Purified stem cells restore muscle in mice with muscular dystrophy

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By injecting purified stem cells isolated from adult skeletal muscle, researchers have shown they can restore healthy muscle and improve muscle function in mice with a form of muscular dystrophy. Those muscle-building stem cells were derived from a larger pool of so-called satellite cells that normally associate with mature muscle fibers and play a role in muscle growth and repair.

In addition to their contributions to mature muscle, the injected cells also replenished the pool of regenerative cells normally found in muscle. Those stem cells allowed the treated muscle to undergo subsequent rounds of injury repair, they found.

"Our work shows proof-of-concept that purified muscle stem cells can be used in therapy," said Amy Wagers of Harvard University, noting that in some cases the stem cells replaced more than 90 percent of the muscle fibers. Such an advance would require isolation of stem cells equivalent to those in the mouse from human muscle, something Wagers said her team is now working on.

Satellite cells were first described decades ago and have since generally been considered as a homogeneous group, Wagers said. While anatomically they look similar under a microscope, they nonetheless show considerable variation in their physiology and function. In a previous study, Wagers' identified a set of five markers that characterize the only subset of satellite cells responsible for forming muscle, which they also refer to as skeletal muscle precursors or SMPs.

In the new study, the researchers analyzed the stem cell and regenerative properties of those SMPs. When engrafted into muscle of mice lacking dystrophin, purified SMPs contributed to up to 94 percent of muscle fibers, restoring dystrophin expression and significantly improving muscle structure and contractile function, they report. (The dystrophin gene encodes a protein important for muscle integrity. Mice lacking dystrophin, also known as mdx mice, are a model for Duchenne Muscular Dystrophy, the most prevalent form of muscular dystrophy.)

" Importantly, high-level engraftment of transplanted SMPs in mdx animals shows therapeutic value—restoring defective dystrophin gene expression, improving muscle histology, and rescuing physiological muscle function," the researchers said. "Moreover, in addition to generating mature muscle fibers, transplanted SMPs also re-seed the satellite cell niche and are maintained there such that they can be recruited to participate in future rounds of muscle regeneration.

"Taken together, these data indicate that SMPs act as renewable, transplantable stem cells for adult skeletal muscle. The level of myofiber reconstitution achieved by these myogenic stem cells exceeds that reported for most other myogenic cell populations and leads to a striking improvement of muscle contraction function in SMP-treated muscles. These data thus provide direct evidence that prospectively isolatable, lineage-specific skeletal muscle stem cells provide a robust source of muscle replacement cells and a viable therapeutic option for the treatment of muscle degenerative disorders."

Wagers noted however that there may be complications in the delivery of cell therapy in humans, particularly for those with conditions influencing skeletal muscle throughout the body. Even so, the new findings present an "opportunity to understand what happens [to these regenerative cells] in disease and identify factors and pathways that may boost their activity," she said. "We may get a handle on drugs that could target muscle impairment" not only in those with muscular dystrophies, but also in elderly people suffering from the muscle wasting that comes with age.

Source: Cell Press