For the past ten years, Angioma Alliance has hosted the International CCM Scientific Meeting. We bring together the key stakeholders, those who will move cavernous angioma therapy from the laboratory bench to the patient’s bedside. No other meeting, conference or workshop attracts the same unique group of researchers to focus exclusively on this rare disease. We again had record attendance this year, with 75 attendees from industry, government agencies and a wide variety of academic disciplines, traveling from three continents to attend this special event.

At our meeting, experts share their data, most of it unpublished, and use these results to inform their own work moving forward. They ask pointed questions of each other to ensure that no major stone has been left unturned. Over the years, numerous research collaborations have developed as a result of our meeting. While competition is still important in driving progress, CCM research has become a team rather than an individual activity. This is critical because no one institution has the knowledge base or resources to move us to clinical trials.

Drs. Brent Derry, Amy Akers, Connie Lee, Kelly Flemming, Issam Awad, Leslie Morrison, Kevin Whitehead, Doug Marchuk.

FEATURED ARTICLE:

Trent Clayton is a busy young man. Most days, depending on the season, you will find him heading to the pool, the soccer field or the track. He is a multi-event athlete in track and field, and currently holds national records for long jump and discus.

And, Trent is a boy with multiple cavernous angiomas who had his first brain surgery when he was just 14 months old.

Read more of his story on page 5.
Graduate students, postdoctoral fellows, medical residents as well as junior and senior faculty presented 22 research talks throughout the course of this two day meeting. Some presented unique unpublished data, and others discussed recently published data. Because most of the data presented was unpublished, we can’t report specific results here. However, published work will be shared through future Angioma Alliance social media and newsletter communications. An expanded version of this article with more information about sessions and attendees can be found on our website at bit.ly/1qDSaY2.

In celebration of the 10th Anniversary, we were thrilled when Dr. Francis Collins, Director of the NIH accepted our invitation to offer a keynote address at this meeting. In what felt like an informal chat, Dr. Collins spoke to our group about the state of research in this country, and provided words of advice to researchers, both young and seasoned, who may be struggling in these challenging economic times.

He encouraged scientists to seek out creative partnerships and be part of the “adventure to improve the human condition.” He also reminded us that biomedical research is not a partisan issue and that he is “guardedly optimistic” that this could be “the century of biology.” Dr. Collins asked scientists and patients to prepare and frequently offer their elevator pitch—a short explanation of the illness and why research is important—to help raise awareness.

Ten years ago, we could not have imagined that cavernous angiomas and Angioma Alliance would have earned the visibility to warrant a visit by the Director of NIH to our scientific meeting. Although progress toward clinical trials has been slower than the patient community would like, Dr. Collins’ address to our researchers was an indication we are at a turning point: cavernous angioma is an illness moving from the shadows of basic research, poking around for answers, to the spotlight of an illness with hope for a real treatment. Angioma Alliance and its Scientific Meeting have been central to this progress.
Clinical Trials Panel

A key feature of this meeting was the moderated panel discussion of clinical trials. The purpose of this session was to host a multi-stakeholder discussion of research progress, needs, and future directions. One of Angioma Alliance’s main goals was to determine what we can do to help prepare for trials, and what messages can we send.

Connie Lee, PsyD – President and Founder of Angioma Alliance

Connie Lee discussed the efforts of Angioma Alliance to help with recruitment and clinical studies, including our patient registry and DNA/Tissue Bank, our social media channels, and our newsletter. These are powerful communication tools that can help connect the patient and research communities.

Angioma Alliance is also undertaking important initiatives to prepare for future studies, such as the Genetic Testing Initiative, development of Clinical Centers, and the drafting of a Clinical Guidelines paper. The Clinical Guidelines paper is currently in development and will be used to help direct the establishment of clinical centers for care as well as drug trial site locations.

