

Obesity hinders chemotherapy treatment in children with leukemia

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David Hockenbery, M.D., is a member of the Fred Hutchinson Cancer Research Center and professor of internal medicine at the University of Washington.
Credit: David Hockenbery, M.D.

Obesity is an important factor contributing to chemotherapy resistance and increasing relapse rates among children with leukemia, according to recent findings published online first in *Cancer Research*, a journal of the American Association for Cancer Research.

Obesity is associated with increased incidence and mortality of many types of [cancer](#). Leukemia is the most common cancer in children, affecting more than 2,000 children each year in the United States alone, according to background materials in the study.

Given the increasing prevalence of obesity worldwide, these findings could have important implications for [cancer treatment](#) and may help explain the increased leukemia relapse rate in obese patients, according to the study's lead researcher Steven D. Mittelman, M.D., Ph.D.

Mittelman is the fellowship research director with the Division of Endocrinology at Childrens Hospital Los Angeles, and assistant professor of pediatrics, physiology and biophysics at the Keck School of Medicine, University of Southern California.

"Obesity could increase cancer incidence and mortality through a variety of ways. It may impair the immune system's ability to stop cancer, or predispose cells to become cancerous," Mittelman suggested. "Once you have cancer, and if you are obese, the fat cells themselves may impair the ability of chemotherapy to fight cancerous cells."

This study was inspired by a previous study led by a colleague, Anna Butturini, M.D., associate professor of clinical pediatrics in the Division of Hematology-Oncology at Childrens Hospital, which showed that obese children diagnosed with leukemia have a 50 percent higher chance of relapsing compared with lean children.

Using preclinical models, Mittelman and colleagues investigated the reason why obese children were more at risk of relapse. They developed a mouse model of obesity and leukemia, cultured fat and [leukemia cells](#) together, and treated the leukemia cells with traditional [chemotherapy drugs](#) used in children — vincristine, nilotinib, daunorubicin and dexamethasone.

Obese mice with leukemia had higher relapse rates than lean mice after treatment with the first-line chemotherapeutic agent vincristine. The chemotherapy treatments all worked less effectively in culture when fat cells were nearby. When the mice relapsed from the leukemia, the researchers found leukemia "hiding out" in the fat tissue during

chemotherapy, according to Mittelman.

"These four drugs attack leukemia cells by different routes, so when we saw fat cells blocking them we realized there could be an important mechanism promoting their ability to live and divide," he said. "We were surprised to find leukemia cells in the fat tissue."

David Hockenbery, M.D., member of the Fred Hutchinson Cancer Research Center and professor of internal medicine at the University of Washington, said "this study provides striking experimental support for the clinical observations that obesity is associated with poor prognosis in multiple cancers."

The researchers demonstrated that co-culture of leukemia cells with adipocytes diminishes response to multiple chemotherapeutic agents. Therefore, adipose tissue may function as a "safe haven" for leukemia cells during therapy, according to Hockenbery. Based on the finding that adipocytes accumulate chemotherapeutic drugs, he advised that careful attention be paid to dose adjustments based on pharmacokinetic measurements.

"In addition, by highlighting a potential communication between adipocyte and leukemia cells, this research will stimulate efforts to find a diffusible factor that protects leukemia cells from chemotherapy," said Hockenbery.

More research is needed to figure out how fat cells are a part of the tumor microenvironment and how they block potentially lifesaving treatments, according to Mittelman. The researchers are currently conducting additional studies to evaluate other chemotherapeutics, how obesity may or may not affect treatment and the effect of [fat cells](#) found in bone marrow on leukemia.

Source: American Association for Cancer Research ([news](#) : [web](#))

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