



ANGIOMA ALLIANCE NEWSLETTER

because brains shouldn't bleed

The Medication Pipeline: Where Are We Now?

In 2009, a research team at the University of Utah identified the first potential medication for treatment of cavernous angioma: simvastatin. The progress in medication identification and development in just seven short years has been nothing short of breath-taking. The diagram below lists nine medications that are being considered for treatment. Our website will soon have an interactive tool that will allow you to follow their progress.

There are four possible ways medications can treat cavernous angioma, and each of the drugs under investigation may perform one or more of these functions. However, we are not sure any will do all of the following: reduce leakiness/hemorrhage, shrink lesions, reduce proliferation in hereditary forms, and prevent regrowth after surgery.

All these medications except propranolol have progressed to animal studies for treatment of cavernous angioma. After animal trials, medications move to Phase I trials. These first human trials are typically quite small and may use healthy volunteers. They focus on determining the safety of a new drug. Simvastatin (Zocor) has completed a small Phase I pilot trial using cavernous angioma patients at the University of New Mexico. Researchers are currently analyzing the data.

Phase II trials are larger studies of patients for whom the drug is intended. They may be placebo controlled, and aim to investigate the effectiveness of the drug. Atorvastatin (Lipitor) will begin a Phase I/II trial through the University of Chicago in late 2016 or early 2017. Our website will have recruitment information when it becomes available.

While statins have many uses, industry partner BioAxxone is working to develop a medication specifically for cavernous angioma patients. This medication does not yet have a name; it is known simply as BA-1049. It is currently being tested in animals that have been genetically altered to develop cavernous angiomas. Fasudil is a similar medication but is not available outside of Japan and has never been tested for cavernous angioma.

Tempol, sulindac metabolites, and B-cell depletion therapy have completed animal trials. The FDA has granted orphan drug status to Tempol, a medication being

developed by Recursion Pharmaceuticals, which could help it move to clinical trials sooner. A group of European researchers are studying sulindac metabolites, specifically sulindac sulfone, which has been granted the equivalent of orphan drug status there. Researchers at the University of Chicago recently published a paper documenting the effectiveness of B-cell depletion therapy for reducing hemorrhage and lesion proliferation.

We have been discussing Vitamin D3 for some time. (See the research summary on Page 6 for a recent study.) Since controlling D3 exposure is impossible (your D3 level increases with sun exposure), this medication will never enter clinical trials. However, measuring Vitamin D3 levels in those who have had hemorrhage helps us to understand that Vitamin D3 levels are associated with negative consequences if they are lower than those recommended by the Food and Nutrition Board (FNB) at the Institute of Medicine of The National Academies.

Propranolol has been used to treat two women at the Barrow Neurological Institute to control hemorrhage and growth of their lesions. Its mechanism of action isn't yet understood, and it hasn't been tested in animal models of the illness.

Our website will soon have more detailed information about each of these medications, including their expected functions and the biology of their actions. This is a very exciting time and we are thrilled to be able to share the progress.

Connie Lee

	Pre-Clinical		Clinical Trials		
	in vitro	Animal models	Phase I	Phase II	Phase III
Rho Kinase Inhibitors					
ZOCOR (Simvastatin)	X		X		
LIPITOR (Atorvastatin)	X		Trial to begin late 2016		
Fasudil	X	X			
BA-1049	X	In progress			
Superoxide Dismutase					
Tempol	X	X			
Inflammatory Inhibitors					
Sulindac Metabolites	X	X			
B-cell depletion therapy	X	X			
Nutritional Supplement					
Vitamin D3	X	X			
Beta Blocker					
Propranolol					

News

Regina's Gift

On March 6, William and Mary professor Dr. Regina Root stood in front of an audience at the Kimball Theater in Williamsburg, Virginia, to share her story at the premiere of the film "Regina's Gift."

Just two years earlier, it wasn't clear whether Regina would survive, let alone stand or speak again. "Regina's Gift" documents her year-long battle with a large, active brainstem cavernous angioma, from diagnosis to surgery through rehabilitation. It is an emotionally honest, medically accurate depiction of the experience of one of our members.

We aired the film at our patient conference in Cincinnati, and many of our attendees, who could relate to Regina's experiences, believed it could help them explain their experience to others.

The documentary is available on DVD through the filmmaker's website at www.stikdawgmediallc.com.

Cavernous Angioma Night at the Cincinnati Reds

This year's Cavernous Angioma Night at the Cincinnati Reds was even better than last year's. We preceded the evening with an afternoon patient conference that drew 40 attendees, including medical professionals from Cincinnati Children's Hospital, and a reception for all ballgame attendees.

