Engineered stem cells carry promising ALS therapy

September 16 2008

(PhysOrg.com) -- Using adult stem cells from bone marrow as "Trojan horses"to deliver a nurturing growth factor to atrophied muscles, Wisconsin scientists have successfully slowed the progression of ALS in rats.

The work, published this week (Sept. 16) in the journal *Molecular Therapy*, provides a tantalizing hint that the approach may provide a new therapy for people with amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease.

At present, there are no effective treatments for ALS, an invariably fatal disease caused by the progressive loss of motor neurons and their connections to muscles.

"We were surprised," says Clive Svendsen, a University of Wisconsin-Madison professor of neurology. "We got nice protection of the nerves connected to the muscle and increased survival of the rats."

The study was led by UW-Madison associate scientist Masatoshi Suzuki of the Waisman Center and builds on previous work that showed motor neurons, the critical cells that connect muscles to the central nervous system, could be protected by stem cells that ferried a key growth factor, glial cell line-derived neurotrophic factor (GDNF).

Past work by Suzuki and Svendsen showed that transplanting neural stem cells releasing the growth factor into the spinal cord could protect motor

neurons that degenerate in an ALS rat model. However, while the motor neurons fared better, they still did not effectively connect with the muscles that waste away due to ALS.

In the new study, Suzuki and his colleagues used the same strategy to pump GDNF directly to muscle. In doing so, they delayed the progression of the disease and extended the lifespan of the afflicted animals.

"The novelty is that this is a combined cell and gene therapy approach," Suzuki explains, noting that the bone marrow stem cells on their own had a modest effect, possibly by releasing their own protective factors. "But only when we engineered the cells to release GDNF did we see a significant improvement. The cells turned out to be quite an important component. It's this combination of cells and drug delivery that seems to be so effective."

The Wisconsin group reported that the engineered cells survive well when introduced to muscle and significantly increased the number of neuromuscular connections and motor neurons in the spinal cord at mid stages of the disease.

The new study is important because it could lead to treatments for a disease that now has no effective therapy, although Suzuki and Svendsen cautioned that much work remains before it could be attempted in humans.

A therapeutic advantage of the new work, however, is that muscle is easy to access and stem cells could be generated from patients themselves, lowering the risk of an adverse immune response. In addition, Svendsen notes, a combined approach using cells to deliver GDNF directly to both motor neurons in the spinal cord and muscles could provide a one-two punch to slow the progression of the disease.

Co-authors of the new Molecular Therapy report include Jacalyn McHugh, Craig Tork, Brandon Shelley and Antonio Hayes, all of UW-Madison; and Ilaria Bellantuono of the Royal Manchester Children's Hospital, United Kingdom; and Patrick Aebischer of the Ecole Polytechnique Fédérale de Lausanne, Switzerland.

The new study was supported by grants from the ALS Association, the National Institutes of Health, the University of Wisconsin Foundation and the Les Turner ALS Foundation.

Journal: www.nature.com/mt/index.html

Provided by University of Wisconsin