dada2 FOUNDATION

DRIVING TOWARD CONSENSUS

April 2022

In the last weeks, the daffodils have arrived in Nashville, Tennessee. These flowers are the first harbingers of Spring. We know that warmer weather is coming soon. But it's also a reminder that we are already a quarter of the way through 2022. We have so much to do before the end of the year!

And to help accomplish our goals, I'm thrilled to announce we have hired Julie Williams as our Research Engagement Director. Julie joins us as a Genetic Counselor with a passion for working with families and children affected by rare disease.

Julie is jumping right in to oversee the development and implementation of our Natural History Study and Patient Registry. You will be hearing more about this over the coming months. The NHS/Patient Registry is a critical step in developing our understanding of the natural progression of DADA2 as it will offer a wealth of de-identified data for researchers working to improve the treatment and find a cure for DADA2.

Join me in welcoming Julie to our ever-expanding DADA2 community.

Sincerely,

Chip

Chip Chambers, M.D.
Founder and President, the DADA2 Foundation

Hello!

I am thrilled to join efforts as a Genetic Counselor trained in Rare Genetic Diseases, and importantly, as a mother of two who can appreciate our shared group sense of urgency to improve care and treatments for loved ones with DADA2.

I truly look forward to meeting and getting to know each and every one of you, and to sharing your excitement as we forge new progress together. The Natural History Study and Patient Registry are exciting projects I'm eager to get started on this month.

Part of my new role will be keeping you up to date on all the new studies coming out about DADA2. Below are two important articles by Dr. Amanda Ombrello's team at the National Institutes of Health (NIH, USA)

and Dr. Pui Lee et al of Harvard Medical School that give new insights about many of the common symptoms and their causes.

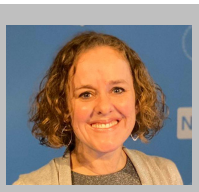
Excited to be here,
Julie Williams

Dr. Pui Lee

Dr. Pui Lee (Boston Children's Hospital / Harvard University), **Dr. Ivona Aksentijevich** (National Human Genome Research Institute), and **Dr. Qing Zhou** (Zhejiang University, China) **released a review article** this month summarizing what we now know about the science behind the vascular symptoms we see in DADA2 patients.

New studies have helped explore the inner workings of our immune system response when the body is missing ADA2 or when this enzyme is not working and the lining of blood vessels become damaged, or vessel walls become thickened or narrow. We are beginning to understand where we may be able to target new treatments in the future to prevent further inflammation and blood vessel damage. Experiments in cells missing ADA2 enzyme have shed light on how the immune system gets turned on and turned off in different ways that can cause blood vessel damage.

This understanding may help us to figure out how medications can help calm the inflammation response in new ways and stop further damage to blood vessels in the body. It also discusses approaches to help those patients with hematologic symptoms who aren't seeing improvement with current treatments. **This review article** tying the ideas of many researchers together is very valuable in helping our doctors gain new insight into the way DADA2 affects our bodies. With more work studying DADA2, we hope to learn better ways to treat many of our patients with vascular symptoms.



Dr. Amanda Ombrello

Dr. Amanda Ombrello and her team of researchers at the NIH studied a group of sixty patients with DADA2 to note the variety of symptoms patients experience and how well anti-TNF medicines such as etanercept and adalimumab managed their symptoms. All patients in the study had DNA tests revealing ADA2 gene changes and underwent extensive examination by subspecialists of their skin, blood vessels, liver, spleen and kidneys. All patients had MRIs done of their brains as well, looking for evidence of prior strokes. Genetic tests were offered to all the reportedly unaffected siblings of the patients and revealed seven additional DADA2 patients. After a closer investigation, all seven of these family members had at least one clinical or immunological finding consistent with DADA2.

An exciting finding was that anti-TNF medicines prevented stroke in ALL patients treated, including those who had had a prior stroke. Some patients saw fewer tender bumps (nodules) and mild relief of livedo racemosa. Others noticed no difference in their visible symptoms, nor in tingling and temperature sensitivity, which can be present in patients with Raynaud's phenomenon. On TNF-inhibitors, blood tests showed a lowering of inflammation among those patients with active inflammation. The researchers did not observe significant improvement in neutrophil levels, antibody production, or red blood cell counts with anti-TNF medication unless the decreased red blood cell counts were related to inflammation suppressing their production. Persistent neutropenia and/or pure red cell aplasia were the primary DADA2 features that prompted referral for stem cell transplant.

Among the six patients in the study who underwent stem cell transplant, four required more than one transplant before they were able to fully engraft. Following successful transplantation, all six patients were able to remain off anti-TNF medications. Importantly, no serious side effects were observed due to anti-TNF medication treatment even in those patients who had immune deficiency secondary to DADA2. We look forward to more large studies like Dr. Ombrello's to increase our knowledge about DADA2.

Our community is growing and spreading the word! The DADA2 Foundation is thrilled to support several local meetings being organized by patients, families and physicians.

- On April 16, Ishaan Jeloka, Dr. Raju Khubchandani and colleagues will be hosting a group of patients and families in Mumbai, India.
- On May 5 in Bologna, Italy, Dr. Francesca Conti has organized an educational physician

conference titled: ***ADA2 deficiency (DADA2): More than one disease. A multidisciplinary approach from the clinic to the bench***.

- In the Netherlands, Linda Swart, Sanne de Jong and Dr. Joris van Montfrans have organized their second Dutch DADA2 meeting in Utrecht on May 20, 2022.

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We would love to be a part of your annual giving. Please consider a donation to the DADA2 Foundation if you are able. Otherwise, know that we are immensely grateful for your engagement!

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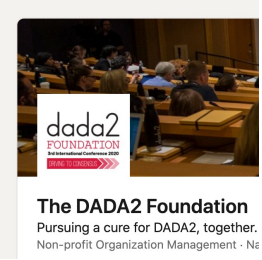

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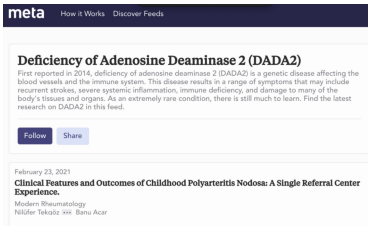

LATEST DADA2 PAPERS
We're partnering with Meta to bring the latest papers.