and Dr. Morini is a

real stepping stone along the path to developing new therapies for FD. It brings together two excellent laboratories and scientists with a track record of successful discoveries in a highly collaborative project, which will, no doubt, move the science forward.

The eye data becomes part of the natural history study, which makes it quite powerful as a clinical end point. To change the sight of a person with FD would be an important breakthrough in medicine. For patients, sight loss limits their lives a lot or becomes another hurdle that can make their world smaller. What emerges from this collaborative effort is a path forward, with the basic science and clinical medicine moving together. That is an important step. We have a target of nerves to save at the back of the eye.

**Funding:**

Familial Dysautonomia Foundation  
National Institutes of Health (R 01)  
The Michael J Fox Foundation



## RESEARCH PROJECT



### Carbidopa therapy for FD

When it comes to managing the blood pressure for patients with FD there is no text book. Unlike regular hypertension, the blood pressure swings widely. These highs and lows are why the disease is called *dysautonomia*. The autonomic nerves are supposed to keep the blood pressure in range and prevent damage to the organs. The heart and the kidney bare all the hallmarks of hypertensive damage, but treating the blood pressure comes at a cost. Drugs like clonidine cause hypotension and valium can cause respiratory arrest. Many patients have spent years successfully weaning off daily use taking them only as rescue medication. It is not that they do not work, it is that the price we pay is too high.

Facing few alternatives, the team was awarded a grant from the FDA's Office of Orphan Product Development. They successfully guided 21 patients through a controlled clinical trial. It was the second grant from the FDA to test carbidopa; they were convinced we were **onto an idea worth testing**. The trial involved wearing blood pressure monitors and measuring urine levels of sympathetic nerve transmitters, which were thought to be responsible for the hypertensive surges. Patients took carbidopa at two doses (100 mg and 200 mg) and placebo. The end point was to see if we could reduce the variability by dampening the peaks. Carbidopa works in the nerves outside the brain, blocking an enzyme catalyzing a decarboxylation reaction. It essentially quietens the function of the sympathetic nerves, so when they are activated, patients don't feel that flight or fight response so much.

The trial showed that with carbidopa the blood pressure doesn't surge so high every day with activities like waking up, eating, or getting anxious. The previous trial had shown it was **helpful for the nausea and retching crises**. For some patients, carbidopa can provide a bridge to being able to lower their dependence on sedatives. When they enter situations that would make them red, sweating, and hypertensive, carbidopa helps block that effect. It doesn't escalate in the way it used to and slowly patients start to see their crises diminish or even stop. Blocking the hypertensive peaks appears to be a good important strategy for the **long-term health of the heart and the kidney**. The side effects of carbidopa are minimal and, most importantly, its safety is well established.

#### Funding:

Food and Drug Administration, Office of Orphan Product Development (R01)

## \_\_\_\_\_ OPPORTUNITIES \_\_\_\_\_

### Current research studies open for patients with familial dysautonomia

#### OPEN and ENROLLING

##### THE NATURAL HISTORY OF FAMILIAL DYSAUTONOMIA

IRB#: S16-01774

ELIGIBILITY: Patients with FD of any age

PURPOSE: To use the clinical information collected during routine medical visits to define the clinical features of FD and how they evolve overtime. The goal of the project is to find biological signals that we can use to track the features of FD to use in clinical trials to test new drug treatments. The study will also measure IKAP protein levels to see how well they correlate with symptoms of FD.

SPONSOR: Familial Dysautonomia Foundation, Inc. and PTC Therapeutics, Inc.

#### ENROLLING

##### A STUDY OF GUT FLORA IN FAMILIAL DYSAUTONOMIA (MIBIOM)

IRB#: s16-00718

ELIGIBILITY: Patients with FD age 4 and older and their family members

PURPOSE: Maintaining a healthy weight is a problem for a number of patients with FD. The aim of this study is to better understand the microorganisms that live in the gut of patients with FD and whether these play an important role in digestive function. In this project, we want to understand if differences in the microorganisms in the gut of patients with FD affect the energy derived from food. We will compare diets between tube and oral fed subjects to better understand the differences and also we will compare it with healthy controls. Better understanding of the microbiome in FD might help also to understand whether fungal overgrowth in the GI tract of FD patients is associated with persistent diarrhea in the absence of known pathogens.

SPONSOR: Familial Dysautonomia Foundation, Inc.

#### OPEN

##### UNDERSTANDING THE MUSCLE IN FAMILIAL DYSAUTONOMIA

IRB#: S14-01192

ELIGIBILITY: People with familial dysautonomia of any age.

