New Avenues of Research Opened!

This edition marks another milestone for ALS research. The announcement in February that mutations in FUS/TLS are linked to familial ALS, together with a growing body of evidence for the potential role of altered RNA processing in ALS and other neurodegenerative disorders, has opened up new avenues of research. How the cell translates DNA messages to RNA from the nucleus to the cytoplasm to correctly assemble proteins is a complex multi-step process (known as RNA processing) crucial to the health of the cell. Experts in this field are now turning their attention to ALS. The focus is on developing new model systems, understanding which genes interact with these binding proteins and the downstream consequences of these changes.

Progress in ALS and the potential of finding new therapies for ALS relies on a vibrant, talented research pool of biomedical researchers and clinicians. In this edition we are pleased to recognize the talents of established clinician scientists as well as the newer fellows committing their energy and expertise to ALS research. Clinician scientists have the unique opportunity to bring research knowledge directly to patients through a focus on clinical trials, biomarker studies and epidemiology.

Participation from those living with ALS is crucial to these studies in order to make progress in developing treatments. I hope this edition inspires scientists and/or clinicians entering the field, people suffering with this devastating disease and established researchers to collaborate together as this is indeed an extremely promising time for ALS research with the potential to develop meaningful treatments.

- Lucie Bruijn, Ph.D.

Cudkowicz and Hardiman Receive Essey Award

The ALS Association joins the American Academy of Neurology in presenting The 2009 Sheila Essey Award for ALS Research to two clinician scientists who have significantly impacted clinical trials, epidemiology and genetics in ALS.

Dr. Merit Cudkowicz, Associate Professor of Neurology at Massachusetts General Hospital, Boston, Mass., is an international leader of clinical therapeutics in ALS. She is co-founder and co-director of the Northeast ALS Consortium (NEALS) a clinical trials network of 76 clinical sites throughout the U.S. and Canada dedicated to performing academic led clinical trials. The trials network has completed six trials: three phase III efficacy studies (topiramate, creatine and celecoxib) and three phase II studies (coenzyme Q10, sodium phenylbutyrate, arimoclomol).

Dr. Cudkowicz is currently playing a leadership role in three clinical trials through this network: ceftriaxone, lithium and arimoclomol in patients with SOD1 mutations. (The latter two trials are featured in this edition on page 6.)

In 2007 through The Association’s Translational Research Advancing Therapies of ALS (TREAT ALS) program, The Association partnered with NEALS to establish the TREAT ALS/NEALS clinical network facilitating broader participation in ALS clinical trials. In addition, Dr. Cudkowicz has been advisor to The Association’s pilot clinical trial program, which is currently funded by The Association for the SOD1 antisense trial in familial ALS and has established a repository for patient samples. (See page 4 and 5.)

Ongoing studies in her group, facilitated by this resource, attempt to find biomarkers or signatures for the disease to allow for earlier diagnosis and improved clinical trials. Furthermore, Dr. Cudkowicz recognizes the importance of encouraging young clinician scientists in ALS and has mentored, among others, Dr. Aggarawal, recipient of this year’s AAN/ALS Association Clinician Scientist Development Award. Her group has focused on adaptive clinical trial design to identify promising treatments for ALS more rapidly.

“It is an honor to receive this award for my research team at the Massachusetts General Hospital Neurology Clinical Trial Unit and our collaborators in the Northeast ALS consortium. The Sheila Essey

Continued on Page 3
Essey Award cont.

Continued from Page 2

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.

The AAN/TREAT ALS Clinician Scientist Development Award is funded through The Neil Brouerman, M.D. ALS Research Fund.

The ALS Association and the American Academy of Neurology (AAN) are pleased to announce that Swati Aggarwal, M.D. from Massachusetts General Hospital, Massachusetts, is this year’s recipient for the 2009 AAN/ALS Association Clinician Scientist Development Award as part of TREAT ALS (Translational Research Advancing Therapies for ALS). The purpose of the award is to recruit talented and promising young clinicians to the ALS research field, and to foster their development to make significant contributions to ALS clinical research. Dr. Aggarwal’s study will focus on selection trial design for promising therapeutics in ALS.

The process of developing new drugs for ALS is particularly challenging. The trials are generally very long and the number of patients that need to be recruited for the trials is large due to the lack of good biomarkers for the disease. This puts a demand on trials to enroll sufficient patients for the now growing number of trials in a disorder which is relatively rare. At least 32 compounds have been tested in safety and efficacy trials (phase II and phase III) over the past 15 years. Currently seven therapy trials are underway, at least four additional trials in planning, and many more drugs in early discovery stages. The focus of the study in Dr. Aggarwal’s three year award will be to use a selection trial design to more rapidly identify the best therapies to test.

“I am honored to receive this award. I am very thankful to Dr. Cudkowicz, The ALS Association and my colleagues at the Neurology Clinical Trials Unit at Massachusetts General Hospital for their guidance and ongoing support,” commented Dr. Aggarwal.

Clinician Scientist Receives Award

New Gene Mutations

Continued from Page 1

(FUS) or translocation in liposarcoma (TLS) was identified. The protein is structurally and functionally similar to TDP-43 with a normal localization predominantly in the nucleus, and when mutated, forms abnormal accumulations in the cytoplasm of motor neurons. It has not yet been reported whether these accumulations are also present in glial cells. Interestingly, as with TDP-43, the mutations reported so far are localized to the c-terminal fragment of the protein, a region also implicated in interacting with other proteins.

The exact roles of TDP-43 and FUS/TLS are not fully determined; however, both are multifunctional proteins that have been associated with several steps of gene expression, regulation including transcription, RNA splicing, RNA transport and translation. Abnormalities in many of these processes have been implicated in other motor neuron diseases such as spinal muscular atrophy, a childhood motor neuron disease. These exciting findings open up a whole new avenue of research with efforts underway to develop new model systems and to determine both the normal and altered functions of these proteins. These new opportunities will ultimately provide us with important clues to develop meaningful therapies for ALS.

References


Dr. Orla Hardiman

Dr. Swati Aggarwal, M.D.