At the pre-game ceremony, we were presented with a check from the Reds organization for \$5,154. The announcer explained the illness to the fans, our 6-Word Stories video was shown on the Jumbotron, and Joe Price, retired Red and Angioma Alliance family member, threw an honorary first pitch. After that, we were all able to sit back and enjoy the game. We are grateful for the generosity of the Reds, for the hard work of Tony Mayer and his family in organizing this event, and for all those who made it to the game.



MadoroM Charity Wine Auction

The MadoroM Foundation held its 11th Annual Charity Wine Auction in late February to a packed house at the Seven Oaks Country Club in Bakersfield, CA. MadoroM Vineyard proprietors Andy and Marissa Amador were hosts to the most generous group in Bakersfield, which included Congressman Kevin McCarthy and many local business owners.

Despite Bakersfield's challenging economy, the event raised over \$100,000, a portion of which will benefit Angioma Alliance. We are deeply grateful for Andy and Marissa and their continuing support as well as for all those who bid to help us drive research for a cure.

Alan Alda's Foundation Brings Improv to Cavernous Angioma Patients and Professionals

On a warm day in February, if you walked into the Domenici Center at the University of New Mexico, you would have seen more than twenty doctors, researchers and patients silently tossing imaginary balls to each other. And you would have seen patients presenting very difficult published cavernous angioma research in lay language. These unusual activities were part of a workshop facilitated by the Alan Alda Center for Communicating Science. In the workshop, doctors, nurses, scientists, cavernous angioma patients and family, including Angioma Alliance Board members Tim Gallegos and Connie Lee, learned to communicate with each other in everyday language. The goal was to reduce power differentials, build group cohesion, and improve communication skills to ensure true two-way communication between all group members. To achieve our goals, we need to be able to understand each other.

After two days of building communication, the real job began. The workshop was preparation for this group to work together to identify patient priorities. What did the patient community feel were the biggest needs in New Mexico to improve cavernous angioma health outcomes? What research could identify the best ways to meet these needs? The group successfully identified four major needs ranging from a Center of Excellence to better early diagnosis to improved training of medical providers.



The Angioma Alliance table at the MadoroM Wine Auction including Angioma Alliance Board member Liz Neuman and Congressman Kevin McCarthy.

A subgroup of workshop attendees is now meeting every two to three weeks to prepare a grant application to submit to the Patient-Centered Outcomes Research Institute (PCORI) to address one of the identified critical needs. Cavernous angioma patients have never been this involved in setting priorities and drafting requests for funding. Angioma Alliance looks forward to supporting this effort through the funding process and beyond.

Read more about our work in New Mexico in the interview with Tim Gallegos on page 9.



Dr. Leslie Morrison portrays a 14-year-old patient while Vivian Reese plays the role of doctor during the Communicating Science workshop.

Interview: Myrna Sarowitz

Connie Lee: I'm here today with Myrna Sarowitz who is a member of the Angioma Alliance Board of Directors. I'm going to be asking her a couple of questions about her experiences with cavernous angioma and also about the project that she's working on for us. Myrna, can you tell us a little about how you came to be diagnosed with cavernous angioma and what has happened since then?

Myrna Sarowitz: Absolutely. This started in 2008 and it started very, very harmlessly. I thought something was itching under my arm. I went to my doctor and said, "Can you give me some salve because I have a rash." She looked under my arm and said, "You don't have a rash." That started the journey. The itching became a burning sensation so I went to my chiropractor. He did all the things he's always done in the past to relieve pain and nothing helped. I do believe in alternative medicine if that's at all possible. After a couple of months of seeing him and it wasn't working, the next symptom I had was this incredible headache like no other headache I'd ever had. It started in the back of my head and felt like my head was in a vise. Then my blood pressure went extremely high. I've always had normal blood pressure, never been on blood pressure medication.

I ended up in the emergency room many, many times. They had no idea what was going on. They just gave me medication to regulate the blood pressure. So that went for about 6 more months. Then I had numbness around my waist. I went to many different doctors. Nobody diagnosed me until I went to the University of Chicago. I saw a wonderful neurologist. This was about 2 years after the symptoms started. He finally said, "I think you need a spinal MRI." Once they did that and the EKG and everything, they found a cavernoma.



I was so happy because they found something, but then I began to realize this was not a simple thing. So, I went to three different neurosurgeons, had three different opinions. Two did not want to operate and one did. I just wanted the pain, the burning sensation, and everything else to go away. This surgeon did say he's operated on cavernomas before. He told me there'd be numbness afterward and that it would be temporary.

So, I recovered pretty well from the surgery. I had rehab, wonderful rehab therapists who taught me how to walk again, how to go up stairs, gave me some balancing because my balance was off. That was in 2010. Now it's 2016 and I still have the numbness, the tingling, the hypersensitivity on both my legs and have since learned that I have scar tissue from the site of the surgery. My cavernoma was in the cervical spinal cord.

