Exciting New Clinical Trials Begin Enrolling Patients

Research continues to focus on understanding the disease process in ALS. Virginia Lee, Ph.D., describes the complexity of the disease and the emerging understanding of the protein changes associated with the various forms of ALS and frontotemporal lobar dementia. In the meantime, efforts continue to bring important laboratory findings into clinical testing with the hope of developing new treatments for the disease. Clinicians emphasize the importance of participation in clinical trials and describe a few of the current trials that are enrolling patients. Understanding the complexity of the disease will also impact clinical trial design as it is very possible that treatments effective in some forms of ALS may not be effective for all patients.

The ALS Association is proud to honor two awardees, Dr. Leonard van den Berg, the Sheila Essey Award recipient, and Dr. Steve Han, TREAT ALS/AAN Clinician Scientist Fellow. With the growing understanding of the complexity of ALS and the need to more directly relate findings in animal models to humans with the disease, there is an increasing collaboration between clinicians and scientists in the field. Dr. van den Berg has made significant contributions in identifying new genes linked to the disease, as well as improving trial design and patient care. Dr. Han will combine his clinical expertise with laboratory skills and develop induced pluripotent stem cells from ALS patients to better understand the disease and develop therapies.

Progress in ALS and the potential of finding new therapies for ALS relies on a vibrant, talented research pool of biomedical researchers and clinicians. Participation from those living with ALS is crucial to these studies and necessary to make progress in developing treatments. I hope this edition inspires scientists and clinicians entering the field, people suffering with this devastating disease, and established researchers, as this is indeed an extremely promising time for ALS research with the potential to develop effective treatments.

- Lucie Bruijn, Ph.D.

Sheila Essey Award 2011

The ALS Association joins the American Academy of Neurology in presenting The 2011 Sheila Essey Award for ALS Research to Leonard van den Berg, M.D., Ph.D.

Leonard van den Berg, Professor of Neurology, University Medical Center, Utrecht, founded the first integrated Netherlands ALS Center. He has initiated a nationwide population-based study aiming at complete ascertainment of incident ALS patients (Prospective ALS study in the Netherlands, PAN). He has established a detailed database and biobank of more than 3,000 individuals. It has generated a combination of large-scale genetic as well as environmental datasets.

To better differentiate motor neuron variants and treatable mimics from ALS he has performed prospective natural history studies of patients suffering from pure lower or upper motor neuron syndromes. In addition to his clinical expertise in ALS, Dr. van den Berg leads a competitive and productive ALS genomics team. His laboratory was amongst the first to use the technology of genome-wide association studies (GWAS) in ALS.

To translate new discoveries in ALS research into treatment for patients effectively, Dr. van den Berg has set up an infrastructure to perform web-based, investigator-initiated placebo-controlled trials. He has introduced the futility, sequential trial designs for ALS as an alternative to

"It is a great honor to receive this internationally recognized and prestigious award. Receiving this award is recognition for the hard and excellent work of the researchers in my group. This award will encourage us to reach our obligation to find a cure for our patients suffering from ALS and related diseases."

–Dr. Leonard van den Berg
Essey Award

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a classic trial design, in which sample size is fixed. This trial design allows trial cessation as soon as a treatment effect can be significantly demonstrated or denied. Trials on creatine and valproate have been completed and a third trial is currently underway using lithium. Capitalizing on his experience in the Netherlands, Dr. van den Berg is leading a European Consortium (European Network for the Cure of ALS or ENCALS) to develop a Clinical Trials and Research Network modeled on the successful initiative of the North Eastern ALS Consortium (NEALS).

His untiring commitment to ALS has produced an international center of clinical excellence in Holland. Dr. van den Berg has integrated his research program into the day-to-day management of people with ALS. He has made important observations about risk factors for ALS including smoking, and has shown that moderate alcohol consumption might be protective. His group has designed and organized a series of clinical trials of drugs that might be beneficial, and his research into trial design has been exciting and innovative. His group has been amongst one of the first to identify new genes for ALS using modern technology, and his observations have been important in improving our understanding of the complexity of ALS.

The $25,000 prize honors the memory of Sheila Essey and was made possible through the generosity of the Essey Family Fund. Past recipients have often used the funds to support research of promising young scientists on their teams.

Clinician Scientist Award

The ALS Association and the American Academy of Neurology (AAN) are pleased to announce that Steve Han, M.D., Ph.D., from the Department of Neurology, Massachusetts General Hospital, Boston, Mass., is this year’s recipient for the AAN/ALS Association Clinician Scientist Development Award as part of The Association’s research program TREAT ALS (Translational Research Advancing Therapy for ALS). The purpose of the award is to recruit talented and promising young clinicians who propose innovative clinical research and to foster their development to make significant contributions to ALS clinical research. Dr. Han has joined Dr. Kevin Eggan’s laboratory at Harvard University, where he will develop the expertise to undertake the proposed study.

The objectives of the study is to test the overall hypothesis that markers of the ALS pathology can be recapitulated in motor neurons generated from patient-specific induced pluripotent stem cells. Having a robust source of patient-specific motor neurons in culture may be useful for the development of “humanized” in vitro disease models and therapeutic drug screens for ALS. The aims of the proposal are to establish four cell lines for each of the different groups of individuals: sporadic ALS patients, familial patients with FUS or TDP-43 mutations and control subjects. Once established, assays will be developed for characteristic markers of disease. These include cell survival, morphological abnormalities, mislocalization of TDP-43 and FUS, ubiquitinated inclusions, and mitochondrial abnormalities.

The proposed experiments will help validate a novel human stem cell-based model of ALS. Once validated they will be adapted for large-scale small-molecule screening to identify potential treatments for ALS.

The project combines expertise from the Eggan laboratory at Harvard University in stem cell reprogramming technology and ALS disease modeling with the clinical expertise and resources of the MGH ALS clinical directed by Merit Cudkowicz, M.D. for ALS scientific and clinical collaboration.

"In the process of planning and coordinating these and subsequent experiments in conjunction with my strong educational plan, I hope to develop the necessary skills and expertise to successfully transition to an independent clinical scientist in the field of ALS. I am delighted to be a recipient of this prestigious award, which will enable me to achieve my career goals," commented Dr. Han.

Directed spinal motor neuron differentiation of iPS cells derived from skin fibroblasts of a 43-year-old man with ALS linked to a mutation in TARDBP. MAP2 (red) and Islet 1/2 (green) double-labeled cells identify motor neurons. 20x magnification.

“...I am delighted to be a recipient of this prestigious award, which will enable me to achieve my career goals.”

–Dr. Steve Han