



Winter 2012

# Angioma Alliance Newsletter

## Scientific Update: 2011 CCM Workshop

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Note: In this newsletter, the terms "cavernous angioma," "cavernous malformation," and "CCM" are used interchangeably.

This November marked the 7th annual Pathobiology of CCM Scientific Workshop, and this year Angioma Alliance partnered with Cavernoma Alliance UK and Genetic Alliance UK to host the meeting in France. The French venue was chosen to help facilitate participation of European labs that have not been able to attend previous workshops. We are thankful to all of the cavernous angioma researchers who attended the workshop—this year there were nearly 50 participants from more than 20 labs who traveled from the United States, Canada, the United Kingdom, Spain, France, Italy, Israel, Germany and Brazil.

Students, postdocs and senior faculty members delivered 20 oral presentations that made up the scientific agenda. The material presented was all new, unpublished, or recently published data. This is an important point; we encourage our researchers to share cutting edge data with one another in a friendly and open environment. This helps to facilitate collaboration and advance the science most quickly. Because much of the work presented at the meeting is unpublished, we will not report on specific findings in this newsletter, but instead provide a

general description of the conference.

One of the great features of this workshop is that it includes presentations on all aspects of CCM research. We had talks from technical bioengineering and computer-based MRI folks as well as basic biologists, translational researchers and clinicians.

The first session of the workshop focused on *Signaling & Molecular Biology*. The research projects described in this session each focused on better understanding the specific biological function of the CCM1, CCM2 and CCM3 proteins. To do this, these researchers took a variety of approaches. Some looked for molecules that physically interact with the CCM proteins—if a protein interacts with another molecule, it can be reasonably assumed that that protein is involved in the same functional pathway. Other groups used assays that involve mutating one of the CCM genes in a laboratory culture of blood vessel cells and then observing the cells for changes in growth, development and/or the ability to form normal tube structures. Through gaining a better understanding of the function of these proteins, and determining with which other molecules they interact, researchers hope to identify potential new targets for CCM therapy.

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Day 2 of the workshop was all about *Animal Models & Vascular Biology*. The talks in this session varied greatly and included discussions of possible drug targets and treatments, the role of inflammation on CCM and how the CCM proteins are involved in the normal growth process of blood vessels. Blood vessel growth is a complicated process that involves changing cell shape, allowing cells to migrate and finally sprout off new vessels from preexisting ones.

Another presentation focused on the question of how neurons are involved with CCM. It is well known that neural cells and blood vessels cells communicate with each other as part of proper development. To determine whether CCM3 is necessary for this communication, these researchers examined mice that are deficient for CCM3 only in the neurons. Also, the recent study of Fasudil treatment of mice was discussed in this session (more on this later).

The final workshop day was dedicated to presentations of *Human Studies & Clinical Trials*. Three presentations described new magnetic resonance imaging technologies that have the power to provide enhanced detection capabilities, 3D modeling, and the ability to measure permeability within the brain and CCM lesions. The permeability MRI is a tool that will be used in a study at the University of New Mexico. Pending approval by the University’s review board, this study will look at the effects of statin drugs on lesion permeability. This group will be specifically working with individuals who have the Common Hispanic Mutation to determine whether statin drugs reduce the “leakiness” of CCM lesions and thereby lead to less bleeding and fewer clinical symptoms.

The design of this study is to assess “baseline” permeability by MRI on CCM patients who are not treated with statins. Then, those individuals will take statins for 3 months and at the end of that time, MRI will again determine permeability. By comparing the pre- and post-treatment MRIs, this research group

may better understand the effects of statin treatment on human patients. Recruitment for this study is planned to begin in the coming months.

So, what about larger-scale clinical trials for statins or Fasudil? The data that has come from mouse research for both of these drugs is exciting and very promising. However, at this point there is no clinical recommendation that statins or Fasudil should be used as a CCM therapy. Prior any recommendation there must be three phases of clinical trials. (For more about the Fasudil study, see the note at the end of this article.)



*Isam Awad, Leslie Morrison and Blaine Hart taking questions from fellow researchers.*

Phase I trials are the smallest studies to show the safety of a drug. Phase I trials must be conducted for statins, Fasudil, and any other medication under consideration for treatment of cavernous angiomas. Statins are currently approved to treat high cholesterol and it is well known that they are safe drugs for the general public. However, there has not been testing to demonstrate that these medications will be effective in treating cavernous angiomas in humans.

