MedicalXpress

Researchers identify a gene responsible for Lou Gehrig's disease

March 31 2008

A team of Canadian and French researchers has identified a novel gene responsible for a significant fraction of ALS (sporadic amyotrophic lateral sclerosis) cases. ALS is commonly referred to as Lou Gehrig's disease, an incurable neuromuscular disorder that affects motor neurons and leads to paralysis and death within one to five years.

Published in the current online edition of Nature Genetics, the study on 200 human subjects with ALS was led by Doctors Guy Rouleau, Edor Kabashi, Paul Valdmanis of the Research Centre of the Centre hospitalier de l'Université de Montréal (CRCHUM). The team identified several genetic mutations in the TDP-43 gene by studying ALS patients from France and Quebec. They established TDP-43 as the gene responsible for up to five percent of the ALS patients.

The breakthrough is the result of teamwork with peers from the Waterloo and Laval universities in Canada and the Fédération des maladies du système nerveux and the Institute of Biology (Unité de Neurologie Comportementale et Dégénérative) in France.

In 1993, Dr. Rouleau and his team also helped identify "superoxide dismutase" as the gene that causes the disease in 10 to 20 percent of all familial cases of ALS. This cornerstone study led to development of several mouse and rat models of ALS that closely resemble the motor neuron disorder observed in ALS patients. These models have been very useful to study molecular and cellular mechanisms of disease and to test treatments for ALS.

TDP-43's normal function is to bind and splice RNA. Two years ago, a team from the University of Pennsylvania discovered TDP-43 in abnormal protein clumps, referred to as aggregates, in motor neurons of ALS patients. However, it was not certain whether TDP-43 causes motor neuron disease or is just a pathological marker.

"The identification of additional mutations in TDP-43 in other ALS patients will confirm that this gene is a prominent cause of this type of disorder," said Dr. Rouleau, director of the Sainte-Justine Hospital Research Centre. "Animal models over-expressing the mutations identified in this study will provide crucial insight into how TDP-43 aggregate and ultimately kill motor neurons."

"This discovery is a step towards the development of therapies for people suffering from this terrible disease and possibly other neurodegenerative diseases," said Dr. Kabashi.

Source: University of Montreal