



# DIAN EXR Newsletter

Volume 3, Issue 1, 2021

## CONTACT US

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

**Jennifer Petranek**  
[j.petranek@wustl.edu](mailto:j.petranek@wustl.edu)

**Ellen Ziegemeier**  
[eziegem@wustl.edu](mailto:eziegem@wustl.edu)

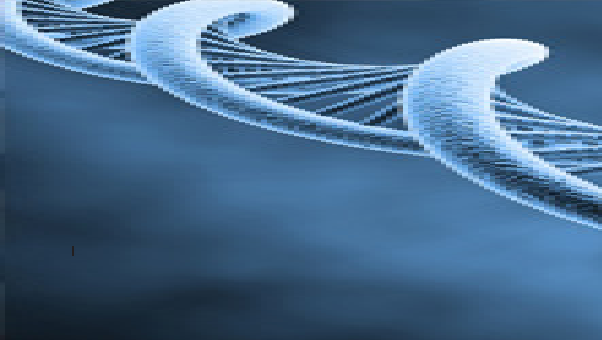


## 2020 - A Year to Forget? Or Remember?

At the end of each year, the DIAN-TU team takes a moment to reflect on our work from the past year, the challenges we faced and overcame, and our accomplishments. It's always a good reminder of what we are capable of doing – even when faced with terrible disappointment or extremely challenging situations. 2020 was no different. Although we were all very disappointed with the main outcome of the DIAN-TU-001 trial of solanezumab and gantenerumab, followed by a pandemic which made the entire world halt, we persevered and continued moving forward.

I continue to hear over and over again about how 2020 was so terrible. Granted, I admit, the trial results hurt; COVID-19 has taken or hurt people we know and love; it's been difficult not to see or hug family and friends; virtual meetings and conferences do not have the same impact as in-person interactions; and being near the kitchen all the time is not helping the waistline. But despite the adjustments and challenges of 2020, with the dedication and commitment of our team members and DIAD families, we still accomplished a lot. So be proud of all we've achieved together and the good things that happened in 2020:

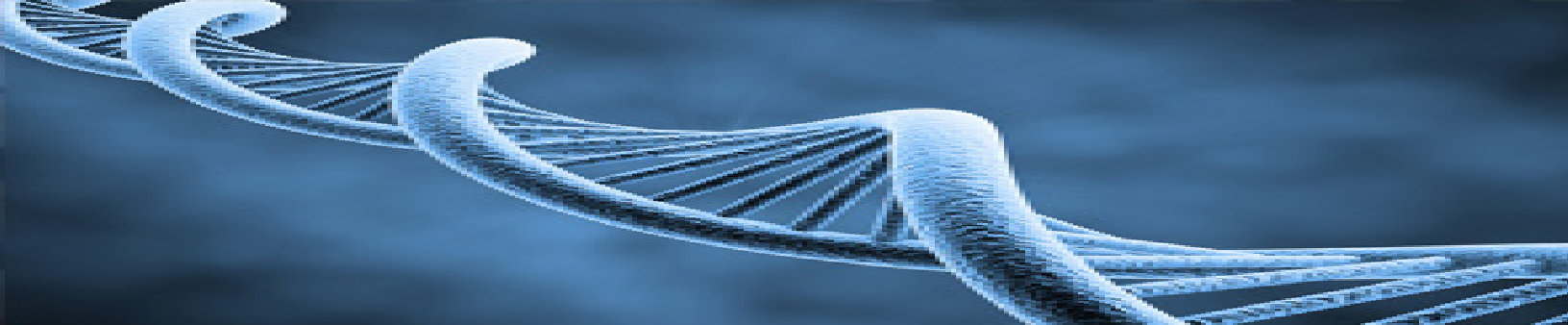
- **Results from the first ever trial in dominantly inherited AD (DIAD) and first prevention trial for Alzheimer's disease using drugs which target amyloid-beta were announced.** Although, neither drug met the primary cognitive endpoint, biomarkers showed positive movement.
- Further analyses of the DIAN-TU-001 trial data demonstrated that **gantenerumab improved biomarkers of disease activity and progression.** Compared to placebo, gantenerumab reduced amyloid plaques in the brain, reduced the tau protein levels in cerebrospinal fluid, and slowed increases in the neurofilament light chain (a marker of neurodegeneration). **This indication that gantenerumab can positively affect the biological course of AD is a critically important finding.**
- The DIAN-TU and Roche launched an exploratory **Open Label Extension (OLE)** to continue studying the effects of gantenerumab in dominantly inherited AD.
- With the successful completion of the DIAN-TU-001 solanezumab and gantenerumab drug arms, **the DIAN-TU demonstrated the success of the innovative DIAN-TU trial platform and a public-private-philanthropic partnership, and the potential for informative global platform trials, even with rare diseases.**
- Site start-up and enrollment continued for the DIAN-TU-001 and DIAN-TU-002 **Cognitive Run-In (CRI)**. The DIAN-TU CRI allows the trial platform to enroll and engage subjects, collect longitudinal data, and immediately randomize subjects into the next available active drug arm to reduce the enrollment duration.
- **COVID-19 safety protocols were implemented to enable study visits** for both OLE and CRI.