Fasudil is a drug that is currently approved for use in Japan to treat individuals who have suffered a specific type of hemorrhage. Importantly, it is only approved for use in a 1-month treatment period. In the mouse study, mice were chronically treated with Fasudil in their water supply for 3 or 4 months (this amount of time aged them from baby mice to fully mature adults). It is unknown whether Fasudil would be safe for humans to take daily, and perhaps for a lifetime, as a preventative medication. Thus, a new safety study is necessary for this drug as well.

Following the safety trial, Phase II and Phase III clinical trials are much larger, and test efficacy to see if the drug of interest provides therapeutic benefit. Measuring therapeutic benefit is a challenge for CCM because the illness is so variable in different



*The Château de Chantilly, near the conference venue, on an overcast day*

individuals—some people have single lesions, other many; some suffer hemorrhage, stroke or headaches, while other may have other symptoms. A few possibilities for measuring therapeutic benefit might include hemorrhage rate, the number of new lesions that develop over time, or permeability of the lesions.

These studies will need a lot of support from the Angioma Alliance community. At least 1,500



*Isam Awad and Rustam Al-Shahi Salman*

individuals will be needed to participate. Currently, the patient registry only has about 370 members. If you are interested in participating in research studies, please sign up for the patient registry! By signing up, you will be contacted about studies that need volunteers and you can help to speed up the recruitment and study process. Sign up today at [www.angioma.org/registry](http://www.angioma.org/registry)

In summary, the CCM research community continues to produce novel and exciting results that are leading us in the direction of new therapies. Each year the workshop continues to grow, new collaborations are developed, and progress is made. We are excited by the scientific advancements that have happened over the past year, and look forward to continuing the momentum towards human studies and clinical trials.

*Amy Akers*

Note: A paper called, “Fasudil decreases lesion burden in a murine model of cerebral cavernous malformation disease,” was published online on Oct. 27, 2011, by Stroke, and in the January 2012 print issue of the journal. You may access the full press release for this paper at [http://www.eurekalert.org/pub\\_releases/2011-10/uocm-dts102411.php](http://www.eurekalert.org/pub_releases/2011-10/uocm-dts102411.php).

For more about this study, see a blog article by Amy Akers: [www.angiomacommunity.org/blog/?p=440](http://www.angiomacommunity.org/blog/?p=440)

## Supporting Each Other

Angioma Alliance has always been an organization whose focus is “People helping people.” This priority is especially apparent in the member and peer support that Angioma Alliance provides. Angioma Alliance’s Community Forum, peer support program, Facebook page, and the caring people who visit hospitals to give support to fellow members having surgery have all been an invaluable part of Angioma Alliance’s mission.

One of the organization’s first goals was establishing an online Community Forum where members could exchange information and support each other through good times and, more importantly, difficult times. Over the ten years that the Community Forum has been in existence, the support given and the lasting friendships formed have been invaluable. In this past year alone, there have been over 5,000 posts! Many vital members of the Community Forum post nearly every day and welcome newcomers as they find us. Libby Davis is the moderator who catches the rare post that goes unanswered. She’s been an active participant of the forum for a long time, and her perspective and support have helped to set the tone in our Community.

People from all over the world use the Community Forum. As Angioma Alliance has grown, so has the forum. The forum includes sections for different languages including English, Spanish, French and German. It also has forums based on geographic location, which include the United Kingdom, Canada and the United States. For many people, Angioma Alliance’s Community Forum is a lifeline to information, emotional support, and a feeling of community. If you are part of Angioma Alliance’s Community Forum, you are part of a group of people who welcome and support you.

Angioma Alliance’s Peer Support Program has also been a tremendous help to people in need, particularly people who have been newly diagnosed, who have newly diagnosed family members, or people who are facing surgery. During these times, people often feel scared, vulnerable and alone. Being able to talk with or e-mail somebody who has experienced what you are experiencing can be very comforting and help people get through this difficult period of upheaval and adjustment. Just knowing that

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somebody is there for you, willing to listen, and truly understands because they have gone through the same thing themselves, can make a difference.

In the five years since the peer support program was launched, Angioma Alliance has matched hundreds of people with peer supporters. Norma Villa heads Angioma Alliance's peer support program. She sends out questionnaires and interviews potential peer supporters and answers requests from people seeking peer support. Once Norma has received all the pertinent information from both the peer supporter and the person needing support, she makes a "match." The categories for matching a peer supporter to a person needing support include which area of the brain is affected and who in the family is affected (for example, matching parents whose children are affected or matching an adult with an adult). Also, if possible, it can be helpful to match people in a similar geographic region (same state, or even same city, if possible). Religious preference and gender requests are also taken into consideration. A man might want another man as his peer supporter, for example. Norma Villa does an excellent job fulfilling these many requests and requirements.

