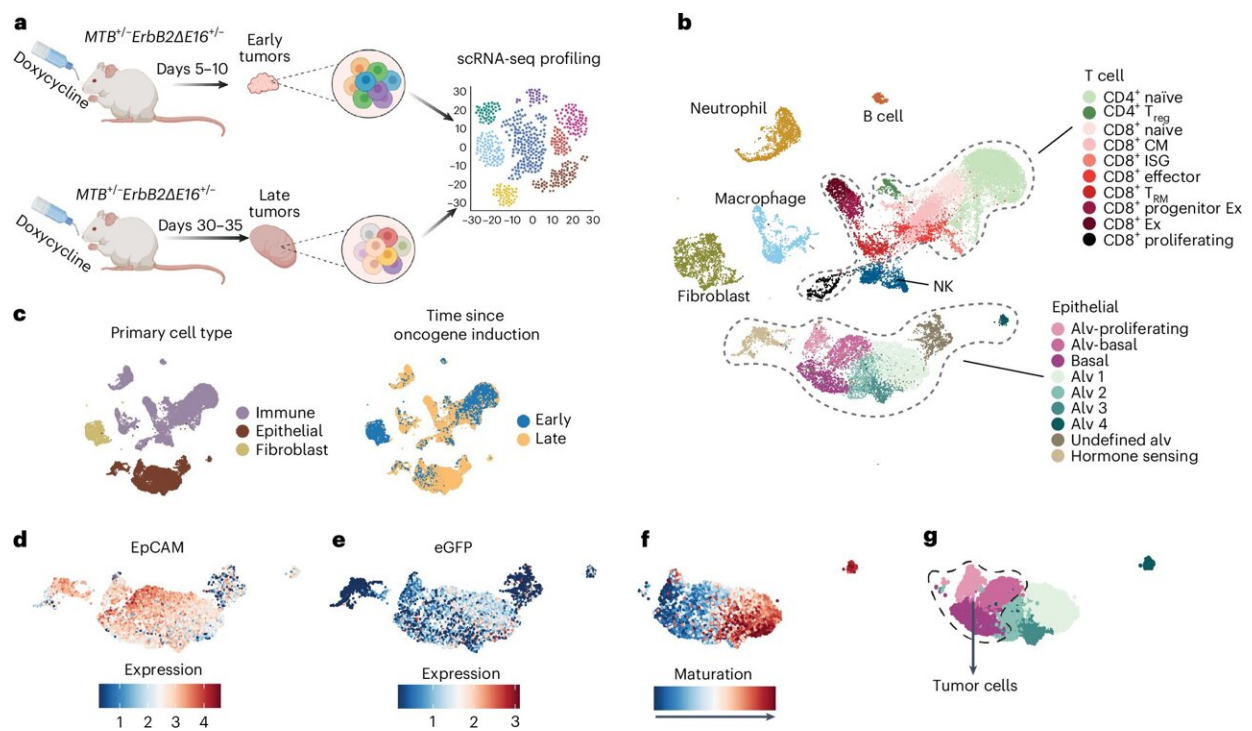


Study reveals how cancer outsmarts immunity—and how to potentially turn the tables

August 26 2024, by Jacqueline Mitchell



Cell mapping by scRNA-seq of early and late tumors in a breast cancer GEMM. Credit: *Nature Immunology* (2024). DOI: 10.1038/s41590-024-01932-8

A new study led by researchers at Beth Israel Deaconess Medical Center (BIDMC) and Boston Children's Hospital and [published](#) in *Nature Immunology* shows how tumors grow by avoiding the immune system.

The researchers revealed how genes in tumors edit themselves to escape the immune system's detection. The study identifies, for the first time, the actual genes that are silenced by tumors, offering a roadmap for better immunotherapies.

The researchers studied [breast cancer](#) in a [mouse model](#), using genome-wide single-cell RNA sequencing to identify which genes were edited by tumors as they developed. The team found that tumors use epigenetic modification, particularly DNA methylation, to suppress genes involved in the innate immune response—the body's first line of defense against pathogens and disease.

This silencing is how most tumors evade current immunotherapies, such as CAR-T cells and checkpoint inhibitors. However, the scientists also found that the FDA-approved drug decitabine, a chemotherapy that slows cancer cell growth, can reverse these gene edits.

At low doses, decitabine reactivates the [immune response](#), leading to a reduction in [tumor](#) growth by boosting the presence of immune cells that attack the tumor.

The findings suggest that gene editing might be a common defense mechanism across various cancers. Further research is needed to explore how these insights apply to other solid tumors such as lung and ovarian cancers. Future studies will focus on gene editing in patients with genetic predispositions to cancer, especially at early tumor stages and during metastasis.

"Our research sheds light on the sophisticated strategies tumors use to hide from the immune system," said Winston Hide, Ph.D., a lead author on the study and co-Director of the Non-Coding RNA Precision Diagnostics and Therapeutics Core Facility at BIDMC.

"By identifying the specific genes that tumors silence to evade detection, we open the door to new therapeutic approaches. These findings could lead to the development of more targeted immunotherapies, potentially improving outcomes for patients with cancer."

More information: Ying Zhang et al, Tumor editing suppresses innate and adaptive antitumor immunity and is reversed by inhibiting DNA methylation, *Nature Immunology* (2024). [DOI: 10.1038/s41590-024-01932-8](https://doi.org/10.1038/s41590-024-01932-8)

Provided by Beth Israel Deaconess Medical Center

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