- The DIAN-TU continued preparations to **add a tau drug arm to the DIAN-TU-001 trial and to launch the primary prevention trial**. Both studies are expected to launch in mid-late 2021.
- With tau being the next biomarker focus, the DIAN-TU has continued to work with our industry partners to **establish tau PET tracer manufacturing centers all over the world** to ensure all DIAN-TU studies and participants will have access to tau PET imaging.
- The DIAN-TU **continued discussions with multiple industry partners regarding their tau-based compounds** (antibodies, genetic therapies, small molecule aggregation inhibitors) and participation in the DIAN-TU trial platform. Several drugs are promising and could potentially be tested in the DIAN-TU in the next few years.
- The DIAN-TU and DIAN OBS continued **expansion with Latin America** performance sites **giving DIAD families in these countries an opportunity to participate in treatment trials**.
- The DIAN EXR continued to work with researchers in Greece to identify DIAD families. The DIAN EXR website was translated into Greek and **4 potential DIAD families in Greece** have been identified, with exploratory testing of 5 additional families underway.
- The DIAN EXR along with other DIAN-TU team members, the Alzheimer's Association and DIAD individuals, **successfully organized the sixth annual DIAD family Conference with a virtual platform** in place of the annual in-person gathering. The virtual format allowed for greater flexibility in accessing presentations and afforded multiple support sessions on 10 different topics which were offered during the second week, facilitated by Alzheimer Association support group leaders and family experts on the featured topic. **Family members created a video message about life during COVID-19 that was shared at the beginning of a live Q&A panel. Preliminary feedback indicates that virtual offerings were well-received and greatly appreciated, and some aspects such as pre-recorded talks could be helpful for future in-person conferences.**
- **The DIAN EXR continued** its work to identify new DIAD families with country-specific liaisons and keep families updated through regular webinars and newsletters.
- **Remote cognitive testing** with the ARC app continued.
- **The DIAN-TU expanded with the addition of several new team members** to help with operations for all the DIAN-TU activities.
- **Participants continued study visits**, including those in-person when possible.
- With all of the Zoom meetings, people were able to put faces to names (as long as people actually turned on their video).

Overall, 2020 was still a highly productive year, despite its setbacks. Results from the DIAN-TU-001 trial provided valuable information for future trial design and the field of Alzheimer's research. The DIAN-TU continued efforts to design and launch innovative and pioneering trials in DIAD. And DIAD families continued participation in DIAN-TU and DIAN OBS studies. **The dedication of our team members and DIAD families is unmatched. We thank you all for making 2020 the best it could be and look forward to working with you to continue to break new ground, make the years to come even better, and find a cure for AD.**

