



# SPIRIT OF HOPE

## Revolutionary FD Mice *The Next Step Towards A Cure*

One morning in May 2010 in the Tel Aviv University lab of Dr. Gil Ast, a very special litter of mouse pups was born. The parent mice had both been genetically altered to carry the FD mutation and the birth of this litter was much anticipated. Two of the pups were carriers like their parents, and one pup, like the children with FD, was born with two copies of the mutation. It was the first mouse, the first ever non-human animal, to have FD.

The implications of this are profound. Researchers now have a mouse model with which they can test potential treatments without putting children at risk.

Creating mice models is relatively easy for most disorders, but because FD is a genetic disorder whose effects are caused by alternative gene splicing, this task was difficult. While smaller than its littermates, the FD mouse pup was nurtured by its mother and has grown and developed. The FD mouse pup is historic; the first transgenic mouse



Dr. Gil Ast

to recapitulate a human alternative splicing disease. From this initial litter, Ast was able to create the requisite colony of over 600 FD mice needed for adequate research.

Ast and his dedicated graduate students at TAU first generated embryonic mouse cells that contained the human gene with and without the mutation causing FD. These cells were inserted into mice that were mated to produce heterozygous mice (carriers of the FD mutation), and finally homozygous mice (FD affected mice).

The FD mice will be used to study how FD causes its effects in children and adults with FD, and to test drugs and supplements that Ast and his collaborators have already identified as possible

treatments, as well as other therapeutic approaches for the treatment of FD. Because children with FD are medically fragile, testing therapies first in mice is vitally important.

The maintenance of the FD mouse colony is an essential part of any treatment-testing program. The lab has been able to establish 100 cages (each with 6-7 mice) and soon will begin screening of treatments for FD. While this news is a much-anticipated and essential

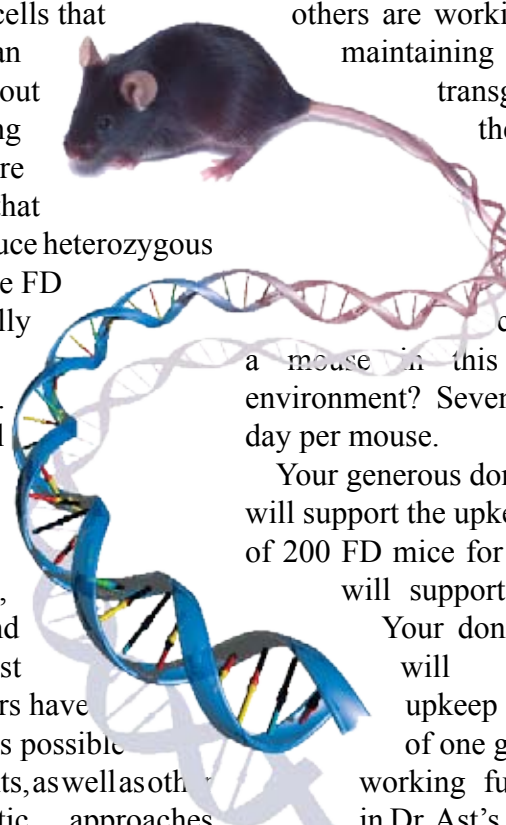
requisite for the development of the cure towards which Ast and others are working, the cost of maintaining a colony of transgenic mice in the appropriate pathogen-free environment is substantial. What is the cost of maintaining a mouse in this pathogen-free environment? Seventeen cents per day per mouse.

Your generous donation of \$1000 will support the upkeep and feeding of 200 FD mice for a month; \$360 will support 72 FD mice.

Your donation of \$2000 will support the upkeep and feeding of one graduate student working full-time on FD in Dr. Ast's lab for a month.

Please make your donation online at [www.fdtype.org](http://www.fdtype.org) or use the enclosed envelope to send in your check today. We applaud Dr. Ast and his colleagues for this accomplishment that benefits not only the FD community, but the many others who suffer from diseases involving alternative gene splicing.

