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

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.

Jamie Bartzel
bartzel@wustl.edu

Ellen Ziegemeier
eziegem@wustl.edu

Washington University in St. Louis
School of Medicine

Looking Ahead to 2023

The end of a new year has come, and the beginning of a new year is here. It's appropriate then that we also reflect on important events from 2022 and look forward to what 2023 will bring. The year 2022 was one of incredible milestones for the DIAN-TU and the field of Alzheimer's disease therapeutics. In the past twelve months, the first combination trial (DIAN-TU-001 NextGen amyloid and tau treatment trial) and the first anti-amyloid primary prevention platform study in dominantly inherited Alzheimer's disease (DIAN-TU-002) were both launched! Additionally, the results of the phase III studies of lecanemab clearly show that removing amyloid plaques has a beneficial effect on Alzheimer's disease progression! These results are revolutionary for Alzheimer's disease treatment and clinical trials moving forward.

In 2023, the results of additional clinical trials of amyloid immunotherapies are expected and will be important additional pieces in the puzzle of this class of treatments and the role of amyloid plaques in Alzheimer's disease. In addition, 2022 marked the 10-year anniversary of the DIAN-TU! We had the chance to celebrate this important landmark here at Washington University and want to let you know how important you are to making this possible.

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Looking Ahead to 2023 (continued)

However, we also recognize the disappointment of the results of the phase III studies of gantenerumab in late onset Alzheimer's disease. Unfortunately, the amyloid plaque lowering effects in these phase III studies were lower than predicted, which likely is a key reason as to why the expected clinical benefit was not reached. These results were incredibly disappointing, especially as they have resulted in the need to stop the planned dosing of gantenerumab in the DIAN-TU Primary Prevention study. We are continuing to evaluate the effect of much higher doses in the gantenerumab Open Label Extension study. We aim to determine if we can fully remove amyloid plaques, if we can reverse Alzheimer's disease downstream processes, and what effects this might have on cognition and clinical function. For those of you unable to attend the DIAN-TU webinar related to this decision, please look for the recording on the Expanded Registry website.

For those of you who were ready to or planning on enrolling in the Primary Prevention study, we are actively working with several other therapeutic programs to replace gantenerumab. We have a head start for the next drug to launch Primary Prevention, with the trial design validated, operations geared up and ready, and continuing Cognitive Run-In to allow for continued enrollment for planned randomization, all of which will help accelerate the launch again. Additionally, it is important to realize that the success of the lecanemab studies in symptomatic Alzheimer's disease, as well as the previous results from the aducanumab trials, only strengthen the decision to move forward with true amyloid prevention studies. We look forward to 2023 being a monumental year for the DIAN-TU-002 Primary Prevention study in spite of the current setbacks.

With this in mind, we wish you all a happy new year and look forward to what we can accomplish together in 2023.

Randall Bateman, MD and Eric McDade, DO

Pictured: The DIAN-TU team at our Tenth Anniversary Celebration on December 8, 2022
Photo by Caroline Arbanas

MyDIAN Portal App: Your Mobile Connection to Everything DIAN

Have you joined MyDIAN yet? Maybe you saw an email message inviting you to download an app called Linkt in the last few weeks or months but didn't know what it was all about. The email may not have the usual Wash U or DIAN logos on it, but this email is from us! The Linkt app is the platform supporting our online participant portal, MyDIAN, which we use to distribute articles, announcements, webinars, and remote research participation opportunities. The happy face shown in the corner of the email is the logo for Datacubed Health, our software development partner company that built the app for us. We realize it can be hard to tell what emails are safe, so we want to make sure our participants know what to look for in our communications.

The app makes study participation and receiving DIAN-related information and easier and more engaging. Complete activities to earn gems and navigate your avatar across colorful maps. The DIAN research team is always working to defeat Alzheimer's disease, but it can't be done without participants like you! MyDIAN makes it possible to contribute to research at any time and from any place. For example, answering short surveys in the app about factors such as diet and exercise will help us analyze the relationship between environment and disease progression in DIAD.

This is an important way for us to advance our understanding of how lifestyle influences the age of symptom onset, cognitive decline, and biomarker changes. Just a few minutes of your time, even from the comfort of your own couch, can help us make new scientific discoveries. Don't forget to have notifications enabled so you receive the latest app content—and we promise not to spam you.

If you lost your email invite to access MyDIAN or haven't received one and would like to, contact us at dianexr@wustl.edu or +1-844-DIAN-EXR (+1-844-342-6397). If you don't have a smartphone but are still interested in MyDIAN, please contact us to discuss a desktop computer-based site we have set up. Let us know if you have any other questions about MyDIAN, its content, or troubleshooting, and we would be happy to help you. We are excited to grow this part of DIAN and hope it provides a valuable research connection to you, the participant!