Issam Awad, MD – Chairman, Angioma Alliance Scientific Advisory Board & Neurosurgeon at the University of Chicago

Dr. Awad discussed the key elements and our understanding of the natural history of the CCM illness, and outlined the progression that we can expect, on average, in CCM patients. This knowledge is important because it provides a baseline for comparison as we plan treatment trials and consider which outcomes are best for measuring drug effect. Potential outcomes for measurement include: re-bleed rate, total number of lesions vs. new lesions, and lesion properties, such as permeability, iron levels and ROCK (Rho kinase) activity. Our knowledge of these parameters will influence study design, as well as help determine the number of participants needed.

Kevin Whitehead, MD – Member, Angioma Alliance Scientific Advisory Board & Cardiologist at the University of Utah

Dr. Whitehead was asked to share his expertise on the use of animal models in pre-clinical research and the feasibility of using biomarkers as a surrogate measure of drug treatment. Possible surrogate markers for investigation include looking at molecules in the blood that may be able to predict risk of hemorrhage or seizures and/or to predict the benefit of therapy by tracking lesion biology. This is currently an active area of research.

Leslie Morrison, MD – Member, Angioma Alliance Scientific Advisory Board & Neurologist at the University of New Mexico

Dr. Morrison discussed her experience designing and recruiting patients into the Statin Pilot Trial at UNM. This study aimed to use dynamic contrast-enhanced MRI to detect abnormalities in brain permeability in patients treated (and untreated) with low doses of simvastatin. The initial eligibility criteria for this study were too rigorous, and no participants could be enrolled for quite some time. These challenges led the research teams to work with the FDA and local regulatory committees to modify the study protocol. Following these changes, 10 of 30 participants have completed the study procedures. Recruitment and study analysis is ongoing.

Claudia Moy, PhD – Program Director, Office of Clinical Research at the National Institute of Neurological Disorders and Stroke

Dr. Moy helped provide the meeting attendees with guidance on NIH funding mechanisms related to translational and clinical research. NIH is currently undergoing a shift where more programs are being offered to cooperatively work with investigators as a partner in drug development and to help move a basic science idea to a potential product that may become useful for patients and the pharmaceutical industry.

Dr. Lisa McKerracher, PhD – CEO & Founder of BioAxone Biosciences, Inc.

We were thrilled to have Dr. McKerracher sit in on this important discussion panel. This meeting is the first in which we have had attendees from the pharmaceutical industry. Dr. McKerracher’s company is a small biotech company that is currently developing drugs for spinal cord injury. However, there is scientific crossover between her field and CCM research, as both involve study of the Rho Kinase pathway and potential drug therapy by blocking activation of a Rho Kinase signals. Dr. McKerracher shared her experiences with
our attendees and highlighted the important role of patient advocacy groups in drug development: organizations like Angioma Alliance that best understand patient needs, manage patient registries, provide financial support, and act as a liaison between academic labs and industry.

KATHRYN O’CONNELL, MD PhD – MEDICAL OFFICER, RARE DISEASES PROGRAM, OFFICE OF NEW DRUGS AND THE FOOD & DRUG ADMINISTRATION

Dr. O’Connell’s professional expertise lies in the regulatory aspects of rare disease drug development. She provided guidance for successful navigation through the FDA process, a process which must begin well before initiation of clinical trials.

What’s Next?

At the end of the discussion, each of our medical advisors was asked what he or she felt was the key message that ought to be delivered to the patient community.

Dr. Awad expressed the importance of the newest mouse data and current studies that will help guide us to clinical trials and make an informed decision about drug choice and dosage. It is important not to rush into a trial without adequate animal data: patient time and willingness to participate, as well as funding, are limited resources that must be utilized wisely.

Dr. Whitehead pointed to the efforts of Angioma Alliance and the importance of establishing Clinical Centers. Not only will these centers provide excellence in care of our patients, but will set up a network of patients and physicians who are equipped, educated, and ready to conduct clinical trials in an effective and efficient manner.

Dr. Morrison’s take-away message is that the first-in-human trial is currently being conducted and the first set of analyzed data will likely be available within the coming year. If significant results are found from this small pilot study, they will inform planning for larger trials that will include more forms of the illness.

