Researchers discover blood biomarker for Lou Gehrig's disease, could lead to new treatments

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Researchers from Brigham and Women's Hospital (BWH) are the first to discover that changes in monocytes (a type of white blood cell) are a biomarker for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. This finding also brings the medical community a step closer toward a new treatment for the debilitating neurological disease that affects approximately 30,000 Americans.

The study will be published online in The Journal of Clinical Investigation on August 6, 2012.

In pre-clinical studies involving mice with an ALS gene mutation, the researchers saw that two months prior to ALS onset, monocytes in the spleen began exhibiting proinflammatory qualities. As disease onset loomed, there was an increase in cell-signaling molecules that directed monocytes to flood the spinal cord. Influx of these inflamed white blood cells was associated with nerve cell death in the spinal cord.

When the researchers treated the mice with antibodies to modulate the inflammatory monocytes, they found that it led to fewer monocytes entering the spinal cord, diminished nerve cell loss and extended survival.

After having observed these activities in mice, the BWH researchers, working with the Massachusetts General Hospital (MGH) ALS Clinic

and research team, found that there were similar monocytes in humans with ALS that also exhibited a disease-specific inflammatory signature.

"People have wondered if the immune system plays a role in neurological diseases like ALS," said Howard Weiner, MD, director of the BWH Multiple Sclerosis Program and senior study author. "The immune system is complicated, and previous immunotherapy trials have not been successful. But now we know what is wrong in the blood, and this opens up new therapeutic targets for ALS and perhaps other diseases in the near future."

Study co-author Merit Cudkowicz, MD, who heads the ALS program at MGH adds, "These findings identify a potential new target for developing treatments for people with ALS."

Oleg Butovsky, PhD, BWH Department of Neurology is first study author and lead scientist on the study.

Each year, approximately 5,600 people in the United States are diagnosed with ALS, a disease that affects nerve and muscle functioning, eventually leading to paralysis. The average age at diagnosis is 55 years old and half of those affected live at least three or more years after being diagnosed. Twenty percent live five years or more, and up to 10 percent will live more than ten years.

More information: Modulating inflammatory monocytes with a unique microRNA signature ameliorates murine ALS, *Journal of Clinical Investigation*.

Provided by Brigham and Women's Hospital