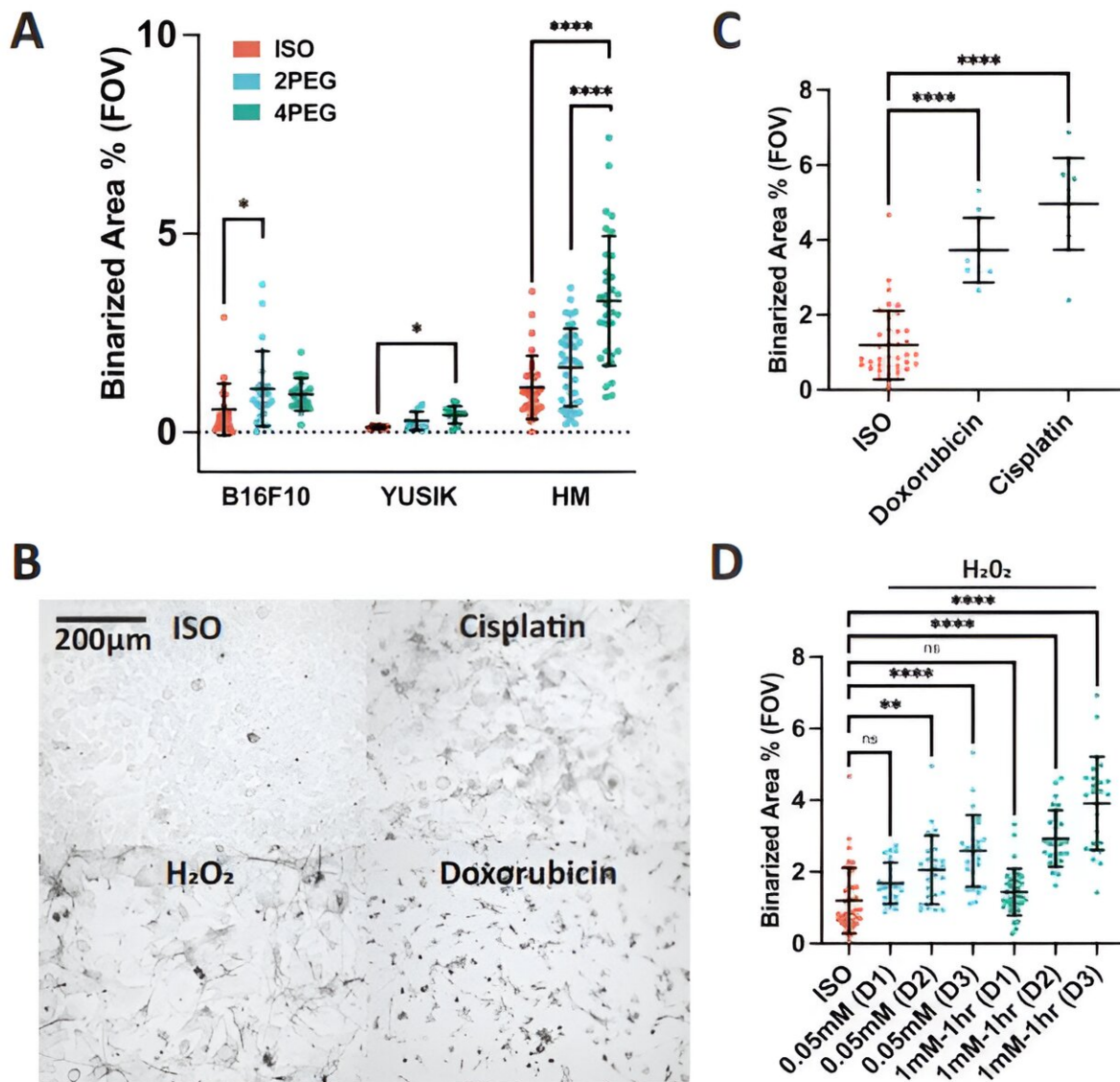


# Compression of cancer cells is a double-edged sword, study finds

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(A) Binarized melanin area percentage (FOV) of the uncompressed and 5-day

compressed B16F10 cells, YUSIK cells and Human Melanocytes are plotted ( $n \geq 6$  for each condition, human melanocytes data are from two independent experiments, all other data are from one experiment). (B) Representative images of B16F0 cells cultured with  $H_2O_2$  (day 2, cells were treated with 5mM  $H_2O_2$  for 1 hour at the beginning of the culture), cisplatin (day 5), or doxorubicin (day 5) without compression. (C) The binarized area percentage of the 5-day 10 $\mu$ M cisplatin and 0.5 $\mu$ M doxorubicin treated B16F0 cells are shown ( $n \geq 10$ , from one experiment). (D) The binarized area percentage on different days after the B16F0 cells were treated with  $H_2O_2$  (0.05mM throughout the culture or 1mM of  $H_2O_2$  for 1 hour at the beginning of culture) is shown ( $n \geq 22$  for each condition, from two independent wells). All error bars are mean with standard deviation. Credit: *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2220062120

Adhering closely to Darwin's theory of evolution, tumors need to adapt to environmental changes to survive. A new study shows that one of those changes—the compression of cells—can both help and hinder the progression of cancer.

The study, which looks specifically at melanoma cells, is published in the *Proceedings of the National Academy of Sciences (PNAS)* and was conducted in the lab of Michael Mak, assistant professor of biomedical engineering. Xingjian Zhang, a former Ph.D. student in Mak's lab, is first author of the study.

As a tumor develops, melanoma cells may experience a range of environmental challenges that prompt adaptations. One of these challenges is the compression of [tumor cells](#), which causes changes in the tumor itself.

It happens when tumor cells proliferate in constrained tissue environments. It also occurs during tumor progression and metastasis,

when cancer cells can migrate in confined microenvironments, causing the cells to deform and sometimes decrease in volume. And in certain cancers, walking and other [everyday activities](#) can lead to compression of the cells.

The effects of compression on cancer cells, though, hasn't been well explored, and it's unclear how these physical forces impact and drive the diverse properties found in tumors. Using a bioinformatics-informed approach, Mak and his research team found that compression-induced changes on melanoma cells are associated with both the improvement and worsening of patient prognoses.

On the one hand, compression inhibits the proliferation and migration of [melanoma cells](#), thereby suppressing tumor progression. Compressions also trigger subcellular activities that contribute to elevated intracellular organelle stress and [oxidative stress](#), which can potentially damage cells and affect their viability and function.

On the other hand, compression drives adaptations to stress and changes in the transcriptome, leading to properties that include the ability to resist chemotherapeutic treatment.

"Surprisingly, compression-conditioning of [cancer cells](#) for only a few days can promote resistance to chemotherapeutic treatment," said Mak, who is also a Yale Cancer Center member.

The researchers said these findings could be useful in developing new treatments for cancer.

"They offer [valuable insights](#) into therapeutic strategies aimed at addressing cancer chemoresistance and improving chemotherapy outcomes for cancer patients," Zhang said.

The researchers said they plan to explore the effects of different types of compression over varying time scales.

**More information:** Xingjian Zhang et al, Compression drives diverse transcriptomic and phenotypic adaptations in melanoma, *Proceedings of the National Academy of Sciences* (2023). [DOI: 10.1073/pnas.2220062120](https://doi.org/10.1073/pnas.2220062120)

Provided by Yale University

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