

Researchers find cancer-fighting drugs help morbidly obese mice lose weight

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Credit: Mayo Clinic

Scientific investigations sometimes result in serendipitous discoveries which shift the investigations from one focus to another. In the case of researchers at Mayo Clinic in Arizona, studies addressing obesity's

impact on cancer treatment resulted in an unexpected discovery that shifted the focus from cancer to obesity. The investigators observed that two common cancer-fighting drugs sparked significant weight loss in the obese mice, even though the mice continued their excessive consumption of a high-fat diet. These results, which are part of a Mayo Clinic study, were reported in the Jan. 17 edition of *Oncotarget*.

"We were surprised to observe that when [morbidly obese](#) mice were treated with certain cancer-fighting drugs, the drugs not only targeted their cancers, but also tended to spontaneously resolve their obesity—even with undiminished gorging on a high-fat diet," says Mayo Clinic cancer immunotherapist Peter Cohen, M.D., who co-led the study with postdoctoral fellow Cheryl Myers, Ph.D. and Mayo Clinic immunologist Sandra Gendler, Ph.D.

"Importantly, two chemotherapy agents—methotrexate and cyclophosphamide—could be dosed to completely reverse obesity without detectable toxicity, even in mice without cancer," explains Dr. Myers. "Interestingly, these drugs are already used to treat some noncancerous conditions, such as rheumatoid arthritis."

More research needs to be done to see if the same outcome can be achieved in morbidly obese patients.

"The ease with which this [weight loss](#) was achieved in mice—even with continued caloric binging—is in stark contrast to the Herculean difficulties morbidly obese patients experience trying to preserve weight loss through dietary restraint," adds Dr. Gendler.

The weight reduction observed in the obese mice was not attributable to trivial explanations, such as a decrease in dietary intake, increased energy expenditure or malabsorption. Instead, the investigators identified multiple effects of methotrexate or cyclophosphamide that worked

together to expedite loss of excessive weight in mice. Much like chemotherapy's well-known ability to decrease red and white blood cell precursors transiently, methotrexate or cyclophosphamide depleted fat cell precursors, leading to much decreased fat storage. "This meant that excessive dietary calories had to go somewhere else in the body instead, such as to the liver," explains Dr. Cohen.

"Surprisingly, the liver maintained a robust level of metabolic activity during methotrexate or cyclophosphamide treatment, but was nearly shut down in regards to fat production and fat storage," adds Dr. Myers.

"Based on our composite data," explains Dr. Gendler, "it appears that methotrexate or cyclophosphamide can induce the livers of [obese mice](#) to burn off rather than accumulate excessive dietary fat. This results in desirable weight reduction instead of increased obesity, even with continued caloric binging."

The study sets the stage for further research, exploring how these metabolic mechanisms could reduce the need for severe dietary constraints in morbidly obese individuals.

Provided by Mayo Clinic

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