The scar from the surgery is what's preventing the nerves from connecting and doing what they are supposed to do. That's where I am. I'm learning to accept, although it was not an easy journey. I went through a lot of anger at the surgeon

for not giving me all the information. I went through depression for a while. I was just so upset. But now I'm learning to - not every day but on the really good days - just be grateful I can walk, be grateful I can drive, be grateful I can take care of myself pretty well. And that's where I am.

CL: You were not the typical age of someone who gets diagnosed with this illness. Can you tell us how old you were when you were diagnosed?

MS: I was 69.

CL: Do you think that made any difference in how seriously your symptoms were taken? The age that you were? Or at least looked at?

MS: I think that they just truly didn't know. They thought it was my rotator cuff. I had MRI and x-rays. No, I think they just did not know, truly.

CL: Can you share with us a little bit about the peer support program that you are restarting for Angioma Alliance.

MS: This is very fulfilling for me. Having a disease - if I can do something for somebody else - that makes me feel better. So, we started a peer volunteer support group. These are peer volunteers who have volunteered to talk to somebody one-on-one if that's what the person requires. Just help them, particularly people who are newly diagnosed, but it can be anybody who wants more support than they are getting. The peer support volunteer will call them, speak to them on the phone, through Skype, and just let them know there is life beyond the diagnosis, the surgery. This can be very, very frightening. It's such a rare disease but everybody has different symptoms. There are a few similarities but the symptoms can really throw you. They threw me because you never expect those things to happen. The peer volunteers are there to support people and to give them hope and to know that they continue with their lives as best they can. I think one of the difficulties is knowing that physically you can't do everything you used to and learning that you have to adjust your life to that.

CL: I just want to share that if folks would like to be matched with a peer support volunteer, they can do that on our website. They just need to go to angioma.org/peer and there is a form they can fill out. Is there anything else you would like to share before we end?

MS: Just that being in the Angioma Alliance has helped me to know that, number one, I'm not alone. Number two, I'm not the only person who has numbness, because if I describe it to my friends and even my family, they try to understand but they really can't. It's a fantastically warm support group and I think everybody in the group really wants to help each other. I recently went to a Reds game [Cavernous Angioma Night at the Reds] and it was so much fun just being on the field and being there. It's a great group and I'm just grateful I found it. I do want to say I thought at first it was just for brain cavernomas but I recently found it's for spine cavernomas as well.

CL: Thank you very much for joining us and talking with us today.

Angioma Alliance Peer Support

Sometimes, online support groups aren't enough. Angioma Alliance has restarted our one-on-one peer support program with trained volunteers. They are ready to talk with members who are newly diagnosed or at a turning point in their illness. Peers and volunteers are matched based on common experiences and continue their relationship for as long as it's helpful. To learn more about the program and to request or become a peer supporter, please visit www.angioma.org/peer.

Free Genetic Testing Initiative: One Year Anniversary

Angioma Alliance has been offering free genetic testing to our members in the United States and Canada who have multiple lesions and cannot get coverage for testing through their insurance. So far, in our first year, we've had 130 requests through our international patient registry. Of these, 60 people were eligible to participate in the program because of multiple lesions, but most had not yet tried their insurance. Fifteen of the 60 have now made it all the way through the process from enrollment in our program to receiving results. About 50 extended family members have also learned about their mutation. While we haven't heard from everyone, some of the 60 eligible participants who have not been tested through our program were eventually able to receive testing through their insurance companies.

Our first year of the initiative has led 70 individuals to learn about their genetic mutation. These individuals and their families can begin receiving care appropriate to their mutation status. Considering that at least one of the upcoming drug trials expects to enroll only 60 individuals, we have already provided a great service to research.

To express your interest in genetic testing, register at www.angioma.org/registry. Learn more about the program on our website at www.angioma.org/testing.

Research Update

Vitamin D3, Cholesterol, and the Course of Cavernous Angioma

A team at the University of Chicago performed a study to determine whether anything that could be measured through a blood test might correlate with the aggressiveness of patients' cavernous angioma disease. The study included 43 patients who were fairly evenly split between sporadic and familial forms of the illness. The researchers defined "chronic" aggressiveness as any of the following: symptom onset before age 18, two or more symptomatic bleeds, 25 or more lesions on SWI MRI, or more than 5 lesions greater than 4 mm in the familial form. The researchers defined "acute" aggressive symptoms as a hemorrhage, lesion growth, or new lesion formation within the last 12 months.

The researchers measured total cholesterol, HDL (good) cholesterol, LDL (bad) cholesterol, and triglycerides. They also measured Vitamin D and C Reactive Protein levels, and performed a leukocyte ROCK assay. C Reactive Protein is associated with inflammation, and ROCK is a protein thought to contribute to the formation of cavernous angiomas in the brain.

