Hunter Nelson Sturge-Weber Center
Kennedy Krieger Institute

Sturge-Weber Syndrome Research Update 2021

RESEARCH STUDY SUMMARY:

Epidiolex Drug Trial
The second Epidiolex drug trial for cognitive impairments has been completed and the data is being analyzed. This trial evaluated pharmaceutical grade cannabidiol for cognitive and social issues, migraines and motor impairments. Look for the results of this study to be out in the coming year. Please contact Dr. Comi if you'd like to learn more. Funding is being sought for follow up trials.

Sirolimus Drug Trial
Our sirolimus trial data was published in Pediatric Neurology (see paper summary). The results suggest that this drug (an mTOR inhibitor and open label drug for cognitive impairment) helps a subset of patients with SWS. We are planning a follow-up trial and working to obtain funding. This is the first targeted drug treatment trial for SWS, following our discovery of the causative somatic gene mutation in *GNAQ* in 2013.

SWS Tissue Analysis
The Comi laboratory continues to work with human SWS tissue in collaboration with a Johns Hopkins scientist. We determined that proteins downstream of the somatic mutant GNAQ (the cause of SWS) have increased activity in the abnormal blood vessels on the surface of the brain and in brain cells. These proteins are targeted by Sirolimus treatment. This work is currently being submitted for publication.

Cell Culture Model
A new collaboration with a Kennedy Krieger scientist has led to the development of a cell line with the SWS mutation. We are currently studying these cells and looking to develop new approaches for studying tissue and testing drugs.

Mouse Model
Work continues on development of a mouse model of SWS, a difficult yet important step in testing potential drug therapies and treatments prior to clinical trials. Since the discovery of the underlying somatic mutation that causes SWS, developing an animal model has become a primary goal. Modeling SWS has been challenging, because standard genetic mouse model approaches do not work for somatic mutations.

Other Clinical Studies
We are currently analyzing data from prior BVMC (Brain Vascular Malformation Consortium) funded work with urine biomarkers and neuroimaging. We are also a site enrolling for the current BVMC studies. Additionally, we are engaged in further research on the genetics of SWS, and the outcome of presymptomatic treatment of infants with SWS.

PAPER SUMMARY: From our group 2020-2021

Quantitative EEG improves prediction of Sturge-Weber syndrome in infants with port-wine birthmark. Clin Neuropyshiol. 2021 Oct. We determined that quantitative EEG (qEEG) adds information to risk prediction in infants with facial port-wine birthmarks (PWB). qEEG can be used to help determine whether to obtain an MRI in the first year of life. The data collected can assist in developing a predictive model risk calculator that incorporates both PWB extent and qEEG results, which can be validated and then employed in the community.

A novel somatic mutation in GNB2 provides new insights to the pathogenesis of Sturge-Weber syndrome. Hum Mol Genet. 2021 Oct. One patient in this study with SWS was negative for the GNAQ mutation, but instead harbored a somatic mutation in GNB2 which encodes a beta chain of the same G-protein complex. The discovery of the GNB2 mutation sheds novel light on the pathogenesis of SWS and suggests future directions for research on targets of treatment.

Multicenter research data of epilepsy management in patients with Sturge-Weber syndrome. Pediatr Neurol. 2021 Jun. Epilepsy in typical Sturge-Weber syndrome is common, and many questions remain regarding the treatment outcomes. We analyzed a large multicenter database with focus on neurological drug treatment in different demographic and SWS characteristic groups. Levetiracetam, low-dose aspirin, and oxcarbazepine were the most frequently used medications. More severely affected patients were frequently on a greater number of antiseizure medications. Surgery for epilepsy was associated with the ability to discontinue antiseizure medication. Longitudinal studies are needed to further investigate medication use in patients with SWS.

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Please support our efforts!
KennedyKrieger.org/SWS

Sturge-Weber Syndrome Research Update 2021-Cont.

RESEARCH STUDY SUMMARY CONT.:

Sirolimus treatment in Sturge-Weber syndrome. Pediatr Neurol. 2021 Feb. Sturge-Weber syndrome is a rare neurovascular disorder associated with capillary malformation, seizures, cognitive impairments, and stroke-like episodes (SLEs), arising from a somatic activating mutation in GNAQ. Studies suggest this DNA change (or mutation) may cause over-activity of an important process in cells called the mammalian target of rapamycin (mTOR) pathway. Sirolimus is a mTOR inhibitor that has been studied in other vascular anomalies and is a potentially promising therapy in Sturge-Weber syndrome. The side effects we saw from sirolimus were generally mild, and it may be beneficial for cognitive impairments, especially in patients with impaired processing speed or a history of stroke-like episodes. A future, larger trial of sirolimus in patients with Sturge-Weber syndrome is being planned, to better understand the potential benefits.

Manuscripts for the following studies are currently being prepared:

- EpiCog trial for cognitive impairments in SWS
- Protein expression SWS brain tissue
- Genetics of SWS
- Outcome in infants SWS presymptomatically treated

Future Drug Trial Development
The protocols are being written, and funding being sought, for three different drug trials for SWS.

EDUCATIONAL EFFORTS:

Dr. Comi worked with the **Vascular Birthmark Foundation** to publish a booklet on answers to common questions about SWS. Find the booklet on our website at KennedyKrieger.org/SturgeWeber and click on "News and Updates."

Dr. Comi will be participating in a Facebook Live session with the **Vascular Birthmark Foundation** on November 26, 2021. Check the foundation website for the recording at www.birthmark.org.

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Dr. Comi gave talks on SWS and participated in the Vascular Birthmark Foundation annual meeting and at the EMBO (**European Molecular Biology Organization)** International meeting. She has been invited to speak and participate in several meetings in the coming year.

Fourth SWS Family Symposium--slated for 2022 in Baltimore. Stay tuned for more information!

New Partnership with Real Estate Charities
Buy a Home, Sell a Home, Do Good.
Real Estate Charities, founded by Mitch Ribak, broker associate at eXp Realty, LLC and the grandfather of Lola, a Kennedy Krieger patient with Sturge-Weber syndrome, adds greater purpose to buying and selling a home. Half of all referral fees collected by the company will support Kennedy Krieger with an additional amount of funds directly supporting the Institute's Hunter Nelson Sturge-Weber Syndrome Center.

Whether you are looking to buy or sell your home, you will have access to a network of more than 48,000 agents. The process is free, personalized and has the added benefit of raising research funds for Sturge-Weber syndrome. It's a win-win for all! Check out the website KennedyKrieger.RealEstateCharities.com to learn more.

Mitch and Lola performing together in 2019.

We look forward to keeping you updated on our progress and thank you for your support of our efforts. If you would like information about research studies, please contact Dr. Comi at 443-923-9127 or via email at comi@kennedykrieger.org.