How work tells muscles to grow

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We take it for granted, but the fact that our muscles grow when we work them makes them rather unique. Now, researchers have identified a key ingredient needed for that bulking up to take place. A factor produced in working muscle fibers apparently tells surrounding muscle stem cell "higher ups" that it's time to multiply and join in, according to a study in the January *Cell Metabolism*, a Cell Press journal.

In other words, that so-called serum response factor (Srf) translates the mechanical signal of work into a chemical one.

"This signal from the muscle fiber controls stem cell behavior and participation in muscle growth," says Athanassia Sotiropoulos of Inserm in France. "It is unexpected and quite interesting." It might also lead to new ways to combat muscle atrophy.

Sotiropoulos' team became interested in Srf's role in muscle in part because their earlier studies in mice and humans showed that Srf concentrations decline with age. That led them to think Srf might be a culprit in the muscle atrophy so common in aging.

The new findings support that view, but Srf doesn't work in the way the researchers had anticipated. Srf was known to control many other genes within muscle fibers. That Srf also influences the activities of the satellite stem cells came as a surprise.

Mice with muscle fibers lacking Srf are no longer able to grow when they are experimentally overloaded, the new research shows. That's

because satellite cells don't get the message to proliferate and fuse with those pre-existing myofibers.

Srf works through a network of genes, including one known as Cox2. That raises the intriguing possibility that commonly used Cox2 inhibitors—think ibuprofen—might work against muscle growth or recovery, Sotiropoulos notes.

Treatments designed to tweak this network of factors might be used to wake muscle stem cells up and enhance muscle growth in circumstances such as aging or following long periods of bed rest, she says. Most likely, such therapies would be more successfully directed not at Srf itself, which has varied roles, but at its targets.

"It may be difficult to find a beneficial amount of Srf," she says. "Its targets, interleukins and prostaglandins, may be easier to manipulate."

More information: Guerci et al.: "Srf-dependent paracrine signals produced by myofibers control satellite cell-mediated skeletal muscle hypertrophy."

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