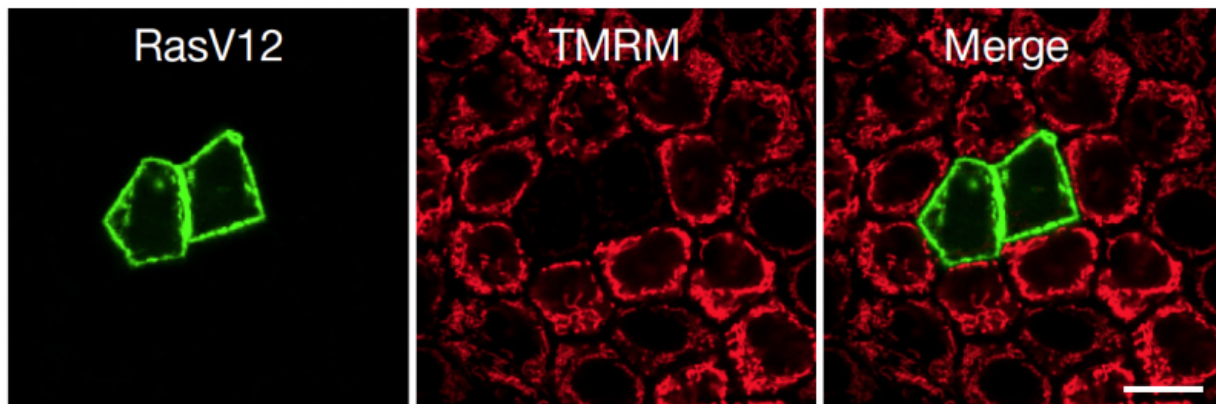


# Natural defense mechanism preventing cancer at the earliest stage

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Transformed cells (RasV12, green) showed reduced mitochondrial membrane potential (TMRM, red) when surrounded by normal epithelial cells. Credit: Kon S., et al., Nature Cell Biology, April 17, 2017

A new study shows cells in the initial stage of cancer change their metabolism before getting eliminated by the surrounding normal cells, providing a novel target for developing cancer prevention drugs.

Most cancers begin when one or more genes in a cell mutate. These newly "transformed" cells get extruded and eliminated after losing a competition against the surrounding normal cells in the epithelium, or the outer layer of the body. However, the mechanism by which normal cells recognize and attack the transformed cells remains elusive.

A research team led by Professor Yasuyuki Fujita of Hokkaido University's Institute for Genetic Medicine explored this natural defense mechanism using cultured mammalian cells and a mouse model. The study uncovered two metabolic changes occurring in the newly transformed cells: mitochondrial dysfunction and an elevated glucose uptake. The changes were significant only when the transformed cells were surrounded by normal epithelial cells, indicating that the changes are induced by the normal cells. Furthermore, according to the study, the metabolic changes play an important role in eliminating the transformed cells.

Interestingly, these metabolic changes are similar to the Warburg effect, which is observed in cancerous cells in the middle and latter stages of cancer. The Warburg effect is generally thought to play tumor promoting roles whereas the newly discovered metabolic changes could suppress cancer in its initial [stage](#). "Although these two processes have similar metabolic alterations, mitochondrial downregulation and increased glycolysis, they are governed by distinct regulators and have opposing effects on the development of cancer," says Fujita.

Their findings shed new light on the inherent ability of [normal cells](#) to eliminate [cancerous cells](#) and opens up potential avenues for cancer prevention. "Considering that the [metabolic changes](#) could either suppress or promote cancer [cells](#) depending on the stage, further elucidation of the mechanism is essential to help develop [cancer](#) prevention drugs while avoiding adverse effects," Fujita commented.

**More information:** Shunsuke Kon et al. Cell competition with normal epithelial cells promotes apical extrusion of transformed cells through metabolic changes, *Nature Cell Biology* (2017). [DOI: 10.1038/ncb3509](https://doi.org/10.1038/ncb3509)

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