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Study provides new clues to leukemia resurgence after chemotherapy

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For the first time, researchers have discovered that some leukemia cells harvest energy resources from normal cells during chemotherapy, helping the cancer cells not only to survive, but actually thrive, after treatment.

The study, published online today in *Blood*, the Journal of the American Society of Hematology (ASH), focuses on acute myeloid leukemia (AML), a cancer of the blood and bone marrow that is the most common type of acute leukemia in adults. Nearly 20,000 U.S. adults are diagnosed with AML each year, and another 10,400 die from it annually, according to the American Cancer Society. Although chemotherapy treatments are often initially successful against this type of cancer, relapse occurs in about two-thirds of treated patients, often resulting in death.

The researchers found that leukemia cells are capable of stealing organelles known as mitochondria from stromal cells, non-cancerous connective tissue cells found in bone marrow and other organs. These stolen mitochondria give an energy boost to the surviving cancer cells that helps fuel the cancer's rebound, they explain.

"There are multiple mechanisms for resistance to chemotherapy, and it will be important to target them all in order to eliminate all leukemic cells," said Jean-François Peyron, PhD, team leader at the Centre Méditerranéen de Médecine Moléculaire (C3M) in Nice, France. "Targeting this protective mitochondrial transfer could represent a new

strategy to improve the efficacy of the current treatments for acute myeloid leukemia."

The team conducted their experiments using cell cultures and mice, examining cells under the microscope. They found that while almost all cancer cells died when exposed to chemotherapy drugs, some stayed alive. Those that survived issued a "mayday" signal that tricked nearby non-cancerous cells to yield their mitochondria to the leukemia cell, thus strengthening the cancer cell.

"Mitochondria produce the energy that is vital for cell functions," said Emmanuel Griessinger, PhD, principal investigator of the study. "Through the uptake of mitochondria, chemotherapy-injured acute myeloid leukemia cells recover new energy to survive. It's like getting new batteries, or refueling during a pit stop."

The leukemia cells were found to increase their mitochondria mass by an average of 14 percent. This increase in mitochondria led to a 1.5-fold increase in energy production and significantly better survival rates. That is, the leukemia cells that have a high level of mitochondria are also more resistant to the chemotherapy.

The researchers observed the phenomenon in several types of leukemia cells, most notably those known as leukemia-initiating cells, which are considered to be responsible for the cancer's resurgence after treatment. Authors say this finding may explain why it is hard to treat some cancers.

Researchers believe these findings offer new hope for developing better treatments for AML. If researchers can find a way to interrupt the "mayday" signal or otherwise interfere with the transfer of mitochondria, that knowledge could lead to chemotherapy drugs that would reduce the risk of relapse.

The study has clear implications for AML, but it may also shed light on other cancer types. It is likely that similar mechanisms may be at play in other blood cancers that involve the bone marrow, and it is also possible that the mechanism could be found in solid tumors as well, according to the researchers.

According to the study authors, the next important step will be to identify the mechanism underlying the transfer of mitochondria to AML.

Provided by American Society of Hematology