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Learn how the NF Center is providing exceptional care through groundbreaking research, highlighted by NF Center director, David H. Gutmann, MD, PhD.

RESEARCH GRANTS
Groundbreaking research requires funding from numerous sources, including the federal government, private foundations, and individual donors. We appreciate the generous support we have received from each of these important sources over the past year.

A YEAR OF GROUNDBREAKING RESEARCH
Get a first-hand look at the discoveries made by NF Center researchers and collaborators, and learn more about early phase findings that bring us closer to offering personalized medicine to individuals with NF1.

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RESEARCH GRANTS
MESSAGE FROM THE DIRECTOR

During our thirteen years as a multi-disciplinary clinic care and research enterprise, the Washington University Neurofibromatosis (NF) Center has many new developments to report. In 2018, we look forward to expanding our research initiatives aimed at developing personalized medical approaches for people affected with NF. We are grateful for the continued partnership with our families that make these high-risk, high-payoff ventures possible.

INTRODUCING NEW MEMBERS

In 2017, Dr. Corina Anastasaki was promoted to the rank of Senior Research Scientist. Dr. Anastasaki has been a leader in the establishment of NF1 patient induced pluripotent stem cell (IPSC) lines from skin and urine samples. These human stem cell lines have been critical resources to study brain cells important to the discovery of new treatments for learning and behavioral problems in NF1. The Washington University NF Center houses one of the largest NF1-patient iPSC repositories in the world, and we have shared the one-of-a-kind resources with many researchers.

The clinical program celebrated the addition of Erika Ramirez, our nurse coordinator, and Jennifer Traber, our Center coordinator, to improve the care we provide for our families. Under Jen’s leadership, we improved our NF1 complementary care programs, including the bimonthly Club NF program for school-age children, the Beat NF jazz music motor therapy program for toddlers, and the Teen NF social skills therapy program for adolescents.

ADVANCING NF RESEARCH

There has been exciting progress in our understanding of neurofibromatosis, with numerous researchers in the Washington University NF Center publishing new discoveries. These include advancing our understanding of why girls with NF1 optic glioma are at greater risk for vision loss, establishing how progressive vision loss in mice with NF1 optic glioma can be stopped, and how immune system molecules affect brain tumor growth. In addition, one of our Pediatric Neurology residents completed the largest study of brainstem tumors in children with NF1, while Dr. Anastasaki identified the first genetic mutation in dermal neurofibromas arising in people without NF1. We also continue to expand our unique collection of resources essential to making these advances, including the NF1 Genome Project used to discover subtle DNA changes that might one day serve to predict the risk of developing specific medical problems in people with NF1.

RAISING NF AWARENESS

In addition, Washington University NF Center neuroscientists participated in the SCIFEST: Brain Matters event, held at the St. Louis Science Center. Visitors to the NF Center booth had the opportunity to learn more about Neurofibromatosis Type 1 (NF1), and NF Center research, through a variety of interactive games and activities. DNA bracelet-making demonstrated how easy it is to isolate DNA, and showed that people can have different NF1 gene mutations. A “spot-the-difference” iPad game had visitors becoming real scientists by spotting the differences between normal and abnormal brain cells. Finally, we welcomed a delegation of freshman Missouri State House Representatives to meet our researchers, clinicians, and families. During this session, they learned more about NF, and how the Washington University NF Center is working to improve the lives of people affected with these conditions.

Warm regards,

David H. Gutmann, MD, PhD
Donald O. Schnuck Family Professor
Director, Washington University NF Center
Vice Chair for Research Affairs, Neurology

RESEARCH GRANTS

NATIONAL INSTITUTES OF HEALTH RESEARCH PROGRAM AWARD

to DAVID H. GUTMANN, MD, PhD. This prestigious eight-year grant allows Dr. Gutmann to devote half of his efforts to study why people with NF1 develop markedly different signs and symptoms. This funding permits him to attack the problem of precision medicine from many angles.

FRANCIS S. COLLINS SCHOLAR AWARD FOR NEUROFIBROMATOSIS CLINICAL AND TRANSLATIONAL RESEARCH

to ANGELA C. HIRBE, MD, PHD. As a result, she will be obtaining additional training in NF clinical practice at the National Cancer Institute and Johns Hopkins University, and will be expanding her role in the care of adults with NF1-associated plexiform neurofibromas and malignant peripheral nerve sheath tumors.

BERLIN INSTITUTE OF HEALTH EINSTEIN FELLOWSHIP AND ALEXANDER VON Humboldt AWARD

to DAVID H. GUTMANN, MD, PHD to establish an international research team at the Max Delbrück Center for Molecular Medicine. In collaboration with Professor Helmut Kettenmann, a leading authority in brain support cells (astrocytes and microglia), Dr. Gutmann will be exploring the role of microglia in autism and brain cell function, as well as to generate human brain microglia from NF1 patient induced pluripotent stem cells.

