New Efforts in the Treatment of Alzheimer's Disease: The Dominantly Inherited Alzheimer's Network (DIAN)

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DIAN consists of an international network of over 11 leading research centers funded through the National Institute on Aging to longitudinally study Alzheimer's disease caused by a rare dominantly inherited genetic mutations. DIAN has the largest and most extensive research network for dominantly inherited Alzheimer's disease, and includes sites in the United States, Australia, and the UK. DIAN is directed by John C. Morris, M.D., of Washington University School of Medicine, director of the University's Knight Alzheimer's Disease Research Center, and former member of the Alzheimer's Association Medical & Scientific Advisory Council.

The genetic mutations in these families are rare (<1% of Alzheimer's cases), but clinically and pathologically, individuals that inherit the gene appear to have an almost identical disease as those that are impacted in late life. Children of individuals who carry one of these genetic mutations have a 50% chance of inheriting the gene mutation and those who do will develop the disease. The average age of onset for this group that inherits one of these mutations is about 45 years of age, although I recently evaluated a 37-year-old mother of two in our DIAN Project at Washington University, who had been struggling with the disease for several years.

At the Alzheimer's Association International Conference 2011, the DIAN team reported on over 150 participants and showed that the biomarker beta amyloid (the protein that is believed to be neurotoxic)starts accumulating as early as one to two decades before the onset of symptoms. The age of disease onset of the parent is generally a good predictor of when the disease will begin for those children that inherit the mutation. Knowing when the onset of symptoms will likely occur sets this network up to test potential drug targets to prevent or delay the onset of the disease.

To date, all drug trials that have been focused on decreasing production or increasing elimination of Alzheimer's disease proteins have not shown efficacy. One explanation for this universal finding may be that once you have developed symptoms, the proteins and brain damage is too widespread for the drugs to work. Thus, treating the disease earlier with these drugs may show efficacy before it is "too late."

We can now diagnosis patients with the brain pathology of Alzheimer's disease before they begin to lose memory or other cognitive abilities. Presymptomatic or preclinical Alzheimer's disease can now be diagnosed with PET scans or cerebrospinal fluid studies to confirm the presence of Alzheimer's disease proteins in participants without clinical symptoms.

The DIAN Therapeutic Trials Unit (TTU) was funded by a generous grant of over $4,000,000 from the Alzheimer's Association and will leverage the current DIAN network to launch biomarker and prevention trials. Our Washington University site enrolled the first three participants in the world in this prevention trial. However, this effort could not be done without support from all the sites since the numbers at any individual site would not be sufficient to obtain meaningful results. This type of prevention trial would be almost impossible without the DIAN network.

Two monoclonal antibodies, drugs given by infusion that target beta amyloid and assist in clearing this neurotoxic protein out of the central nervous system, are currently being studied. It is hoped that this approach, if successful in these families with genetic mutations, can be adopted for treatment for Alzheimer's disease at all ages. It is anticipated findings will be available in about two years. It is estimated that even a six-month delay in symptom onset could prevent over 2,000,000 new cases of the disease. We are indeed fortunate to have such cutting edge research here in our St. Louis area and also

have such tremendous partners and collaborators as the Alzheimer's Association. Please consider being a volunteer to help fight this disease. Contact our local chapter of the Alzheimer's Association to find out how you can help.