FIRST HUMAN MODELS OF NF1-ASSOCIATED NEUROFIBROMAS DEVELOPED BY NF CENTER COLLABORATIVE TEAM

The most common tumor in children and adults with NF1 is the neurofibroma, a peripheral nerve sheath tumor composed of Schwann-like cells. While mouse models of plexiform neurofibromas have been developed, Dr. Lu Le, Professor of Dermatology at the University of Texas-Southwestern joined forces with Drs. Corina Anastasiaki and David Gutmann to develop a human model of neurofibroma.

To do this, the team took advantage of human stem cell engineering methods, called CRISPR, to develop a series of NF1 patient-specific human induced-pluripotent stem cells (hiPSCs), which they used to create human Schwann-like cells. They found that implanting human NF1 Schwann-like cells into the nerves of mice resulted in the formation of bona fide neurofibromas, thus creating the first human model of this common tumor.

Moreover, they identified the cell that gives rise to cutaneous neurofibromas, and used this information to design mice that develop classic cutaneous neurofibromas, similar to those found in people with NF1. Dr. Le and his team then used these mice to show that drugs that block MEK activity decrease the growth of cutaneous neurofibromas.

Together, these two laboratories established complementary humanized neurofibroma explant and first-in-kind mouse genetically engineered cutaneous neurofibroma models amenable to future therapeutic target discovery and evaluation.

This report was published in the Journal of Clinical Investigation.
COMPLEMENTARY CARE PROGRAMS GO VIRTUAL

At the Washington University NF Center, we believe in the value of extending medical care for our families beyond the walls of the clinic. As such, we have pioneered several successful therapy programs, including Beat NF, Club NF and Teen NF.

The COVID-19 pandemic has challenged our team to find creative ways to offer these essential therapy programs in a safe manner. To overcome these obstacles, we have transitioned all therapy programs to a virtual format via Zoom.

Our entire Beat NF program was reimagined this spring, and now provides quality musical programming and therapy in a virtual Zoom format. Prior to each live session, video recordings were made of each song introducing the weekly instrument and highlighted musician. Each of the five weekly sessions were performed live, with our music therapist leading participants in video recordings, while our physical therapist guided children through the weekly gross motor skill. After each session, participants were emailed their weekly “homework”, representing the skills learned in the session, to practice themselves at home. We look forward to continuing this virtual program for the spring 2021 season.

Club NF participants are still able to enjoy meaningful and rewarding events virtually, while our skilled physical therapists work with each child to improve gross motor, fine motor and/or social skills. At our first Virtual Club NF event in October, children were able to visit a working farm from the safety of their own living room. The NF Center Coordinator and our team physical therapist interacted with the animals and provided education about the farm (social/emotional therapy). In addition, children were led through a corn maze (social therapy), and then worked on craftwork (fine motor/executive function therapy). All Club NF participants had a wonderful time! Stay tuned as more events are announced.

Teen NF was also successfully transitioned to a virtual Zoom format. Participants were able to join with the NF Center Coordinator and Teen NF psychologist, Dr. Kimberly Sirl, for six bi-weekly sessions. These sessions included four meetings with group format interactions with Dr. Sirl to build confidence, work on social skills and foster leadership skill development, followed by two “Life Skills” classes led by an educational specialist from the Saint Louis Science Center. Our newly added Life Skills classes focused on “Health and Well-being” and “Networking and Developing Your Brand”. We are looking forward to providing the same 6-session, bi-weekly format for our spring 2021 session.

UPCOMING EVENTS

BEAT NF - SPRING 2021 - MARCH 2 - 30, 2021
CLUB NF - LEARNS TO SING! - APRIL 9, 2021
TEEN NF - SPRING 2021 - MARCH 8 - MAY 17, 2021

If you have any questions about our programs or would like to attend one of our future events, please contact our NF Center Coordinator: Jennifer Traber, jtraber@wustl.edu.
ALEXANDER CHEN AWARDED TRAINING GRANT FROM THE CENTER OF REGENERATIVE MEDICINE

Alexander Chen, PhD, a postdoctoral fellow in the Gutmann Laboratory, was recently awarded a “Training in Regenerative Medicine” training grant (T32) from the National Institute of Biomedical Imaging and Bioengineering. This program aims to develop highly-trained individuals by providing a unique, multidisciplinary experience for postdoctoral fellows. Dr. Chen is honored and privileged to be one of the three postdoctoral candidates to receive this prestigious grant in its inaugural year. He is excited to use the generous resources offered by the grant to investigate the cell of origin for brain tumors, specifically low-grade gliomas.

