

THE WASHINGTON UNIVERSITY NEUROFIBROMATOSIS (NF) CENTER

Making a Difference Together



DAVID H. GUTMANN, MD, PHD, RECEIVES WASHINGTON UNIVERSITY DISTINGUISHED INVESTIGATOR AWARD

On February 12, 2013, David H. Gutmann MD, PhD, the Donald O. Schnuck Family Professor of Neurology was honored by the Washington University School of Medicine with the Distinguished Investigator Award for his outstanding contributions to the understanding of Neurofibromatosis Type 1 (NF1) and Neurofibromatosis Type 2 (NF2) and the biology of brain tumors.

Gutmann, also a professor of neurosurgery, pediatrics and genetics, is a world leader in neurofibromatosis research and clinical care. A set of complex genetic disorders, neurofibromatosis can affect almost every organ system, causing a predisposition for tumors to grow on nerves in the brain and throughout the body.

Considered the ultimate physician-scientist, Gutmann's generosity as a collaborator and mentor and his talent for multidisciplinary investigation epitomize the power of translational research. He has made many seminal contributions to the understanding of NF, including developing critical mouse tumor models, identifying several therapeutic drug targets, and establishing the molecular bases for several clinical problems affecting patients with NF1 and NF2. He has published more than 300 peer-reviewed papers.

Gutmann has played a critical role in advancing the care of patients with NF. He is the founder and director of the Washington University and St. Louis Children's Hospital Neurofibromatosis Clinical Program, and he established the Washington University Neurofibromatosis Center in 2004, now one of the world's largest NF research centers. He is an international thought leader in NF clinical practice and research, and has received many honors for his contributions, including the National Neurofibromatosis Foundation Crystal and Center of Excellence Awards, the Walker Lecture in Neurofibromatosis, the Takao Hoshino Lectureship, and the Frederick von Recklinghausen Award.

He earned his doctoral degree in 1984 and his medical degree in 1986, both from the University of Michigan. He completed his residency at the University of Pennsylvania and a fellowship at the Howard Hughes Medical Institute, working with Francis Collins, MD, PhD. He joined the Washington University faculty in October 1993.



WELCOME!

The Washington University Neurofibromatosis (NF) Center is composed of clinicians and laboratory scientists focused on accelerating the pace of scientific discovery and its application to the care of individuals with NF.

Our mission is to galvanize and promote research on NF, achieving significant breakthroughs in the diagnosis and treatment of this condition. We believe that these breakthroughs are possible when researchers, medical professionals, and families partner together.

The Washington University Neurofibromatosis (NF) Center team offers detailed patient evaluations and assessments. They work seamlessly with families, referring physicians, allied health professionals and other agencies to deliver the most advanced medical services available to children and adults affected by NF.



Washington University
Neurofibromatosis Center

SAVE THE DATE!

<p>CLUB NF APRIL 6, 2013</p> <p>•</p> <p>Join us for roller-skating and shoelace tying! Kim Sirl, PhD will speak.</p>	<p>CLUB NF JUNE 1, 2013 Ropes Course</p> <p>•</p> <p>AUGUST 2, 2013 Dance Therapy</p>	<p>BACK-TO-SCHOOL PICNIC AUGUST 10, 2013</p>
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RESEARCH AT THE WASHINGTON UNIVERSITY NF CENTER

WASHINGTON UNIVERSITY NF CENTER RESEARCHERS COMPLETE FIRST WHOLE GENOME SEQUENCE OF NF1 BRAIN TUMORS

In collaboration with the Genome Institute at Washington University, David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor in Neurology and Director of the Washington University NF Center, recently completed an advanced whole genome sequence analysis of three NF1-associated low-grade brain tumors, called pilocytic astrocytomas. This effort represents the first detailed genetic study of pilocytic astrocytomas. Their findings were recently published in the journal *Genome Research*.

In this landmark study, Gutmann, along with collaborators Li Ding, PhD and Elaine Mardis, PhD from the Genome Institute, demonstrated that *NF1* gene loss is the primary genetic alteration in these tumors, confirming the primary role of this important tumor suppressor gene in NF1-associated brain tumors.

In addition, this study demonstrated that there are multiple ways to inactivate the *NF1* gene in brain tumors, including potentially reversible mechanisms. Future work will be required to determine whether the *NF1* gene can be re-activated as possible therapy.

Finally, these investigators showed that nearly half of the cells in these tumors are not cancer cells, but rather immune system-like cells. These immune system-like cells, called microglia, are currently under intense investigation in the Washington University NF Center as prime targets for future cancer therapies.

MULTIPLE FACTORS CAUSE LEARNING PROBLEMS IN NF1

Researchers at the Washington University NF Center have recently shown that learning problems and attention deficits associated with NF1 could be caused by multiple factors.

Past studies have shown that mutations in the *Nf1* gene can disrupt the activity of an important protein, known as RAS, in the hippocampus, a region of the brain associated with learning and memory. In contrast, previous studies by researchers at the Washington University NF Center have shown that nerve cells in *Nf1* mice have lower levels of a neurotransmitter called dopamine.

The most recent study, by post-doctoral fellow Kelly Diggs-Andrews, PhD, suggests that both factors might play a role in learning problems and attention deficits. Diggs-Andrews showed that in *Nf1* mice dopamine-producing nerve cells extending into the hippocampus were reduced in size. This reduction caused less dopamine to be present in the hippocampus and the lowered dopamine levels disrupted communication between nerve cells causing interference in memory creation.

When researchers gave the *Nf1* mice L-DOPA, a drug which increases dopamine levels, normal nerve cell length and communication within the hippocampus was restored ending the memory and learning deficits previously seen.

