



The Sturge-Weber Foundation
12345 Jones Road, Suite 125
Houston, TX 77070

 **believe**
you. us. progress.



A PUBLICATION OF THE STURGE-WEBER FOUNDATION

Branching Out

DECEMBER | JANUARY



973.895.4445 | www.sturge-weber.org | swf@sturge-weber.org



The Sturge-Weber Foundation MAGAZINE

CONTACT INFORMATION

12345 Jones Road, Suite 125
Houston, TX 77070
973-895-4445
swf@sturge-weber.org
www.sturge-weber.org

DESIGN/EDITOR

Susan Finnell

EDITORIAL CONTRIBUTIONS

Karen L. Ball, SWF CEO
Anne Howard, SWF Writer
Susan Finnell, Marketing/Home Office
Julia Terrell, Community Relations Director

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Oon Tian Tan, MD

The SWF is a member of the Brain Vascular Malformation Consortium (BVMC), American Brain Coalition (ABC), The Coalition of Skin Diseases (CSD), and the Association for Research in Vision and Ophthalmology (ARVO).

Branching Out

December | January

On the Cover: Laura and David Powers with daughter Kaylee Embrey

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Port Wine Birthmarks (PWB) on the skin are developmental abnormalities in blood vessel formation (capillary malformations) that are more extensive and darker than the pink capillary birthmarks often seen at the nape of a baby's neck. Sturge-Weber syndrome (SWS) is a rare congenital condition usually consisting of a facial port wine birthmark, glaucoma, and seizures, (although not all of these symptoms may be exhibited).

SWF POLICY STATEMENT:

In implementing the purpose of The Sturge-Weber Foundation to improve the quality of life for individuals

with SWS and their families, the Foundation will act as a clearinghouse of information, provide emotional support and facilitate research on PWB and SWS.

The Foundation will seek information regarding management and treatment techniques and suggestions concerning education and emotional support and will facilitate the dissemination of appropriate information.

If, in facilitating research on PWB, SWS and KT, the Foundation provides financial or other support to a particular research project, the Foundation will base its decision upon need, the Foundation's financial resources and medical advice.

INVOLVEMENT = PROGRESS

That's You and Us! \$700,000



- OVER 2,000 (patient) x 4(family) impacted by SWS & Birthmarks
- 275 invested Clinicians & Scientists



Global Research Requests from Germany, United Kingdom, Italy, North Carolina, Texas, Massachusetts

YOUR INVOLVEMENT

- 2 donated tissue
- 3200 individual donors
- 68 volunteers at SWF events



2018-2019 Requests

- 16% increase in assistance
- 25% increase in research grants

TISSUE DONATIONS

PATIENT ADVISORY COUNCIL

DONATIONS

RESEARCH PARTICIPANTS

INVOLVEMENT = FUTURE

TOP NEEDS OF FAMILIES & RESEARCHERS



Tissue Biobank \$25K	Family Meetings \$75K	Knowledge Transfers \$100K
Fellowships \$150K	SWS Registry \$20K	Calcification Study \$50K
Seed Grants \$100K	Travel Grants \$30K	
Animal Research Consortium \$50K	Delphi Glaucoma Advocacy \$20K	



THE STURGE-WEBER FOUNDATION
12345 JONES ROAD, SUITE 125
HOUSTON, TEXAS 77070

www.sturge-weber.org | swf@sturge-weber.org





CHERISH EACH SEASON OF YOUR YEAR AND LIFE!

Karen L. Ball
Founder and CEO



The approaching holiday season brings delight for many and painful reminders for others. A Birthmark or Sturge-Weber syndrome diagnosis can hasten those feelings either way. The diagnosis has brought us together for a reason, a season or a lifetime. Some of you will come and go like the ebb and flow of the seasons others stay with us for a lifetime. It's been so heartwarming to watch babies with SWS grow up into young adults! There are some people who battle SWS from birth and others it evolves over a lifetime. The best gifts I've known other than my family are all of you who have shared your lives, stories of sorrow or triumph and you have made all my seasons much richer for it!

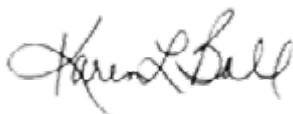
The conference this summer was just sooo fun! I look forward to seeing more of y'all at our regional forums in conjunction with our national Clinical Care Network. The SWF will host a leadership meeting this Spring of all the various countries who have SWS organizations ever expanding our collective ability to create impact and Progress. Together we are enriching our lives and uplifting others along the way!

Your commitment to raise critical funding online, through **Amazon Smile**, or by holding fundraising events in your local neighborhood is the lifeblood of hope that binds all of us through the seasons of our lives. Those donations gave us funding for new clinical and basic research goals and grant awards that hint at another season for promise and celebration. The Falmouth road race gave staff and the Board some breathing room to not have to do all the heavy financial lifting and to generate new funding relationships while supporting patient engagement and research. The funding for Lisa's Fellowship enabled a new crop of researchers to gain a foothold on their scientific career and increase the pace of discovery for SWS and Birthmarks. The NIH funding gave us the GNAQ gene mutation! The BVMC collaboration was a game changer but there is much more needed to be done! The new BVMC award will bring all the key pieces together so researchers have a comprehensive profile of how your SWS is expressed and treated.

The SWF is your "Roots to a Cure"! The comprehensive patient engagement and research program has been the solid bedrock of knowledge for a lifetime of clinical and basic research that have improved your quality of life and care. In this issue, the "Roots to A Cure" supplement highlights progress on 2018 grants awarded and announces the latest grants for 2019-20. We welcome your input and participation! Look forward to hearing from you!