NF CENTER TRAINEE PUBLISHES GROUNDBREAKING STUDY ON THE ORIGINS OF NF1 OPTIC GLIOMAS

Dr. Nicole Brossier, Instructor in the Division of Pediatric Hematology and Oncology at St. Louis Children’s Hospital, recently reported that numerous factors explain why children with NF1 develop optic gliomas. In her study, Dr. Brossier, who is a pediatric neuro-oncologist specializing in the care of children with NF1-associated brain tumors, showed that the cells which likely give rise to optic gliomas in mice with Nf1 mutations exhibit different capacities to grow as a function of the type of germline Nf1 gene mutation, the age of the mouse, and the location of the progenitor cells within the brain. Her detailed work demonstrates that Nf1 brain tumor formation in mice must occur during embryonic development, in specific progenitor cells in the brain, and in mice with some, but not all, germline Nf1 gene mutations.

This exciting report was recently published in Neuro-Oncology. Future studies by Dr. Brossier will focus on examining risk factors that underlie brain tumor formation in children with NF1.

GUTMANN RECEIVES AWARD FROM THE AMERICAN NEUROLOGICAL ASSOCIATION

David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor and Vice Chair for Research Affairs in the Department of Neurology at Washington University School of Medicine in St. Louis, has received the George W. Jacoby Award from the American Neurological Association for his discoveries on the role of the immune system in brain tumors.

The award is given once every three years to a scientist who has done especially noteworthy experimental work on any neurologic or psychiatric subject. Gutmann was recognized for a body of research showing that two kinds of immune cells – microglia and T cells – control the formation and growth of brain tumors in mice, similar to those arising in children with Neurofibromatosis type 1 (NF1). The findings could lead to new ways to help doctors predict which brain tumors are most likely to become life-threatening, and opens up new avenues to prevent or treat brain tumors.

Dr. Gutmann accepted the award at the American Neurological Association annual (virtual) meeting.
MEET MAKENZIE SLEDD
PHYSICAL THERAPIST FOR THE NF CENTER PROGRAMS

A wife, a mother of two kiddos, and a physical therapist at St. Louis Children’s Hospital, Makenzie has been practicing since 2008 following graduation from St. Louis University with a master’s degree in Physical Therapy.

Makenzie has extensive experience in providing continuity of care, consultations, and education to patients and families. She thrives in a multidisciplinary environment where she has the opportunity to collaborate with occupational and speech therapists, and Washington University physician teams. She has spent her career not only working directly with patients, but also with physicians in Orthopedics, Neurology and Hematology.

She has developed and streamlined physical therapy protocols and teaching tools for her department to use, while fostering continuity of care between therapists and improving patient outcomes. Additionally, she has developed departmental resources that provide therapists and parents with a centralized repository of educational resources and information. Makenzie loves to share these resources and information with other therapists, patients, and families.

Makenzie approaches her practice by looking at the entire picture. She believes in looking beyond the medical diagnosis and treating the whole patient – even if that means spending an extensive amount of personal time and energy researching problems outside of the realm of physical therapy. She tries to make sure that her families have all of the information and resources they need to best care for themselves.

The highlight of Makenzie’s summers is her long tenure as co-director of the Gateway Hemophilia Association Camp Notaclotamonugus. In response to the 2020 COVID-19 pandemic, Makenzie led the team in pivoting their programming to a virtual setting to optimally serve the kids she adores so much. She also is a member of the National Hemophilia Association Physical Therapy Working Group, which plans and executes the annual NHF Bleeding Disorder Conference. Recently, she has helped form an organization, from the bottom up, composed of physical therapists across the country to continue her work to share knowledge and create resources to better the management of patients. Makenzie considers all of these activities a “pastime” and in essence, her passion for pediatric health does not fall far from her personal life.

Although it’s nearly impossible for Makenzie to turn off her “PT Brain”, she enjoys unwinding with her husband and two daughters by gardening, crafting, camping, and hiking. Through Makenzie’s Motor Minute, Makenzie will address a variety of topics that support children with NF achieve the best versions of themselves.