SUMMER 2016
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Pathways to a Cure

The CAA Newsletter

MESSAGE FROM THE DIRECTOR

Summer is upon us! Since our last newsletter hit your mailboxes I've participated in multiple panel discussions about CAA and attended a very successful CAA research fundraiser in the Netherlands. One of the most moving experiences during these was hearing numerous families and caregivers tell their stories about living with someone afflicted by dementia. They reminded me of the invaluable role family and patient advocates play, not only in day-to-day care, but in research.

The growth in this kind of 'grassroots' support comes at a time of increasing national-level recognition and support for the small vessel brain diseases like CAA. The National Alzheimer's Project Act (NAPA), unanimously passed into law six years ago, was designed to address Alzheimer's disease and the AD-related dementias (ADRDs) which encompass Vascular Contributions to Cognitive Impairment and Dementia (VCID). The NAPA and ADRD initiative have meant more government research funding and more scientific attention to VCID. This matters because VCID contributes to the kinds of memory loss caused by CAA. While this act is not a cure for CAA, it is an acknowledgment of the importance of matching national focus with biomedical research.

As physicians we will continue to offer the best possible care to our patients – as researchers we will continue to design studies that (hopefully) influence treatment development. What we cannot do is walk in your shoes – as patients, families and caregivers. History has shown that disease research often gains increased funding, support and national recognition when patients, families and caregivers become an organized community and make their voices heard. I encourage you to acknowledge how valuable your voice is at the table.

In this edition of *Pathways to a Cure,* you will read about the value of our studies that collect biologic samples and our inaugural Caregiver Spotlight. We hope you enjoy this edition, and as always, thank you for your continued interest in our newsletter!

Sincerely,
Steve Greenberg, MD, PhD

Biologic samples and CAA research

The term "biologic samples" is used to describe anything that originates from the human body, such as blood, urine, or even skin tissue. Most biologic samples can be collected quickly and safely, making them an ideal source of medical information. These samples also have the potential to provide critical information about what is happening at a microscopic level, a perspective essential for both doctors and researchers alike.

While the field of neurology has seen exciting advancements in "high-tech" methods like MRIs and PET scans, the analysis of biologic samples remains an irreplaceable component of our research efforts. The J. Philip Kistler Stroke Research Center, in partnership with MGH's Center for Human Genetic Research, has conducted research with biologic samples for nearly twenty years. In our cerebral amyloid angiopathy (CAA)-specific research studies, we primarily focus on two sample-types: blood and cerebrospinal fluid (CSF).

One question we often receive is whether or not these biologic samples can be traced back to a specific person, i.e. our research participants. Since every person's biologic samples are unique and contain genetic information, they are considered potentially identifiable. However, we take this concern

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— Role of biologic sample collecting and testing

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very seriously and have extensive measures in place to protect both the identity of the participant and the physical samples we collect. In the twenty plus years that our center has obtained biologic samples, we have never experienced a breach in confidentiality.

One of the largest challenges we face in CAA/stroke research is the overall accessibility of the brain. The brain is protected not only by a hard, bony skull, but also by an internal "firewall" called the blood-brain-barrier. This firewall tightly regulates which substances are allowed to pass between the blood and the brain tissue, often times making it difficult to perform research on blood samples alone. For this reason many researchers have turned to CSF, which comes into direct contact with the brain, in order to obtain a more complete analysis. The collection of CSF (the colorless fluid that bathes the brain and spinal cord) is performed via lumbar puncture. When our team collects CSF for research, it is analyzed for certain types of proteins, for example amyloid ß-peptide. If present in decreased levels, these proteins may provide a set of clues about CAA.

As previously mentioned, analyzing blood samples comes with its own set of challenges. Unlike CSF, blood is separated from the brain by the blood-brain-barrier. However, blood is still heavily utilized in our research because it provides access to a participant's genetic information. Any cell, such as a red blood cell, that contains genetic information contains all of your genetic information. This makes it possible to collect a blood sample from your arm and know that the deoxyribonucleic acid (DNA) found is identical to the DNA in your brain. Therefore, when we collect blood samples we carefully extract the DNA to be analyzed for possible genetic influence in CAA and stroke.

Performing this type of genetic research requires a large number of samples – sometimes hundreds or thousands – and significant funding. In our group, we most commonly perform genome-wide association studies (GWAS), which are an examination of many common genetic variants from lots of different people. These variants are then tested for specific traits (a characteristic expressed by genetics). CAA in particular demands a very large sample size because it's considered a complex and spontaneous disease – involving multiple genes – and therefore we need more samples to increase the chances of seeing the modified genes. Once we obtain enough blood samples, we thaw the DNA, carefully mount it in tiny droplets onto microscope slides, and perform sophisticated analyses that we hope will tell us more information about CAA at a cellular level. While it may seem like a rather slow process, the first GWAS results in the world were only published 11 years ago! In that time, our group has collected enough samples to perform multiple GWAS studies from which we've discovered five different variants associated with hemorrhagic stroke and one variant associated with CAA, the ApoE genotype.