I am excited for the New Year! Thank you to those of you who take time out of your day to say thank you or send encouraging notes...they are cherished! I wish y'all a year filled with joy which will lead to peace and for good health!

With faith hope and love,





just
believe
you. **us.** progress.

*Wishing you a happy holiday season!
Thank you for your support and helping us make progress!*

The SWF Board of Directors and Staff





2018-2019 BY THE NUMBERS

DIRECT MEMBER SUPPORT

7782 Registered Members

4892 registered people with SWS/PWB

3060 registered adults with SWS/PWB

908 registered Klippel-Trenaunay Cases

SOCIAL MEDIA MEMBERS

6869

(Facebook, Twitter, Instagram, Inspire)

TOTAL PATIENT ENGAGEMENT GATHERINGS

11

CLINICAL CARE NETWORK

27 National Centers

STRATEGIC RESEARCH

- GNAQ discovery 2013
- 2 Sponsored Meetings (SWFIRN)
- \$25K invested in Registry
- 4 medical consensus articles
- 2 SWS Research Symposiums
Sponsored (July and September 2019)
- 1 Biorepository Launched

ON THE ROAD TO GROWING GOLDEN



“We need to think forward on how to prepare for his years ahead as he leaves the school system and becomes an adult. We are always thinking forward - of how to support him today and in the future, not only as he ages but as we do too.”

Linda Cohen

Pictured: Marco celebrating his 14th birthday.

ON THE ROAD TO GROWING GOLDEN



My son, Marco, is 14 years old and was born with bilateral Sturge-Weber Syndrome. He is a music-loving boy whose laughter and smiles are contagious. He is also incredibly resilient. He has recovered from so many difficult medical issues, including twenty-eight eye surgeries, a retinal detachment that we thought for months would not repair itself even after surgery, and seizures that almost killed him. But Marco does not walk or talk (nor has he learned to use an alternative means of communication). He is starting to stand for brief periods (after regaining strength from a prolonged ICU stay last year) and recently learned to pedal an adaptive bike (thanks to the amazing therapists at his school) but he is fully dependent on all of us for his care.

We need to think forward on how to prepare for his years ahead as he leaves the school system and becomes an adult. We are always thinking forward - of how to support him today and in the future, not only as he ages but as we do too.

Currently, we are preparing for the challenges ahead by creating an adaptive home environment and establishing the support base that we will need as he grows bigger and older. Through the school's equipment clinic, we have requested a Hoyer lift, a special bed (www.sleepsafebed.com) and a toileting/showering system. We are working to renovate what will be Marco's area with a wheelchair accessible bathroom. In NY state, the

individuals enrolled in the Home and Community Based Services waiver (as part of the Office for People with Developmental Disabilities) can receive up to \$60,000 in environmental modifications during a five-year period. They also used to provide environmental modifications for vehicles (ramps and lifts). I advocated for an increase in homecare hours (as it gets harder to take care of him alone as I age) and have taken steps to enroll him in Self Direction, which allows individuals more control over funding

for certain services to buy their preferred mix of programs. To help Marco enroll in Self-Direction (<https://opwdd.ny.gov/self-direction>), I went to a training in Willowbrook, on Staten Island. The training was only a few days before I read Ann Nehrbauser's essay in the June/July 2019 issue of Branching Out. When I first read her essay, I was full of mixed emotions –

sadness that there ever was a place like Willowbrook, happiness to hear that Stephen had overcome all the difficulties surrounded by the support of his family, and gratefulness for people like Ann and Stephen who have paved the way for our kids to now have a range of services to help them live at home or live independently with the supports they need.

The Willowbrook I visited has been repurposed and reclaimed and it was there where I learned more about the history of Willowbrook and the advocates who paved the way for a program like Self Direction to come about. I am grateful for all the services

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ON THE ROAD TO GROWING GOLDEN



that now exist. The system may not be perfect, and it may take a lot of headaches of paperwork and unreturned calls and perhaps even a fair hearing to get the services lined up, but they are there for Marco.

The budget for Self-Direction will almost double for Marco once he leaves the school system and having it already set up will allow us to have a smooth transition to the day habilitation programs or other post-school services. Signing up right now allows us to take advantage of the program's flexibility and build the experience and a deep understanding of the system for the future. While I have been working on these actions, I have also continued my informal research on the next steps, such as guardianship.

But how do I “research” all the options for Marco? Where is the guide that explains the complexity of the programs and the numerous agencies involved for all the different services, goods, and care that Marco needs?

Unfortunately, as most of you probably know, no such guide exists. When Marco was younger, I naively searched for guides with detailed information for services and in some cases, couldn't even find a description! There are probably many reasons why it is hard to come by the information easily – each individual is unique with different needs and preferences (for example, some individuals may want and be able to live independently whereas we are preparing for Marco to live with us); there is great variation in the range of programs in different states and cities; the information that is received may be dependent on the knowledge and experience of the social workers or care managers that are assigned to the

individual; and last but not least, because the programs seem to be in continuous flux with changing rules and regulations.