What can Angioma Alliance do to prepare for trials?
- Continue to grow our patient registry, educate the patient community and facilitate genetic testing,
- Develop a network of clinical centers for treatment and for use as study sites,
- Continue to facilitate research and act as a communication liaison,
- Explore unique funding opportunities,
- Continue to host the annual CCM Scientific Meeting.

At the meeting, more than a handful of medications were identified and discussed as having potential benefit in treating cavernous angiomas. It is now time for comparisons using mice to make sure we are testing the best possible medications in humans. We are stepping up our efforts as a patient community to prepare ourselves for clinical trials that could begin in the near future. Everyone left our 10th anniversary meeting energized, excited, and prepared for the next decade to bring us real treatments for cavernous angioma.

Amy Aker & Connie Lee

Tracy Brown, Angioma Alliance Board Member and mother of Zach Brown, talking with Dr. Issam Awad.
Trent Clayton is a busy young man. Most days, depending on the season, you will find him heading to the pool, the soccer field or the track. He is a multi-event athlete in track and field, and currently holds national records for long jump and discus, and is also accomplished in target archery.

Like many other 11 year olds, Trent loves video games and amusement parks, especially roller coasters. He lives in Pennsylvania with his mother Darla, father Gary, and younger sister, Amarisa.

“He’s a thrill seeker,” Darla told me. She thinks that’s why he likes video games so much: if he can’t be in the action, he can create it on the screen. But Trent has another side. He also studies the French horn, and has a role in the school musical.

If you are wondering how Trent and his family juggle all of these activities and still have time to eat, sleep, and go to school, prepare to be amazed.

**NINE YEARS EARLIER**

A little over nine years ago, Darla Clayton was sitting in a hospital waiting room while 14-month-old Trent was undergoing an MRI. Because he was so little, he has been sedated. Darla was told the scan would take about 45 minutes, and she was counting each one of them. She was anxious to be with him when he awoke. Finally, nearly two hours after they had taken Trent in, the doctor emerged and delivered a sentence which consisted of exactly fourteen words. It would be ingrained in her memory forever:

“I need to let you know that there is a mass in Trent’s brain.” The MRI had shown a growth, the size of a fist, in Trent’s fronto-parietal lobe.

Darla became concerned when Trent was between six and nine months old. He never seemed to use his right hand. The first time she expressed this concern to a pediatrician, he replied that maybe Trent was a lefty. When Trent reached twelve months, wasn’t walking and still wasn’t using his right hand, Darla, a clinical psychologist, insisted the pediatrician take a closer look. It was at that appointment that Trent was referred to a neurologist who recommended further examination, and thus the MRI.

With little time to adjust to the news, the Claytons were told that Trent required immediate surgery. It was a steep learning curve. They hit the medical library and began researching. “I learned quickly,” Darla said, “that I didn’t know anything.” Trent was not permitted any food or drink by mouth. Darla remembers how difficult this was. “He wanted to nurse and I just wanted to nurse him…” They wheeled Trent into surgery, and it would be several hours before the neurosurgeon appeared and told them Trent was in the recovery room. He reported that as they attempted to excise the mass, “black blood that looked like motor oil came oozing out all over the OR table.” Apparently, no one expected that.

Trent was ultimately diagnosed with a cavernous angioma. He has a mutation on the CCM2 gene, a hereditary form of the disorder. Before his 11th birthday, Trent would undergo two surgeries, survive more strokes than the doctors can document, and endure hundreds of hours of therapy. The part of Trent’s brain responsible for motor skills had been affected. He does not have full function on the right side of his body. He wears a brace on his right leg. He suffers from seizures for which he takes medication; he requires a one-to-one aid at school.

Trent was born with a second genetic condition: Von Willebrand Disease, a bleeding disorder. Three times a week, Darla administers an IV infusion of clotting factor. Trent’s bleeding disorder is treated very aggressively. Since no one can know when a cavernous angioma will
bleed, he always has to have clotting factor in his system just in case.

