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The Washington University NF Center hosted our 3rd biennial research symposium on Friday, April 1 at the Eric P. Newman Education Center on the Medical School Campus. At this enlightening day-long event, faculty, researchers, residents and families learned about new discoveries in the world of NF. There were exciting presentations from our keynote speakers, Drs. David Largaespada and Alcino Silva, as well as Washington University NF experts.

David A. Largaespada, PhD, of the University of Minnesota delivered a presentation on “Using Model Systems and Functional Genomics to Develop New Treatments for NF1 Syndrome-Associated Tumors.” Alcino Silva, PhD, from UCLA talked about “Developing treatments for cognitive disorders.” Additional talks were delivered by Washington University NF researchers, including John Constantino, MD, Kimberly Johnson, MPH, PhD, Matthew Dobbs, MD, NF Center Director David Gutmann, MD, PhD, Angela Hirbe, MD, PhD, Courtney Dunn, PT, DPT and Nicole Weckherlin, OTR/L.

During the lunch break, attendees enjoyed an array of oil portraits titled “The Many Faces of NF,” by Rachel Mindrup of Omaha, Nebraska. Each portrait, inspired by an actual person living with NF, included a detailed autobiography of that person, providing a powerful and tangible connection between the researchers in attendance and the people whose lives are touched by their dedication to NF research. The day ended with a lively cocktail reception, accompanied by music from the Jazz St. Louis All-Stars.
**NEW CLUES IDENTIFIED IN CHILDHOOD CANCER SYNDROME**

Children with the inherited cancer syndrome neurofibromatosis type 1 (NF1) are prone to developing brain and nerve tumors as well as myriad other medical problems, including autism, epilepsy and bone defects. While the disorder is caused by a mutation in a single gene, the range and severity of clinical abnormalities vary widely, making the impact of NF1 on children and adults difficult to predict and treat.

But new research at Washington University School of Medicine in St. Louis may help doctors determine which issues are likely to manifest in patients with NF1. The findings indicate that varying mutations in the NF1 gene may lead to different clinical outcomes. The research is published online in Human Molecular Genetics.

“This discovery could enable us to better predict how NF1 will affect specific individuals, showing us what problems are likely to develop and how best to address them,” said senior author David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor of Neurology. “These early-phase findings bring us one step closer to being able to individually tailor how we monitor and treat people with NF1.”

While all individuals with the disorder are born with a mutation in the NF1 gene, there are thousands of different NF1 gene mutations. To determine whether specific mutations of the gene increase the risk of developing optic gliomas, one of the most common brain tumors affecting children with NF1, the researchers used mice genetically engineered with patient-specific NF1 gene mutations.

Surprisingly, Gutmann and his colleagues found that mice harboring one specific patient-derived NF1 gene mutation developed optic gliomas, while mice with another patient-derived NF1 gene mutation did not. The mice with optic gliomas also had greater eye dysfunction. Optic gliomas are known causes of vision loss in children with NF1. To determine why the specific mutation had such a dramatic effect on optic glioma formation and vision, Toonen discovered that the number and activity of microglia, immune cells in the central nervous system that defend against invaders in mouse brain tumor growth. Toonen discovered that the number and activity of microglia were affected differently by each mutation. There were more microglia in mice with one patient-derived mutation, leading to greater tumor growth and increased optic nerve injury. In striking contrast, these findings were not observed with the other patient-derived mutation. The scientists now are researching how microglia promote optic glioma growth and vision loss.

*Based on these exciting results, we can now envision using a mini-clinic of mice with different NF1 gene mutations,” said Gutmann, who also directs the Washington University NF Center. “This would offer us a valuable representation of the spectrum of clinical variability in this very heterogeneous disorder.

*Moreover, should specific gene mutations play a major role in determining brain tumor development, families could be better informed about the risk that their children may develop such tumors,” Gutmann said.

For this reason, the researchers are incorporating the mice into preclinical drug-discovery and evaluation efforts as a means of developing precision medicine strategies for children and adults with the disorder.

This article, written by Jessica L. Williams, first appeared in the Washington University School of Medicine News Hub on March 30, 2016. View additional news stories at https://medicine.wustl.edu/news/

**BEAT NF PROGRAM FEATURED IN JAZZTIMES**

The sight of a group of children dancing happily to live music never gets old. And when those kids have been diagnosed with a genetic disorder called neurofibromatosis type 1 (NF1), and exposure to jazz has proven to have a positive factor in their therapy, the joy factor skyrocketed. NF1, which can cause a myriad of problems, affects one in 2,500 to 3,000 people of all ages—it’s more common than muscular dystrophy. In young children, it can lead to numerous medical, motor and learning issues, as well as problems with socialization. Traditional therapies can help, but for many kids, they’re not enough.

That’s where Dr. David Gutmann comes in. A professor of neurology and director of the Washington University Neurofibromatosis (NF) Center in St. Louis, Mo., Dr. Gutmann and his team, in tandem with St. Louis Children’s Hospital and Jazz St. Louis, two years ago created Beat NF, a therapy program that uses live jazz to treat toddlers with NF1, for which there is no known cure as yet.

“We noticed that kids that have NF1 require a multidisciplinary approach,” he says, “and we needed to bring a number of different ideas and approaches to bear. The reason that we decided to use jazz is that the 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.”

Why jazz? “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 to try to solve medical problems with information and tools that are immediately at hand, as you 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 to the situations that we’re dealing with.”

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. “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 on the piano actually produces music, what’s happening with the innards of the piano. The kids are fascinated by that.”

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,” jazz, with its pronounced rhythms, seems to have a more noticeable effect than other genres of music. “We can vary the music in terms of speed and tailor it to just the right challenge for these kids,” he says.

He hopes to expand the program within St. Louis at first, but eventually it could be used in other locations, and could possibly be applied to other conditions, including cerebral palsy and autism.

This article, written by Jessi Tomarkin, originally appeared in JazzTimes on March 24, 2016. View additional JazzTimes articles at jazztimes.com
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To determine why the specific mutation had such a dramatic effect on optic glioma formation and vision, Joseph Toonen, Toonen, PhD, a postdoctoral research fellow, built upon previous research in the Gutmann laboratory that demonstrated a critical role for microglia - immune cells in the central nervous system that defend against invaders - in mouse brain tumor growth.

Toonen discovered that the number and activity of microglia were affected differently by each mutation. There were more microglia in mice with one patient-derived mutation, leading to greater tumor growth and increased optic nerve injury. In striking contrast, these findings were not observed with the other patient-derived mutation. The scientists now are researching how microglia promote optic glioma growth and vision loss.

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During the lunch break, attendees enjoyed an array of oil portraits titled “The Many Faces of NF,” by Rachel Mindrup of Omaha, Nebraska. Each portrait, inspired by an actual person living with NF, included a detailed autobiography of that person, providing a powerful and tangible connection between the researchers in attendance and the people whose lives are touched by their dedication to NF research. The day ended with a lively cocktail reception, accompanied by music from the Jazz St. Louis All-Stars.