Due to the difficulties in accessing clear information, I have learned that the task lies in my hands to research the programs. Although Google searches and talking to social workers or attending information sessions may lead to some information and ideas, I have initially learned about the options for Marco from fellow parents or a knowledgeable therapist. I could make a long list of everything I have learned from other individuals in Marco's community over the years. Some examples that come to mind are that I could apply for a special handicap tag for city street parking even though Marco was still quite young, that there were special car seats for big kids and that these were covered by insurance, that there was a program that subsidized modifications for vehicles (e.g. ramps and lifts in a van), that I could call 311 to have a handicap taxi come to our door (this was in the early years of wheelchair accessible





taxi in NYC), and that there were flotation swimsuits and pool diapers for special needs big kids (www.mypoolpal.com). Most of the times I have been lucky to come by these pieces of information in a timely way and sometimes- unfortunately – I stumbled on the helpful information after struggling for months on one issue or another.

I will never forget one of the first moments that I realized how haphazard the information flows and how lucky I was to have a knowledgeable person guiding me! When Marco was only one and a half years old, Marco's wonderful early intervention physical therapist, Linda Montas, suggested that I start requesting a wheelchair for him. Marco still fit into a small stroller and special education preschool seemed far away, so I did not quite understand the need. But I followed through with her advice and started the process for the wheelchair. The first hurdle was to find an equipment provider that accepted our insurance. For nine months (and I am not exaggerating!), the insurance company sent me lists of surgical supply stores that were in network but none of them were a vendor for pediatric wheelchairs. But finally, after much perseverance, I got the right person on the phone who provided me with the right type of vendor so I could proceed with the order. The wheelchair arrived just a couple of months before Marco started preschool and the wheelchair was essential for him because it was required for transportation on the school bus.

If it weren't for that knowledgeable therapist (who knew it took a long time to obtain the chair), I would have never thought of requesting a wheelchair so early on and his transition to preschool would have been difficult. From that experience, I quickly learned how important it was to listen to advice, explore options and talk to others.

I also have made a point of sharing my knowledge with those around me. There is one moment that I think worth sharing since it also highlights the haphazardness of the information flow and how important it is to reach out and share with other parents. One day when Marco was about 9 years old, I was chatting with a fellow parent at my son's school about an agency that managed our kid's cases. I shared that Marco had been receiving diapers and Chuxs monthly for a few years because the care manager at the agency had helped set him up. She was astonished that she had never been told this was an option. We were even more surprised when we discovered we had the same person managing our cases in the same agency, yet my friend's daughter had never been offered the diapers even though she was equally eligible. It was a stark example of how there can be variation in the information each participant is provided even within the same program!

I guess I do not have a perfectly curated list of steps to take and programs to access to prepare for the adult years, but I am hopeful that my experiences are a reminder to always keep on searching and exploring. I sometimes feel exhausted by all the work required to look up and set up the services and there are moments when I feel I cannot deal with one more agency or more paperwork. In these moments, I slow down my searches and take a good break.

I guess, in the end, the best piece of advice that I can give is to keep your ears and eyes open for information on programs and services, go to information sessions (even when you think you have heard it all because there just may be something new) and talk to others with similar needs (whether they have SWS or not) in your local community. This way, when you have the energy to work on a plan, you have the information you need to move forward.



WHAT TO DO: OUT THE DOOR TO THE EMERGENCY ROOM

It is reasonable and prudent to worry about the welfare of our spouses, elder parents and adult children who have SWS especially when you must make a run to the Emergency Room or call the local First Aid Squad because of a sudden fall or accident. You always have to be prepared to face emergency medical situations that have no direct connection to SWS, but you also have to be vigilant about drug and treatment interactions if your loved one is taking seizure meds.



With the widespread concern about the opioid epidemic and the over-use of prescription pain medications, families need some guidelines on how to be reasonable advocates in an emergency situation.

Like any other adult, people with SWS have varying tolerance to pain. Some people have taken only the minimum dose pain relief med all their lives. Some need more in different circumstances.

How do you know what hospital administered pain meds are being used when, for instance, your spouse is in the ER with a cracked rib due to a fall from a ladder?

What are the seizure meds most SWS patients use and what pain killer meds should or should not be used?

Out the door to the ER

A folder in your car or at home should be kept up to date with the following information about the person with SWS. Keep a link or download on your phone for portable access: name, date of birth, diagnosis (SWS, facial port wine birthmark, seizures), treating doctors (your neurologist, primary care physician, any other, including phone numbers), what hospitals do you normally visit, access info to any scans or recent lab tests, any prosthetic devices (eye), medications currently taken – how often are they taken – when was the last dose taken, medications to avoid.

A medical ID bracelet or necklace that all EMT and ER staff look for which give basic diagnosis is an alternative. There are many kinds you can pick from. Your local pharmacy or primary doctor might be able to provide information. The Internet has many items to choose from. These are different from the Medic Alert devices which are more elaborate and connect directly to emergency services when activated.



You also have to be prepared to face emergency medical situations that have no direct connection to SWS, but you also have to be vigilant about drug and treatment interactions if your loved one is taking seizure meds. With the widespread concern about the opioid epidemic and the fear of over-use of prescription pain medications, families need some guidelines on how to be reasonable advocates in an emergency situation. While you have to be a concerned advocate for your loved one, you also have to respect the expertise and experience of the medical staff. You can assist with proper information.

Like any other adult, people with SWS have varying tolerance to pain. Some people have taken only the minimum dose OTC pain relief medication all their lives. Some need more in different circumstances. How do you know what hospital administered pain meds are being used when, for instance, your spouse is in the ER with a cracked rib due to a fall from a ladder? Becoming familiar with the names of common pain meds is essential so you can alert the ER staff and not have to rely on “we gave her something for pain”.

What are the pain meds that should or should not be used for adults who take seizure medication? Always consult with your neurologist or primary doctor to keep this information current.

