Sunnybrook
HEALTH SCIENCES CENTRE

New Gene Identified as Common Cause of ALS:
Huge stride for research and treatment implications

Two new studies are bringing scientists closer to slowing down the progression of ALS, as a new gene has been identified as the most common cause of the genetic form of the disease.

The studies, published in the September 21 online issue of *Neuron*, report the identification of the long-sought genetic abnormality which authors say is the most common cause of two different but related forms of neurodegenerative disease: Frontotemporal Dementia (FTD) and ALS.

One of these studies was an international collaboration led by Dr. Bryan Traynor at the National Institutes of Health (NIH) and included University of Toronto-based investigators Dr. Lorne Zinman (Sunnybrook Health Sciences Centre) and Dr. Ekaterina Rogaeva (Centre for Research in Neurodegenerative Diseases) who were co-authors.

A mutation was discovered, where a short DNA sequence on chromosome 9 is repeated many more times as compared to healthy individuals. The mutation was found in around 1/3 of patients with familial ALS and is more than twice as common as the previously identified mutation SOD1. The defect is also the strongest genetic risk factor found to date for the more common, sporadic forms of ALS and FTD. It was found in four percent of sporadic ALS samples and three percent of sporadic FTD.

The discovery of this gene underlying the largest proportion of familial ALS and FTD cases to date is a significant finding.

“This is a critical step that will help us determine how the disease develops and progresses, why its presentation and course is variable, and provide a new target for intervention,” says Dr. Zinman who is also chair of the Canadian ALS Research Network (CALS). “The next step is to determine how this mutation causes ALS and FTD. We can also develop cell and animal models using this novel mutation to improve our understanding of the diseases and for screening of therapeutics that may halt progression.”

Investigators worldwide have been committed to identifying the gene alteration in patients with ALS and FTD linked to chromosome 9, and until now it had remained elusive. This gene mutation was identified by collecting blood samples from hundreds of ALS and FTD patients worldwide and using state of the art next-generation sequencing technology.

“Finding a mutation representing the majority of patients with familial ALS is a major milestone for the ALS community,” says Zinman. “There has never been more reason to be hopeful and optimistic that ALS research will provide effective therapies for those living with ALS.”

In past decades, there was an inaccurate belief that there is no known cause of ALS. In cases where ALS is inherited as a familial trait, researchers have now identified the causative mutations in the majority of cases thanks to this new finding.

Mutations in a number of genes, such as those found in these recent studies, account for a large fraction of those familial cases. In addition, studies in recent years have demonstrated the involvement of many of those genes in cases of sporadic ALS. This means that experimental models based on mutant genes will provide important insights relevant to both the sporadic and familial forms of the disease.

Dr. Zinman’s research is funded by the ALS Society of Canada.

-30-

Media contact:
Nadia Norcia Radovini
416.480.4040