Brooke Kinsaul

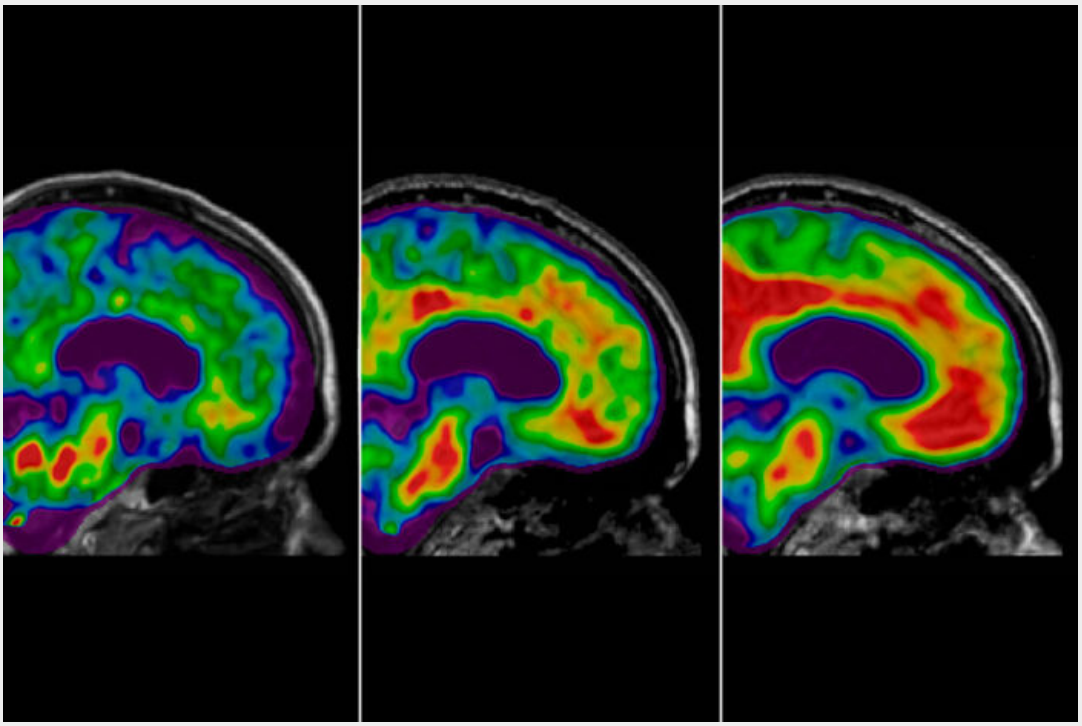
Supplemental Study on Sleep for Select DIAN Participants in the United States

Sleep is essential for good health, and poor sleep may cause health problems. Many studies are showing that disturbed sleep may be a marker for very early Alzheimer disease. The vast majority of sleep and Alzheimer disease studies looked at individuals with, or at risk for, sporadic Alzheimer disease (not dominantly inherited Alzheimer disease). To better understand the timing of changes in sleep and changes in Alzheimer disease, Dr. Brendan Lucey at Washington University in St Louis is interested in studying sleep in individuals with dominantly inherited Alzheimer disease.

In this study, participants complete all sleep assessments at home. Interested individuals will be consented to participate via telephone or video call, and sleep monitoring devices will be shipped to them. Participants will be asked to wear a device on the forehead to measure brain activity during sleep, as well as two devices on the wrist to measure movement and blood oxygen levels. After completing the monitoring at home, the devices are shipped back for evaluation.

Eligible participants have been contacted by email. There may be future opportunities for participation in this research study and/or additional studies on sleep. We will notify you via the MyDIAN portal and email you if you qualify. If you have additional questions about sleep studies, please reach out to dianexr@wustl.edu.

Ellen Ziegemeier



Brain scans of an Alzheimer's patient taken over the course of years show growing yellow, orange and red areas, reflecting the spread of the Alzheimer's protein amyloid beta through the brain. At the first scan (left), the patient was cognitively normal; by the last (right), the patient had developed cognitive impairments.

Image by Brian Gordon

Source: *https://medicine.wustl.edu/news/washu-eisai-form-drug-discovery-collaboration/*

Alzheimer's in the News

WashU, Eisai form drug discovery collaboration
Focus is on therapies for Alzheimer's, other neurodegenerative diseases
https://medicine.wustl.edu/news/washu-eisai-form-drug-discovery-collaboration/

$9 million to fund study of 'jumping genes' in Alzheimer's
Researchers from several labs to study role of transposable elements
https://medicine.wustl.edu/news/9-million-to-fund-study-of-jumping-genes-in-alzheimers/

Study yields clues to why Alzheimer's disease damages certain parts of the brain
Findings could help explain rare symptoms such as problems with language, vision
https://medicine.wustl.edu/news/study-yields-clues-to-why-alzheimers-disease-damages-certain-parts-of-the-brain/

Risk of Alzheimer's dementia may be predicted with help of new tool
Demographic data, imaging results, biomarkers of study participants help determine risk
https://medicine.wustl.edu/news/risk-of-alzheimers-dementia-may-be-predicted-with-help-of-new-tool/