Lindsay Higson, MD of Thomas Jefferson University in Philadelphia, an SWF consultant, tells us: *“I worry much more about the effects of seizure medications on each other, birth control, antibiotics, and medication for anxiety or depression.*

In regard to pain medications, in most cases normal dosing of most opioids such as morphine, oxycodone, Dilaudid are fine with patients with epilepsy as long as they take their seizure medications. There is some concern with Fentanyl, but that is rarely given outside of a surgery or ICU setting. The combination of opioids and seizure meds can lead to increased sleepiness.

Non-opioid medications such as Tylenol and NSAIDs are considered safe in my book. Toradol is an IV NSAID analgesic that won't cause sedation. Patients can ask for topical treatments with lidocaine patches. (NSAIDs are non-steroidal anti-inflammatory drugs such as aspirin, ibuprofen, and naproxen – these are the chemical names of several OTC (over-the counter) medications. Ask your pharmacist if you are not sure).

Warning: Benadryl is also known to affect seizure threshold which is in a.m. and p.m. formulations of common OTC medications such as Nyquil, Advil PM, etc. SWS patients should be warned of that.

I found some information via the Epilepsy foundation:
<https://www.epilepsy.com/learn/professionals/resource-library/tables/drugs-may-lower-seizure-threshold>
<https://www.epilepsy.com/learn/professionals/diagnosis-treatment/procedures-epilepsy-patients/non-opioid-analgesics>



A large part of the Sturge-Weber Foundation's responsibility to patients and families is to stay current on new medical treatments, government policy and regulations, pharmaceuticals and research related to SWS and other PWB conditions. To do this, SWF staff gets on the road and travels to various conferences and meetings to be educated and collaborate with others in industries that are directly aligned with patient needs. Because of your continued support and BELIEF in our work, we can continue to attend events such as the following in update.



2019 AAD ANNUAL LEGISLATIVE CONFERENCE

On September 7, the Sturge-Weber Foundation, together with the Coalition of Skin Diseases and the American Academy of Dermatology, went to Washington DC. for its annual Legislative Conference. Brian Fisher, Julia Terrell, and Thomas and Molly Speer represented SWF. We learned a great deal about advocacy and were able to use those skills to work. Thank you Thomas and Molly, for doing a great job on your first trip and for this great report on your trip!

From Thomas and Molly Speer:

We are so grateful for the experience and new adventures that the Sturge-Weber Foundation are sending us on. We never wanted to end up where we are today, but life happens and it led us to an AMAZING group of people with the Sturge Weber Foundation. In September we were blessed with the offer to travel to Washington DC to advocate for our daughter; the Sturge-Weber Foundation, and every other patient affected by skin diseases.

We met people from all over the country and learned about many rare diseases that we had no idea existed (Much like Sturge-Weber Syndrome). The first day we were in DC we met with the AAD to learn about what we would be doing the next couple of days. The next day was very important so we knew how to advocate as well as what we were advocating for! The Third day we went to Capital Hill. Which was great to experience as we had never been to Washington DC let alone be talking to our legislators to try to get them to pass something that would be helpful to us and our Sturge-Weber community.



ON THE ROAD AGAIN | SWF TRIP UPDATES



The three bills we were advocating for were:

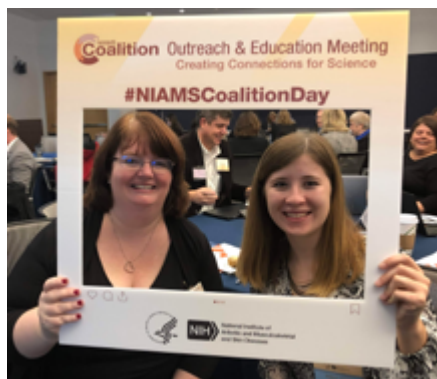
- Strengthen Pharmaceutical access and affordability
- Ensure a strong and sustainable Medicare
- Promote Skin Cancer Prevention and Access to Sunscreen

The one that we spoke on the most is Affordable and access to pharmaceuticals. Overall, we learned so much over the few days we were in Washington DC. We learned that Advocating is difficult to do but very worth it and rewarding!

Again, we are so thankful for the Sturge-Weber Foundation and giving us this opportunity to grow ourselves as people but to help the Sturge-Weber Foundation in some way and give back to them!

NIAMS 2019 OUTREACH & EDUCATION MEETING

The SWF went to the National Institute of Health on October 16, for the 2019 Outreach and Education Meeting by the National Institute of Arthritis, Musculoskeletal and Skin Diseases Coalition. The day consisted of hearing from the Acting Director, Dr. Robert Carter, who spoke about the state of the institute and also funding opportunities. We also learned how to Amplify the Patient's Voice and Integrative Approaches to Pain Management.



There were breakouts on Collaborations to Foster Innovative Research and Training, as well as an educational information on clinical trials. One the most enjoyable parts of the meeting was the Unconference Session during lunch. Earlier in the day we picked topics to discuss during this session and were able to present our findings. It was a great networking opportunity.

It was a great learning experience to hear from so many talented and knowledgeable people at NIH. Who knows, you may even be at an Unconference Session at the next SWF International Family Conference where YOU get to pick the topic of discussion!