Purpose: Patients with FD frequently develop muscle atrophy. Moreover, the incidence of rhabdomyolysis (episodes of muscle destruction) is increased in people with FD. To investigate this, we aim to examine muscle function in patients with FD and other hereditary sensory neuropathies by studying muscle samples. Small pieces of muscle are obtained during programmed surgery (scoliosis, hip replacement, etc) and studied.

SPONSOR: Familial Dysautonomia Foundation, Inc.

#### ENROLLING

##### BRAINSTEM REFLEXES IN FAMILIAL DYSAUTONOMIA

IRB#: S07-938

ELIGIBILITY: People with familial dysautonomia of any age.

PURPOSE: To understand if dysphagia and dysarthria in FD are due to a reduction in number and/or excitability of afferent trigeminal nerve fibers. In order to achieve this, we are studying brainstem reflexes in familial dysautonomia using electrophysiological techniques.

SPONSOR: Familial Dysautonomia Foundation, Inc.



## NATURAL HISTORY INFO

**W**e need you. The closer we can follow you, the sooner we can understand your issues and the closer it brings us to finding a treatment. Our Natural History Study is currently open and recruiting patients with FD.

There are several ways to be involved:

- Patients with FD being evaluated at the NYU Dysautonomia Center in New York, at the Hadassah Hebrew University Medical Center or at the Sheba Medical Center in Israel will have the option to be enrolled in the Natural History Study. All three centers share the same database regardless of the different locations.
- If, for whatever reason, you are unable to visit New York or Israel, you can still send medical records from your local doctors. In addition to receiving medical recommendations by the FD doctors, your information will be included in the database.

What type of clinical information should you send?

- Your most recent sleep study report
- Your most recent swallow study report
- Your most recent office visit notes from your neurologist or other specialist
- Your most recent chest-CT or Chest x-ray report. Ideally you should also send a CD/DVD with the images.
- Your most recent eye evaluation, ideally including retinal optical coherence tomography (OCT) and other visual function tests
- Your most recent pulmonary function tests
- 24-hour blood pressure recordings
- Results from regular blood or urine tests
- Notes from hospital admissions or surgical admissions
- A current medication list

These tests are routinely recommended for patients with FD as part of their standard medical care. They help screen for potential problems and determine when treatments are necessary. If you are still unsure of what to send, send us your information from any visit to a doctor.

**The FD Questionnaire:** The FD Questionnaire has been developed over several years to provide doctors with the information they need in clinical practice. It is a series of questions that cover all the body systems, how they function, and identify common complications at different stages of the disease. The questionnaire is specifically designed for patients with FD, to be filled on a yearly basis. Filling it out will help families prepare for their visits with doctors. The FD Center will send you a copy of the questionnaire as soon as you schedule your appointment (212-263-7225).

**What will happen with my information?** The information received will be stored in specially designed databases, an idea originally implemented by Dr. Felicia Axelrod. It will be used by the research team to answer pressing clinical research questions. It allows us to look at trends overtime and examine which treatments are truly effective for treating FD. It allows us to look for patterns to provide guidelines that will shape clinical practice. The study is designed to support clinical trial readiness to speed up drug development to improve the lives of patients with FD. The goal is to help other researchers working and collaborating on FD to use this information to support their scientific work.

**Official sites for the Natural History Study of FD:** In the United States - NYU Dysautonomia Center, 530 First Avenue, Suite 9Q, New York, NY, 10016. In Israel - Sheba Medical Center, Tel Hashomer, Derech Sheba 2, Ramat Gan, Israel and Pediatric Pulmonology and Sleep, Hadassah Hebrew University Medical Center, Jerusalem, Israel.

**How is my information protected?** The information collected in the natural history study is stored in a secure encrypted server supported by NYU Langone Health MCIT. Access to identifying information is restricted to NYU Langone Health administered terminals. Patients should transmit their medical records through data-protected safe channels, including MyChart and NYU Langone Safe-Email Portal. Information and support for this can be provided. Data shared for research is de-identified and entered into a secure online data collection platform (RedCap), with controlled access.

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## DYSAUTONOMIA CENTER

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### Staff

Horacio Kaufmann, MD  
Director

Lucy Norcliffe-Kaufmann, PhD  
Associate Director

Jose Martinez, MS  
Clinical Trials Manager

Bhumika Balgobin, MD  
Neurology Fellow

Miguel Perez  
Data Manager

Maria Cotrina, PhD  
Research Scientist

Patricio Millar, MD  
Research Fellow

Jose-Alberto Palma, MD, PhD  
Assistant Director

Lee-Ann Lugg, BS  
Administrative Assistant

Isabella Schneider  
Project Assistant

Kaia Dalamo, DNP  
Nurse Practitioner

Zenith Kahn, FNP  
Nurse Practitioner

### Collaborators

Susan Slaughenhaupt, PhD  
Frances Lefcort, PhD  
Howard Trachtman, MD  
Bat-el Bar, MD  
Joseph Levy, MD  
Amal Dakka, PhD  
Monica Salani, PhD  
Leela Raju, MD

