New insight into factors that drive muscle-building stem cells

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A report in the January issue of *Cell Metabolism*, a publication of Cell Press, provides new evidence explaining how stem cells known as satellite cells contribute to building muscles up in response to exercise. These findings could lead to treatments for reversing or improving the muscle loss that occurs in diseases such as cancer and AIDS as well as in the normal aging process, according to the researchers.

The researchers showed that a transient and local rise in an inflammatory signal, the cytokine known as interleukin-6 (IL-6), is essential for the growth of muscle fibers. The findings offer the first clear mechanism for the stem cells' incorporation into muscle and the first evidence linking a cytokine to this process, said Pura Muñoz-Cánoves of Universitat Pompeu Fabra in Barcelona, Spain. "As we learn more about how muscles grow in adults, we may uncover new methods for restoring lost muscle mass in the elderly and ill," she added.

Skeletal muscles are made up of individual myofibers, each with many nuclei containing genetic material. As muscles are made to work harder, they adapt by bulking up each of those individual fibers, the researchers explained, but the mechanisms responsible have largely remained elusive.

Mounting evidence has shown that the growth of myofibers is limited by the need to maintain an equilibrium between the number of nuclei and the fibers' overall volume. Because mature myofibers are incapable of cell division, new nuclei must be supplied by satellite cells (muscle stem

cells). Once activated, satellite cells follow an ordered set of events, including proliferation, migration, and incorporation into the myofiber, leading to its growth.

Now, the researchers have found that IL-6 is an essential regulator in that process. While IL-6 was virtually undetectable in the muscles of control mice, animals whose muscles were made to work harder showed an increase in IL-6 after one day. That cytokine rise was maintained for two weeks before it declined again.

Interestingly, systemically high levels of IL-6 had earlier been implicated in the muscle wasting process, Muñoz-Cánoves noted. “Having excess IL-6 is bad, but its local translation is required for muscle growth.”

The researchers further found that IL-6 was produced both within myofibers and in their associated satellite cells, leading to muscle growth. In contrast, the muscles of mice lacking IL-6 did not show any significant increase in size after several weeks of overloading. The researchers also showed that IL-6 exerts its effects by inducing the proliferation of satellite cells.

While Muñoz-Cánoves said that the findings are “just the beginning” of a new line of investigation into how adult muscle grows, she added that they might ultimately provide a new avenue for muscle-building therapies.

“Treatments could be designed to compensate for or block the pathways leading to muscle loss,” she said. “In muscles that have already lost mass, you might also be able to stimulate muscle growth.”

Source: Cell Press