*To learn more about the FD mouse & the science behind it, visit the research page at [www.fdtype.org](http://www.fdtype.org)*



## In Tribute...

*It is with great sadness and mourning that we mark the passing of the many children and adults with FD who died in 2010. Among these were the children of two former FD Hope Board members, Zak Rosen and David Orton.*

### David Orton

David Zachary Orton, age 22, died in his sleep at home on March 1, 2010. Born on March 12, 1987 in Madison, the son of Barry and Marilyn Orton, David was a graduate of West High School and worked in data support for The Road Home Dane County, a non-profit specializing in providing temporary and permanent shelter for homeless families. David enjoyed collecting videos and playing video games, and was a wizard with a mouse and keyboard.

Familial Dysautonomia compromised his body, but never his spirit or his will. David charmed most all who met him with his incredible sense of humor, complete lack of guile, and his sweet disposition. He taught us more about life than we taught him. He never complained about his health; he was known for saying "I have a wonderful life." The pain of his loss is indescribable, but he will live forever in our hearts.



David Zachary Orton  
1987 — 2010

### Zak Rosen

On August 11th, just 4 days before his 18th birthday, Zak Rosen succumbed to FD. Despite a life defined by his illness, Zak was always smiling. He loved to shake hands and had a passion for playing games. At his funeral, his uncle Chuck said, "If there's one word that describes Zak, it'd be love. Zak exuded love, whether it was a hug or a prank, or just sidling up to you as you sat." This was evident in Zak's last wish, to donate his organs to FD research, so that someday in the future no child would have to suffer as he did. You may remember Zak as the talented poet whose words graced the FD Hope bookmark. Ever eloquent, spiritual, and wise, Zak wrote the following poem, which his parents did not discover until after his death. In a thank you to the FD community for its support, his parents wrote, "Zak left us with one last poem, something he wrote earlier this year. We never spoke with him about how serious FD is (we were always hopeful) but he apparently figured it out himself."

*I woke up one day  
Searching, where I am  
Astonished to find my body  
My cold blue lifeless body*

#### *Ghost*

*Shocked to see my self  
I quickly left  
Happy to find that I can move, quicker than lightning  
I travel the globe in nanoseconds*

*I could see everyone  
I could see the baker making delicious bread  
The police officer handcuffing a filthy criminal  
A baseball player hitting homeruns*

*But most important  
I can go to the glorious heaven  
I could see my past relatives  
I also could see the great Jewish G-d*



Zak Rosen  
1992 — 2010

# Preventing Autonomic Crises

## The Role of Probiotics

Without a doubt, the most difficult symptoms of FD are the episodes of autonomic crisis, during which kids with FD vomit or retch for days, and experience high blood pressure and heart rates, abdominal pain, anxiety, and poor sleep. High levels of noradrenaline have long been implicated as a possible cause of crisis. For years, FD Hope has worked to find answers to reduce the incidence and severity of autonomic crisis.

In 2005, FD Hope funded researchers determined that individuals with FD exhibit decreased levels of monoamine oxidase A (MAO-A), an enzyme responsible for the metabolism of noradrenaline. Individuals with low MAO-A levels cannot adequately metabolize noradrenaline and levels remain high. Because noradrenaline is derived from the amino acid tyramine and tyramine comes from food, diets low in tyramine have been recommended as a way to reduce the amount of noradrenaline that needs to be metabolized.

But tyramine does not only come directly from food. It can be produced in the gastrointestinal (GI) tract from another, more common amino acid called tyrosine and a significant amount of tyramine can come from this source. Both normal and pathogenic bacteria and yeast found in the GI tract can convert tyrosine into tyramine if they produce the enzyme tyrosine decarboxylase.