The Claytons will never know exactly when the cavernous angioma developed, or when he had his first stroke, but Darla thinks it was very early on.

“I just remember, every time I laid him down on his back to sleep, he would be miserable; this was around 3-6 months. He could only sleep sitting up in the little infant swing. I was so sleep deprived, I swear one night I started hallucinating. We think now that lying on his back, the pressure inside his head was excruciating.”

**DOING MORE**

Ability is defined as the power or skill to do something. Darla and Gary Clayton wanted their son to be as active and engaged as safely possible. Contact sports were out, as were activities with high G-force. They found ways for Trent to not just participate, but excel. Darla founded Strong As Steel Adaptive Sports, a team to allow children with physical disabilities to compete on an even playing field. They looked at nearly every instrument in the band and orchestra to find one which was suitable. Darla became active in Angioma Alliance, and is hopeful that research will ultimately offer more treatment options. When I asked Darla where she thought research money should be allocated, she paused for a moment and said “brain surgery; we have to find alternatives to conventional brain surgery. No one should have to go through that.” She also encourages any parent going through a similar situation to “connect with others, it is a very powerful tool.”

I asked Darla how she maintained balance, deciding what she would or would not let Trent do. She reminded me how much Trent loves roller coasters. When he was small, the little kiddy rides were fine. As he grew he wanted to go on bigger, faster rides. At a park one day he was begging to go on the roller coaster.

“So there I am, walking all around this roller coaster, estimating the height, trying to calculate the G-force in my head.” She let him go on that one, but often has to say no.

I asked her what are the greatest challenges raising a child with such complex medical issues?

“Some days it’s something as basic as shoes.” Because of the brace, he cannot be fitted with shoes very easily. Other days, it is the behavioral issues. A simple request to turn off the video game for dinner can involve compromises, bribes, sometimes scenes. As a psychologist, she knows the appropriate ways to deal with such behaviors. As a mom, it’s not always so easy.

But from these challenges, Darla has learned so much.

“I think as a psychologist I am better equipped. When I meet with a patient going through a rough time, I get it. Believe me, I get it”.

So, who is Trent Clayton? He is a student, an athlete, a musician, a little boy who has been significantly impacted by cavernous angioma, but he is a warrior. Darla is determined to ensure he experiences life to the fullest, and has a well-equipped army behind him.

*Donna dePasquale*
Anywhere Walks

During the month of October, Angioma Alliance members around North America walked to raise awareness of cavernous angiomas. Some walked individually, some with family and friends, and some in large events they organized. In the photos on the following page, you'll see a combination of Angioma Alliance Awareness shirts, Zach Brown 5K shirts, and signs; there were many ways to express support. In addition to raising awareness, the 2nd Annual Angioma Alliance Anywhere Walks raised over $40,000 toward our work for a cure.

We want to thank all participants and hand out a few awards:

Largest Walk: With some 200 participants, the Zach Brown Virtual 5K, at YMCA Camp Letts in Edgewater, MD, was more than double the size of any other. In addition to being a beautiful walk through the woods, the event, which raised almost $20,000, featured barbecue and hot dogs donated and served by Fired Up to Help, a DJ, a bounce house, and a lively volleyball game.

Coldest Walk: Dana Betz and her family walked in Springside, Saskatchewan, Canada, on October 17. It was a nippy 4º C (40º F), with a wind chill below freezing.

Greatest Number of Angioma Alliance families: Chesapeake, VA with eight unrelated Angioma Alliance families participating (this was also the only walk that included scientists: John Mably and Joanne Chan from Hampton University).

Best Integration into a public event (tie): Michelle Wilkinson walking in her town’s Homecoming Parade on a stormy night.

The Pittsburgh group (three families) walking during the Pittsburgh Zoo’s ZooBoo (because brains that bleed are scary!).

