

New 'exercise hormone' promotes physical endurance

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A new study in mice shows that exercise causes muscle to release a peptide that builds the muscle's capacity for energy production and increases physical endurance, allowing for longer and more intense exercise.

The findings establish that the peptide, called musclin, is an "[exercise factor](#)"—a hormone-like substance made by skeletal [muscle](#) in response to exercise and released into the bloodstream. The study shows that increased levels of circulating musclin trigger a signaling cascade that improves muscle performance and promotes production of mitochondria in [muscle cells](#). The study was published online the week of Dec. 14 in the *Proceedings of the National Academy of Sciences* Early Edition.

"Exercise is an extremely powerful way to improve people's health, but unfortunately, increasing physical activity can be really difficult in many circumstances," says senior author Leonid Zingman, MD, associate professor of internal medicine at the University of Iowa Carver College of Medicine and a physician scientist at the Iowa City Veterans Affairs Medical Center. "We don't want to replace exercise by using this exercise factor, but if we can learn more about the mechanism it might help us to increase [exercise tolerance](#) and make it easier for people to actually exercise. And if it is easier, people may exercise more."

The scientists used genetic engineering to make [mice](#) that don't have musclin. Although these animals look and act like wild type mice, they have lower exercise tolerance and are not able to exercise as long or as hard as wild type mice. However, infusing the musclin peptide back into these modified mice allows the animals to regain normal exercise capacity.

"The musclin infusion into the [knockout mice](#) was effective in rescuing the animal's exercise capacity in just one week," says first author, Ekaterina Subbotina, PhD, a post-doctoral scholar in Zingman's laboratory.

The researchers also showed that infusion of wild type mice with musclin increased the animals' voluntary treadmill activity; the mice ran faster and longer on the treadmill than wild type mice that received a placebo infusion of saline.

Further investigation showed that musclin signaling promotes production of mitochondria in muscle cells. Mitochondria are the cells' power plants, producing the energy required for everything the cell does. The study links the increase in mitochondria to improved aerobic capacity in the mice.

Although the research focused primarily on the effect of exercise on musclin levels, even when mice were sedentary, mice that lack musclin had decreased exercise endurance compared to sedentary wild-type mice, suggesting that musclin may promote muscle health even during the low level exercise of normal everyday living.

More information: Ekaterina Subbotina et al. Musclin is an activity-stimulated myokine that enhances physical endurance, *Proceedings of the National Academy of Sciences* (2015). [DOI: 10.1073/pnas.1514250112](https://doi.org/10.1073/pnas.1514250112)

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