A newsletter distributed by The Dominantly Inherited Alzheimer Network Expanded Registry (DIAN EXR), Washington University School of Medicine, Department of Neurology

Washington University in St. Louis
SCHOOL OF MEDICINE

DIAN EXR Newsletter

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CONTACT US

If you have an idea for a story or have questions about the information in this newsletter, please contact the editors.

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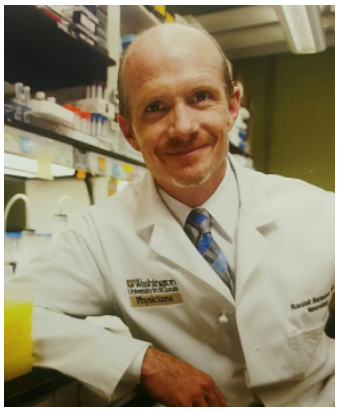
Greetings from Dr. Randall Bateman



Dear DIAN Expanded Registry Participants,

Welcome to the first quarterly electronic newsletter of the DIAN EXR! It is exciting to see the DIAN EXR grow in both membership and scope of what is being done. The DIAN EXR has already supported enrollment into DIAN, and several drug trials in DIAN-TU, while also referring to additional Alzheimer's disease research studies. As the broadest world-wide registry for dominantly inherited (or autosomal dominant) Alzheimer's disease, the DIAN EXR will continue to accelerate research into the causes, mechanisms, tests and treatments of Alzheimer's disease.

2018 has been an exciting year for progress in Alzheimer's disease, with several breakthroughs by DIAN and other studies. Some of these exciting advancements include:

1) Tracking DIAN changes over time have found faster and slower rates of decline compared to single time measures in several measures

http://n.neurology.org/content/neurology/91/14/e1295.full.pdf

2) Researchers from London, UK, have found that ADAD and SAD are similar when compared across domains using novel analytic approaches

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5920320/

3) Stop Alzheimer's before it starts. A primary prevention trial has been called for based on DIAN findings and now has NIH grant support

https://www.ncbi.nlm.nih.gov/pubmed/28703214

4) Neuropathological findings in DIAN and ADNI show similar findings in the key pathologies, but later onset AD also has other co-pathologies of stroke and protein deposition

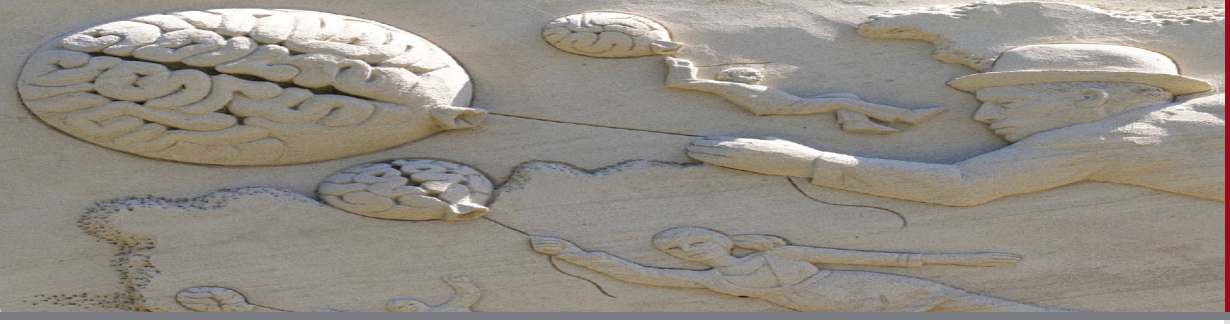
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4521391/

5) Amyloid PET, a measure of amyloid plaques, correlates with cognitive decline and suggests a link between plaques and the memory thinking changes of Alzheimer's

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4553024/

6) Non-cognitive neurologic findings in DIAN and the literature have found that other neurological findings occur in ADAD, some of which are similar to late onset AD

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5116769/



7) Symptom onset by EYO provides prediction of stage of disease, allowing times to predict onset of symptoms

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4117367/

With these achievements, we are looking forward to the conclusion of the first two drugs arms at the end of 2019, and the launch of the third cycle of the DIAN Observational study in mid-2019. We are excited about our prospects to one day be able to slow and stop the disease with your help and partnership.