THE ST. LOUIS MEN’S GROUP AGAINST CANCER

awarded a second grant to ANGELA HIRBE, MD, PHD to continue her research on a deadly cancer seen in young adults with NF1. Dr. Hirbe will be using these funds to develop cancer cell lines from people with NF1-associated malignant peripheral nerve sheath tumors (MPNSTs) as a first step toward identifying and evaluating more effective therapies for these malignancies.

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My introduction to the world of Neurofibromatosis began when I was only three years old. It started with a bug bite on my neck and fevers. This was in 1998, and at that time, not a lot was known about NF. On a visit to our local pediatrician, he could not explain the fevers that I was experiencing at night. Also, on further examination while looking at my back, they noticed that it appeared to be curving to one side. After a CAT scan, he decided to send me to the “big guns” St. Louis Children’s Hospital. After a CAT scan and an MRI, the doctors discovered a tumor in my back. They then performed surgery to try to remove the tumor. At this point, I was diagnosed with Neurofibromatosis—a childhood cancer with a survival rate of 50%. As a result of this diagnosis, I stayed on the oncology floor for five days. At this time in my early life, Batman was my hero, so I had a Batman doll at my side at all times, through the various tests and even surgeries.

After the fifth day, before I was to begin chemotherapy, a young doctor entered my hospital room with tears in his eyes, and told us that I did not have Neurofibromatosis, but rather something called Neurofibromatosis Type 1 (NF1). Soon after this diagnosis and more tests, I was introduced to Dr. David Gutmann, who over the past eighteen years, has always been there for us whenever we had any questions or concerns regarding NF1.

I ended up developing severe scoliosis as a result of the neurofibroma in my back. It was necessary to have instrumentation, or rods, put into my spine, which was followed by six months of wearing a hot, plastic brace. The upside to that, was that my brace was decorated with kittens, which was very important to a three-year-old girl. That is what we did—making the most of each situation. Each new challenge always looked like a new adventure.

After all of that, I had one more challenge. More surgery faced me in the fall of my sixth grade year. The curvature of my spine had become more severe, so I went through six weeks of traction. I was in the good hands of a world-renowned orthopedic surgeon at St. Louis Children’s Hospital. My mother and I had a seven week stay in the hospital and to say the least, we made the most of it. To begin with, I had a halo put into place for traction, and it was decorated with the most beautiful rhinestones. My stay was during the month of October, so my hospital room was decorated for Halloween, which allowed me to go on many “journeys” throughout the hospital. The last night before my six-hour surgery just happened to be Halloween, and in the spirit of St. Louis Children’s Hospital, there was trick-or-treating and fun Halloween festivities to take our minds off where we were heading. Oh, and I dressed up as a leopard with great face paint. The next day began with a six-hour surgery, now the fun was over; but it was worth it, because the traction had made me straighter and a few inches taller.

Fast forward a few years. I have always had big dreams, so when I was in high school, I really wanted to attend the most prestigious school, but through hard work and dedication, I made it, and entered The University of Illinois to study graphic design. Through high school, I was in love with biology, music, and the NF. Those were the classes that I excelled in, but I had always had problems with mathematics (I had found out later that could be caused by NF1), which sometimes did make high school a little difficult for me. I was always worried that I wasn’t good enough to get into a prestigious school, but through hard work and dedication, I made it, and entered The University of Illinois as a freshman in the fall of 2014. The University of Illinois has provided me with some of the best times of my life. I am taking design classes to prepare me for my future career, and have joined various clubs and a sorority on campus. In addition, I cheer for my school in sporting events until my voice gives out. I can’t begin to count the number of amazing people that I have met and I am continuing to meet.

Halfway through my college career, I became more curious about NF1 and what it could have in store for me. I remember one night after I researched it for hours, I learned so many things about the condition I have had my entire life. Why or how I would do things and why I looked the way I did, and also why I had gone through so many of those tribulations as a kid.

NF1 has made me a very strong person, and continually makes me stronger every day. I will never let it stop me from doing the things that I love. During my junior year, I decided to combine my interest in graphic design with a deep passion for medicine. I’m not sure if that stemmed from being in and out of the hospital as a kid or from reading countless National Geographic magazines. After researching potential career options in medicine and graphic design, I stumbled upon The Association of Medical Illustrators website. These are the people who design all of those colorful pictures in your biology or anatomy book. This is exactly what I want to do with my life.

In the summer of 2017, I was awarded an internship as a graphic designer at the Washington University Neurofibromatosis Center, where I have been creating medical illustrations. I am so appreciative for this opportunity. A big thank you to Dr. Gutmann and his staff. This internship has provided me with an amazing opportunity to have a taste of what my dream job would look like.