They found that none of the measures correlated significantly to acute aggressive symptoms. In other words, they couldn't tell which patients had recent worsening based on their lab values. However, there were differences on two measures in patients who presented with chronic aggressiveness versus those who did not: Vitamin D and non-HDL cholesterol.

First, individuals with chronically aggressive disease were more likely to have Vitamin D levels under 25.68 ng/ml (a value above 30 is considered an optimal level of Vitamin D for the general population).

Second, people with chronic aggressive disease were also likely to have low non-HDL cholesterol. This is a somewhat surprising result. Non-HDL cholesterol is all of what we have been told is the bad stuff, including LDL cholesterol and triglycerides. The value for non-HDL cholesterol is found by subtracting HDL cholesterol from total cholesterol (Total Cholesterol – HDL cholesterol = non-HDL cholesterol). For cavernous angioma, lower non-HDL cholesterol levels correlated with more aggressive disease. Those with a non-HDL cholesterol value below

138.5 were more likely to have chronically aggressive disease. Previously, researchers who are part of the Brain Vascular Malformations Consortium had found that higher BMI (body mass index) was correlated with lower disease aggressiveness in people with the Common Hispanic mutation. The new finding that the lower your non-HDL cholesterol, the higher your odds of having chronically aggressive cavernous angioma is consistent with this previous study.

Furthermore, combining Vitamin D and non-HDL cholesterol into one value is even more predictive of chronic disease aggressiveness. The researchers developed a formula to combine the values: $0.74(\text{Vitamin D}) + 0.73(\text{non-HDL cholesterol})$. A combined value below 118.8 was highly correlated with chronic disease severity. Apparently, a combination of low Vitamin D and low bad cholesterol is associated with having more difficulty with the illness in the long term than either alone.

Atorvastatin, a drug which has several functions including lowering non-HDL cholesterol, will be moving into clinical drug trials for treatment of cavernous angioma soon. Atorvastatin has been identified as a possible treatment because it can inhibit the activity of ROCK protein. This could lead to a slowing of the rate of lesion formation in people with the familial form, and possibly a reduction in hemorrhage for everyone with the illness.

However, it's not clear if lowering cholesterol will conflict with its efficacy as a treatment. Only a controlled trial with regular monitoring of Vitamin D and non-HDL cholesterol will be able to determine this. The authors also encourage additional blood test studies with a larger number of patients over a longer period of time and as well as a study measuring a greater variety of inflammatory markers.

Choquet H, Nelson J, Pawlikowska L et al. Association of cardiovascular risk factors with disease severity in cerebral cavernous malformation type 1 subjects with the common Hispanic mutation. *Cerebrovascular Disease*. 37(1), 57-63 (2014).

Girard R, Awad IA et al. Peripheral plasma vitamin D and non-HDL cholesterol reflect the severity of cerebral cavernous malformation disease. *Biomarkers in Medicine*. (Epub ahead of print, 10 February 2016).

Connie Lee

Brian J. Fair joins Angioma Alliance as Director of Resource Development



Brian Fair brings to Angioma Alliance more than 15 years of experience in all aspects of building and growing earned income sources for non-profits. Brian has also has trained staff and boards in best practices in solicitation and development program creation. His ability to assist Board members and volunteers with their own fundraising efforts through mentoring, assistance, and guidance makes him an invaluable resource for our entire community.

For nearly six years, he served as the Director of Development for Nauticus/USS Wisconsin in Norfolk, VA, where he launched the museum's first successful annual fundraising program, encompassing individual and corporate gifts, grants, special events, and membership. His last tenure was as Development Officer for Major Gifts at Physicians for Peace. In this position, he identified, cultivated, and solicited major donors to fund the organization's teaching trips. During these trips, medical providers from the United States visit developing countries to teach their counterparts.

Brian had asymptomatic epilepsy until the age of 35, when he suffered two violent tonic-clonic seizures resulting in skull fractures, cerebral hemorrhage, dual shoulder surgery, and mild traumatic brain injury. "When I discovered Angioma Alliance, I knew I could use my experience to help further its important mission," he says. "I know what it's like to be fine, then have my life turned upside down. The stories of the survivors with Cavernous Angioma resonated with my own." This personal experience combined with his technical skill and experience in nonprofit development inspired him to apply.

You can reach Brian at bfair@angioma.org or (206) 446-8051 to learn more about these opportunities and valuable benefits for your company. Please consider how he can help you to reach out to your network.

Help Angioma Alliance Get Us Closer To a Non-Invasive Cure

Since starting as Director of Resource Development at Angioma Alliance in mid-March, I've been impressed by what I've learned. When Angioma Alliance was created 14 years ago, patients and their families felt lost. With a baffling illness that doctors knew little about, they couldn't even turn to each other for support. Cavernous angiomas were not on the radar of drug manufacturers or scientists.