Carlos Mendoza, MD  
Vaughan Macefield, PhD  
Mikhail Kazachkov, MD  
Alex Gileles-Hillel, MD, PhD  
Joel Gutierrez, MD  
Elisabetta Morini, PhD  
Yvonne Lui, MD, PhD

### Support for the Program

Familial Dysautonomia Foundation, Inc.  
Food and Drug Administration  
MSA Coalition

National Institutes of Health  
Michael J. Fox Foundation  
PTC Therapeutics

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## 2020 HIGHLIGHTS

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Dr. Horacio Kaufmann chosen for the Irwin Schatz Award from the American Academy of Neurology

Expert review on dysautonomia published in the New England Journal of Medicine

FD Scientific Advisory Board meets at NYU School of Medicine

The Natural History Study opened at sites in the US and in two new sites in Israel

Familial Dysautonomia Foundation commits to continued support of the center and research program

Montreal Chapter of the Dysautonomia Foundation renews grant to support a mental health program at the Center

Dr. Norcliffe-Kaufmann invited as Visiting Professor at Innsbruck Medical Center to talk about FD

Lee-Ann Lugg promoted to Administrative Coordinator

Clinical Trials Manager Jose Martinez celebrates 10-year service award

Dr. Lucy Norcliffe-Kaufmann highlighted by the British Heart Foundation as a notable alumni

Nurse Practitioner Dr. Kaia Dalamo receives her Doctorate of Nursing degree

Theravance BioPharma provides grant to support research for new scientist and neurologist Dr. Patricio Millar

Telemedicine service started for FD patients during the COVID pandemic

NP Zenith Kahn accepted into NYU's Doctorate of Nursing Program

Dr. Patricio Millar accepted into NYU's TRAIL leadership training Program

Data Manager Miguel Perez received MSA research award from the American Autonomic Society

Dr. Millar and Dr. Balgobin chosen to give platform presentations at the American Academy of Neurology

Dr. Alberto Palma completes the NYC marathon

Dr. Lucy Norcliffe-Kaufmann and Dr. Kaia Dalamo run the NYC Half Marathon for the FD Foundation

Dr. Palma awarded a million dollar grant from Biogen to study the natural history of degenerative brain disease MSA

Carbidopa trial completed with positive end results and accepted in top journal Hypertension

FD Patient Art show proceeds go to support vital computer upgrade

Fellowship award pledged to support visiting professorship

FD patient samples shared with Israel to boost scientific work

Project assistant Vivian Cao accepted into Ivy league graduate program at Columbia University

Project assistant Joy Wang accepted into Medical School

## WAYS TO HELP

**Stay up to date:** New studies for patients with FD open throughout the year. There are several places where you can learn about new research opportunities: sign up for our blog at [DysautonomiaCenter.com](http://DysautonomiaCenter.com); follow the Dysautonomia Center on Facebook; read the Foundation's Dyscourse magazine; and ask the clinicians at your annual evaluation visit.

**Give samples:** By giving a small sample of blood, we can measure gene production and protein levels. We hope to develop measure to test the outcome of different treatments to preserve neurological function in patients with FD. You can also donate muscle samples when undergoing routine surgeries.

**Send your doctors reports:** Have you visited your eye, kidney, or lung doctor recently? By sending us your clinical results or reports, we can add the information to our natural history study and help better understand how to treat patients with FD.

**Support the Familial Dysautonomia Foundation:** No single organization has done more to change the face of treatment of FD. The Foundation's unwavering support over the last 50-years has helped to centralize the care of patients with FD and to bring new treatments to the clinic. The Foundation and its chapters around the world have regular fund-raising events to support the cause. They make it possible for us to make important equipment upgrades, have a mental health program, maintain a dedicated team, and provide 24h emergency care to families at times of need.

**Call us:** Keep in touch. Periodically calling to find out about new research opportunities is an important way to find out what is new at the Center. Our staff can tell you about new studies and discuss whether our clinical trials may be right for you. Dr. Maria Cotrina is available to answer questions about studies you may be interested in joining and how to enrol.

**Tell your friends.** Talk to your friends about studies that you participate in. This will hopefully encourage them to be consider participating. Research in rare diseases like FD relies on having a committed community. Each time you give up your time for research the knowledge gained helps pave the way for other potential treatments.

## STAY CONNECTED



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<https://familialdysautonomia.org/news/newsletter>



<https://nyulangone.org/locations/dysautonomia-center>

NYU Dysautonomia Center  
530 First Avenue, Suite 9Q  
New York, NY, 10016  
[www.dysautonomiacenter.com](http://www.dysautonomiacenter.com)