Researchers isolate human muscle stem cells

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UC San Francisco researchers have successfully isolated human muscle stem cells and shown that the cells could robustly replicate and repair damaged muscles when grafted onto an injured site. The laboratory finding paves the way for potential treatments for patients with severe muscle injury, paralysis or genetic diseases such as muscular dystrophy.

"We've shown definitively that these are bona-fide stem cells that can self-renew, proliferate and respond to injury," said Jason Pomerantz, MD, an assistant professor of plastic and reconstructive surgery at UCSF.

The findings appeared Sept. 8 in the open access Cell Press journal, *Stem Cell Reports*.

When muscles are badly damaged, they can lose the native populations of stem cells that are needed to heal. This has posed a major roadblock for treating patients crippled by muscle injury and paralysis, particularly in the critical small muscles of the face, hand and eye, Pomerantz said.

Surgeons have shown remarkable success at restoring nerves in damaged muscles, but if the process takes too long the stem cell pool and capacity for regeneration is lost, these injured muscles fail to connect to the nerve tissue, causing their power to wither away.

"This is partly why we haven't had major progress in treating these patients in 30 years," Pomerantz said. "We know we can get the axons there, but we need the stem cells for there to be recovery."

Grafted "Satellite Cells" Repair and Replace Damaged Muscles

So-called "satellite cells" dot the borders of muscle fibers and – at least in mice – were known to act as stem cells to contribute to muscle growth and repair. Until now, however, it wasn't clear whether human satellite cells worked the same way or how to isolate them from human tissue samples and adapt them to help treat patients with muscle damage.

To address these shortcomings, Pomerantz and colleagues obtained surgical biopsies of muscles of the head, trunk and leg, and used antibody staining to show that human satellite cells can be identified by their co-expression of the transcription factor PAX7 with surface proteins CD56 and CD29.

This molecular signature enabled the research team to isolate populations of human satellite cells from the patient biopsies and graft them into mice with damaged muscles whose own muscle stem-cell populations had been depleted. Within five weeks, the human cells successfully integrated into the mouse muscles and divided to produce families of daughter stem cells, replenishing the stem cell niche and repairing the damaged tissue.

Potential "Huge Leap" toward Therapy for Paralysis Patients

This characterization of human muscle stem cells and the ability to transplant them into injured muscles has wide-ranging implications for patients suffering from muscle paralysis, whose damaged muscles have lost the ability to regenerate.

"This gives us hope that we will be able to extract healthy stem cells from other muscles in the patient's body and transplant them at the site of injury," Pomerantz said. "If replenishing a healthy muscle stem cell pool facilitates reinnervation and recovery, it would be a significant leap forward."

The ability to isolate and manipulate human stem cells also may have applications for understanding why our muscles lose their regenerative capacity during normal aging or in genetic diseases such as muscular dystrophy.

Pomerantz's interest in regenerative medicine is inspired by animals like salamanders and zebrafish, which can grow whole new body parts following injury. In addition to his translational work he studies zebrafish regeneration in hopes of using insights from such creatures to improve the self-healing capacity of humans.

More information: "Human Satellite Cell Transplantation and Regeneration from Diverse Skeletal Muscles," *Stem Cell Reports*, Volume 5, Issue 3, 8 September 2015, Pages 419-434, ISSN 2213-6711, dx.doi.org/10.1016/j.stemcr.2015.07.016

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