Darla Clarke-Clayton is one of Angioma Alliance's peer supporters. She has been a peer supporter for over 3 years and has supported approximately 20 people in that time. Darla loves being a peer supporter. She says that she hopes that she gives people a sympathetic ear, but at the same time, Darla says that she often learns from the people she supports. Also, she often gets ideas and new perspectives from the people she supports and says that it is definitely a reciprocal relationship. She feels that she gets as much as she gives, and that she is grateful to have the opportunity to help people and sometimes form lasting relationships.

Holly Ayala is one of the people that Darla Clarke-Clayton supports. Holly has a two year-old son who has been diagnosed

with cavernous angiomas. Holly Ayala and Darla Clarke-Clayton were matched for peer support because they both have sons with the condition. Holly says that Darla is a wonderful support to her in so many ways. The medical tests, procedures and medical terms used to describe cavernous angiomas can be confusing and difficult to understand. It can also be frustrating and exhausting to have to explain to numerous friends and family what all these medical terms mean. But when Holly speaks with Darla, she doesn't have to explain. Darla has been through the same medical experiences with her son and she understands. When Holly and Darla speak, there is an understanding between them that would be difficult to find anywhere else.

In addition to Darla's peer supporter responsibilities, she also coordinates the Traveling Awareness Bears program for those with cavernous angiomas where two teddy bears named

Charlie and Charlise visit children from all over the world. Each bear wears a t-shirt stating its name and diagnosis (the same diagnosis as the child) and the Angioma Alliance little red man logo. The child keeps the bear for companionship and comfort and then, when ready, sends the bear on its way to visit another child. Darla is the bear's steward and sends the bears on their travels to bring comfort and awareness wherever they are needed. Visits from the bears can be requested at: <http://www.trackpatforpsa.org/invite-pat-to-visit/>

Angioma Alliance also supports its members through its Facebook page. Angioma Alliance has had a presence on Facebook since 2008, and the Facebook group has grown rapidly and now boasts over 1,500 members!

Angioma Alliance is also lucky to have members who take the time to visit other members who are having surgery in the hospital. Becky Schnee and Angioma Alliance Board member Savannah Hollis are two of these special people.

Becky Schnee had surgery herself in December, 2006, and since then has been visiting members who are having surgery at the Barrow Neurological



*Darla Clarke-Clayton and family*



*Holly Ayala*



*Becky and Kevin Schnee*

Institute in Arizona. Becky tries to visit people both before and after surgery just to say “Hi” and give comfort and reassurance if needed. Sometimes patients have family members with them when they have surgery, but for the patients who are on their own for the surgery and recovery, Becky’s visits are a much needed reminder that they are not alone and somebody is there to listen and assist them, if needed.

Angioma Alliance Board member Savannah Hollis also visits members who are having surgery at the University of Texas Southwestern Medical Center. Savannah visits members before surgery to emotionally support them, answer any questions they may have, and connects them with community resources, if needed. Savannah goes out of her way to help members in any way she can. If they are from out of state, she helps find hotels, runs errands for them, and even buys food or takes them out to lunch to help them feel that they are not alone. Savannah says that it helps people to know that she has been where they are right now and that she understands.

Through all of these programs and the time and effort of so many people, Angioma Alliance has been able to offer support to its members both person-to-person and online. Angioma Alliance has always been about people helping people and we hope to maintain this high standard into the future.

*Kristen Dehn*

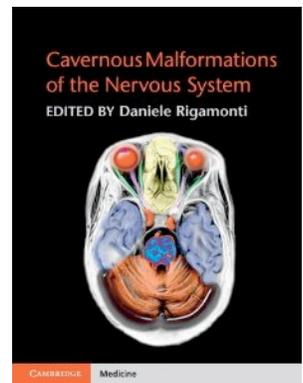
Remember, without you there can be no cure. Sign up for the Patient Registry today at [www.angioma.org/registry](http://www.angioma.org/registry)

## News

### **New Medical Textbook about Cavernous Angioma**

A new medical textbook about cavernous angiomas has just been released; this is the first major book on the topic in four years. It contains a wealth of information about diagnosis and management of cavernous angiomas. Topics of interest include: pros and cons of conservative and surgical management, management in children and pregnancy, and genetic counseling. If you do look at this textbook, remember that information quickly becomes out of date and that any medical decisions should be made with your doctor. The book is edited by Daniele Rigamonti, MD, and published by Cambridge University Press. It sells for \$135, and a Kindle edition is available for less.

