New medication gives aging mice bigger muscles

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It is common knowledge that as people grow older they lose muscle mass and bone. Researchers from Aarhus University, Denmark, working together with researchers at Erasmus Medical Center in Rotterdam, have now studied a new group of medications that could prove beneficial for the elderly and the chronically ill who suffer a loss of bone and muscle mass.

They have named the group of medicinal products IASPs, for inhibitors of the activin-receptor signaling pathway. "IASPs inhibit a signal pathway which is found in virtually all cells. The difference between the various medications in the group is that they inhibit different routes into the pathway," explains Ph.D. student Andreas Lodberg from the Department of Biomedicine at Aarhus University.

The researchers report that it is possible to achieve an effect on different tissues such as muscle tissue, bone tissue or blood cells, depending on the IASP they used. "We found an increased muscle mass of 19 percent in mice after just one week. At the same time, we saw that the drugs also counteracted osteoporosis," says Andreas Lodberg.

However, the effect on the blood cells presented the researchers with a challenge. Thus far, the drugs in the group of medicinal products have stimulated the formation of red blood cells as vigorously as EPO. "This isn't bad if we're dealing with someone suffering from anaemia, low muscle mass and osteoporosis all at once, as is the case for some. But for the majority of patients with a normal blood percentage, this increases

the risk of blood clots," he says.

The researchers have therefore been working on a solution. They have succeeded in creating a molecule in the IASP group that works on bones and muscles, but does not affect the blood. The results have just been published in the international journal *The FASEB Journal*.

Andreas Lodberg and his colleagues have now begun investigating how IASPs specifically act when building up bone. They use different models in mice to create a loss of muscle mass before examining the tensile strength of the bones and the activity in the cells which break down and build up bones.

"Our earlier results could indicate that IASPs inhibit cells which break down bone tissue while at the same time the cells which build up bone tissue are stimulated, a phenomenon known as 'dual-action'," he explains.

A different IASP that the researchers tested led to a 48 percent increase in the bone strength of the neck of the femur after three weeks compared to the group that did not receive treatment. "If the results of the clinical studies continue to show such promise, it may make sense to treat frail elderly patients suffering muscle loss as a result of chronic diseases with an IASP. Both for the individual patient and for the national economy, as falls and broken bones in elderly patients are a costly affair with high mortality, and also because the loss of muscle mass due to chronic diseases impacts on quality of life and mortality rates," says Andreas Lodberg.

More information: Andreas Lodberg et al, A follistatin-based molecule increases muscle and bone mass without affecting the red blood cell count in mice, *The FASEB Journal* (2019). DOI: 10.1096/fj.201801969RR

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