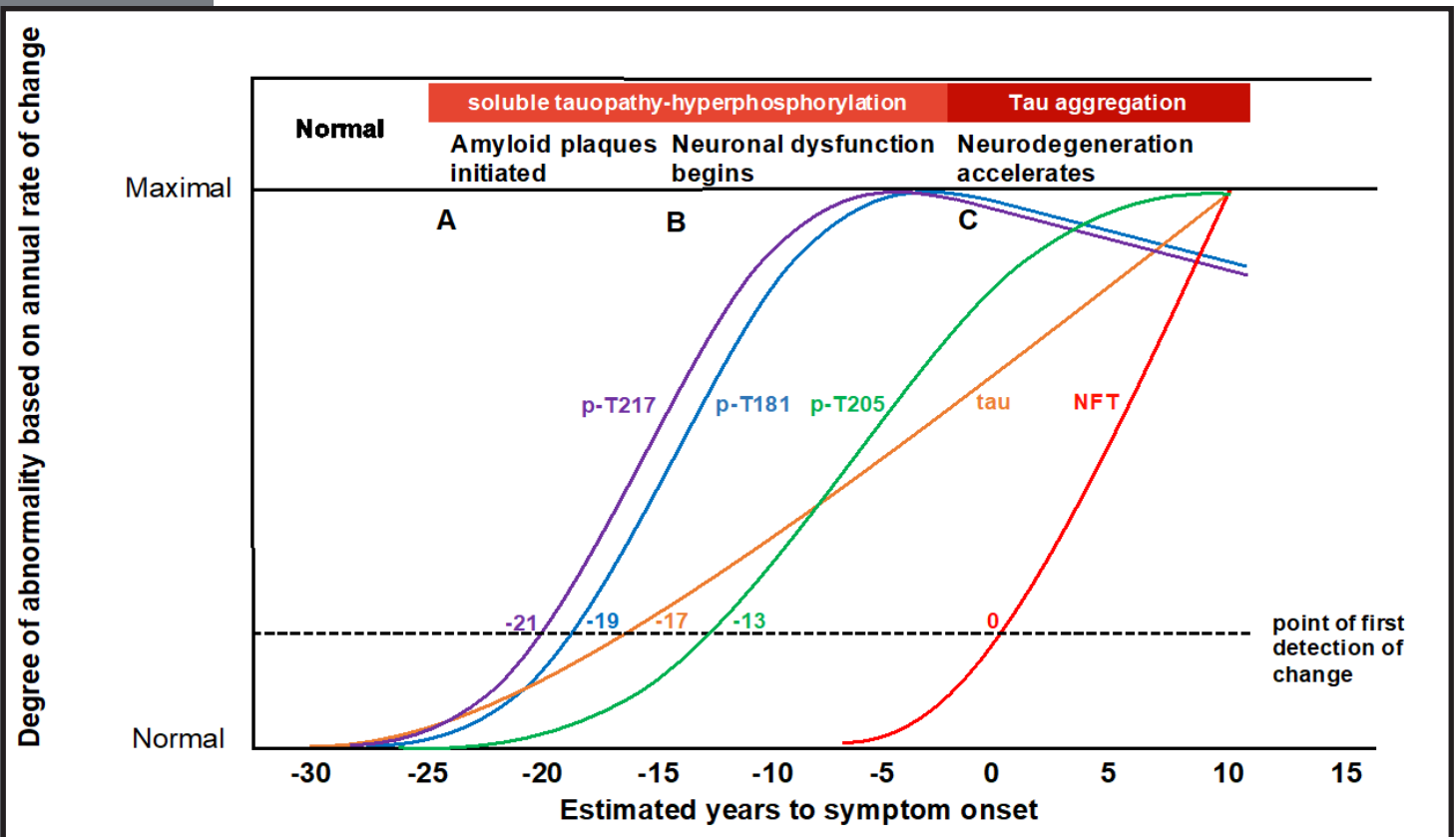
*Anna Santacruz - Administrative Director*