In just two months, I have learned that because of you, all that has changed. Your community is strong, and patients and families can reach out to each other online, in one-on-one peer support, and at family conferences.

Patients can get free genetic testing courtesy of Angioma Alliance. This year marks the 12th Annual Scientific Meeting in Washington, D.C., the only one of its kind, where scientists and medical professionals gather to present their latest findings as they work toward creating better treatments for cavernous angiomas.

Now, nine drugs are in various stages of research and development to take away the uncertainty in the lives of angioma patients.

The most impressive thing is that this tremendous progress is all due to your support! With your continued help, families will have a little more connection each day, and we will be closer to a cure.

Fundraising isn't just about money. By working together, we connect passionate people to projects that help us meet our mutual goals. In doing this, we help our supporters fulfill their need to make a difference.

Fundraising is about your willingness to tell a business partner over lunch how sponsoring an Angioma Alliance program will help him do good while exposing his brand to a greater audience.

Fundraising includes those of you who are parents and patients telling the story of how your family was impacted by cavernous angiomas. Sharing a glimpse into our challenges and the promise of Angioma Alliance can increase support one person at a time.

Fundraising means being willing to consider all the people, companies and organizations in your life and ask: "How can I get them to think about Angioma

Alliance more often?" I urge you to invite people to be a part of our extended family.

My goal is to increase our financial support and broaden our base through different forms of donations. To do this I am working with the Board to launch our first-ever Major Gift program. There are many ways individuals and corporations can help. If you think of a contact, please send their information on to me to research. Your connections can help by:

- Making a personal donation,
- Having your employer or company sponsor our Scientific Meeting or other event,
- Making an in-kind donation of services or valuables,
- Putting Angioma Alliance in your will, or creating other planned gifts to ensure our future. (This is a great way to leave a legacy and save on taxes.)

Please invite anyone you know to be join our family of supporters. When you do so, our efforts are magnified and we move closer to a cure.

Brian Fair

Q: How does baseball analytics help Angioma Alliance?

A: Through a weekend seminar in Boston in August.

"Sabermetrics, Scouting, and the Science of Baseball" is the premier baseball analytics event on the East Coast. Organizer and Angioma Alliance member Chuck Korb gets front office insiders, scientists, scouts, and sabermetricians into the same room to have them talk about the game they love. The seminar is a charity event; this year's proceeds will be split between Angioma Alliance and the Jimmy Fund.

Chuck is crowdfunding to raise money to cover expenses for the event, a model that we can use in other fundraisers.

Learn more at www.generosity.com/sports-fundraising/saberseminar-2016.

Please look at our Upcoming Events list below to see other upcoming fundraisers in September and October. If you are planning an event, please let us know at clee@angioma.org so we can share the information on our Facebook page and website.

Upcoming Events

Here is a sampling of large events planned by our members:

CCM Support Group Meeting, July 30 at 1 pm

Location: Epilepsy Support Education Services, Albuquerque, NM

Featuring an invited speaker, children's table, and discussion

More info: www.3cs.info

Sabermetrics, Scouting and the Science of Baseball Seminar, August 13-14

Location: Boston, MA

Benefits Angioma Alliance and the Jimmy Fund

More info: www.generosity.com/sports-fundraising/saberseminar-2016 and www.saberseminar.com.

Jared's Journey of Hope, Sept 10 at 10 am

Memorial Stadium, Indiana State University, Terre Haute, IN

Facebook event page: www.facebook.com/events/278878599111677.

2nd Annual Angioma Alliance Wine Tasting, Sept 16

Location: Torrington Country Club, Goshen, CT

More info will be available at www.facebook.com/AngiomaAlliance and on our website.

4th Annual Zach Brown 5K for Angioma Alliance, October 8

Location: Edgewater, MD

More Info: www.facebook.com/ZachBrownVirtual5kForAngiomaAlliance.

International Cavernoma Awareness Month in June:

Angioma Alliance Canada Conference, June 11

Location: Peter Gilgan Center for Research and Learning, Toronto, Ontario

More info: www.fb.com/AngiomaAllianceCanada and www.Angioma.ca.

Cavernoma Alliance UK 10th Anniversary Forum, June 11

Grange Holborn Hotel, London, United Kingdom

More information: www.cavernoma.org.uk and www.facebook.com/Cavernoma.Alliance.UK

Interview: Tim Gallegos

Connie Lee: I am here today with Tim Gallegos who has recently joined the Board of Angioma Alliance. He is from New Mexico and he is going to be sharing his story and his family's story with us. Tim can you tell us a little bit about your family's experiences with cavernous angioma?