2019 ROOTS TO RESEARCH REPORT

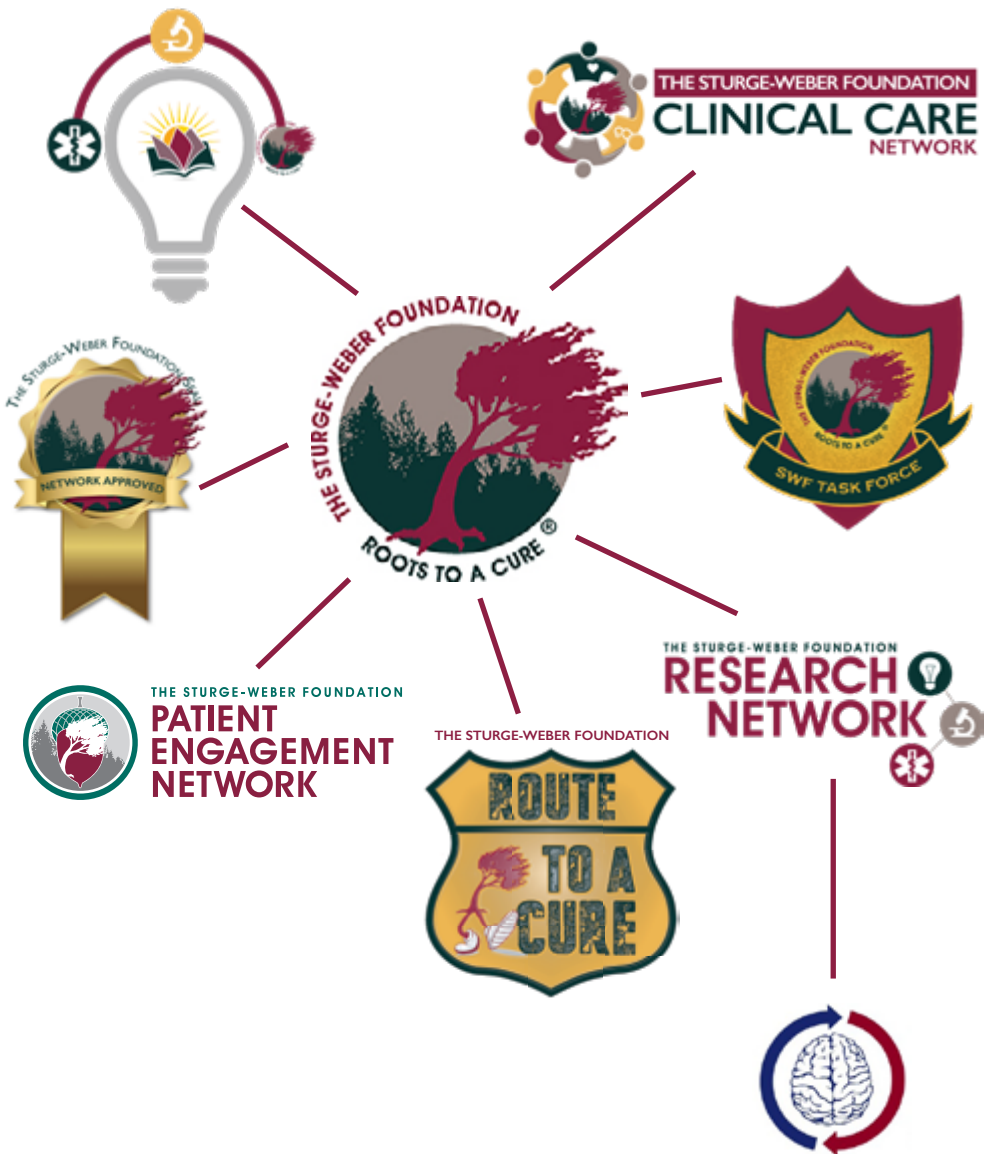
The clinical care of a Sturge-Weber syndrome patient involves many specialties throughout their lifetime. The Sturge-Weber Foundation's strategic plan for clinical care involves diverse specialists to address any medical and psychosocial issues which will arise. These specialists work in collaboration with each other and across specialties to gain new knowledge on best treatment practices, unusual case reports etc. Dr. Jeff Loeb, Chief Clinical Strategist, is in charge of guiding the clinical care and research portion of the SWF Research Program. Dr. Jonathan Pevsner, Chief Scientific Officer, directs the overall SWF research program and leads the basic research endeavors. The following are a few highlights that your generous donation's create for lasting patient and family impact.



A WAR IS WON ON MANY FRONTS!

*Comprehensive Investigative Clinical and Basic Research
at the Sturge-Weber Foundation*

The SWF has always believed in a comprehensive investigative clinical and basic research approach to increase our understanding of SWS and diversity of funding for research. As you can see in the following graphic, this approach has worked successfully and encourages collaboration across specialties and industries.





Sturge-Weber Foundation International Research Network (SWFIRN)



The SWFIRN meeting in Delaware was attended by researchers comprising the international dedicated SWS research network. The meeting brings scientists together to discuss their research progress and to generate new collaborations and goals. Invited guest speakers this year were Dr. Catherine van Raamsdonk (University of British Columbia), who identified **GNAQ** as an oncogene that drives uveal melanoma and who discussed the role of **GNAQ** in affecting signaling pathways. Dr. Michael Onken (Washington University in St. Louis) discussed **GNAQ** signaling pathways and the roles of peptide inhibitors of **GNAQ**. Dr. Nathan Lawson (University of Massachusetts Medical School) described the use of zebrafish as a model system to study SWS. Meeting participants heard many other interesting and important talks, and focused on community-wide goals such as biobanking and developing animal models.