Additionally, an alternative way to study genetics, called sequencing, is rapidly evolving. This method requires far fewer samples than GWAS studies and also produces more precise results. It is our hope that sequencing will provide results that can be more easily applied to medical care, potentially enhancing our ability to individualize treatments for patients in the future.

We want to extend a special THANK YOU to all of our past and present research participants who have generously donated their time and biologic samples to further our research here at the J. Philip Kistler Stroke Research Center!

Cure

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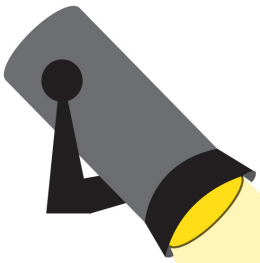
CAREGIVER SPOTLIGHT:



This edition of *Pathways to a Cure features our first ever Caregiver Spotlight. In it you'll read about Virginia's experience as a caregiver to her husband, John, who was diagnosed with CAA after surviving a hemorrhagic stroke. John generously participated in several of our genetic and imaging research studies, feeling lucky to have almost no lasting effects from his stroke. Over time, however, John's memory has begun to interfere with his daily life. Virginia kindly shared with our research staff what it's been like to become a caretaker to her husband and why they chose to participate in research at MGH.*

What was your initial impression when we asked your husband to participate in research?

John's neurologist in the clinic at MGH told us John was eligible for a research study. After the appointment we met two lovely research coordinators and our initial impression was, "wow, we've been so lucky (John having made an excellent recovery from his bleed) that if we can help someone else in some way we want to do that."

After coming in for a study visit, did that impression change? How so?

From the first research visit we felt very cared for. Everyone was so caring and understanding and compassionate; they seemed to really want to help John and help me get through it. At every research visit, even after one year had passed the staff was equally caring. We were glad that we did it, so many people were willing to give up time ... this might be able to be the one thing that could help someone in the future ... your staff truly made it easy so we were happy to help.

Has there been a "silver lining" to the diagnosis/research that you can share?

For us, the "silver lining" lies in the hope that the research will help someone else down the line.

Do you have any advice or strategies for staying positive?

The toughest part of this disease, for us, has been the memory loss. My husband was the most brilliant man I'd ever met. At times I cry a lot of tears as I try to accept our reality and live with it. I think the best advice I can offer is to try to accept and live your new norm. I know that John still has my back, which is comforting and makes me feel lucky. When I accept things the way they are John and I have better days. We still take a walk around the block twice a day and see old friends and whenever possible we're with our children and grandchildren.

Are there any resources you have found particularly helpful/informative during this process?

To be honest, thus far I haven't felt like I needed anything just yet. Still, it's a wonderful feeling knowing that you (the Stroke Research Center) are there and that there are people to lean on if we need to.

Do you have any advice for a newly diagnosed patient and his/her family members?

Not that anybody can really hear this because it's so difficult but ... accept the diagnosis and do everything the doctor tells you to do. Stay positive, take care of yourself so you stay healthy and are able to help keep your loved-one healthy. For me, I've found that it just isn't worth getting upset over; that is too painful. Instead, I've come to accept the diagnosis and our new norm and have begun going out with friends and my children to take a little time for myself.

"Like" us on Facebook for updates and more information about CAA!
https://www.facebook.com/CerebralAmyloidAngiopathy

J. Philip Kistler MGH Stroke Research Center
175 Cambridge Street, Suite 300
Boston, MA 02114

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Contact Information:

Please send your comments, questions and suggestions to: pathwaystoacure@partners.org. For more information on our CAA research and for FAQs, please visit: www.angiopathy.org

Looking to support CAA Research?
Many patients and families have lent their time and heartfelt dedication to finding a cure for CAA by helping raise funds for our clinical research program. The CAA Research Team at MGH encourages your interest in hosting a charity event or fundraising among friends, family and colleagues, and appreciate the efforts many of you have already made to this end!

If you would like to learn more about how to support CAA research at MGH, please visit this link: *https://giving.massgeneral.org/crowdfunding-community-fundraising/*

Individual donations can also be mailed to:
MGH Development Office c/o
Shawn Fitzgibbons
125 Nashua Street, Suite 540 Boston, MA 02114

***Please make checks payable to Mass General Hospital, memo: #1200-028184**