Scientists said to restore some youthful strength to old mice

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Courtesy of Stanford University School of Medicine
and World Science staff

Scientists have announced that they were able to restore the strength of some muscles in old mice to youthful levels, through a treatment applied to muscle cells.

The treatment—which researchers hope to eventually try on people—involved removing muscle stem cells from the mice, treating them and putting them back inside the rodents.

"Two months after transplantation, these muscles exhibited forces equivalent to young, uninjured muscles," said Postdoctoral scholar Benjamin Cosgrove of Stanford University School of Medicine in California, one of the researchers.

The investigators found that over time, stem cells, or immature cells, in muscle tissues dedicated to repairing damage become less able to generate new muscle fibers and struggle to self-renew.

"In the past, it's been thought that muscle stem cells themselves don't change with age, and that any loss of function is primarily due to external factors in the cells' environment," said Helen Blau, a Stanford microbiologist. But "when we isolated stem cells from older mice, we found that they exhibit profound changes with age," two thirds of them being "dysfunctional," said Blau. She is senior author of a report on the findings published online Feb. 16 in the journal *Nature Medicine*.

The scientists found that many muscle stem cells from mice that were two years old, equivalent to about 80 years of human life, showed high levels of activity in a chemical process called the p38 MAP kinase pathway. This hampers the proliferation of the stem cells and encourages them to instead become another type of muscle progenitor cell that proliferates less.

Using a drug to block this chemical pathway in old stem cells, while also growing them on a soft substance called hydrogel, allowed them to divide rapidly and make many potent new stem cells that can robustly repair muscle damage, Blau said.

The treatment "stimulates stem cells from old muscle tissues that are still functional to begin dividing and self-renew," she explained. When transplanted back, the treated stem cells migrate to their natural places and provide a long-lasting stem cell reserve to contribute to repeated demands for muscle repair, she added.

"We can take cells from an old animal, treat them for seven days—during which time their numbers expand dramatically, as much as 60-fold—and then return them to injured muscles in old animals to facilitate their repair," Blau said.

The process depended on use of the hydrogel; growing cells on the standard, hard plastic lab

plates didn’t work, the scientists added, probably because the soft hydrogel is more like the cells’ natural environment.

The researchers tested the ability of the rejuvenated stem cells to repair muscle injury and restore strength in old mice. “We were able to show that transplantation of the old treated muscle stem cell population repaired the damage and restored strength to injured muscles of old mice,” Cosgrove said.