

## To keep muscles strong, the 'garbage' has to go

December 1 2009

In order to maintain muscle strength with age, cells must rid themselves of the garbage that accumulates in them over time, just as it does in any household, according to a new study in the December issue of *Cell Metabolism*. In the case of cells, that waste material includes spent organelles, toxic clumps of proteins, and pathogens.

The researchers made their discovery by studying mice that were deficient for a gene required for the tightly controlled process of degradation and recycling within cells known as autophagy. Those animals showed profound <u>muscle</u> atrophy and muscle weakening that worsened with age.

"If there is a failure of the system to remove what is damaged, and that persists, the <u>muscle fiber</u> isn't happy," said Marco Sandri of the University of Padova in Italy. Damaged and misfolded proteins pile up along with dysfunctional <u>mitochondria</u>, distended endoplasmic reticulum, free radicals, and other aberrant structures. Eventually, some of those <u>muscle cells</u> die, and "the muscles become weaker and weaker with age."

The muscle wasting observed in the mice seems to bear some resemblance to certain forms of muscle-wasting diseases, Sandri said. He now suspects that this kind of mechanism may offer insight into some of those still-unexplained conditions, as well as the muscle weakening that comes with normal aging (a condition known as sarcopenia).



Researchers knew before that excessive autophagy could also lead to muscle loss and disease. The new findings highlight the importance of maintaining a normal level of autophagy to clear away the debris and keep muscles working properly. Although the discovery seems to make perfect sense in retrospect, it wasn't what Sandri's team had initially anticipated.

"We thought if you reduced autophagy it might protect against atrophy," he said. "Instead, it's the opposite. We realized, OK, of course, if you don't remove the damage, it triggers weakness."

The findings may have clinical implications, he says. There has been interest in developing therapies to block proteins' degradation for treating certain muscle-wasting disorders. But in some cases, at least, "it may be better to activate autophagy and remove the garbage in the <u>cells</u>," Sandri said.

The researchers think similar treatments might combat aging sarcopenia as well, noting that another study has shown a decline in the efficiency of autophagy during aging.

Source: Cell Press (<u>news</u> : <u>web</u>)

Citation: To keep muscles strong, the 'garbage' has to go (2009, December 1) retrieved 4 May 2024 from <u>https://medicalxpress.com/news/2009-12-muscles-strong-garbage.html</u>

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