Most visible to strangers: Becky Moyers sporting Mickey ears and an Angioma Alliance t-shirt at Disneyworld.

Best awareness-raising by a dog: Romeo, companion of Jo Macaluso, in Austin, TX.

Walk furthest from home: Linda Fuchser’s California family walking in Kauai, Hawaii.

Walk with the most first responders: Newport News Fire Department in Newport News, VA.

New Angioma Alliance Logo

Angioma Alliance rolled out our new logo in September. Gone is the little red guy, and replacing it is a powerful illustration of cavernous angiomais with a statement about our purpose. We want to thank all those who submitted design ideas, and especially Amber Blakesley whose design was chosen and who then worked with Connie Lee and Crystal Shaulis to refine it. Finally, we’d like to thank Ryan Lisiak for coming up with the new tagline. We hope you like the logo as much as we do and find it useful in explaining cavernous angiomas to those around you. Below you can see two versions of the logo:
International News

Cavernoma Alliance, UK

Cavernoma Alliance UK held a very successful CaverHub in Cambridge, in September. Mr Ramez Kirollos, Consultant Neurosurgeon, discussed “Management and Treatment of Cavernomas,” which covered decision-making options and the factors involved when exploring surgery. Mr Kirollos discussed management and individualised care for cavernomas based on the person, not on literature or protocols. He provided a relaxed and informative talk, and very kindly gave his time at the end to answer questions from the group.

The annual tradition of the Autumn London CaverHub was continued at the National Hospital, Queen Square, on 25th October, with over thirty members attending a stimulating talk on cavernoma given by Mansoor Foroughi and Dr. Nick Coffin.

Progress with the Cavernoma Priority Setting Partnership steams ahead. This research project between CAUK and the medical profession is taking forward the process of discovering the top priority research questions that need to be addressed to improve the treatment and management of those with cavernoma.

CAUK is pleased to announce that many of our one year targets for the Big Step project have been met and exceeded. For example, our social media target for 2018 has already been reached, and has exceeded our expectations. In the last twelve months, CAUK has also registered over three hundred new members from the UK, Europe, and around the world, held over eleven meetings, and many people have begun to volunteer as CaverBuddies along with a volunteer organiser. Registration is just closing for another event to be held in the North of England for our CaverFamilies in March 2015: a study day with a neurologist, geneticist, two neuroradiologists and a paediatric neurosurgeon. Sponsored by the Big Lottery and CAUK, this day includes free transportation and accommodation. It will be closely followed by our 3rd Annual free residential weekend for children affected by cavernoma and their parents and/or carers.

CAUK have also begun a new round of conferences with our first successful attendance at the British Association of Neuroscience Nurses. Simon Temple (Trustee) and Ian Stuart (co-ordinator) spoke to many nurses, from those in emergency departments to those who assisted with neurological operations.

Ian Stuart & Angie Yeomans

Mansoor Foroughi at the Autumn London CaverHub in October.
Angioma Alliance Canada

Angioma Alliance Canada continues with our goal to raise awareness in Canada. We are working on an exciting project, distributing our informative brochures to the community. Our plan is to reach as many hospitals, doctors’ offices, clinics, nurses, medical students etc. as possible.

For many people, when they receive a diagnosis it is the first time they have heard of CCMs. We feel that this needs to change. Having access to accurate information and a community of people who understand is crucial.

In order to reach our goal we continue to raise funds. It’ not too early to begin thinking about Christmas and/or Birthday gift ideas. Consider asking people for monetary donations in lieu of a gift. We also have a partnership with “Donate a Car Canada” where you can donate a vehicle in exchange for a tax receipt. Angioma Alliance Canada (AAC) will then receive a donation in the sale amount of the car. Donations can be made via www.workingtowardsacure.ca.

Planning is already in full swing for our 4th annual AAC conference which will take place in Toronto, ON, on June 6, 2015; stay tuned for more details. Our board members are excited about the speakers we have invited; already, Dr. Derry from the Hospital for Sick Kids has agreed to be a presenter. We look forward to seeing people from all over Canada and the U.S. again. Contact us for details on how to get a DVD from last year’s conference, available soon.

