

# Research Update 2022

## RESEARCH STUDY SUMMARY

### Epidiolex Drug Trial

The second Epidiolex drug trial for cognitive impairments has been completed and the paper is in press. This trial evaluated pharmaceutical grade cannabidiol for cognitive and mood issues, migraines and motor impairments. Funding is being sought for follow up trials.

### Sirolimus Drug Trial

Our Sirolimus trial data was published in Pediatric Neurology (see paper summary) last year. This was the first targeted drug treatment trial for SWS, following our discovery of the causative somatic gene mutation in *GNAQ* in 2013. 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 multi-center follow-up trial and have submitted a grant application to the National Institutes of Health to fund this trial.

### 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 has been published (see paper summary) and additional tissue studies are underway. The goal of these studies has been to identify cells with the mutation and markers of progression in the tissue.

### 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 using them to develop new probes for use in tissue sections from subjects with SWS.

### 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. We now have a genetic mouse model with the SWS mutation in blood vessels of the brain, with which we are testing new probes and studying for new treatment targets. Look for this paper in the next year.

### Other Clinical Studies

We are currently analyzing data from prior Brain Vascular Malformation Consortium (BVMC) funded work with urine biomarkers and neuroimaging. We are also a site enrolling for the current BVMC studies. Additionally, we recently submitted a manuscript with our further research on the genetics of SWS. We anticipate that this recent research will guide future clinical and genetic evaluations. We continue to work on the planning, and funding, of a new presymptomatic treatment trial in infants with SWS.

## PAPER SUMMARY: From our group 2021-2022

**Study protocol: retrospectively mining multisite clinical data to presymptomatically predict seizure onset for individual patients with Sturge-Weber.** [BMJ Open](#). 2022 Feb. We aim to retrospectively mine clinical data for SWS at two national centres to develop presymptomatic biomarkers. We will retrospectively collect clinical, MRI and neurocognitive outcome data for patients with SWS who underwent brain MRI before 2 years of age at two national SWS care centres. Expert review of clinical records and MRI quality control will be used to refine the cohort. The merged multisite data will be used to develop algorithms for abnormality detection, lesion-symptom mapping to identify neural substrate and machine learning to predict individual outcomes (presence or absence of seizures) by 2 years of age. Presymptomatic treatment in 0-2 years and before seizure onset may delay or prevent the onset of seizures by 2 years of age, and thereby improve neurocognitive outcomes. The proposed work, if successful, will be one of the largest and most comprehensive multisite databases for the presymptomatic phase of this rare disease.

## PAPER SUMMARY CONT.

**Updates on Sturge-Weber Syndrome.** Stroke. 2022 Dec. Patients with SWS have impaired perfusion to the brain and are at high risk of venous stroke and stroke-like episodes, seizures, and both motor and cognitive difficulties. While the activating R183Q *GNAQ* somatic mutation is the most common somatic mutation underlying SWS, recent research also implicates that *GNA11* and *GNB2* somatic mutations are related to SWS. Recent retrospective studies suggest the use of low-dose aspirin and vitamin D in treatment for SWS and prospective drug trials have supported the usefulness of cannabidiol and Sirolimus. Presymptomatic treatment with low-dose aspirin and antiepileptic drugs shows promising results in delaying seizure onset in some patients. This review focuses on the latest progress in the field of research for Sturge-Weber syndrome and highlights directions for future research.

**Vitamin D and Neurological Status in Sturge-Weber Syndrome.** Journal of Vascular Anomalies. 2021 Dec. This study investigated the frequency of vitamin D deficiency and insufficiency, as well as the relationship between vitamin D levels and neurologic function in Sturge-Weber syndrome (SWS). Vitamin D deficiency and insufficiency are common in patients with SWS. Improvements in neurologic function may be seen with supplementation, especially in Black or African Americans as well as in severely affected patients, suggesting the utility of vitamin D as a therapeutic intervention. More research is needed to confirm and extend these findings.

**Phosphorylated-S6 Expression in Sturge-Weber Syndrome Brain Tissue.** Journal of Vascular Anomalies. 2022 Sept. We studied human brain tissue samples from SWS subjects and epilepsy controls. SWS brain tissue was more likely to have a protein (called p-S6) in the abnormal blood vessels, compared with epilepsy controls. This finding in SWS brain tissue implicates mTOR as a potential treatment target for Sturge-Weber Syndrome, and is consistent with the possible treatment with mTOR inhibitors. We recently published our pilot trial of an mTOR inhibitor called Sirolimus in SWS. Further drug trials with Sirolimus are needed and funding being sought to complete a multi-center trial.