Clinical Care Network (CCN)



THE STURGE-WEBER FOUNDATION
**CLINICAL CARE
NETWORK**

There were 14 CCN's represented at the annual meeting in Chicago, IL September 19-20, 2019. Karen Ball and Brian Fisher began the meeting by talking about grants for researchers. Dr. Jeffrey Loeb gave a presentation from multi specialties with treatment consensus issues not just in pediatrics but through transition into adulthood and in adulthood. Breakouts discussed what are successes and challenges and what are the next steps. The groups then reconvened and proposed goals for the 2019-2020 fiscal year. Several new collaborations on publications began.

Jo Anne Nakagawa, Director, Clinical Projects and TSC Clinic Liaison, gave a presentation on clinical trials. The attendees went on to discuss what clinical trials we should work on next. We finished the conference with Dr. Miller Shivers discussing the importance of mental health early in life and the need for neuropsychology for symptoms like memory loss, difficulty paying attention, ADHD treatments and risk-benefit analysis. The mental team can even help in a patient's educational plan as well as transition of care.

On Friday, the group also took a tour of the Cranial Facial Department at UIC with state-of-the-art 3D imaging and printing program, maxillofacial program and much more. Many thanks to Dr. Loeb, Terenda and their great team at UIC in hosting our successful CCN meeting.

Follow up to the CCN meeting was the formation of a clinical advisory committee needed to evaluate potential clinical trials that the Foundation will support and a subgroup interested in improving transition of care from pediatric to adulthood.



Brain Vascular Malformation Consortium

The BVMC is a Rare Disease Clinical Research Network (RDCRN) funded grant from the National Institutes of Health (NIH). Three brain vascular malformation related diseases work separately on their respective research goals and share information with each other throughout the year. Dr. Loeb was unanimously approved as the lead investigator for our round three of funding. As a M.D. and Ph.D, Dr. Loeb has the skill set needed to direct a new phase of SWS research for Project 2-Sturge-Weber syndrome. The BVMC was awarded this third round of funding with an outstanding score from the NIH review process. We are excited that project 2 will focus on developing a clinical longitudinal database that will enable us to understand the natural history of SWS from kids to adults as well as the underlying changes in the brain that can lead to seizure, headaches, and stroke-like episodes. This is critical as this information will inform us of what treatments work and what treatments do not. It will also suggest new lines of preventative treatments that could prevent SWS from progressing as patients get older.



Biorepository

Thuy Phung, MD, Ph.D., Director of Pathology Strategies, is working on the submission of Internal Review Board (IRB) approval to launch the Sturge-Weber Syndrome Virtual Biobank, which will establish standard protocols for the collection, storage and distribution of tissue samples for research. The SWF needs your participation in tissue and blood contribution for research into genetic and specialty specific investigations which will impact your dail life and care.

SWF RESEARCH GRANTS 2019-2020

Research funding is a lifeline for patients battling SWS every day. The SWF continually receives questions around the world asking for answers to why a certain issue has developed or what types of medication is needed. The Strategic Research Plan addresses many areas of research needed to give a complete snapshot which will lead researchers in a united and collaborative front to answer your questions and theirs! This year the SWF Research program is funding a record number of research grants and a record **\$101,245 in research grant funding! Thank YOU!**



IMAGE OF GNAQ



Lisa's Research Grant went to two researchers



\$25,000 Sebastien Gauvrit, Ph.D.

"Investigating Sturge-Weber syndrome vascular defects using zebra fish"

Max Planck Institute for Heart and Lung Research/Department of Developmental Genetics

Dr. Gauvrit proposes to investigate how somatic mutations in GNAQ, such as those that occur in SWS, lead to vascular defects. To do this he will develop a zebrafish model, study how vascular defects occur, and then search for new drugs that may be used to treat SWS by performing a screen of many small molecules.



\$19,245 Lisa Arkin, M.D.

"Towards a precision-based approach to patients with port wine birthmarks"

University of Wisconsin School of Medicine & Public Health/Department of Dermatology

Dr. Arkin proposes to enroll a group of patients and deeply characterize the phenotype with methods such as colorimetric and angiographic imaging. She will study the genotype (i.e. identify **GNAQ** or other DNA mutations) and the gene expression changes. This may allow her to identify novel downstream targets. Ultimately these targets may provide avenues for therapeutic intervention.

Six Catalyst Awards were provided



\$25,000 Sarah E. Wetzel-Strong, Ph.D.

"Characterizing lesion development in a mouse model of Sturge-Weber syndrome"

Duke University School of Medicine/Department of Human Genetics

Dr. Wetzel-Strong will develop and characterize a mouse model of SWS. The proposed studies will allow us to understand the developmental conditions that influence port-wine birthmark formation and the influence of severity and progression of the disease.



\$7,000 Nathan D. Lawson, PhD

UMass Medical School

Developing a Sturge-Weber syndrome Zebrafish model



\$5,000 Naiem Issa, Ph.D.

University of Miami Miller School of Medicine

GNAQ inhibitor compound study

2019 ROOTS TO RESEARCH



\$5,000 Jonathan Pevsner, Ph.D.
Pevsner Lab at Kennedy Krieger Institute
SWS registry and SWS research



\$5,000 Sara Sabeti
University of California, Irvine
SWS Consensus paper



\$10,000 Thuy Phung, MD, Ph.D.
Baylor College of Medicine
Bio-repository seed funding

LURIE'S EDUCATION DAY CONFERENCE CHICAGO, IL | OCTOBER 5, 2019

On October 5, 2019, Dr. Sarah Chamlin Kiolbasa, RN and their team held their 2nd Education Conference at Ann & Robert Lurie Children's Hospital of Chicago, Clinical Care Network of the SWF. There were 28 attendees including our very own Dr. Jeffrey Loeb, who spoke about transitioning to adulthood.



