FALL 2015

WASHINGTON UNIVERSITY NEUROFIBROMATOSIS CENTER

EXCEPTIONAL CARE *through* GROUNDBREAKING RESEARCH

RESEARCHERS SEPARATE NF1/RAS FUNCTION IN BRAIN STEM CELLS

Children with Neurofibromatosis type 1 (NF1) are prone to the development of clinical problems that reflect abnormalities in both nerve cell (learning and behavior) and glial cell (brain tumors) function. In this regard, nerve cells and glial cells originate from stem cells in the brain (called neural stem cells); however, it was not known how the *NF1* gene precisely controlled neural stem cell (NSC) growth and differentiation (the formation of nerve and glial cells).

Dr. Yi-Hsien Chen, a post-doctoral fellow in the laboratory of Dr. David Gutmann, used a combination of experimental strategies to demonstrate that the *NF1* gene regulates NSC growth and differentiation by shutting off the activity of the RAS protein. Importantly, Dr. Chen found that the decision to form more NSCs versus differentiate into nerve and glial cells are controlled by two different RAS signaling pathways. In this study, he showed that RAS control of NSC growth is mediated by the AKT molecule, whereas NSC differentiation is regulated by the MEK signaling pathway. In addition, Dr. Chen discovered that MEK controls NSC formation of new nerve and glial cells through a mechanism not previously ascribed to NF1.

Together, these novel findings clearly establish that *NF1* gene control of brain stem cell function operates through distinct RAS signaling pathways, which can be individually targeted to block abnormal cell growth or differentiation.

Dr. Chen's paper was published in the journal, *Genes and Development*.

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PATIENT SPOTLIGHT: MOLLY MCNEILL

Molly McNeill is eight, and was diagnosed with NF1 four years ago. She was born with several café-a-lait spots, so we began to watch for development of a second NF sign. Her pediatric ophthalmologist found Lisch nodules on her irises when Molly was four, and a diagnosis of NF1 (spontaneous mutation) was confirmed by Dr. David Gutmann at the Washington University NF Center soon thereafter.

Molly loves to read, and other than some mild attention issues, hasn't struggled much in the classroom. However, she has had both physical and occupational therapy to improve her gross and fine motor skills. One of the more obvious struggles Molly has had is in the area of balance. From a young age, walking up and down stairs and running have both been difficult for her. A physical therapist suggested dance classes to help with Molly's balance issues, but I, as her mom, was hesitant. I didn't want her to have a frustrating experience or stand out in a negative way because of her delays. But she was willing to try and I could see the potential benefit, so I enrolled her in a tap/ballet combination class. She's done both styles of dance for the last four years, and we've tried other types of activities, as well: acrobatics, volleyball, basketball, swimming, tee ball, soccer, cheerleading, drawing/painting, pottery, piano and theatre.

Now, before you think we live in our car, I need to stress we've tried all these things; we don't do them all at once! A great way to try stuff, we've found, is through camps and short workshops. There is a volleyball camp, for example, at a local college that lasts two days each summer, and a one-day pottery workshop Molly loves. When trying out new activities, we check local park and recreation centers, Molly's school, other schools and colleges, and arts organizations (many classes are reasonably priced at all these places with scholarship offerings for many of them). We look for activities that target different areas, like a swimming class that helps with the development of gross motor skills, a theatre workshop for focus, and piano lessons for fine motor engagement.

If I sense a new interest is going to be a struggle, I speak privately with someone in charge before Molly tries it. I explain what NF1 is, how it can affect children, and where I could foresee some possible issues with this particular endeavor. Most people understand if I contact them well before the activity starts (not trying to catch them five minutes before class). When Molly pursues a new activity, we do a short "debriefing" after each session. We talk about what she enjoyed and went well, and what she didn't enjoy and didn't go well. Then we talk about our achievable goal for each session: for Molly to participate the whole time and do her best.

There are times Molly can't do some things that others in the class can do. For example, she can't do a cartwheel in her acrobatics class. She notices when others can do cartwheels, and sometimes it bothers her. So we think about the goal: Did she stay involved in the class the whole time? Did she try her best to learn how to do a cartwheel? Still, there are times of frustration for her. But there are also times of joy. Because Molly is small for her age, it was easier for her to do a tripod (a headstand with knees balances on the elbows) than others in the class. In theatre class, because she isn't always socially attentive, she's willing to throw herself fully into a character, without fear of what others think, while still learning to focus on her lines.