The results suggest that there are a variety of ways that NF1 may cause cognitive problems in people. Researchers at the Washington University NF Center are now working to find what specific contributions RAS and dopamine play in determining cognitive deficits in people with NF1.

WASHINGTON UNIVERSITY NF CENTER RESEARCHERS PUBLISH STUDY ON THE CELL OF ORIGIN IN *Nf1* AND OPTIC GLIOMA

To identify the cells that give rise to NF1-associated optic glioma, Ms. Anne Solga, a graduate student in the research laboratory of David H. Gutmann, MD, PhD analyzed a progenitor cell previously shown to give rise to malignant brain tumors in mice. Using a battery of experiments, she showed that inactivation of the *Nf1* gene in this progenitor cell population does not lead to increased growth or cause optic gliomas in mice. These experiments exclude these cells as the potential source for mouse optic glioma. Her findings were recently published in the journal *Oncogene*.

Scan the QR Code to learn more about research at the
Washington University NF Center!



FOR OUR FAMILIES

CLUB NF GOT ITS GAME ON!

On January 26 and February 2, 2013, the Washington University Neurofibromatosis (NF) Center in collaboration with the St. Louis Children's Hospital Foundation hosted their Winter 2013 Club NF Event **Get Your Game On!** The winter program highlighted the benefits of playing as a family and focused on building community amongst our families.

The January 26, 2013 session was held at Tropicana Bowling Lanes. Families spent the first hour bowling as a team and then switched up lanes and did a Crazy Bowl while meeting new families and friends. The bowling session encouraged kids to practice gross motor and attention skills as well as fostered team spirit and community building.

The February 2, 2013 session was a board game relay held at the Maryland Heights Community Center. Families explored new games by rotating through various game stations every 15 minutes. No family member had the exact same path to ensure everyone got a chance to meet and play with someone new. The board game session encouraged kids to practice fine motor skills, gross motor skills, attention skills and communication skills.

Club NF is changing its schedule! Starting on April 6, 2013 the Washington University NF Center will host Club NF events every first Saturday bi-monthly. Want to learn more? Contact Kirsten Brouillet at brouilletk@neuro.wustl.edu.



GET TO KNOW TEAM NF!

Kirsten Brouillet (pictured right)

Kirsten Brouillet is the new Washington University NF Center Team NF Coordinator. Kirsten is responsible for all phases of Club NF. Kirsten is also the glue of the team, ensuring that everyone is communicating and sharing all their awesome ideas for growing the Washington University NF Center as a community. If you have questions comments or ideas for Club NF or if you have ideas for growing our community, please contact Kirsten at brouilletk@neuro.wustl.edu.

Alicia Vallorani (pictured above in bottom picture, green shirt)

Alicia Vallorani is the Clinical Program Coordinator for the Washington University NF Center. Alicia is responsible for managing all on-going clinical studies at the Washington University NF Center as well as for managing Washington University NF Center publicity. Alicia also ensures quality educational materials are available to our families. If you have questions about getting involved in research or if you have ideas for new projects at the Washington University NF Center, please contact Alicia at vallorania@neuro.wustl.edu.



CLINICAL STUDIES AT THE WASHINGTON UNIVERSITY NF CENTER

FIRST NEUROFIBROMATOSIS TYPE 1 PATIENT REGISTRY (NPRI) REPORT PUBLISHED

Dr. Kimberly Johnson, MPH, PhD and her colleagues recently described the Washington University Neurofibromatosis (NF) Center NF1 Patient Registry Initiative (NPRI) in a report published in the journal *Contemporary Clinical Trials*.

One of the major challenges to clinical research focused on people affected with NF1 is the inability to assemble large numbers of individuals for study. To overcome this barrier, Dr. Johnson developed an online patient registry (<https://nf1registry.wustl.edu/>), which was officially launched in May 2011. This one-of-a-kind registry allows anyone with NF1 from across the world with internet access to enroll in the registry and participate in research. The goal of the NPRI is to help physicians and researchers conduct clinical research studies aimed at defining the risks for cancer and other health outcomes in children and adults with NF1. Researchers hope that the information gained from these studies may one day help clinicians to develop personalized treatment strategies that improve the quality of life for individuals living with NF1.

During the inaugural year of the NPRI, a total of 308 individuals from 44 U.S. states, the District of Columbia, and 19 countries on six continents participated in the registry. The registry includes participation of individuals from all races and the vast majority of participants agreed to future contact about research. The results from the registry's first year strongly indicate that the internet is providing an unprecedented opportunity to rapidly connect individuals with rare diseases from across the world to researchers for studies that will ultimately improve the health of people living with these conditions.

We congratulate Dr. Johnson and her colleagues on this important milestone.

GET INVOLVED IN RESEARCH

NF1 Genome Project: Blood samples are collected and DNA is extracted for future research aimed at identifying children at greatest risk for specific medical problems associated with NF1. Participation is open to all ages. Blood draws can also be performed during a sedated brain scan.



NF1 Brain Trust Project: Small skin biopsies are donated to the Washington University Neurofibromatosis (NF) Center in order to generate brain nerve cells used to discover better treatments for learning, memory and behavior problems associated with NF1. Neurofibromas are removed by our plastic surgeon as part of routine clinical care



To get involved in our clinical studies, please email Alicia Vallorani at NFClinicalStudies@neuro.wustl.edu.

STAY CONNECTED!

FACEBOOK

"Like" The Washington University Neurofibromatosis (NF) Center to follow us and get regular updates about everything we're doing from research to Club NF!



APPS FOR NF

Check out our recommended Apps for kids with NF by scanning the QR Code with your iPhone or iPad. Learn about great tools for teaching skills from organization to classroom productivity.

THE WASHINGTON UNIVERSITY NEUROFIBROMATOSIS (NF) CENTER WEBSITE

Visit our website at:
www.nfcenter.wustl.edu