## A Better Understanding of Tau in Alzheimer Disease

The protein tau is a complex protein that plays a fundamental role in neuronal/brain function. However, for reasons that remain not fully understood, tau also plays a role in the pathology of Alzheimer disease and other neurodegenerative dementias as well. With the development of tau-targeting therapies now accelerating, it is critical to understand as much as possible about the when and how of tau pathology. Fortunately, there have been major advancements in methods for measuring tau in the brain using positron emission tomography (PET) scans, cerebrospinal fluid and blood. Recently, Nicolas Barthélemy, PhD, Assistant Professor of Neurology in the laboratory of Randall J Bateman, M.D., has developed a method that can measure multiple fragments of the tau protein in a single spinal fluid sample. In doing so he, Dr. Bateman, Eric McDade, D.O. and DIAN Collaborators have demonstrated for the first time that there are multiple stages during which different components of the tau protein begin to increase in the spinal fluid (**See Figure**). Importantly, because of the wealth of additional data collected from DIAN participants, Dr. Barthélemy and the team were able to demonstrate that the different changes in the tau protein appear to be related to specific biomarkers (amyloid plaques, MRI changes, brain metabolism changes) and begin up to 20 years before memory problems and “tau tangles” measured by tau PET. Although further work is required to replicate and understand the cause for these tau changes, they come at an important time as they are likely to help in understanding the effects of tau-targeting therapies and, as was recently demonstrated in the DIAN-TU-001 study, even treatments that target amyloid plaques. Groundbreaking work like this simply would not be possible without dedication of DIAN participants and researchers and will continue to push the field forward.

*Eric McDade, DO - Associate Director, DIAN-TU*



A soluble phosphorylated tau signature links tau, amyloid and the evolution of stages of dominantly inherited Alzheimer's disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309367/>





Marty Reiswig with his family during the 2019 DIAD Family Conference in Los Angeles

## I Still Exist

For 25 years, the photographer Carl Cordonnier has been documenting Alzheimer's disease in the world in collaboration with Dr Florence Lebert, (Psycho-geriatrist at the CHRU of Lille in France).

The photographic film series "I Still Exist" explores representations of young onset patients and their loved ones affected by Alzheimer's disease, Lewy Body Disease and Frontotemporal Lobar Degeneration.

The testimonies of Gérard, Corinne, Alexis, Jean-Marie, Marie-Jeanne, Carmen, Marty, Kobayashi and Wagner, photographed in five countries around the world express the cultural diversity and universality of these diseases. The originality of the approach rests on the characters' involvement in the creative process, which gives particular strength to the stories. Each film plunges the spectator into the interiority of feelings and forces concentration. They express the wanderings of memory, confusions, relational difficulties, violence, emotions but also the "victories" of everyday life. Beyond borders, their testimonies forcefully express a need for recognition, as patients and citizens. Their films tell us the desire to "still exist" in a period of their lives when they are very often excluded from their own history.

Carl dialogued for a year with Marty Reiswig in an empowering process to write the story before photographing Marty and his family in Denver and Los Angeles. Each of the five sequences in Marty's film expresses a perception or an issue Marty claims: his father's heredity and illness; his commitment to his company and to associations to prevent and protect his family; his doubts and frailties in a vulnerable period; his hopes and involvement in research; and his energy to take advantage of the present for his children. The project seeks to understand from the inside, in an original form, the complexity of living with the risk of developing a disease that has not yet declared itself.

"J'existe Encore" is produced by Dailylife with the support of the Nord department, the Distalz and Pictanovo laboratory of excellence and the Hauts-de-France Region, the University, the CHRU of Lille, the EPSM of Flanders and international partners.

Film presentation of Carl Cordonnier with Dr Lebert - Code MEMORYA with english translation

Film of Marty Reiswig: <https://www.jexisteencore.com/films> - Second Life - Code: 2021E

©Carl Cordonnier/Dailylife

Dailylife@orange.fr



## MyDIAN Portal App: Have You Seen This Email?

Have you seen an email message inviting you to download an app called Linkt in the last few weeks or months? 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 participant portal, MyDIAN, which we use to distribute articles, announcements, and alerts for research participation opportunities. The happy little face shown in the corner of the email is the logo for Datacubed Health, our software development partner company who built the app for us. We realize it can be hard to tell safe emails from spam, so we want to make sure our participants know what to look for in our communications.

