

Protein released from fat after exercise improves glucose

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Laurie J. Goodyear, Ph.D., Section Head and Senior Investigator at Joslin Diabetes Center, and Professor of Medicine at Harvard Medical School. Credit: John Soares

It's well-known that exercise improves health, but understanding how it makes you healthier on a molecular level is the question researchers at Joslin Diabetes Center are answering.

After performing experiments in both humans and [mice](#), the researchers found that [exercise](#) training causes dramatic changes to fat. Additionally, they discovered that this "trained" fat releases factors into the bloodstream that can have positive effects on health. The study was published online February 11, 2019, in *Nature Metabolism*.

It's known that fat cells secrete proteins called adipokines, and that many adipokines increase with obesity, having [harmful effects](#) on metabolism and health.

"In contrast to the negative effects of many adipokines, our study identified transforming growth factor beta 2 (TGF-beta 2) as an adipokine released from adipose tissue (fat) in response to exercise that actually improves glucose tolerance," says Laurie J. Goodyear, Ph.D., Head of Joslin's Section on Integrative Physiology and Metabolism and study co-author.

Not only did exercise-stimulated TGF-beta 2 improve glucose tolerance, treating obese mice with TGF beta 2 lowered blood lipid levels and improved many other aspects of metabolism.

"The fact that a single protein has such important and dramatic effects was quite impressive," says Goodyear, Professor of Medicine at Harvard Medical School.

Two years ago, the international research team first demonstrated that [adipose tissue](#) offers beneficial metabolic effects in response to exercise.

"Our hypothesis was that exercise is changing the fat, and as a result of that change, the fat releases these beneficial proteins into the bloodstream," says Goodyear. "Before this discovery, we always just focused on the positive effects of muscle."

Building on this insight, Joslin researchers sought to identify the adipokines released from fat in exercise. To do so, they ran a series of molecular experiments in both humans and mice. They identified levels of adipokines in men before and after a cycle of exercise. They also studied exercising mice.

Their analysis identified TGF beta 2 as one of the proteins upregulated in exercise in humans and mice. Additional investigation confirmed that levels of this one adipokine actually increased in the fat tissue as well as in the bloodstream with exercise, in both cases.

To find out if the protein promoted beneficial metabolic effects, they treated the mice with TGF beta 2. The experiment showed a number of positive metabolic effects in the mice, including improved glucose tolerance and increased fatty acid uptake.

Next, they fed the mice a [high fat diet](#), causing the animals to develop diabetes. To know if TGF beta 2 was actually responsible for the metabolic effects, they treated the diabetic mice with TGF beta 2. This reversed the negative metabolic effects of the high fat diet, similar to what happens with exercise.

"Our results are important because it's really the first demonstration of an exercise-released adipokine that can have beneficial metabolic effects on the body," says Goodyear.

Another significant finding was that lactic acid, which is released during exercise, serves as an integral part of the process. Lactate is released by the muscles during exercise then travels to the fat where it triggers the release of TGF beta 2.

"This research really revolutionizes the way we think about exercise, and the many metabolic effects of exercise. And, importantly, that fat is

actually playing an important role in the way exercise works," says Goodyear.

These findings suggest that TGF beta 2 may be a potential therapy for treatment of high blood sugar, and eventually a potential therapy for type 2 diabetes. Long-term studies will be needed to determine the safety of TGF beta 2 treatment.

More information: Takahashi et al. TGF-B2 is an Exercise-Induced Adipokine that Regulates Glucose and Fatty Acid Metabolism. *Nature Metabolism*, February 11, 2019. [DOI: 10.1038/s42255-018-0030-7](https://doi.org/10.1038/s42255-018-0030-7) , www.nature.com/articles/s42255-018-0030-7

Provided by Joslin Diabetes Center

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