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Fasting boosts stem cellsâ?? regenerative capacity

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A study finds that a drug treatment that mimics fasting can also provide the same benefit.



As people age, their intestinal stem cells begin to lose their ability to regenerate. These stem cells are the source for all new intestinal cells, so this decline can make it more difficult to recover from gastrointestinal infections or other conditions that

affect the intestine.

This age-related loss of stem cell function can be reversed by a 24-hour fast, according to a new study from MIT biologists. The researchers found that fasting dramatically improves stem cells' ability to regenerate, in both aged and young mice.

The researchers say that in fasting mice, cells begin breaking down fatty acids instead of glucose, a change that stimulates the stem cells to become more regenerative. The researchers found that they could also boost regeneration with a molecule that activates the same metabolic switch. Such an intervention could potentially help older people recovering from GI infections or cancer patients undergoing chemotherapy.

"Fasting has many effects in the intestine, which include boosting regeneration as well as potential uses in any type of ailment that impinges on the intestine, such as infections or cancers," says Omer Yilmaz, an MIT assistant professor of biology, a member of the Koch Institute for Integrative Cancer Research, and one of the senior authors of the study. "Understanding how fasting improves overall health, including the role of adult stem cells in intestinal regeneration, in repair, and in aging, is a fundamental interest of my laboratory."

David Sabatini, an MIT professor of biology and member of the Whitehead Institute for Biomedical Research and the Koch Institute, is also a senior author of the paper, which appears in the May 3 issue of *Cell Stem Cell*.

"This study provided evidence that fasting induces a metabolic switch in the intestinal stem cells, from utilizing carbohydrates to burning fat," Sabatini says. "Interestingly, switching these cells to fatty acid oxidation enhanced their function significantly. Pharmacological targeting of this pathway may provide a therapeutic opportunity to improve tissue homeostasis in age-associated pathologies."

The paper's lead authors are Whitehead Institute postdoc Maria Mihaylova and Koch Institute postdoc Chia-Wei Cheng.

The findings suggest that drug treatment could stimulate regeneration without requiring patients to fast, which is difficult for most people. One group that could benefit from such treatment is cancer patients who are receiving chemotherapy, which often harms intestinal cells. It could also benefit older people who experience intestinal infections or other gastrointestinal disorders that can damage the lining of the intestine.

The researchers plan to explore the potential effectiveness of such treatments, and they also hope to study whether fasting affects regenerative abilities in stem cells in other types of tissue.

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