If you lost your email invite to access MyDIAN or haven't received one and would like to, contact us at [dianexr@wustl.edu](mailto:dianexr@wustl.edu) or 1-844-DIAN-EXR (1-844-342-6397). Don't have a smartphone but still interested in MyDIAN? Please contact us to discuss a desktop computer-based site we have set up.

In news for active MyDIAN users, the DIAD Lifestyle Surveys project has launched and you have probably seen at least one activity (survey) in the app regarding it. The first activity you will see gives you information about the study, which aims to examine how lifestyle factors such as sleep and diet impact risk of Alzheimer's disease, and asks if you would like to participate. If you have agreed to participate, be on the lookout for related study questionnaires to pop up every few months or so to ask you about your daily activities and habits. This data will eventually be analyzed to look for relationships between lifestyle factors and the other types of data DIAN collects, like age at symptom onset, disease progression, biomarkers and imaging.

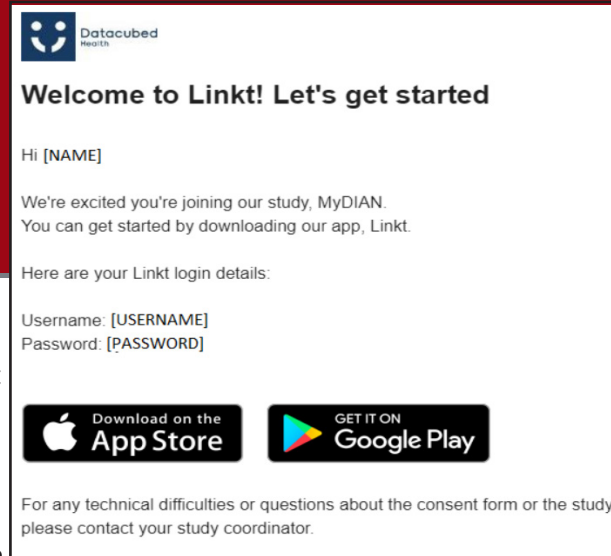
If you have questions about MyDIAN invites, surveys, or troubleshooting, please contact us at any time ([dianexr@wustl.edu](mailto:dianexr@wustl.edu) or 1-844-342-6397) and we would be happy to help you. We are excited to grow this new facet of DIAN and hope it provides a valuable research connection to you, the participant!

*Sarah L. Adams - Clinical Research Coordinator II*

## DIAN in Latin American Countries

DIAN recently increased the outreach to Latin American (LatAm) countries. DIAN LatAm centers are being established for the DIAN OBS and DIAN-TU in the region and will offer DIAD families opportunities to participate in longitudinal research and experimental therapies to prevent, delay, or treat AD. As DIAN establishes new sites in LatAm, a cohort-ready population will be critical for recruitment and enrollment in upcoming observational studies and clinical trials. A recent [paper](#) by Latin American and DIAN researchers described a comprehensive review of DIAD families and mutations in LatAm, leading the way for the characterization of these families in future studies. Key findings suggest unique characteristics within the LatAm populations, including: relative high frequency of DIAD, presence of common ancestors, and large extended families usually related to founder effects.

*Jorge J Llibre-Guerra, MD - DIAN-TU Fellow*





## Meet the New Executive Director of DIAN

Hi, I'm Dr. Alisha Daniels, the new Executive Director of DIAN, and am truly honored to be given the opportunity to contribute to such a unique and groundbreaking program. I joined Washington University's Neurology Department in January 2021, bringing a slightly non-traditional background to DIAN. My professional career started in clinical research at the Medical College of Wisconsin which provided the ability to obtain experience as a clinical research assistant, coordinator, and more recently as an administrator at the University of Florida, prior to attaining my medical degree. I have also volunteered in Phase I trials wanting to understand the study participant's perspective of being in a study. Clinical research has made a profound impact on my life, and I hope to help further the aims of DIAN.

Outside of work, I literally try to get outside as often as possible, enjoying activities such as running, hiking, kayaking, and traveling with my husband and two kids. My husband and I are both originally from the Midwest, he's from Chicago (sorry, not sorry he's a Cubs fan!) and myself Oshkosh, WI; we're excited to be back in the region we consider home. While we will miss last minute trips to Disney and cooling off in freshwater springs, we are very much looking forward to having four seasons again while enjoying St. Louis' festivals and cuisine.