Tim Gallegos: Sure. It all started back in 2005 when our whole family was genetically tested for CCM. This was a few months after the loss of our 9-year-old daughter Jenae. She had a hemorrhage in her cerebellum. It wasn't until a month after she passed away that we knew she had CCM. The test results for our entire family revealed that my oldest son Jordan and I were negative. My wife Sandra and my youngest son Joel were positive for CCM1. Eight months after losing our daughter Jenae, our youngest son Joel had similar symptoms as our daughter Jenae did when she got sick. We took him to our local hospital and it was a shock to find out that in the ER they had no knowledge of CCM, what CCM was. They were trying to Google what it was. Our daughter had been through those doors eight months prior. With a CAT scan, Joel was found to have a micro-bleed at that time.

Now, we drive 55 miles away to Albuquerque for all our CCM issues because they are knowledgeable about it there. With my wife Sandra, she had an MRI here at the local hospital and she was given a clean bill of health. We thought we should get a second opinion so we went to Albuquerque and worked with Dr. Morrison. We showed her the slides and even though they weren't the right sequence - they were of a lower resolution or sequence pattern - she was able to detect something on the slide within seconds. She ordered an MRI with the right sequence and with contrast, and it was found that my wife had a couple of small lesions. It's just hard because here locally we just don't have

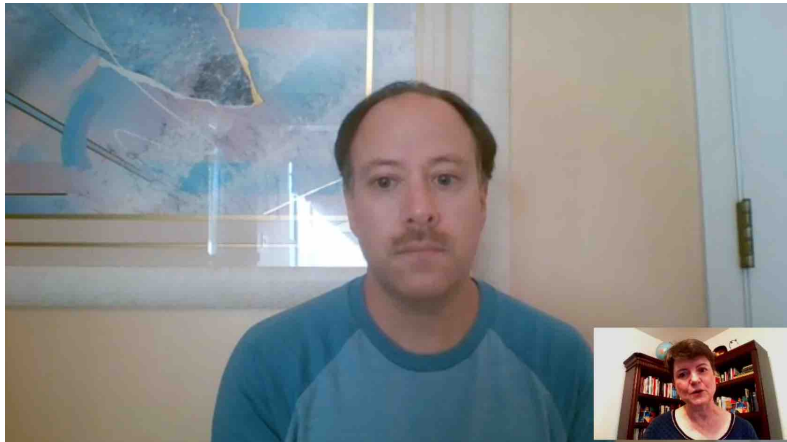
support and we found that a lot of rural areas don't really have expertise with CCM.

The last part of our experience with CCM is with Joel. He started having seizures in 2010. This was after he came home tired from a vacation. He was put on Keppra. After 3 years of being on the medicine, the seizures started getting more frequent. Though Dr. Morrison had increased his Keppra levels, the seizures were still breaking through. We had gotten 3 different opinions for Joel about having surgery and being that he wasn't able to go to school and function we didn't have any choice. It was the hardest decision we had to make to put him through brain surgery. In March 2013, Dr. Yonas removed a lesion in his right frontal lobe. Since then, his seizures have stopped. His Keppra levels have been brought drastically down. He is still taking some Keppra because there is another lesion in the parietal region that we're keeping a watch on. Basically, 2005 started our nightmare; we were not able to be proactive with Jenae. We didn't know she had the illness. We didn't know anyone in our family had the

illness. Knowing about it afterward, we were able to be proactive with Joel and it has made a difference.

CL: Tell me a little bit about what you've been doing in New Mexico, why New Mexico is so important, and what your plans are going forward.

TG: To address why New Mexico is so important - I think it spans into the Southwest area - there seems to be a common ancestor who had the CCM1 mutated gene and is the ancestor for hundreds to thousands of people in this area who have CCM1. This illness has been misdiagnosed for hundreds of years. We're really trying to spread awareness, trying to let people know about the illness so they don't face the same consequences we did with Jenae. Also, to prevent deficits because being proactive is key.



Some of the things we've been doing – for the last 3 years we been members of the New Mexico Brain Network. We're a group of volunteers who represent all the different types of brain illnesses. We support each other with spreading awareness, obtaining resources and raising advocacy. Also, to spread awareness my wife and I have done newspaper and radio interviews. We also recently created a pamphlet in collaboration with Dr. Morrison. The pamphlet is our family's story. The other purpose for the pamphlet was to let others know about research studies that are being done at UNM by Dr. Morrison. We nicknamed the pamphlet "The Persuader" because we strongly feel that with our family's story those people who have been reluctant to get diagnosed - especially maybe stubborn family members - the story would inspire them to be proactive based on the fate of Jenae. The other effort we just started is a CCM support group that's face-to-face. We thought with our experience and what we've gone through, no one should have to suffer with CCM alone. There are so many issues with CCM, and we can all learn from each other and support each other through thick and thin. We had our first meeting a week ago and we got some positive feedback from the group. We're really excited.

