

# How it works: The protein that stimulates muscle growth

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In the gym, you are not just pumping iron, you are oxygenating muscle cells which keeps those muscles healthy, strong and growing—a process called hypertrophy, or an increase in muscle mass due to an increase in

muscle cell size. Conversely, under the covers, lounging, your muscles may begin to atrophy, or shrink.

Scientists understand that a few [signaling proteins](#) are activated in various conditions of muscle atrophy and hypertrophy, but they have been stumped about the role and mechanisms by which TAK1, a protein that regulates innate immunity and the proinflammatory signaling pathways, regulates [skeletal muscle mass](#), until University of Houston researchers began exploring.

"We demonstrate that supraphysiological activation of TAK1 in skeletal muscle stimulates translational machinery, [protein synthesis](#) and myofiber growth," reports Ashok Kumar, UH College of Pharmacy Else and Philip Hargrove Endowed Professor and chair, Department of Pharmacological and Pharmaceutical Sciences, in *Nature Communications*.

Using genetic approaches, Kumar and research assistant professor Anirban Roy demonstrated that TAK1 is indispensable for maintaining healthy neuromuscular junctions, which are involved in transmitting nerve impulses to skeletal muscle and allow muscle contractions.

"Our findings demonstrate that targeted inactivation of TAK1 causes derangement of neuromuscular junctions and severe muscle wasting, very similar to muscle wasting observed during nerve damage, aging and cancer cachexia. We have also identified a novel interplay between TAK1 and BMP (Bone Morphogenetic Protein) signaling pathway that promotes muscle growth," said Roy.

Nutrients, growth hormones and weight training all result in an increase in skeletal muscle mass in healthy individuals. Conversely, many disease conditions often lead to a loss in lean muscle mass. Understanding the mechanisms regulating protein and organelle content is highly important

to identify drug targets for various muscle wasting conditions and neuromuscular disorders.

The team also reports that activation of TAK1 in [skeletal muscle](#) beyond normal levels can prevent excessive muscle loss due to nerve damage. Loss of [muscle mass](#) has a devastating impact on standard-of-care treatment during aging and terminal illnesses, such as cancer, COPD, kidney failure and in many genetic neuromuscular diseases.

"Recognizing the impact of TAK1 signaling in supporting muscle growth, our research opens up new avenues to develop therapies for these and many other pathological conditions and improve quality of life," said Roy.

Future studies will investigate whether the activation of TAK1 using small molecules is sufficient to promote muscle growth and prevent atrophy in the elderly and various disease states.

**More information:** Anirban Roy et al, Supraphysiological activation of TAK1 promotes skeletal muscle growth and mitigates neurogenic atrophy, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-29752-0](#)

Provided by University of Houston

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