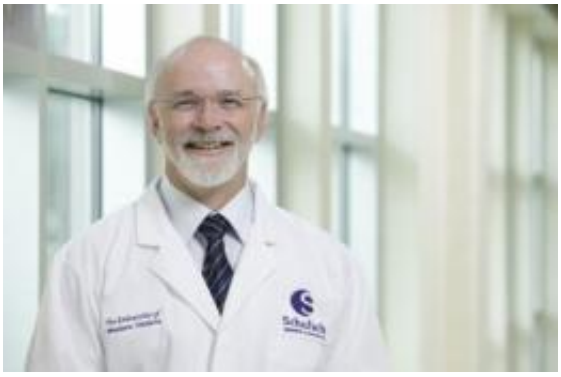
Researchers identify new genetic mutation for ALS

January 15 2013



This is Dr. Michael Strong, Dean of Western University's Schulich School of Medicine & Dentistry, and ALS scientist at Robarts Research Institute. Credit: Schulich School of Medicine & Dentistry, Western Unviersity

Researchers at Western University in London, Canada, have identified a new genetic mutation for amyotrophic lateral sclerosis (ALS), opening the door to future targeted therapies. Dr. Michael Strong, a scientist with Western's Robarts Research Institute and Distinguished University Professor in Clinical Neurological Sciences at the Schulich School of Medicine & Dentistry, and colleagues found that mutations within the ARHGEF28 gene are present in ALS. When they looked across both familial and sporadic forms of the disease, they found that virtually all cases of ALS demonstrated abnormal inclusions of the protein that arises from this gene.

The research is published online in Amyotrophic Lateral Sclerosis *and Frontotemporal Degeneratio*, the official journal of The World Federation of Neurology Research Group on Motor Neuron Diseases.

ALS, sometimes called Lou Gehrig's disease, is a progressive disease that affects the motor neurons that connect the brain to muscles throughout the body. It is a devastating disease with 90 per cent of patients dying within five years of diagnosis. As many as 30,000 Americans and 2,000 Canadians are living with ALS.

Strong's team is convinced ALS is a disorder of RNA metabolism. RNA is the intermediary or messenger between genes and the protein being made. This new protein appears to play a critical role. "Every time we look at a cell degenerating, this particular protein was deposited abnormally in the cell. It was a common denominator," explains Strong, who is also the Dean of Schulich Medicine & Dentistry. "Working with Dr. Rob Hegele at Robarts, we found there was a genetic mutation in the gene coding for this protein. So it's a huge discovery."

Unlike most proteins which have one key function, this one has two. "One side works with RNA. The other side has the capacity to regenerate or to deal with an injury. We think those are competitive activities so if it's doing one, it's not available to do the other," says Strong. In the case of ALS, Strong believes the protein is disturbed on the RNA side so it's no longer able to respond to cell injury. "We need to understand what causes the switch between the two functions, and then can we modulate it."

Provided by University of Western Ontario