Hunter Nelson Sturge-Weber Center
Kennedy Krieger Institute

Sturge-Weber Syndrome Research Update 2020

RESEARCH STUDY SUMMARY:

Epidiolex Drug Trial
The second Epidiolex drug trial for cognitive impairments continues with all slots filled. This trial will evaluate pharmaceutical grade Epidiolex for cognitive and social issues, migraines and motor impairments and will run for the next year. The COVID-19 pandemic slowed us down a bit but we have resumed and the trial is entirely virtual! Please contact Dr. Comi if you'd like to learn more.

Sirolimus Drug Trial
Our Sirolimus trial data was recently accepted for publication in Pediatric Neurology (more details to follow soon). 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.

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. Mouse colonies with the GNAQ mutation have been established, and we have been imaging abnormal vascular structures and working on staining mouse brain tissue to understand the effects of the mutation. 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.

PAPER SUMMARY: From our group 2019-2020

Atypical Intracerebral Developmental Venous Anomalies in Sturge-Weber Syndrome: A Case Series and Review of Literature. Ped Neurol. 2020 Mar
This series of patients presents the issue of enlarged draining vessels which can have the appearance of arteriovenous malformations (AVMs) and how MRA and MRV sequences during an MRI of the brain can rule out AVM in SWS without the need for an invasive angiogram.

Suicide Screening in Sturge-Weber Syndrome: An Important Issue in Need of Further Study. Ped Neurol. 2020 Mar. This study analyzed the results of suicide screening for patients seen at our SWS Center, as compared to general neurology patients seen at Kennedy Krieger. The study found that patients with SWS were more likely to report suicidality than were general neurology patients. These results emphasize the importance of this issue for patients with SWS, the need to screen for suicidality and urges further study of mood disorders and suicidality in SWS.

Identification of a Mosaic Activating Mutation in GNA11 in Atypical Sturge-Weber Syndrome. J Invest Dermatol. 2020 Aug. About 90% of all SWS tissue samples in reported studies have the somatic mutation we discovered in 2013. We analyzed tissue samples and found another mutation associated with SWS: a somatic mutation in a gene called GNA11. GNA11 and GNAQ are similar in sequence and the proteins they code for have similar functions. This discovery adds to our understanding of the causes for SWS and provides further insights into the role of genetic testing in SWS.

Manuscripts for the following studies are being prepared:

- Medication in SWS
- Vitamins in SWS
- Pre-symptomatic treatment of SWS
- Protein expression SWS brain tissue
- Mouse Model of SWS

EDUCATIONAL EFFORTS:

Third Annual Family Symposium
This year the symposium was held virtually and was very successful; more than 80 participants registered for the webinar. Talks reviewed our recent publications; discussions on the first year after diagnosis; COVID-19 and school; our multidisciplinary clinic; mood disorders and Epilepsy; and fundraising.Next year we hope to be back in person combined with virtual access for participants.

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

Hunter Nelson Sturge-Weber Center
at Kennedy Krieger Institute

Please support our efforts!
KennedyKrieger.org/SWS