New center's aim: to ID biomarkers of neurodegenerative diseases
Tracy Family SILQ Center to accelerate progress toward better diagnostics, treatments
https://medicine.wustl.edu/news/new-centers-aim-to-id-biomarkers-of-neurodegenerative-diseases/

Recent DIAN Publications

Immunotherapy for Alzheimer's disease: targeting β-amyloid and beyond
https://link.springer.com/article/10.1186/s40035-022-00292-3

Amyloid-Related Imaging Abnormalities in the DIAN-TU-001 Trial of Gantenerumab and Solanezumab: Lessons from a Trial in Dominantly Inherited Alzheimer Disease
https://onlinelibrary.wiley.com/doi/full/10.1002/ana.26511

Evaluation of dose-dependent treatment effects after mid-trial dose escalation in biomarker, clinical, and cognitive outcomes for gantenerumab or solanezumab in dominantly inherited Alzheimer's disease
https://alz-journals.onlinelibrary.wiley.com/doi/full/10.1002/dad2.12367

Avoid or Embrace? Practice Effects in Alzheimer's Disease Prevention Trials
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9244171/

The Future of AD Clinical Trials with the Advent of Anti-Amyloid Therapies: An CTAD Task Force Report
https://link.springer.com/article/10.14283/jpad.2022.48

The DIAN data are increasingly published in scientific reports to enable investigators worldwide to learn of our progress and to advance scientific understanding of Alzheimer's disease. Because of this, there is a small but possible risk that a DIAN participant reading or hearing of these scientific reports might guess, correctly or incorrectly, information about themselves. This includes guessing one's own or a family member's mutation status. We at DIAN take every step to minimize this risk, including ensuring that all DIAN data in journal articles, scientific meetings, press coverages, etc., lack identifying information for any participant, but it is possible than even such de-identified data may reveal a pattern of symptoms or a relationship with other medical disorders that could suggest that a particular person is mutation positive. You can avoid reading these scholarly articles or listening to presentations related to the DIAN study to decrease this risk.

Meet the Team: DIAN-TU Fellows, Dr. Haiyan Liu & Dr. Olivia Wagemann

Haiyan Liu, MD, MSc

Dr. Haiyan Liu earned her MD and MSc degrees in China. She completed four years of physician training in China and rotated in Internal Medicine, Neurology, and Dermatology. She pursued her postdoctoral training at the University of Michigan, studying central nervous system sensitization, synaptic plasticity, and circuit-level interactions in chronic visceral pain.

Dr. Liu conducted seven years of biomedical research in CCR at Washington University School of Medicine related to lysosome function and pathways in Cardiovascular disease, Type II Diabetes Mellitus, and Alzheimer's Disease. She then Joined Dr. Lucey and Dr. Bateman's lab in the Department of Neurology, Washington University School of Medicine. Her work focused on Amyloid β and Tau measurement in human plasma and CSF, and the effect of Sleep-Deprivation on plasma Aβ and Tau dynamics.

Olivia Wagemann, MD, MSc

Dr. Olivia Wagemann earned her medical degree at the University of Regensburg (Germany) in 2020, where she also obtained her thesis in the field of translational cardiology, investigating the effect of SGLT2-inhibition on ion homeostasis in models of murine and human heart failure.

Dr. Wagemann is now a neurology resident in training at the LMU University Munich (Germany) and specializes in clinical research of neurodegenerative diseases. Her primary interests include Alzheimer's Disease in adults with Down-Syndrome as well as evaluating sociocultural and care-related influences on diagnosis and prognosis in patients with dementia. Through her work in the Outpatient Clinic for Clinical Neurodegeneration at the LMU and the German Centre for Neurodegenerative Diseases (DZNE), she is strongly involved in phenotyping of patients with Alzheimer's Dementia and Frontotemporal Dementia.

Meet the Team: Clinical Research Specialist, Brooke Kinsaul

Brooke Kinsaul

Brooke Kinsaul joined the DIAN Expanded Registry Team as a Clinical Research Specialist in August 2022 and also manages MyDIAN communications. She is a multi-disciplinary scientist who comes from a diverse research background, ranging from early stage drug development to late stage clinical trials. She most recently left the pharmaceutical industry to return to her academic roots, having previously worked in the Department of Psychiatry at Washington University and in Clinical Pharmacology at Vanderbilt University. She is passionate about analyzing and visualizing data in order to interpret complex information, solve problems, and expand knowledge. Outside of work, she enjoys traveling, learning new artistic techniques, and nurturing her ever-expanding plant collection.

The DIAN website is a great place to learn more about our research and find additional information. Please visit our News page for articles related to DIAN and Alzheimer's disease. Family members share their stories on the Family Voices page. If you are interested in research opportunities, please contact the DIAN Expanded Registry at dianexr@wustl.edu. If you are not part of the registry and would like to be, please visit dian.wustl.edu to register.

KNIGHT FAMILY DIAN TU Dominantly Inherited Alzheimer Network Trials Unit

DIAN Dominantly Inherited Alzheimer Network

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