CL: You had speakers there as well.

TG: Yes, we had Joyce Gonzales who talked about the history and genealogy of CCM here in New Mexico. We had Christine Petranovich from UNM who has a study underway researching the psychological aspects of CCM with children who have the illness. My son was able to meet two other children because there was a children's table there. He was able to meet other children who have CCM, who have issues, who have had surgeries. The other thing we've been working on is we're with a team of clinicians, researchers, and other CCM family members. We're getting together with the purpose of planning for a grant to expand awareness and our knowledge of CCM.

CL: Is there anything else you would like to share before we end?

TG: I would just say to the people out there that CCM can be very fearful. Hang in there. Find a good doctor and find other people who have gone through the same or similar circumstances. Together we can all get through it and we hope that with more people

raising advocacy and spreading awareness that we'll some day have the magic pill that will keep lesions from growing or forming in the first place. Until then, we just need to hang in there and do what we can collectively to move forward.

CL: Thank you.

Activities in New Mexico

Because of a shared ancestor, New Mexico has more people with a hereditary form of cavernous angioma than anywhere in the world. The Common Hispanic Mutation, as scientists have named it, has led to thousands of individuals with the illness, many of whom have not been diagnosed. Angioma Alliance has participated in years of outreach and legislative efforts in New Mexico. Most recently, Tim Gallegos has formed a patient and family support group that meets quarterly in Albuquerque. The meetings feature expert presentations, time for discussion, and an opportunity for affected children to meet. See www.3cs.info for more information.

In addition, the University of New Mexico has received several grants to understand and assist our New Mexico members, including a grant to study the effect of the illness on children and a large, long term grant to understand what other factors might affect the severity of the illness in an individual. Tim Gallegos, Connie Lee, other New Mexico patients, and UNM medical professionals are currently preparing a grant application related to early diagnosis.

The fact that New Mexico CCM families have a shared ancestor makes for a unique and critically important population. The studies mentioned above are just the tip of the iceberg in terms of researcher and drug company interest. Every major study involving humans in the United States would like to include UNM as a partner and New Mexicans as participants. If you live in New Mexico, please consider joining the Susan Sukalich Angioma Alliance International Patient Registry at www.angioma.org/registry so that we can let you when studies are recruiting.

International News

Cavernoma Alliance UK

March 2016 was "Together for Cavernoma Month." The CAUK office were involved from the outset, organising our members, volunteers, supporters, and staff in a Walk for Cavernoma to the impressive Maiden Castle iron-age hill fort. Most of this intrepid group succeeded in ascending the hill to the fort's ramparts, and the walk successfully raised awareness with the local media who reported extensively on the event.



The concept of "Together for Cavernoma Month" seemed successful with many members contributing to the appeal. One member, Kirsten Macpherson, and her colleagues also participated in the event, raising awareness of cavernoma at the dental practice where she works, offering free dental checks for a day, holding a raffle, and selling cakes and coffee.

CAUK secured its first much-coveted Virgin London Marathon place this year, bravely taken up by member Dave Overy. David ran the London Marathon for CAUK in support of his daughter Poppy who has a cavernoma.

Exciting news. CAUK has been awarded £10,000 (about \$15,000) from BBC Children in Need. Part of this money will be used to pay for the 2016 CaverFamilies programme, which supports families and carers of children and young people who have

cavernomas. The CaverFamilies Residential Weekend is to be held at Woodlands Tipis and Yurt, set in seventeen acres of mixed woodland. CAUK has hired the entire site for the penultimate weekend in July. Also planned is a meeting for children in Northern England and a Young Persons' CaverHub meeting in the south.

The charity has attended four conferences in the past 3 months: The Society of British Neurological Surgeons. The British Neurovascular Group, BritSpine, and the European Association of Young Neurological Surgeons. Having a presence at these conferences is vital for CAUK to raise awareness amongst the medical profession.

CAUK has also been awarded a grant from The Goldsmiths' Company Charity, which will be used to partly fund the services CAUK provide at its annual Forum for those affected by cavernoma. The Forum is our international meeting open to everyone from anywhere in the world. The Forum is free to attend, and CAUK hope that with this being our tenth anniversary, members from Angioma Alliance will come and have supper with us in London on June 10, and stay for the Forum on June 11. Details are on the website: www.cavernoma.org.uk/cauks-2016-international-forum-and-supper/

Additional funding for the charity comes from The Morrisons Foundation. These dedicated funds will be used to establish four more regional CaverCentres in 2016 enabling CAUK to provide more local meetings and support networks.

Whilst it is wonderful to have such exciting opportunities, the charity remains unable to be self-sustaining without the support of the Big Lottery. Why? Because with the exception of Alice Ellen Cooper Dean Charitable Foundation, no foundation has supplied us with funds not designated for a specific project. We are relying on the support of our superb members and the skills of our grant writers to secure our present position.