From the publisher’s description of this book: "Questions regarding the nature and appropriate management of cavernous malformation (CM) have clouded researchers and those faced with making clinical decisions for several decades. CMs may be seen as an incidental finding on MRI studies, or they may present with symptoms, such as seizures or intracranial hemorrhage, often causing severe neurologic deficit. Cavernous Malformations of the Nervous System provides a comprehensive and authoritative review of the current practice in diagnosis and management of these cerebrovascular disorders. Emphasis has been laid on the understanding of basic sciences with chapters committed to understanding of CCM1, 2 and 3 genes and their role in CCM biology, as well as clinical genetics. Controversial topics which continue to pose treatment challenges such as safety of anticoagulation and prophylactic management during pregnancy are also discussed. This book will be of interest to basic science researchers, neurosurgeons and vascular neurologists both in academic institutions and private practice."



## Angioma Alliance Canada is Formed

In the fall 2011 newsletter of the Angioma Alliance, there was a call to start your own action group. It read: "Action groups will focus on a particular problem, such as brainstem lesions, or a location, such as New Mexico." So, without further ado, we are pleased to announce the launch of Angioma Alliance Canada (AAC). AAC is a local affiliate of Angioma Alliance, seeking to provide information, resources and support for sufferers of Cavernous Angiomas, as well as to increase awareness and support research into this disorder. In addition, this local branch will provide information specific to Canadians—ranging from ongoing studies, to tax implications, and everything in between—as well as connecting Canadian sufferers of this disorder.



The AAC, a newly recognized Canadian charity, will have a web site at <http://www.angioma.ca>, and will contribute generally applicable information back to the global Angioma Alliance site. Henk van der Wilt, a Canadian with a recent diagnosis of the familial form of cavernous angioma, found the lack of knowledge within the general population as well as within the medical field problematic. Having been an educator for more than ten years, he felt compelled to organize the Canadian sufferers and give them an opportunity to get their condition to the forefront. Assembling other sufferers together, united with a common goal, the group soon took its first steps—becoming a charity, and setting the goal of working towards a cure.

While this local branch does contain information specific to Canadians, all are welcome to be a part of it, be it by contributing information, sharing an experience, or simply stopping by to read the content.

As a united Angioma Alliance Canada we would like to thank Connie Lee and the entire Board of the Directors for their support and guidance in this process. We will fight side by side, together as one, as we are Working Towards a Cure!

*Henk van der Wilt*

## The “Stemmies” Facebook Group

My name is Gary and I am a stemmie. According to one member, Crystal, anyone that has or had a brainstem Cavernous Angioma is a stemmie and I believe that makes us unique enough to warrant our own Facebook group.

For nearly 5 years, I believed myself unfortunate, yet unique, after each bleed. After a January, 2011, episode, a team of neurologists told me I had a Cavernous Angioma and suggested I have it removed as soon as possible. But the neurosurgeon I was referred to could not perform the resection due to its "valuable real estate." He sent my records off to someone else and told me he would get back to me in 3 or 4 weeks.

Meanwhile, I had the name for the condition, and went straight home and Googled it. This is how I learned of the Angioma Alliance and eventually found my surgeon in a little hospital in Dallas.

Prior to surgery, I lived near Kansas City and only my wife could go along; I set up a Facebook group called CA so friends and family could follow the procedure. Many of them read nearly real-time updates that my wife Joni and fellow stemmie Savannah provided from the hospital waiting room. When Joni read the get well wishes from everyone, some from people in prayer groups that I didn't even know I was in; it was the silver lining on my dark cloud.

As for the stemmies Facebook group, it is made up of people that have had resections in the past, or are about to undergo surgery. The group allows all of us to share our experiences with those that don't know what to expect.

I chose the Facebook format because it is familiar to most of us and made it "closed" so that it is not as public as many of the other support groups. New members may be added by any current member whether they are interested in learning what to expect or willing to share their experience with new members. This allows members to interact and truly get to know one another. Many of us feel as if we are now family thanks to that approach.

We now have "stemmies" in many parts of the US as well as Argentina, Sweden, and the UK, and offer peer support to anyone requesting it.