Probiotics are beneficial bacteria that support healthy intestinal and immune function. Hundreds of different microbial species live in the GI tract, some essential for health, others pathogenic. The GI tract is home to over one hundred trillion individual bacteria. For years, many parents of children with FD have understood intuitively that giving their

children probiotics can help their GI tracts. But not all probiotics it seems, are the same. Some of these beneficial bacteria can produce high levels of tyramine.

When FD Hope began to research the bacteria that produce tyramine, we consulted with Stephen Olmstead, MD, of Klaire Labs. The Lab, founded in 1969 with the goal of providing nutritional support for individuals with severe food allergies, develops probiotic blends designed to assist GI, neurological, detoxification, and immune system functions. According to Dr. Olmstead, there are blends of specific probiotic species available that have little tyramine production.

The Bifidobacterium species don't make tyramine, but common probiotics such as Lactobacillus brevis (which make large amounts) and Lactobacillus plantarum both do. Taking probiotics high in Bifidobacteria species and avoiding those with Lactobacillus brevis and plantarum may help minimize tyramine production in the GI tract. Ther-Biotic Infant Formula by Klaire Labs is one example of a probiotic blend that provides this spectrum of healthy bacteria.

Reducing tyramine intake is an important strategy for preventing autonomic crises, but this means more than just reducing the amount of foods that contain tyramine. Taking probiotics that do not express tyrosine decarboxylase and therefore, do not make tyramine, can help shift the gut flora towards a balance that can positively impact the frequency of autonomic crises.

*Some probiotics may help prevent autonomic crises....*





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### Make a Tax-Free Gift from Your IRA:

An IRA owner, age 70½ or over, can directly transfer, tax-free, up to \$100,000 per year to FD Hope. This option, created in 2006 and extended through 2009, is available to eligible IRA owners, regardless of whether they itemize their deductions. Distributions from employer-sponsored retirement plans, including SIMPLE IRAs and simplified employee pension (SEP) plans, are not eligible. Just give instructions to your IRA custodian and alert FD Hope about the gift. And remember, every dollar you give us this fund drive is quadrupled!

Thank you!

#### FD HOPE:

Mission: *To find a cure.*  
Method: *Fund top rate researchers.*

Means: *The generosity of our donors.*

Message: *We are not powerless. The day when there is a cure for FD is on the horizon. We shall hasten its arrival.*

## Focus On The Child



Sam Peltzer, pictured here with his little sister Sarah.

### Meet Samuel Nathan Peltzer

Sam is an active thirteen year old from Chapel Hill, NC. The third of four children, Sam's little sister, Sarah, also has FD. Sam attends public middle school, where he is in the 7th grade and excels in math. He was the manager for his school's baseball team. Sam enjoys sports (especially UNC teams), cooking and eating gourmet food, reading, origami, and watching Modern Family. He loves all kinds of animals, but especially dogs. He campaigns for environmental consciousness, and animal rights. Lately he also campaigns his mother for a dog. Sam isn't sure what he wants to do when he grows up, but he knows it will include some form of caring for others and for the earth.

About FD, Sam says he doesn't let it slow him down, and he hopes that there will be a cure someday soon so that all the people with FD can feel better.

Sam has taken nutritional supplements, including those identified by FD Hope funded researchers, since he was a young child. Despite a rocky start his first three years, Sam has not had significant autonomic crises in ten years. He takes growth-hormone injections and has doubled his growth rate.

As a result of his good health, in August he was able to have his gastrostomy tube removed. His mother attributes Sam's relative good health to nutritional supplements, the avoidance of pharmaceutical drugs such as clonidine and valium, with their side effects and rebound, and first and foremost, a solid nutritional foundation. Sam never received formulas through his G-tube, but instead got blended purees of whole food vegetables, grains and proteins.

Sam's mother, Sonia Rapaport, MD, the current FD Hope president and a founding board member, practices holistic and integrative family medicine in North Carolina.

#### FD Hope Board of Directors

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