Shawn Mulvihill

Donate to Angioma Alliance

Angioma Alliance has big plans for 2015, and, with your help, we can make them reality. Expect to hear about a family conference, clinics, and genetic testing. And, of course, we continue to support our researchers as they work toward clinical drug trials.

Your support is critical. As the year is coming to a close, please give as generously as you can. Together, we can help every family affected by cavernous angioma to a better tomorrow.

Please visit angioma.org/donate to donate online and to find information for mailing in a donation.

Aliança Cavernoma Brasil

We are proud to announce that our website, cavernoma.org.br, went on line in October 2014. Patients, family members and doctors—or anyone seeking information about cavernomas in Brazil—can now access this resource. We also link to associations affiliated with Angioma Alliance, so we can strengthen our network of information about cavernomas.

In addition, we are happy to announce that a group of researchers from the Federal University of Rio de Janeiro (UFRJ), coordinated by Dr. Jorge Marcondes, has received a grant from FAPERJ, a Rio de Janeiro state foundation for research, and the D’OR Institute. This is for a new project aimed at identifying potential drug candidates to treat cavernous malformations.

The research group said: “Taking advantage of the robust advances in cell and molecular biology, promoted in the last two decades by several researchers dedicated to the understanding of the mechanisms of the disease, this group is hoping to be in line with other centers of excellence in the search for the next generation of treatment for cavernous malformation so far restricted mainly to observation or surgical intervention. The Laboratories of Pharmacology and Endothelial Investigation, in close collaboration with the Department of Neurosurgery of the UFRJ, has created a joint effort looking for chemical compounds that may act in a more selective, effective and safe way to interfere with the way blood vessels acquire the cavernoma’s configuration, which leads to clinical manifestations.”

Selva Paraguassu Lopes
About Angioma Alliance

Angioma Alliance is a non-profit, international, patient-directed health organization created by people affected by cerebral cavernous angiomas (also known as cavernous malformations or CCM). Our mission is to inform, support, and empower individuals affected by cavernous angioma and drive research for treatments and a cure. We are monitored closely in our educational efforts by a Scientific Advisory Board comprised of leading cerebrovascular neurosurgeons, neurogeneticists, and neurologists.

Angioma Alliance
520 W 21st Street, Suite G2-411
Norfolk, Virginia 23517
Phone: 571-306-2873
Fax: 757-623-0616
info@angioma.org
www.angioma.org
www.facebook.com/AngiomaAlliance
Twitter: @AngiomaAlliance

How You Can Help

Your contributions help fund our research initiatives toward a cure and our patient support programs. To donate, please send a check or money order in the enclosed envelope or visit our website at www.angioma.org to donate with a credit card.

Sponsorships can maintain essential programs or help us expand the way we support the patient and research community. Sponsors are acknowledged with logo placement, naming opportunities, or appropriate other recognition.

Sponsorships are available for the following:

**Newsletter**

This newsletter reaches thousands of patients and donors both in print and online. It is the only patient-directed source of news and information for the cavernous angioma community. If you have an interest in reaching this community to support our efforts, please contact us.

**Website**

Our website has a global reach, and is always in the top three search results for cavernous angioma. It is the first place newly diagnosed patients look for information and support. In addition to being a patient resource, the website provides information to medical support staff, researchers and the general public.

**Children's Book**

A sponsored printing of the children’s book under development would allow us to give the book to our families for free.

**Scientific Meeting**

Our scientific meeting offers a variety of opportunities to support and reach the research community, including travel awards and sponsored speakers, breaks, and meals.

**DNA and Tissue Bank and Genetic Testing**

The DNA and Tissue Bank is the major source of cavernous angioma biological samples for labs around the world, and we have provided the raw materials for several major published studies.

Contact us at info@angioma.org to discuss any of these sponsorship opportunities.