

Donor immune cells accelerate recovery of muscle strength in older mice

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A single dose of healthy immune cells sped the recovery of muscle function in older mice following two weeks of physical inactivity, according to University of Utah Health scientists. They say the finding

could eventually lead to the development of treatments that accelerate muscle repair and help older people recover from falls and other injuries as quickly as younger individuals.

"Many people may not realize it, but the immune system plays a vital role in [muscle repair](#) and restoration," says Micah Drummond, Ph.D., a professor of physical therapy and [athletic training](#) at U of U Health and corresponding author of the study, which appears in the *Journal of Applied Physiology*.

"However, as we age, immune cells often become less responsive to muscle tissue injury. We believe that, if we could find a way to reinvigorate the immune system in aging muscle, then we might be able to help [older people](#) retain or restore their ability to get out of chairs, climb stairs, and live better lives."

Older, weaker muscle contributes to falls, injuries

With age, muscles get smaller and weaker, making a person more susceptible to injury from falls and other accidents. In fact, one out of every five falls causes an injury, such as broken bones, and at least 300,000 older adults are hospitalized for hip fractures annually, according to the Centers for Disease Control and Prevention.

"Every year, far too many older people lose their ability to move, stand, and go about their everyday lives," Drummond says. "We want to prevent that from happening and get their muscles back to performing the way they should."

Normally, when an injury such as an ankle sprain occurs, muscle in the affected area sends out signals to the immune system that attract white blood cells to the damaged tissue. Some of these [white blood cells](#), called macrophages, cause swelling but also remove debris from the injury site

and prompt stem cells to coordinate regrowth of muscle tissue.

However, as we get older, the immune cells involved in this process can't stimulate muscle repair as effectively as they did when we were younger, according to Drummond.

Making old muscle act young again

To determine if some of this repair activity could be restored, Drummond and his colleagues from U of U Health and Miami University in Oxford, Ohio, conducted a series of experiments in laboratory mice.

In their first experiment, the researchers weakened muscles in young and old [laboratory mice](#) by restricting the movement of their hind legs for 14 days. These mice were then given a dose of macrophages taken from a set of young and [old mice](#) that were allowed to move freely around. Another set of mice with restricted movement were given saline treatment as a control.

The researchers found the experimental young mice that received immune cells from other young mice showed no difference in their muscle recovery compared to the control group. However, the older experimental mice, when given immune cells from younger mice, had improved muscle strength recovery to virtually the same levels as older mice that remained physically active.

In contrast, when younger experimental mice received immune cells from older mice, their muscles became weaker, suggesting that the old immune cells were somewhat dysfunctional, Drummond says.

Interestingly, when older mice were given old donor immune cells, their muscle strength dramatically improved during recovery, he says.

"When we gave the old immune cells to the older animals, we thought that it might make them worse," Drummond says. "But to our surprise, they actually improved."

Drummond theorizes that even though the old immune cells are a bit less effective than young immune cells, they still have the potential to make a difference, particularly if enough of them are introduced to the muscle.

"They may not be 100% effective, but if you get a bunch of them together in a muscle, they probably can still do their job," Drummond says. "Whereas in a younger animal not as many are needed because their immune cells are in their prime and very efficient."

Better cell communication accelerates muscle rejuvenation, too

The researchers note that immune cell dysfunction is only one of several factors that contribute to poor muscle recovery in older muscles. In some cases, it's possible that muscle cells aren't sending out enough of the right signals to the immune system, Drummond says. As a result, fewer macrophages are available to help restore muscle.

To test this notion, the researchers gave some of the older experimental mice a [growth factor](#) called macrophage colony stimulating factor (MCSF) that normally alerts the [immune system](#) to begin repairing damaged muscle. Overall, the aged mice given MCSF had more macrophage immune cell production and had greater [muscle strength](#) than control animals.

Although this research shows promises, Drummond emphasizes that much more work is needed before it can be used in humans.

"We're looking at many factors that may rejuvenate [immune cells](#) and allow them to more effectively restore muscle function," he says. "But

we still have more experiments to do."

More information: Patrick J. Ferrara et al, Macrophage immunomodulation accelerates skeletal muscle functional recovery in aged mice following disuse atrophy, *Journal of Applied Physiology* (2022). [DOI: 10.1152/jappphysiol.00374.2022](https://doi.org/10.1152/jappphysiol.00374.2022)

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