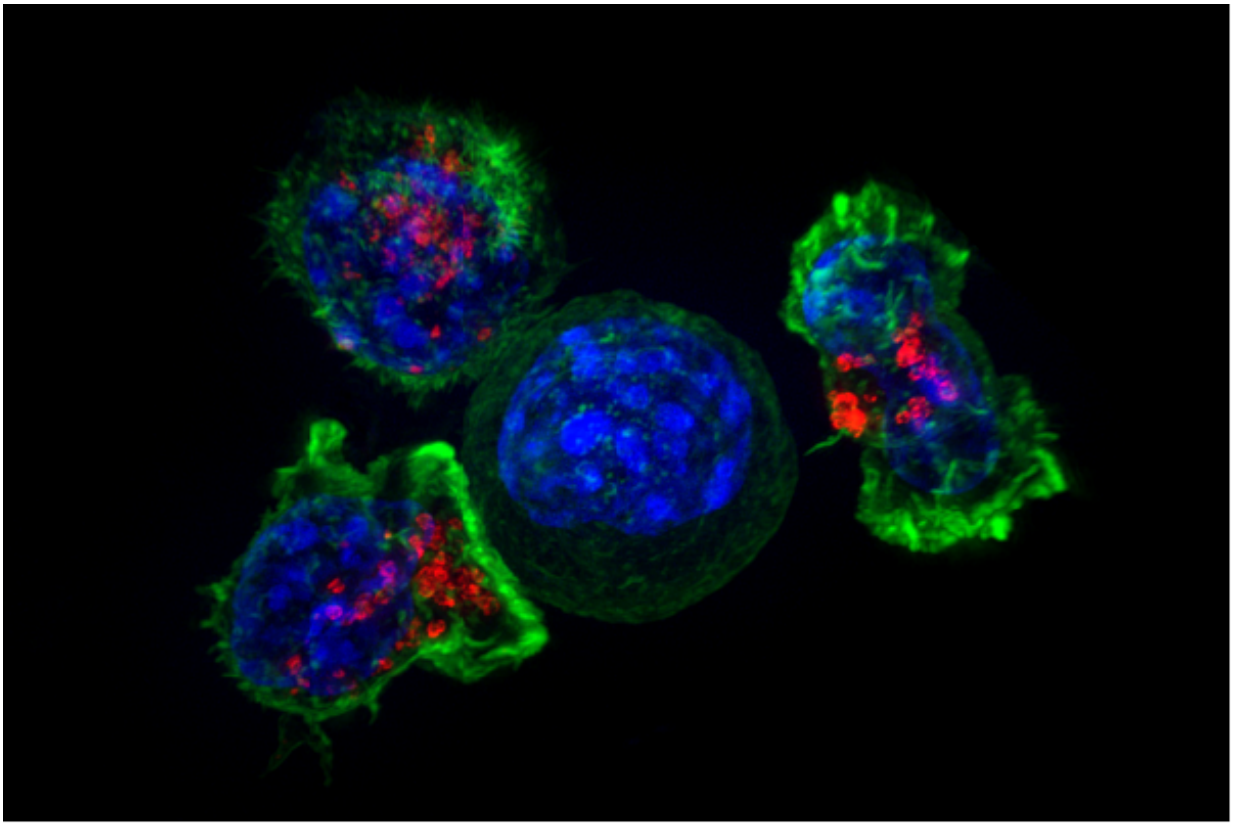
MedicalXpress

Researchers discover novel cancer pathway, opening new treatment options

May 1 2019



Killer T cells surround a cancer cell. Credit: NIH

Mount Sinai researchers have broken new ground in the understanding of the MDM2 gene—which is often overexpressed in cancer—finding that when it acts with a specific protein, it can lead to cancer cell death.

The study appears in the May 2, 2019, print edition of *Molecular Cell*.

Their findings provide fresh insights into the cellular pathways that cause cancer, and may open new therapeutic opportunities for cancer treatment.

Cancer cells are known for altering the methods by which they consume and produce energy. The exact role and function of MDM2, the chronic expression of which is seen in cancer, was previously unclear to scientists. This was in part because MDM2 is characterized as both an oncogene—a mutated gene that has the capacity to transform normal cells into cancerous cells—as well as a tumor suppressor.

By studying human cancer cells, fruit flies, and genetically engineered mice, the researchers were able to show that when extra copies of the MDM2 gene occur in cancer, their presence disrupts cellular processes. Specifically, they found that MDM2 interacts with a protein found in cancer cells' mitochondria—the part of a cell that produces its energy, and thus its life—in a process that eventually promotes cancer cell death.

In addition, the team found that nutlin-3A, a promising therapy, enhanced the interaction between MDM2 and the mitochondrial protein, and thus would help kill cancer cells. This research also shows that MDM2 can be targeted in novel ways to promote its interaction with the mitochondrial protein in cancer cells to spur their death.

"Future research should involve delving into MDM2 biology and its pharmacological regulation and examining cellular respiration and mitochondrial dynamics. Understanding the exact nature of the cellular responses to MDM2-induced stress will help advance our efforts to develop concrete therapeutic treatments for cancer," explains lead investigator Jerry Chipuk, Ph.D., Associate Professor of Oncological Sciences, and Dermatology, and Associate Director for Basic Science

Shared Resources at The Tisch Cancer Institute.

Provided by The Mount Sinai Hospital