With best wishes,

Randall J. Bateman M.D.
Charles F. and Joanne Knight Distinguished Professor of Neurology
Director, Dominantly Inherited Alzheimer Network DIAN (DIAN.wustl.edu)
Director, Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU, DIANTU.info)

Greetings from Dr. Eric McDade

Dear DIAN Expanded Registry Participants,

It is my pleasure to introduce the first issue of the DIAN EXR electronic newsletter. The newsletter will kick off 2019 and provide updates on DIAN-related topics, as well as other points of interest, on a quarterly basis. This is an exciting time for the Expanded Registry, and this communication will let us share with you all that is going on and future initiatives. Dr. Bateman has highlighted the many ways that the DIAN EXR has helped move research forward in dominantly inherited Alzheimer disease. We hope to accomplish more and to provide you all with a better sense of how you are making this possible.

I am excited to announce that changes will be coming to the DIAN EXR. Over the next 6-12 months, we will be developing a new electronic interface (web portal) that will make it easier for all participants to know what is going on with DIAN. This new interface will help each person know what they are involved in, provide available research opportunities and helpful links, and serve as way of communicating with us. We think that the changes will make it easier to launch more research opportunities through the EXR, with less burden to you.

As the Principal Investigator of the DIAN Trials Unit Primary Prevention Trial, I am exceptionally excited to get this trial started in 2019-2020. This will be the first trial focusing on starting treatments in those at risk for

dominantly inherited AD who do not yet have any clear signs of the disease. As part of this, we plan to host 1-2 webinars specifically focusing on this trial, so that when it starts, it will be successful. The EXR will continue to be the way that we send out announcements, so stay tuned.

Lastly, I want to especially thank Ellen Ziegemeier, Jennifer Petranek and Sarah Adams for all that they do to keep the EXR up and running and continuously work to make it better. The newsletter is another reflection of the work that they do. Please let us know how we are doing so we can continue to move forward towards a cure.

Sincerely,

Eric McDade, D.O.

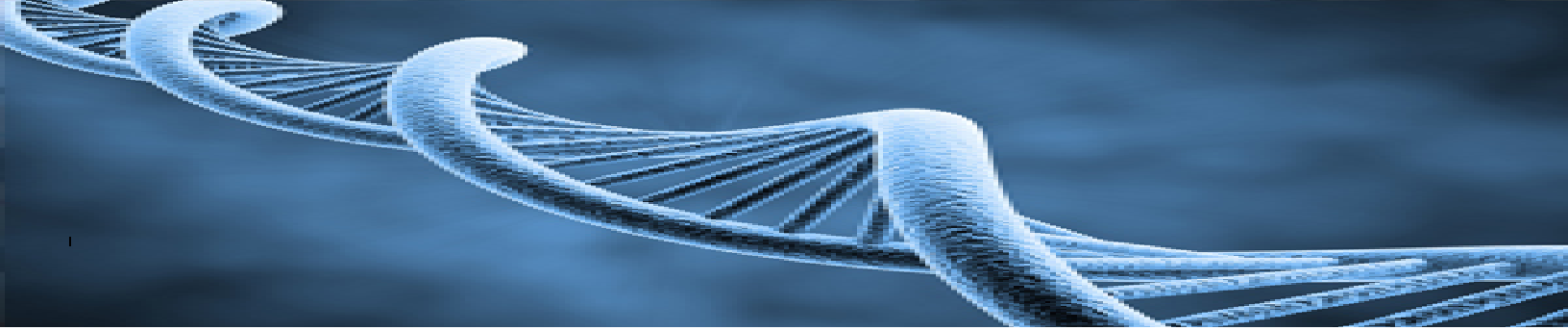
Associate Professor of Neurology

Principal Investigator, DIAN EXR

Don't miss out:

Registration for DIAD Family Conference: 04 March 2019, 2pm CST

DIAD Family Conference: 13 July 2019



Opportunities to get involved

➢ DIAN-TU Clinical Trial-001: Cognitive Run-In (CRI)

The DIAN-TU trial will begin enrollment into the CRI period of the study in spring 2019 at US/Canada sites, with study sites in partner countries opening throughout the year. The CRI period allows participants to enroll when no study drug is available for immediate enrollment. This means that those individuals that are at risk or known carriers of a DIAD mutation have an opportunity for enrollment and contribution in advance of the next drug arm starting. Participation in CRI may help better identify the effectiveness of study drug arms once new drugs are added to the trial, and may help with learning results of the trial faster by decreasing the time it takes to enroll participants once a drug arm is open.

