Research in rodents suggests potential for 'in body' muscle regeneration

September 2 2014

What if repairing large segments of damaged muscle tissue was as simple as mobilizing the body's stem cells to the site of the injury? New research in mice and rats, conducted at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine, suggests that "in body" regeneration of muscle tissue might be possible by harnessing the body's natural healing powers.

Reporting online ahead of print in the journal *Acta Biomaterialia*, the research team demonstrated the ability to recruit stem cells that can form muscle tissue to a small piece of biomaterial, or scaffold that had been implanted in the animals' leg muscle. The secret to success was using proteins involved in cell communication and muscle formation to mobilize the cells.

"Working to leverage the body's own regenerative properties, we designed a muscle-specific scaffolding system that can actively participate in functional tissue regeneration," said Sang Jin Lee, Ph.D., assistant professor of regenerative medicine and senior author. "This is a proof-of-concept study that we hope can one day be applied to human patients."

The current treatment for restoring function when large segments of muscle are injured or removed during tumor surgery is to surgically move a segment of muscle from one part of the body to another. Of course, this reduces function at the donor site.

Several scientific teams are currently working to engineer replacement muscle in the lab by taking small biopsies of muscle tissue, expanding the cells in the lab, and placing them on scaffolds for later implantation. This approach requires a biopsy and the challenge of standardizing the cells.

"Our aim was to bypass the challenges of both of these techniques and to demonstrate the mobilization of muscle cells to a target-specific site for muscle regeneration," said Lee.

Most tissues in the body contain tissue-specific stem cells that are believed to be the "regenerative machinery" responsible for tissue maintenance. It was these cells, known as satellite or progenitor cells, that the scientists wanted to mobilize.

First, the Wake Forest Baptist scientists investigated whether muscle progenitor cells could be mobilized into an implanted scaffold, which basically serves as a "home" for the cells to grow and develop. Scaffolds were implanted in the lower leg muscle of rats and retrieved for examination after several weeks.

Lab testing revealed that the scaffolds contained muscle satellite cells as well as stem cells that could be differentiated into muscle cells in the lab. In addition, the scaffold had developed a network of blood vessels, with mature vessels forming four weeks after implantation.

Next, the scientists tested the effects of several proteins known to be involved in muscle formation by designing the scaffolds to release these proteins. The protein with the greatest effect on cell recruitment was insulin-like growth factor 1 (IGF-1).

After several weeks of implantation, lab testing showed that the scaffolds with IGF-1 had up to four times the number of cells than the

plain scaffolds and also had increased formation of muscle fibers.

"The protein effectively promoted cell recruitment and accelerated muscle regeneration," said Lee.

Next, the scientists will evaluate whether the regenerated muscle is able to restore function and will test clinical feasibility in a large animal model.

Provided by Wake Forest University Baptist Medical Center