KYUSHU UNIVERSITY

Public Relations Initiative, Kyushu University
744 Motooka Nishi-ku Fukuoka, 819-0395
TEL: +81-92-802-2443 FAX: +81-92-802-2139
E-MAIL: koho@jimu.kyushu-u.ac.jp
URL: https://www.kyushu-u.ac.jp

PRESS RELEASE (2026/07/24)

Japanese scientists find compound that may help muscles stay strong as we age

The compound strengthens HGF, a protein that helps activate muscle repair, offering hope for future treatments of age-related muscle loss in humans and pets

Fukuoka, Japan—Skeletal muscle is one of the first tissues to decline with age. This decline can lead to weakness, scarring, fat accumulation inside muscle, and the loss of fast-twitch muscle fibers that are important for quick and powerful movements.

A research team led by Professor Ryuichi Tatsumi at Kyushu University's Faculty of Agriculture has now identified a molecule that may help protect and even strengthen one of the body's key muscle-repair signals. The findings were published on July 24, 2026, in *Scientific Reports*.

The study centers on hepatocyte growth factor, or HGF, which acts like a wake-up signal in skeletal muscle. In healthy muscle, HGF sits quietly in the supportive network surrounding muscle fibers. When muscle is injured or mechanically stimulated, HGF is released and binds to c-met receptors on satellite cells—the resident stem cells of skeletal muscle—awakening them from a resting state, enabling them to proliferate, differentiate, and contribute to muscle fiber repair.

However, aging can interfere with this process. The team's earlier work showed that HGF undergoes a chemical change called nitration, in which a nitro group is added to two specific sites on the protein, Y198 and Y250—the very region HGF uses to bind c-met. Once nitrated, HGF loses its ability to dock with the receptor, like a rusted key that no longer fits its lock. This is thought to be a root cause of age-related muscle wasting and impaired regeneration.

"HGF is not necessarily missing as we age," explains Tatsumi. "Rather, it can be chemically altered after it is made. That led us to wonder whether a compound with strong antioxidant capacity might protect HGF, either by preventing nitration or by compensating for the functional loss it causes."

The team turned to two sulfur-based compounds known for strong antioxidant activity: glutathione trisulfide (GSSSG) and lipoic acid trisulfide (LASSS). Both belong to a class of molecules called trisulfides, which carry three consecutively linked sulfur atoms. Their unusual sulfur chemistry and redox properties have recently attracted attention for pharmaceutical development.

In initial experiments, both GSSSG and LASSS suppressed nitration of HGF at Y198 and Y250. But receptor-binding activity was not fully restored, so the team raised the molar ratio of HGF to trisulfide, from 1:4000 up to 1:8000.

A surprise followed. At this higher ratio, HGF's binding affinity for c-met increased more than two-fold compared with untreated HGF, while also becoming more resistant to nitration-

induced dysfunction, especially at Y198. This enhancement appeared with LASSS alone; GSSSG showed no such effect.

“This exceeded our expectations,” comments Tatsumi. “We knew trisulfides had diverse biological functions, but we never expected that simply mixing HGF with LASSS would produce such a striking effect.

“What this tells us is that LASSS does more than simply neutralize reactive molecules. It may interact directly with HGF and induce a subtle structural change, creating an enhanced ‘Super HGF’ form that binds c-met more strongly and resists nitration.”

To test whether this effect holds up in living tissue, the researchers used a mouse model of muscle atrophy caused by tail suspension. Mice pretreated with LASSS showed significantly reduced nitration compared with untreated animals, while GSSSG again showed no protective effect, confirming that LASSS's protective effect carries over from the lab. Further studies in aging animals will be needed to confirm LASSS's effectiveness and safety *in vivo*.

The findings may open a new path toward strategies for maintaining muscle repair during aging, prolonged bed rest, or other conditions involving muscle disuse. The team believes LASSS's effects on HGF are likely to apply broadly, from humans to companion animals such as cats and dogs, and ultimately help preserve independence, quality of life, and healthy lifespan in later years.

###

For more information about this research, see "Enhanced HGF with increased receptor affinity and nitration-dysfunction resistance through interaction with lipoic acid trisulfide” Kahona Zushi, Miyumi Seki, Ryota Mizuochi, Kazuki Shitamitsu, Alaa Elgaabari, Sakiho Tanaka, Junri Miyamoto, Kaoru Mizoguchi, Reina Fujimaru, Jiaxi Han, Takashi Nakashima, Shoko Sawano, Wataru Mizunoya, Takahiro Maeno, Issei Yokoyama, Takahiro Suzuki, Judy E. Anderson, Ryuichi Tatsumi. *Scientific Reports*, https://doi.org/10.1038/s41598-026-60835-w