Criteria for CRI enrollment:

- Ages 18-80
- Have a qualifying mutation in PSEN1, PSEN2 or APP genes OR be at 50% risk of inheriting such mutation. You do not have to know whether or not you are a carrier of the mutation in order to participate.
- Have no memory problems OR mild memory impairment/ mild dementia
- Not already enrolled in a DIAN-TU trial or other research without sponsor approval

➢ DIAN-TU Clinical Trial-002: Primary Prevention

In September 2018, the US National Institutes of Health (NIH) awarded Dr. Eric McDade one of the largest grants in Institute history. The Primary Prevention study will offer young family members the opportunity to participate in a clinical drug trial in 2020.

Until that time, the DIAN-TU invites interested family members to enroll into the CRI, as described above. Enrolled individuals will continue to participate in CRI until a study drug is identified for Primary Prevention.

Additional webinars focusing on the Primary Prevention Study, including a discussion on **family planning**, will be scheduled in the next few months. Please look out for them and participate.

➢ Ambulatory Research in Cognition (ARC) EXR

Researchers and participants alike in Alzheimer's disease research are familiar with the importance of measuring changes in cognitive function, but also familiar with the frustration and difficulty involved in trying to do so accurately. Lengthy neuropsychological tests taken once or twice a year in labs can be both exhausting for participants and not as accurate as researchers would like. The Ambulatory Research in Cognition (ARC) studies aim to change how cognitive testing data is collected using something most people already own and use every day: a smartphone. Participants download the ARC app to their personal smartphones and complete four very short tests (usually taking only two to five minutes each) throughout the day for seven days in a row. The ARC app then launches a new week of testing every few months. This model is known as "burst testing". Looking at participants' average performance across many short tests has been demonstrated to be more sensitive to any real changes in cognitive function when compared to longer, "single-shot" paper tests. Testing in a participant's normal environment using an already familiar device may also help to reduce "white coat effects" (differences in test results caused by participants feeling nervous in a clinical setting). Many areas of research are taking advantage of mobile devices to develop new strategies for data collection and the DIAN team is excited to add the power of ARC to the fight against Alzheimer's disease. If you have questions about ARC or would like to know about your eligibility to participate, please contact Sarah Adams by phone at 314-273-7112 or by email at neuro-dianarc@email.wustl.edu .

Please contact the DIAN Expanded Registry at dianexr@wustl.edu if you are interested in research opportunities. If you're not part of the registry and would like to be, please visit dian.wustl.edu to register.

2019 DIAD Family Conference

The Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) and the Alzheimer's Association are very pleased to announce the 2019 DIAD Family Conference for families impacted by dominantly inherited Alzheimer's disease (DIAD). Many thanks to the Alzheimer's Association and National Institute on Aging (NIA) for their support of the DIAD Family Conference.

The conference will be held on Saturday, July 13th in Los Angeles, CA, USA, and will offer attendees information, support and opportunities to share insight with each other and with researchers in the field, pharmaceutical companies, government funding agencies and regulators.

Registration will begin March 4th and close when capacity is reached. A wait list will be maintained, and family members will be notified if/when spots become available.

For any questions about the Family Conference, please contact Jennifer Petranek or Ellen Ziegemeier at DIAD-FC@email.wustl.edu.

To see presentations given at past conferences, please visit: https://dian.wustl.edu/for-families/family-conferences/

We are excited to see you in LA!

Funding for this conference was made possible by the Alzheimer's Association and by grant #AG055232 from the National Institute on Aging. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Alzheimer's disease in the news

Alzheimer's Disease May Develop Differently in African-Americans : A biological clue that could help explain why African Americans appear to be more vulnerable than white Americans to Alzheimer's disease.

https://www.npr.org/sections/health-shots/2019/01/07/682036486/study-suggests-alzheimer-s-disease-may-work-differently-in-african-americans

2018-A Year in Research

https://www.alzforum.org/news/research-news/2018-year-research

Decreased deep sleep linked to early signs of Alzheimer's disease: Toxic brain protein tau elevated in older people who sleep poorly.

https://medicine.wustl.edu/news/decreased-deep-sleep-linked-to-early-signs-of-alzheimers-disease/

New hope for old disease: Doctors may soon be able to predict, prevent Alzheimer's disease

https://outlook.wustl.edu/new-hope-for-old-disease/

The DIAN website is a great place to learn more about our research and find additional information. Please visit the "News" page at https://dian.wustl.edu/news/ for articles related to DIAN and Alzheimer's disease. Family members share their stories on the "Family Voices" page at https://dian.wustl.edu/for-families/family-voices/.