Study shows fasting kills cancer cells of common childhood leukemia

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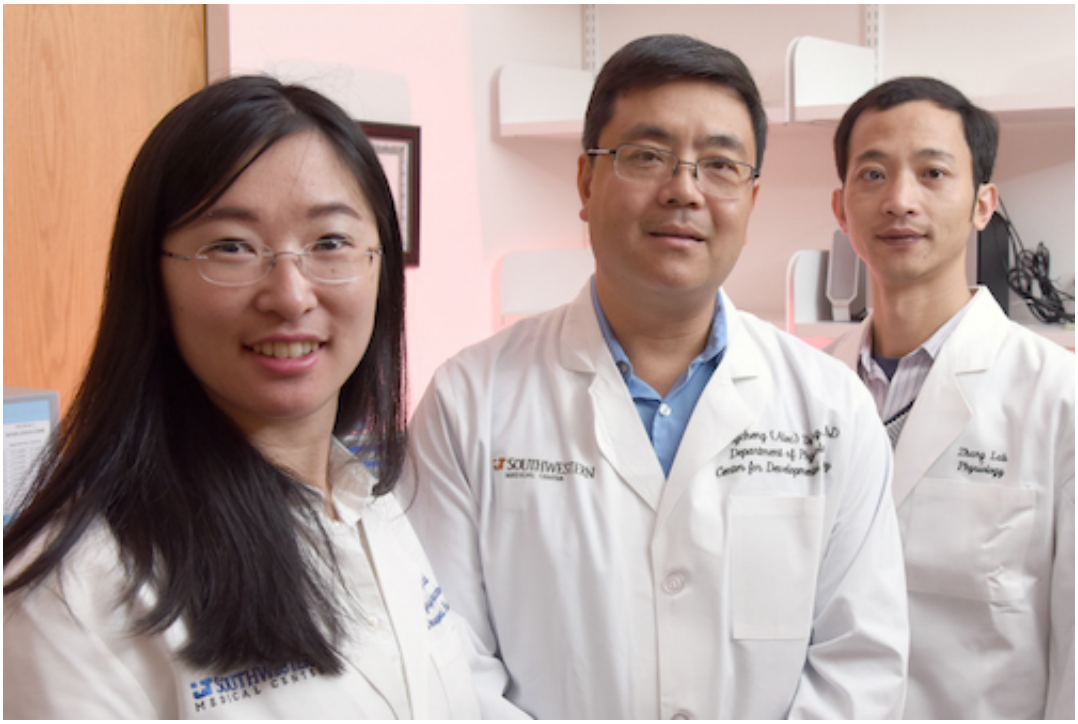

Dr. Jingjing Xie, Dr. Chengcheng "Alec" Zhang, and Dr. Zhigang Lu. Credit: UT Southwestern Medical Center

UT Southwestern Medical Center researchers have found that intermittent fasting inhibits the development and progression of the most common type of childhood leukemia.

This strategy was not effective, however, in another type of blood cancer

that commonly strikes adults.

"This study using mouse models indicates that the effects of fasting on blood cancers are type-dependent and provides a platform for identifying new targets for leukemia treatments," said Dr. Chengcheng "Alec" Zhang, Associate Professor of Physiology at UT Southwestern and senior author of the study, published online today by *Nature Medicine*. "We also identified a mechanism responsible for the differing response to the fasting treatment," he added.

The researchers found that fasting both inhibits the initiation and reverses the progression of two subtypes of acute lymphoblastic leukemia, or ALL - B-cell ALL and T-cell ALL. The same method did not work with acute myeloid leukemia (AML), the type that is more common in adults.

ALL, the most common type of leukemia found in children, can occur at any age. Current ALL treatments are effective about 90 percent of the time in children, but far less often in adults, said Dr. Zhang, who also holds the Hortense L. and Morton H. Sanger Professorship in Oncology and is a Michael L. Rosenberg Scholar in Medical Research.

The two types of leukemia arise from different bone marrow-derived blood cells, he explained. ALL affects B cells and T cells, two types of the immune system's disease-fighting white blood cells. AML targets other types of white blood cells such as macrophages and granulocytes, among other cells.

In both ALL and AML, the cancerous cells remain immature yet proliferate uncontrollably. Those cells fail to work well and displace healthy blood cells, leading to anemia and infection. They may also infiltrate into tissues and thus cause problems.

The researchers created several mouse models of acute leukemia and tried various dietary restriction plans. They used green or yellow florescent proteins to mark the cancer cells so they could trace them and determine if their levels rose or fell in response to the fasting treatment, Dr. Zhang explained.

"Strikingly, we found that in models of ALL, a regimen consisting of six cycles of one day of fasting followed by one day of feeding completely inhibited cancer development," he said. At the end of seven weeks, the fasted mice had virtually no detectible cancerous cells compared to an average of nearly 68 percent of cells found to be cancerous in the test areas of the non-fasted mice.

Compared to mice that ate normally, the rodents on alternate-day fasting had dramatic reductions in the percentage of cancerous cells in the bone marrow and the spleen as well as reduced numbers of white blood cells, he said. The spleen filters blood.

"In addition, following the fasting treatment, the spleens and lymph nodes in the fasted ALL model mice were similar in size to those in normal mice. Although initially cancerous, the few fluorescent cells that remained in the fasted mice after seven weeks appeared to behave like normal cells," he said. "Mice in the ALL model group that ate normally died within 59 days, while 75 percent of the fasted mice survived more than 120 days without signs of leukemia."

Fasting is known to reduce the level of leptin, a cell signaling molecule created by fat tissue. In addition, previous studies have shown weakened activity by leptin receptors in human patients with ALL. For those reasons, the researchers studied both leptin levels and leptin receptors in the mouse models.

They found that mice with ALL showed reduced leptin receptor activity

that then increased with intermittent fasting, he said.

"We found that fasting decreased the levels of leptin circulating in the bloodstream as well as decreased the leptin levels in the bone marrow. These effects became more pronounced with repeated cycles of fasting. After fasting, the rate at which the leptin levels recovered seemed to correspond to the rate at which the cancerous ALL cells were cleared from the blood," he added.

Interestingly, AML was associated with higher levels of leptin receptors that were unaffected by fasting, which could help explain why the fasting treatment was ineffective against that form of leukemia. It also suggests a mechanism - the leptin receptor pathway - by which fasting exerts its effects in ALL, he said.

"It will be important to determine whether ALL cells can become resistant to the effects of fasting," he said. "It also will be interesting to investigate whether we can find alternative ways that mimic fasting to block ALL development."

Given that the study did not involve drug treatments, just fasting, researchers are discussing with clinicians whether the tested regimen might be able to move forward quickly to human clinical trials

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