Thank you Dr. Chamlin, Carolyn, and the entire team for a job well done! Thank you for taking the initiative to keep our patients well informed!

Thank you, Dr. Loeb, for speaking about the transition to adulthood.



To the patients and caregivers who attended, please let us hear about your experience by emailing us at jterrell@sturge-weber.org.



SWF CLINICAL STUDIES AND TRIALS

Calling all participants! It's an amazing time for those living with Sturge-Weber syndrome (SWS) and Port Wine Birthmarks (PWB). The hope created through research discoveries and clinical trials has never been greater!

The Sturge-Weber Foundation (SWF) will be posting and sharing a variety of blogs, documents and shared wisdom to help you better understand your rights if you choose to participate in research and what benefits and risk you can expect. The following are just a few points to ponder and remember as you ascertain if you wish to participate in any upcoming investigations.



A few terms you will need to be aware of and understand prior to participation:

- **Informed Consent -Institutional Review Board (IRB) -Protocol -Subject Recruitment/Retention**
- **Ethics -Patient Compensation -Physician payment -Vulnerable Populations -Pharmaceutical Company Sponsored -Investigator Led. These are very important documents to read and sign.**

The role of the SWF Clinical Trials Committee is to review applications for study design, patient protection (physical and financial), and validity of a hypothesis to mention a few points. The Committee reviews applications which request patient participation and some applications which request information on natural history data. The Committee will also when requested comment on other studies and trials that have synergies to SWS, PWS, Glaucoma etc.

It is our belief that having this Committee review and comment on studies which come before the committee (and also ones we know about) is a valuable tool for you to make an informed decision. Ultimately, living with a SWS diagnosis is a lifelong matter and weighing your participation in a trial is an individual decision.

For some people, if they have to pay out of pocket for their participation it is not an issue because money doesn't matter but for others if an investigator led study



requires you to pay costs which a pharma company only supplies the drug or compound to be tested it will preclude their participation. Other times a pharma company will cover travel, lodging etc.

Look to the Clinical Trials Advisory Committee to put the “Good Housekeeping Seal of Approval” on current and future trials.

UNDERSTANDING CLINICAL RESEARCH

Clinical research is a lengthy and costly process. Subject recruitment and retention is an essential step to help lowering the cost and the length of clinical trials. Good quality research is crucial for determining the clinical and cost effectiveness of health care systems, at the same time recruitment of sufficient participants is a cornerstone for good quality research that tests hypotheses with confidence and minimizes bias.

This research should also address some ethical concerns and considerations related to recruiting human subjects in clinical research. Recruitment and retention of research subjects is crucial for medical advancement and providing data that contribute in directing practice and policy.

Informed consent is a critical element in the subject recruitment and enrollment phase of the trial and it is a crucial step for conducting an ethical research. Understanding the concept of vulnerable subjects is another area clinical research personnel need to focus on and understand.

Human subjects in clinical trials

Good Clinical Practice (GCP) is the international guideline to ensure that clinical trials are designed, conducted, implemented, monitored, audited, recorded, analyzed, and reported scientifically and ethically. It also aims to protect human subject rights, integrity, and confidentiality.

According to the ICH-GCP guidelines all clinical trials should be conducted in compliance with ethical standards, clear scientific proof that benefits outweigh risks; and a clear well-documented protocol is required as well as obtaining an informed consent and affirming confidentiality.

Informed consent process

The process of informed consent is tailored to inform the subject of rights, risks, and benefits when participating in a clinical trial. Informed consent is an essential element for conducting an ethical research that involves human subjects. The process of informed consent is crucial in achieving these principles. The informed consent process should also involve the verbal discussion with the possible subject along with the paper document. The Principal Investigator is accountable to explain the informed consent and determine the subject or their legal guardian has understood the information and any potential financial obligations clearly and given his/her voluntary approval for participating in a particular trial.

2019 ROOTS TO RESEARCH



When obtaining the informed consent from the subject or their legal guardian, the possibility of coercion or undue influence must be minimized. The aim, the expected length of the study, and all required procedures the subject will go through should be stated clearly in the ICD. In addition, ICD should describe the risks (medical, physical, financial), the benefits of the research for subjects or others, other treatment options, and confidentiality of subjects' data.

In research that may lead to minimal risk for future subjects, regulatory bodies acquire explanation of whether medical care or compensation will be provided in case of injury. Beside their right of free participation in research, subjects have the right to know that they are free to withdraw from the trial at any given point. Any protocol or advertisement should not promise providing free treatment or claim the safety or effectiveness of the investigational or experimental drug, device, or biologic.



Institutional review board (IRB) is responsible to identify the degree of risk in a clinical trial. Before study approval, IRB must determine the risks and benefits for a child subject in a research study that involves children and to ensure its compliance with regulatory guidelines. Whenever indicated, the IRB must assess the potential risk/benefit and decide the importance of the presence of a legal guardian and the assent (the child agreement to participate in the study) of the child accordingly.

Consent can be valid when it includes the understanding of voluntary participation, purpose of the research, financial and physical risk and benefit ratio, and the procedures that may be required throughout the study. A patient may like to take higher risk to get better benefit, for example, taking part in an innovative promising therapy. Conversely, an end stage patient may wish to participate in research for the sake of benefiting others or future generations.

Subject recruitment and retention

Recruitment refers to the process of selection— from notification of the study to the enrolment of participants. It starts with communication between the researcher and the potential participants and aims to recruit appropriate participants who are representative of the target population. Many researchers have highlighted the issue of insufficient recruitment. The process of keeping subjects in the study is known as retention.