## 2021 Virtual DIAD Family Conference

Preparations for the 2021 Virtual DIAD Family Conference are underway, and we are excited to bring you an improved virtual experience this year!

The most important thing to us has been and will always be the safety of our DIAD families. Due to the ongoing pandemic, which can cause uncertainty with health and travel, we have decided to hold a virtual conference again this year.

The family conference planning committee, along with generous support from the Alzheimer's Association, is making every effort to make this year's conference more streamlined and user friendly to ensure the best virtual conference experience possible. Stay tuned for upcoming information on how to register for this year's conference.

## Gantenerumab Exploratory Open Label

The DIAN-TU is happy to report that enrollment into the Gantenerumab Exploratory Open Label Extension (OLE) is nearly complete! The baseline/entry OLE visit will provide very valuable data and insight on the drug's effect from the double-blind period. These baseline assessments will allow us to better evaluate the effects of the higher doses for participants who did not have repeat biomarker assessments beyond year 4 but had continued dosing; as well as evaluate any sustained benefits from prior drug exposure. We cannot express enough gratitude to the participants and family members who have contributed and continue to do so in this very valuable extension period during a pandemic, and to the PIs and Study Coordinators for their work in making it happen!

The DIAN-TU is finalizing the next drug arm for secondary prevention and for the primary prevention study. Please stay tuned for coming announcements in the next few months. Meanwhile, enrollment into the cognitive run-in period (CRI) and completion of tau PET scans is a critical active step towards success of these next drug arms.

## Alzheimer's Disease in the News

Protein involved in removing Alzheimer's buildup linked to circadian rhythm

<https://medicine.wustl.edu/news/protein-involved-in-removing-alzheimers-buildup-linked-to-circadian-rhythm/>

Improving emergency care for people with dementia is focus of new grant

<https://medicine.wustl.edu/news/improving-emergency-care-for-people-with-dementia-is-focus-of-new-grant/>

Lewis receives national award for volunteerism

<https://medicine.wustl.edu/news/lewis-receives-national-award-for-volunteerism/>





Alzheimer's in adults with Down syndrome focus of multicenter NIH grant

<https://medicine.wustl.edu/news/alzheimers-in-adults-with-down-syndrome-focus-of-multicenter-nih-grant/>

Racial differences in Alzheimer's research focus of \$15 million grant

<https://medicine.wustl.edu/news/racial-differences-in-alzheimers-research-focus-of-15-million-grant/>

## Recent DIAN Publications

Presymptomatic Dutch-Type Hereditary Cerebral Amyloid Angiopathy-Related Blood Metabolite Alterations

<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad201267>

Biphasic cortical macro- and microstructural changes in autosomal dominant Alzheimer's disease

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12224>

Ante- and postmortem tau in autosomal dominant and late-onset Alzheimer's disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7732239/>

Sequence of Alzheimer disease biomarker changes in cognitively normal adults: A cross-sectional study

<https://n.neurology.org/content/95/23/e3104.long>

Association of education with A $\beta$  burden in preclinical familial and sporadic Alzheimer disease

<https://n.neurology.org/content/95/11/e1554.long>

Single-subject grey matter network trajectories over the disease course of autosomal dominant Alzheimer's disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7475695/>

Neurofilaments in disease: what do we know?

<https://www.sciencedirect.com/science/article/pii/S0959438820300398?via%3Dihub>

*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 that 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.*

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/>. If you are interested in research opportunities, please contact the DIAN Expanded Registry at [dianexr@wustl.edu](mailto:dianexr@wustl.edu). If you are not part of the registry and would like to be, please visit [dian.wustl.edu](https://dian.wustl.edu) to register.

## Save the Date!

DIAD Family Webinar

SATURDAY, April 17, 2021

4:00 - 6:00 PM CDT (22:00 – 00:00 BST)

Featured topics: DIAN-TU Trial Updates: Tau NexGen and Primary Prevention

Instructions on registration for the webinar will be sent via email in March