About Kyushu University

Founded in 1911, Kyushu University is one of Japan's leading research-oriented institutions of higher education, consistently ranking as one of the top ten Japanese universities in the Times Higher Education World University Rankings and the QS World Rankings. Located in Fukuoka, on the island of Kyushu—the most southwestern of Japan’s four main islands—Kyushu U sits in a coastal metropolis frequently ranked among the world’s most livable cities and historically known as Japan’s gateway to Asia. Its multiple campuses are home to around 19,000 students and 8,000 faculty and staff. Through its VISION 2030, Kyushu U will “drive social change with integrative knowledge.” By fusing the spectrum of knowledge, from the humanities and arts to engineering and medical sciences, Kyushu U will strengthen its research in the key areas of decarbonization, medicine and health, and environment and food, to tackle society’s most pressing issues.

Fig. 1. Japanese scientists find compound that may help muscles stay strong as we age
The compound strengthens HGF, a protein that helps activate muscle repair, offering hope for future treatments of age-related muscle loss in humans and pets.

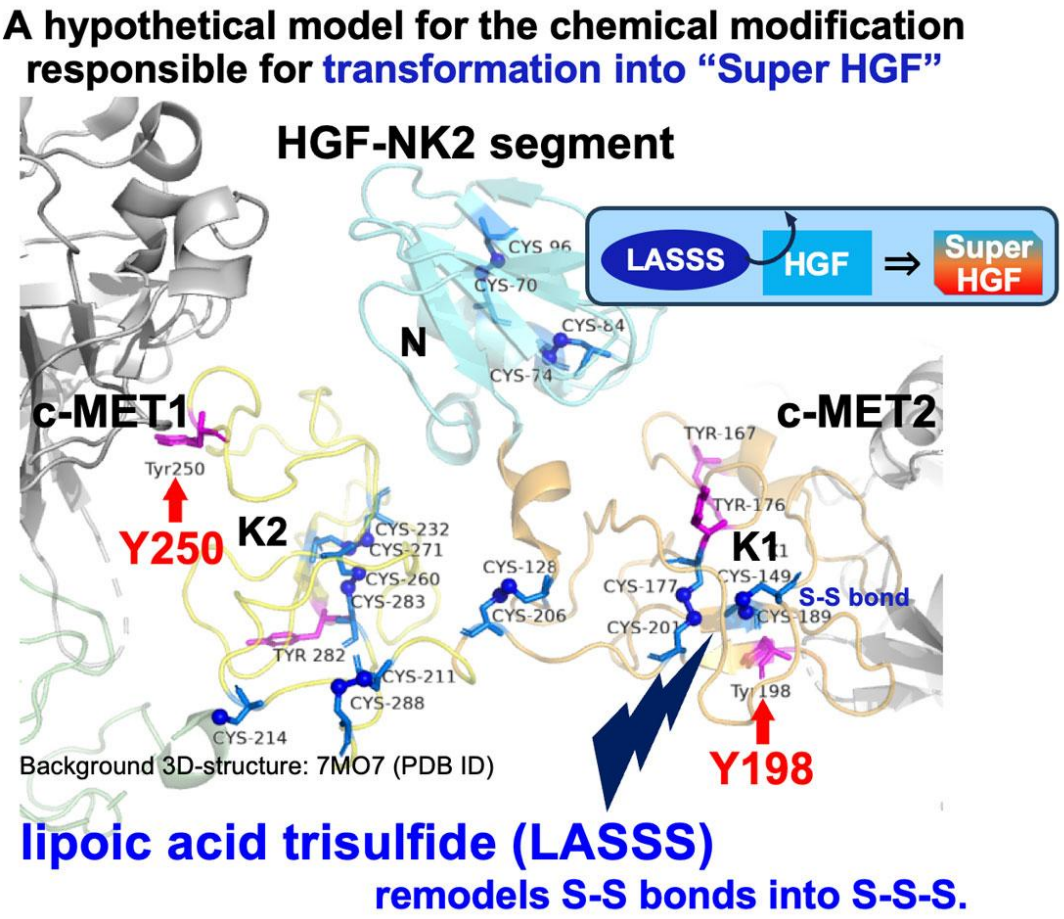

Fig. 2. Lipoic acid trisulfide (LASSS) may turn HGF into "Super HGF"
HGF is a key activator of muscle stem cells that normally resides in the extracellular matrix, but becomes dysfunctional with age due to nitration. Researchers show that interaction with lipoic acid trisulfide (LASSS) can convert HGF into "Super HGF," a form with enhanced receptor-binding affinity and resistance to nitration-induced dysfunction. Disulfide bonds may be potential targets for LASSS-mediated remodeling into trisulfide bonds.

[Contact]
Ryuichi Tatsumi, Professor
Faculty of Agriculture
Tel: +81 92 802 4593
rtatsumi@agr.kyushu-u.ac.jp