Written by Alexandra Schroeder

Please check out Alexandra’s wonderful illustrations as they are posted on the Gutmann Laboratory website this fall (gutmannlab.wustl.edu).
During 2017, researchers in the Washington University NF Center made many groundbreaking discoveries. Additionally, we... patient stem cell lines). These critical resources only exist because of the enthusiastic involvement of our families.

GUTMANN, postdoctoral researcher Joseph A. Toonen, PhD, and colleagues studied mice with NF1 gene mutations specifically engineered to develop tumors on the optic pathway. Both male and female mice developed tumors that were identical in size and growth rates; however, only the female mice exhibited significant nerve damage and vision loss. The researchers found that the tumors contain a type of immune cell called microglia. Strikingly, female mice had three times more microglia within these tumors than male mice. When activated, microglia release a range of toxic compounds that can cause collateral damage to nearby nerve cells. When they are activated, they release those compounds and sometimes cause collateral damage to nearby cells. They also found that the microglia within the optic tumors from female mice were activated, and the neurons near the tumors were damaged.

To test whether sex hormones could account for these differences, Dr. Toonen removed the ovaries from female mice and the testes from male mice. The number of damaged and dying cells in the retina - a light-sensitive layer of nervous tissue in the eye - did not change in the castrated males. But in the females without ovaries, fewer cells in the retina died and the number of activated microglia within the tumors was also decreased. These findings suggest that female sex hormones may cause microglial activation and subsequent neuronal damage.

When researchers used a drug to block the action of the female sex hormone in female mice carrying the NF1 mutation, they saw a drop in the number of activated microglia and a decrease in retinal damage and nerve cell death. Moreover, their team identified the specific sex-damaging toxins produced by these activated microglia. Future therapies to attenuate vision loss in children with NF1-optic tumors might target these compounds. Gutmann stressed that boys with NF1 also experience vision loss, just not as frequently as girls, and that male NF1 mice harbor some activated microglia within their tumors. He believes that the process of microglial activation and ensuing neuronal damage is the same in males and females, but that the presence of female sex hormones increases the microglial activation, leading to greater optic nerve damage and vision loss.

This article, written by Yamasa Bhadani, originally appeared in the Washington University School of Medicine News Hub on December 13, 2016. Read more of about this article at https://mednews.wustl.edu/news/female-hormones-increase-risk-vision-loss-rare-genetic-disease/
Because children with NF1 can experience such a wide variety of physical, social and scholastic challenges, we have partnered with St. Louis Children’s Hospital to establish programs that support general development while also empowering families to manage the types of medical, behavioral, and school problems common in this condition.

Targeting toddlers with NF1, Beat NF is a jazz music motor therapy program that uses live jazz to treat toddlers with Neurofibromatosis type 1 (NF1). The toddlers, of course, do not know what’s happening with the innards of the piano. The kids are fascinated by the music being made, how the fingering of the piano actually can’t play a wrong note, allows educational instruments, where you can try to do when you’re onstage improvising. We don’t always have all the information. We don’t always have the most advanced tools at any one time. We have what we have and we apply that to the situations that we’re dealing with.”

Dr. Gutmann says that the program, which uses “kid-friendly jazz, nothing too extreme,” has produced measurable results. “The more you activate parts of the brain, the more the kids become functional and new connections are made. It could be healing in that respect,” Gutmann says. “Jazz and medicine share a bunch of common principles,” Dr. Gutmann says. “One is improvisation and the other is collaboration. What we do all the time with our kids, particularly our young kids, is try to solve medical problems with information and tools that are immediately at hand, as you try to join in. “They’re mesmerized,” says Dr. Gutmann. “And the inclusion of [specialized educational] instruments, where you actually can’t play a wrong note, allows them to become further engaged. It’s the same sort of feedback that we get in a live jazz concert. You get to see how the music is made, how the fingering of the piano actually produces music, what’s happening with the innards of the piano. The kids are fascinated by that.”

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The toddlers, of course, do not know they are hearing jazz played by area pro musicians. For them it’s just fun to respond to music, which is always performed live, never in recorded form. But for many of the children, it’s their first exposure to live music of any kind, and thus the therapeutic process also becomes a teaching moment. They even get to join in. “They’re mesmerized,” says Dr. Gutmann.

“Beat established in jazz provides a framework for us to begin to address movement and timing and attention, things that are really problematic for these young kids. The live interaction helps them make connections. It provides visual cues and a more interactive experience.”

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As we celebrate our successes in 2017 and look forward to 2018, we want to thank everyone who has supported our mission. We are particularly indebted to our partners at the St. Louis Children’s Hospital Foundation and Schnuck Markets Inc. Washington University NF Center 2017 Annual Report created and designed by Jennifer N. Traber.