## Future Drug Trial Development

Funding is being sought for three different drug trials for SWS.

**Manuscripts for the following studies are currently being prepared or in press:**

- EpiCog trial for cognitive impairments in SWS-in press
- Genetics of SWS
- Clinical data from neuroimaging biomarker study
- Longitudinal biomarker and neurologic study in SWS
- Mouse model of Sturge-Weber syndrome

## EDUCATIONAL EFFORTS:

Dr. Comi worked with the **Vascular Birthmark Foundation** and port-wine birthmark experts to define guidelines for treatment.

Dr. Comi participated in a Facebook Live session with the **Vascular Birthmark Foundation** on November 26, 2022. Check the foundation website for the recording (and prior sessions) at [www.birthmark.org](http://www.birthmark.org). Watch to see how the treatment and study of SWS has changed over time!



Dr. Comi gave talks on SWS and participated in the **Vascular Birthmark Foundation annual meeting** and a program for families in Europe. Her group has also given talks and presented posters at the **Child Neurology Society** and the **International Society for the Study of Vascular Anomalies** meetings in the past year.

The fourth **SWS Family Symposium**, co-hosted with Celebrate Hope Foundation and supported by the Vascular Birthmark Foundation, was a successful virtual meeting in September 2022 with excellent talks from glaucoma, epilepsy and brain surgery experts. Stay tuned for more information on the upcoming SWS Family Symposium in fall of 2023!



## EVENT HIGHLIGHTS FROM 2022

We'd like to share a few highlights from SWS supporters across the country.

### Calvin's Crusade 5K Walk/Run

The first annual Calvin's Crusade 5K Walk/Run for Sturge-Weber Syndrome Awareness was held May 28 in Pennsylvania. Exceeding all expectations, the event brought in more than \$31,000 for SWS research at Kennedy Krieger. Special thanks to the 200 participants, sponsors, volunteers and all who made this special event possible.



L to R: Katie Irvine, James, Calvin, Natalie and Eloise Torrance and Nanette and Bob Harford.

### Rooting for Rainey 5K Fun Run/Walk

The second annual Rooting for Rainey 5K Fun Run/Walk was held October 29 in Texas. The event had 375 participants and raised \$38,000 for SWS research at Kennedy Krieger. Over the past two years, this event has raised a total of \$78,000. Thank you to all who made this event such a success.



L to R: Knox, Ricky, Cindy and Rainey LaPrade at the second annual Rooting for Rainey.

### J. McLaughlin Holiday Fundraiser

The J. McLaughlin clothing store in Belleair, Florida hosted a holiday shopping event on December 17. Fifteen percent of the day's sales will benefit Sturge-Weber syndrome research at Kennedy Krieger. Special thanks to Michele Wanger for hosting this event.



J. McLaughlin

holiday shopping  
and good cheer



### Lizzie and The Yellow Line

Lizzie Click, a long-time patient of Dr. Comi's, donated 40 holiday gift bags she created for Kennedy Krieger inpatients. Included in the bags are DIY art kits from The Yellow Line Art Studio where Lizzie works with owner/artist Carrie Patterson. Lizzie has been involved with the studio for the past 14 years and most recently she's taken on the role of assisting Carrie in her community arts classes at St. Mary's College. For more information on the studio and art kits, visit [theyellowline.co](http://theyellowline.co).



L to R: Carrie Patterson, owner of The Yellow Line Art Company and Lizzie Click prepare holiday bags for patients at Kennedy Krieger.

If you would like to have your event featured or if you are interested in hosting your own event to raise funds for Sturge-Weber syndrome research, please contact Jen Doyle at Kennedy Krieger Institute via email at [DoyleJ@KennedyKrieger.org](mailto:DoyleJ@KennedyKrieger.org) or 443-923-4324.



Kennedy Krieger Institute

*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](mailto:comi@kennedykrieger.org).

*To make a donation, visit [KennedyKrieger.org/SWS](http://KennedyKrieger.org/SWS)*



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