Recruitment and retention of research subjects is crucial for the progress of medical advancement and to provide data that help in guiding practice and policy. Furthermore, poor recruitment consumes the resources, increases the cost, and may lead to moving research outside United States.

Payment for human subjects

In the United States, payment for human subjects is a deep-rooted and a well-known practice that has been reported for more than 100 years ago. The practice of paying subjects continues to be an issue. Some consider paying subjects as coercion where others believe it is an essential method for a successful recruitment process; others see payment as fair and appropriate, especially for healthy subjects.



Some argue that money may impair judgment or jeopardize voluntary decision making. However, making decisions is usually a multifactorial and complicated process and it is rarely based only on money, as I have mentioned earlier people may participate in clinical research for many different reasons other than money. Frequently, subjects are being offered incentives to encourage their participation in clinical research. However, this practice usually raises ethical considerations and concerns. For instance, undue inducement, bias, and clinical research exploitation stay on the top of these ethical concerns. The reasons behind paying subjects include enhancing recruitment process and to compensate subjects for their time, effort, and travel. Studies have shown that offer of financial incentives is the main driving force that encourages individuals to participate in clinical research. Gaining access to medical treatment or contributing to the advancement of medical knowledge may encourage subjects to participate in clinical research.

Conducting an ethical research requires a fair distribution of benefits and risks. So, research subjects deserve to get some benefits that compensate their time and effort and placing themselves at risk.

On the contrary, paying human subjects a very small amount of money may lead to exploitation. As the research sponsors, institutions, and investigators they are going to benefit from the study compared with a limited and unfair benefit for a research subject's benefit. Exploitation might also happen with pediatric subjects, considering that parents might enroll their children to get the financial incentives for themselves. Enrollment bias is another aspect to be considered, as paying incentives may attract higher rates of subjects with a lower socioeconomic status.

Payment for physicians

The lack of incentives in clinical research is considered as a major potential barrier for subject recruitment. For example, physicians who refer subjects do not get any compensation, faculty members are rarely promoted for being investigators in



multicenter trials, and the research staff payment is unassociated to recruitment success. There are some ethical concerns for the protection of research subjects, based on historical research abuses, regarding incentives for researchers and subjects. However, some limited researches have falsified the concerns related to incentives leading to undue inducement.

At some point, finder's fees (a payment for referrals) used to be given to referring physician to compensate their efforts and their critical role for recruiting subjects. Concerns of conflict of interest led to their prohibition in academic centers.

Proper disclosure of incentive planning and studying patients' feedback is crucial for assessing their ethical impact. It has been reported that the response rate of health professionals to postal surveys was significantly increased by offering them monetary incentives. However, to alleviate the concern of conflict of interest the physician can disclose the payment he is going to receive for the subjects during the informed consent process.

Pharmaceutical Companies

Others argue that most trials are sponsored and funded by pharmaceutical companies and their main goal is commercialization. Doctors who are going to recruit the subjects have little or no influence over the study hypothesis, design, protocol, methods, reporting, safety monitoring, or even the decision to publish the study outcomes. These trials rely on the amount of payment given to clinicians as motivation to recruit subjects not on the importance of research itself. Well-designed trials by non-commercial sponsors with the aim to answer an important question that do not pay recruiters usually fail to attract doctors. Hence, a commercialized driven system that does not take into consideration the importance of subjects' altruism in clinical trials can be unethical and unacceptable.

One American study found that just over half of patients questioned found payments to clinicians unacceptable. "An even greater proportion (80%) believed that the patient had a right to know that their doctor would be paid for enrolling them. Fully informed consent should include all information and a frank disclosure of payments provided to physicians that recruits the future subjects.



Vulnerable population

Vulnerable population is a term that refers to the disadvantaged sub-segment of the general public requiring maximum care and particular special protections in research. Vulnerable population require close and careful attention during the clinical trial design with notable recruitment considerations and high-quality observation methods of overall safety and efficacy strategies ensuing research. The vulnerable populations include but not limited to children, minors, pregnant women,



prisoners, employees, critically ill, unconscious, disabled individuals, elderly people, ethnic minorities, international research, and economically and educationally disadvantaged.

The IRBs are responsible to protect the rights, well-being, safety, and privacy of vulnerable subjects. The role of regulatory bodies is crucial in biomedical research and it becomes more critical when a study involves vulnerable population. A special attention should be given to informed consent process when dealing with vulnerable population.

As a result of the continuous attention on the rights, interests and well-being of research subjects, the need for community involvement in research development and approval has become apparent. Despite the concentration of the ethical guidelines on individuals, frequently, community consultation has become a common practice of involving communities. Some argue the need for establishing ethical guidelines that require community disclosure, consultation, and consent. There should be clear ethical guidelines that guide the practice of community involvement in research.

Conclusion

When obtaining the informed consent from the subject or the legal guardian, the possibility of coercion or undue influence must be minimized. It is important to adhere to the principles of GCP through the clinical research process to protect vulnerable population.

Adhering to GCP guidelines is a key element for conducting an ethical clinical research. Community consultation is another crucial element that might foster the recruitment process as when you involve the community in research design and development this may foster their commitment for the success of the study. Their involvement helps them to understand the goals of the study thus may enhance the “buy in” attitude.

**The above article is summarized from multiple on-line public access sources.*

**Stay tuned for updates on the
SWF Pregnancy Survey,
coming out in January.**