Read more about Molly's story at nfcenter.wustl.edu/patient-spotlight-molly-mcneill/

– Written by Stacy McNeill

HELP US WELCOME A NEW CLINICIAN-RESEARCHER TO OUR TEAM!

Stephanie Morris, MD is completing her training in Pediatric Neurology at St. Louis Children's Hospital and Washington University. She was recently awarded a position on the Neurological Sciences Academic Development Award (NSADA) training grant to allow her to study autism in children with NF1. Working with Dr. John Constantino in Pediatric Psychiatry and Dr. David Gutmann in Neurology, she hopes to more completely characterize the autistic-like behaviors in children with NF1 as a first step towards identifying those individuals most at risk for these problems.

WASHINGTON UNIVERSITY NF CENTER TO HOLD RESEARCH SYMPOSIUM

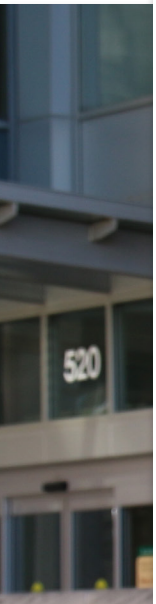
We are pleased to announce that the third biennial Washington University Neurofibromatosis Center Research Symposium will take place on Friday, April 1st, 2016 at the Eric P. Newman Education Center (EPNEC) located on the campus of the Washington University School of Medicine in St. Louis, MO.

Dr. David H. Gutmann, Director of the Washington University NF Center and the Donald O. Schnuck Professor of Neurology at the Washington University School of Medicine, is pleased to announce that David A. Largaespada, PhD from the University of Minnesota and Alcino J. Silva, PhD from the University of California, Los Angeles are the two keynote speakers. Along with other Washington University NF Center investigators, this day-long symposium will highlight advances in NF research and clinical care.

Dr. Largaespada is Professor of the Department of Cell Biology and Development Genetics, where he serves as the Margaret Harvey Schering Chair in Cancer. He and his colleagues pioneered the use of insertional mutagenesis to discover new cancer genes relevant to NF1-associated brain and nerve sheath tumors.

Dr. Silva is the Director of Behavioral Testing Core and Professor of Psychology Behavioral Neuroscience at the Tennenbaum Center for the Biology of Creativity. Dr. Silva has been a leader in mouse learning and behavior, and was the first to use *Nf1* genetically-engineered mice to discover new treatments for cognitive disorders.

For more information about this event, please visit nfcenter.wustl.edu or contact Kirsten Brouillet at brouilletk@neuro.wustl.edu.



WASHINGTON UNIVERSITY NF CENTER

JOIN US FOR BEAT NF THIS FALL!

WHO: Toddlers (2 ½ - 5 years old) with NF1 & their parents
WHAT: Beat NF - Jazz Music Motor Therapy
WHEN: Wednesday mornings
September 23 - October 21, 2015,
9:30 - 10:45 AM
WHERE: The Harry and Dorothy Steward Center for Jazz
3536 Washington Ave., St. Louis, MO 63103

MARK YOUR CALENDAR!

Interested in attending any of these events? RSVP to Kirsten Brouillet at brouilletk@neuro.wustl.edu

CLUB NF HEADS TO FUNFEST!

Please join us on Saturday, October 3, at the Walk Family's 5th annual FuNFest, which will also include Club NF. FuNFest is an annual fundraiser sponsored by the Walk family at Gatch Lake — near Vandalia, Illinois. FuNFest includes games, bounce houses, face painting, a silent auction and a bake sale, along with the infamous Cow Patty Bingo!

If you are interested in riding a free charter bus from the Washington University Danforth Campus (leaving campus at 9:30 a.m. and returning to campus at about 5:30 p.m.), please contact Kirsten Brouillet at brouilletk@neuro.wustl.edu no later than September 30.

WHO: Children in grades K - 8 with NF1 & their families
WHAT: Walk Family Fundraiser - FuNFest and Club NF
WHEN: Saturday, October 3, 2015, noon - 6 PM
WHERE: Gatch Lake, Rt. 51 south out of Vandalia, IL
COST: FREE entry to FuNFest - $10/person unlimited games,
Food and drink available for $1 - $3

5th Annual FUNFEST JORDAN

STAY CONNECTED >> nfcenter.wustl.edu

This newsletter is provided through the generosity of the Doris and Donald Schnuck Fund for Children in Need and the St. Louis Children's Hospital Foundation.