*Gary Wescott*



## Cavernoma Alliance UK Update

Parts of the United Kingdom have recently been experiencing mild weather, and this Autumn has been so unseasonably warm that the Young Persons' CaverHub (YPC) could have been held outside the National Hospital for Neurology and Neurosurgery in beautiful Queen Square. But actually the meeting was held inside where Brana Thorn, YPC co-ordinator, ably assisted by Frank Gent, trustee, and a band of willing volunteers, ran a YPC, sponsored by Roald Dahl's Marvellous Children's Charity, Paula and Steve Wheeler and Kevin and Paula Cavill.

A stimulating talk was given by Mr. Christopher Chandler, consultant paediatric neurosurgeon, King's College Hospital, followed by a discussion with parents of young people affected by cavernoma, led by Brana Thorn and Paula Wheeler. Meanwhile, during the morning's events, activities were held for the young people in an adjoining room. Thanks to our sponsors, lunch was provided at a nearby pizza restaurant prior to being taken by private bus to the Science Museum.



*Crystal Shaulis and Desrae Van de Wetering, members, and Frank Gent, trustee, run a workshop for the Young People*

CA UK is pleased to announce that the charity has been short-listed for its 2012 London sponsorship of YPCs by Jeans for Genes. CA UK would also like to introduce regional CaverHubs (for groups outside of London). Sponsorship has been applied for these meetings through BBC's Children in Need. (CA UK will discover whether we have met with success by the middle of February 2012). In addition, the charity hopes that the trustees of Roald Dahl's Marvellous Children's Charity will favorably consider a further grant to CA UK for a much-needed break for children and their parents with cavernoma.

Ongoing research into cavernoma is an area that CA UK has wanted to undertake for a long time. So when an opportunity arose to work with the generous support of Genetic Alliance UK (GAUK) on a set of clinical guidelines for CCM, CA UK jumped at the chance. CA UK funds were invested in research undertaken by a team at the University of Edinburgh led by one of CA UK's medical advisers, Dr. Rustam Al-Shahi Salman, with additional input by Mr. Neil Kitchen and Dr. Jonathan Berg.

When fully available in March, 2012, these guidelines should offer clearer information for doctors many of whom are presently resistant to relying on volunteer support groups in the Third Sector. Having been made aware of the condition by recognized neurological, neurosurgical and genetic experts, clinicians and doctors may be more sympathetic to the support and information about the condition which CA UK can provide.

Beginning recommendations for the CCM guidelines were presented to scientists by Dr. Salman at the Angioma Alliance 7th Annual Pathobiology Workshop, Chantilly, France (16–18 November 2011). As outlined by Dr. Salman, 196 articles regarding cavernoma were cited but only 6 studies met the required admissible criteria.

During the grey months of January and February, 2012, the air in the cavernoma office will be buzzing with the organization of the International Cavernoma Alliance UK London Brain Awareness Week Lecture on 17 March 2012 with Mr. Kerr, consultant neurosurgeon, from John Radcliffe, Oxford. And our annual presentation at the Society for British Neurosurgeons which this year is to be held in Aberdeen, Scotland.

The Sixth Annual International CA UK Forum will feature guest speakers including our confirmed keynote speaker Mr. Owen Sparrow, consultant neurosurgeon, Southampton. Please note: due to the British public holidays in early June, 2012, the Forum will be held at the Grange Hotel slightly later than normal, Saturday 16 June 2012. Make those international reservations now. CA UK will be pleased to welcome you to our international meeting.

*Ian Stuart*

**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 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 will help fund conferences and forums, increase research, and enhance outreach and support efforts. Our pins, car decals and wristbands support the mission and growth of Angioma Alliance. Share these meaningful gifts with your friends and family.

Each donation of \$10 or more will come with a CCM lapel pin as a thank you gift. Our “little red guy” pin is a wonderful way to increase awareness of cerebral cavernous malformation (CCM). Increasing public awareness can go a long way toward increasing research funding and improving quality of life for those with cavernous angioma. Each pin comes with cavernous angioma business-size information cards that can be handed to anyone who might have questions.



Angioma Alliance also offers a wide range of apparel and other items featuring the Angioma Alliance logo. There are t-shirts, sweatshirts, hoodies, mugs, stickers and much more available. You can find these items in our Café Press store. To purchase Angioma Alliance merchandise, go to our web site and click the Store link at the top of the page.

To donate to Angioma Alliance, send a check or money order (using the enclosed envelope) or visit [www.angioma.org](http://www.angioma.org). You can also donate on line using a credit card with our Paypal connection.

**We Need You:** Angioma Alliance needs volunteers in many areas. If you have time to give, please visit [www.angioma.org/volunteer](http://www.angioma.org/volunteer)

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