Ian Stuart and Angela Yeomans

5th ANNUAL

6.11.2016

Angioma Alliance Canada Conference

Peter Gilgan Centre for Research and Learning
The Hospital for Sick Children
686 Bay Street
Toronto ON, M5G 0A4

"Hosted By Shawn Mulvihill AAC President"

KEYNOTE SPEAKERS:

Dr. Brent Derry, PhD

The Hospital for Sick Children, Senior Scientist
Developmental & Stem Cell Biology



GUEST SPEAKERS:

Connie Lee

Connie Lee is the founding President of Angioma Alliance in the U.S.A. Connie is a clinical psychologist and the mother of a daughter with cavernous malformations.



Meet and Greet on Friday evening
Details @ angioma.ca

Dr. Peter Dirks, MD, PhD

The Hospital for Sick Children,
Staff of Neurosurgery



\$15 PER PERSON

\$25 PER COUPLE

\$40 PER FAMILY OF 3 OR MORE

KIDS UNDER 6 FREE

Please register via

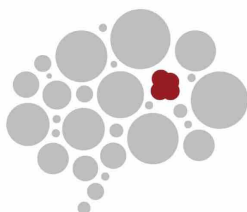
www.angioma.ca

1-800-717-2146

Registration: 8:30 am

Event: 9:30 - 4:30 pm

Lunch Provided



Angioma Alliance Canada
Working Towards a Cure



CCM Italia

2015 has been a very active year for both the CCM Italia research network and the Associazione Italiana Angiomi Cavernosi (AIAC) patient organization.

CCM Italia has further expanded and strengthened the cooperative network among clinical and basic research centers in Italy through the participation of new Units, including major Centers of Excellence in cerebrovascular research and healthcare, such as the C. Mondino National Institute of Neurology in Pavia and the Neuromed Mediterranean Neurological Institute in Pozzilli, Isernia.

To date, the CCM Italia cooperative networking effort has produced a large framework for multidisciplinary and integrated research approaches. This has resulted in novel insights into the understanding of CCM disease pathogenesis and treatment (Marchi et al., 2015 EMBO Mol Med; Marchi et al., 2016 Rare Diseases), and the identification of factors that may modify the range of phenotypic features, determining the large interindividual variability in disease severity (Choquet et al., 2016, Free Radic Biol Med).



AIAC has significantly contributed to provide patients and families with access to current information about CCM disease and leading clinical centers with renowned expertise in cerebrovascular research and comprehensive care delivery, offering support services. It has also helped spread knowledge and raise awareness of CCM disease among Italian people and healthcare institutions through various activities, including comprehensive educational initiatives and the participation to popular regional and national radio and TV programs.

Many CCM patients have received major psychological benefits from the AIAC support, including the possibility to share their clinical stories and interact with people who can listen to them and understand their feelings, offering help to face the disease without feeling alone. One example of this is a letter of a 30-year-old girl from Sicily, stating as follows: "I wished to work, study, dance. I love dancing but I could not and I cannot realize my dreams [...] I still hope to be able to realize my dreams: it would be enough if just one of them can come true." (See the full text at the Clinical Stories section in the CCM Italia website).

While providing some benefit to patients, such letters constitute strong stimuli and deep motivational input for researchers, who feel the duty of carrying out the best research efforts focused on changing the course of CCM disease in order to provide real and effective help to those who need it. Surely, this achievement would be more gratifying and rewarding than any publication of outstanding and prestigious academic value in renowned journals.

Francesco Retta

For more information, please visit the CCM Italia website: www.ccmitalia.unito.it.

References:

1. Micieli G. et al., Cerebrovascular diseases at the C. Mondino National Institute of Neurology: from Ottorino Rossi to the present day. *Funct Neurol.* 2011; 26(2):87-95.
2. Squitieri F. et al., Cavernous angiomas of the nervous system in Italy: clinical and genetic study. *Neurol Sci.* 2000; 21(3):129-134.

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.

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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 our support for the patient and research community. Sponsors are acknowledged with logo placement, naming opportunities, or appropriate other recognition. Sponsorships are available for the following:

Scientific Meeting - \$35,000 to \$1,000

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

Newsletter - \$10,000 to \$5,000/year

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

Website - \$10,000 to \$1,000/year

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.

Events - Range of opportunities

Angioma Alliance members host multiple events throughout the year, from Cavernous Angioma Awareness Night at major league sporting events to smaller Fun Runs and tournaments. Sponsorship opportunities are always available with varying levels of public exposure depending on the event.

DNA and Tissue Bank - \$20,000/year

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 Brian Fair at bfair@angioma.org or (206) 446-8051 to learn more about these opportunities and valuable benefits for your company.