Autophagy helps fast track stem cell activation

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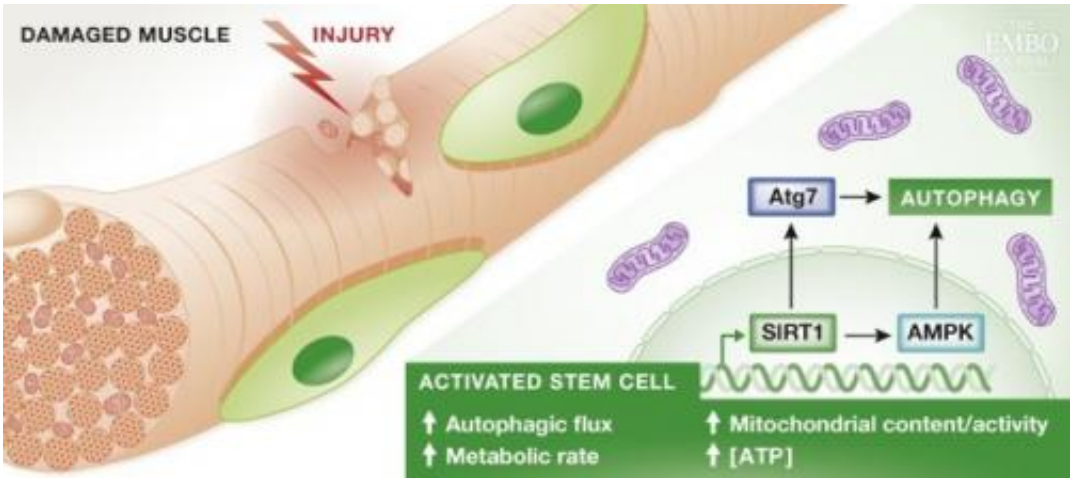

Enhanced autophagy is important to meet the increased energetic and biosynthetic demands of activated stem cells. Credit: Uta Mackensen, EMBO Press.

Researchers from Stanford University School of Medicine have discovered a link between a protective mechanism used by cells and the activation of muscle stem cells. Cells use autophagy to recycle cellular "building blocks" and generate energy during times of nutrient deprivation. The scientists report in The *EMBO Journal* that when this protective mechanism is operational it also seems to assist in the activation of stem cells.

"Our study reveals that when stem cells emerge from a quiescent state

there is a rapid and dramatic change in their metabolic activity," says Thomas Rando Professor at Stanford University School of Medicine and the lead author of the study. "The induction of autophagy seems to be a critical component of these metabolic shifts and allows stem cells to cope with the stressful demands for nutrients and the building blocks for the synthesis of large molecules like proteins and DNA that arise due to the rapid growth of the cell."

Autophagy involves the engulfment of cellular organelles into specialized vacuoles surrounded by a double membrane. The contents of these vacuoles are delivered to the lysosome, another organelle within the cell, where they are degraded to useful small molecules and help to generate energy and biomass for the synthesis of macromolecules and new organelles.

When stem cells are activated, cells experience large changes in their metabolism since they require increased biosynthesis of proteins and other large molecules. The scientists discovered that autophagy is turned on when muscle stem cells are activated. They also showed that when autophagy was inhibited the activation of the stem cells was delayed.

The researchers were also able to demonstrate that a known nutrient sensor, SIRT1, regulates autophagy in the muscle stem cells. When they interfered with this protein using genetic methods or treatment with chemical inhibitors they were able to delay the activation of muscle stem cells. "This study identifies increased autophagy as a crucial checkpoint in the activation of muscle stem cells," says Professor Amy Wagers, a Professor the Department of Stem Cell and Regenerative Biology at Harvard University and Harvard Stem Cell Institute who is not an author of the study.

More information: "Induction of autophagy supports the bioenergetic demands of quiescent muscle stem cell activation." The *EMBO Journal*.

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