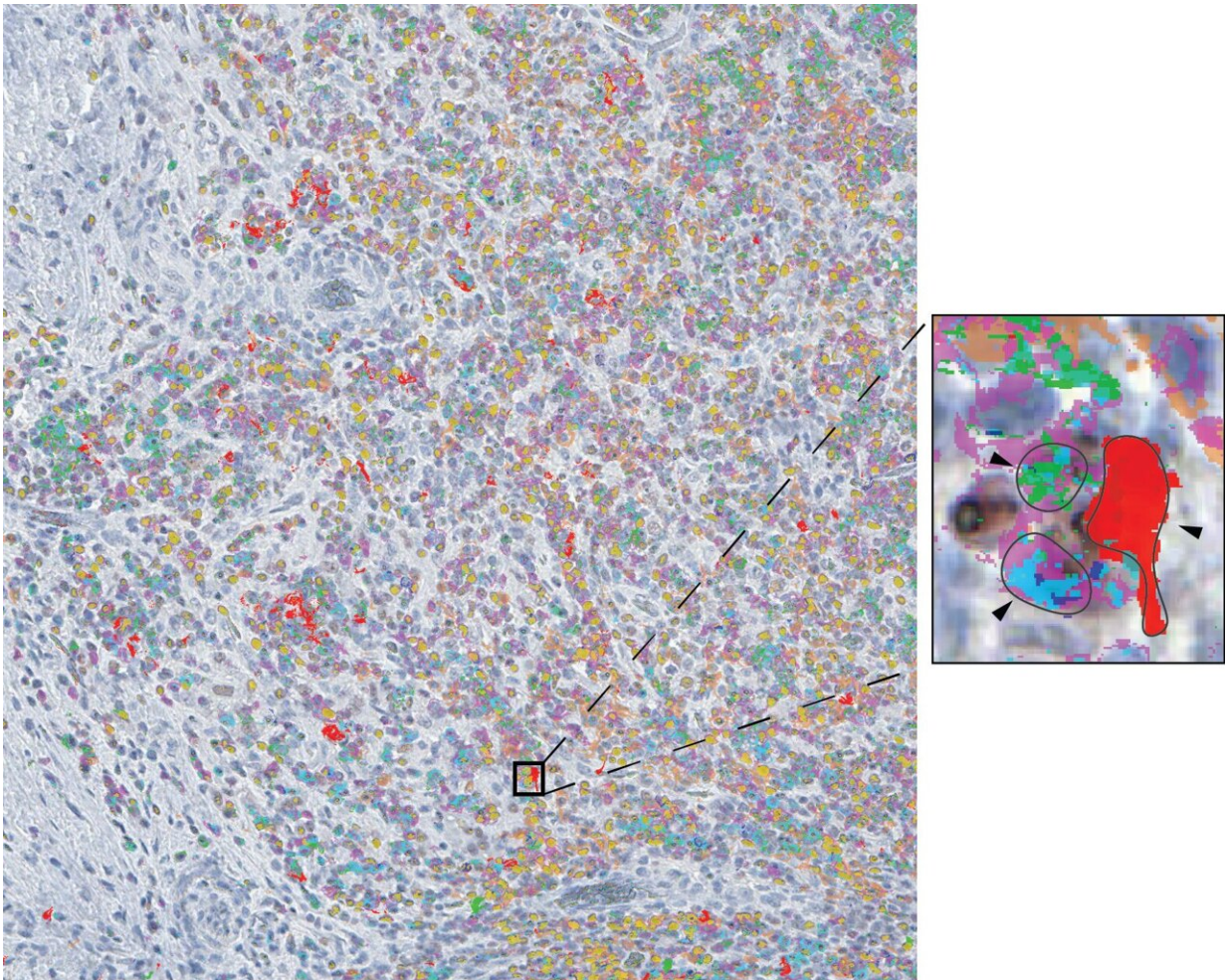


# Study reveals a trio of immune cells vital in response to liver cancer immunotherapy

June 15 2023

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The study revealed how certain immune cell interactions in tumors facilitate response to checkpoint blockade, pointing to potential new approaches to cancer immunotherapy. Credit: Magen et al., *Nature Medicine*

Researchers at the Icahn School of Medicine at Mount Sinai have uncovered a trio of immune cells within tumor niches that are associated with immunotherapy response in hepatocellular carcinoma (HCC). HCC is the primary type of liver cancer and one of the most deadly cancers worldwide. The findings—which help explain which patients benefit from immunotherapy and which do not—were described in the June 15 issue of *Nature Medicine*.

The investigators discovered that a specific niche of immune cells in tumors may be critical for reactivating exhausted T cells and enabling them to attack liver tumors upon treatment with checkpoint blockade. Also known as a PD1 inhibitor, checkpoint blockade is a type of cancer immunotherapy that can unleash the cancer-killing activity of T cells.

"While checkpoint blockade has unquestionably revolutionized cancer treatment, most patients do not respond to this immunotherapy. Understanding at the [molecular level](#) why only some patients respond will help identify novel targets for improving [cancer treatment](#)," says senior study author Miriam Merad, MD, Ph.D., Director of the Marc and Jennifer Lipschultz Precision Immunology Institute and Director of the Human Immune Monitoring Center at Icahn Mount Sinai.

The researchers designed a trial that would both benefit patients and provide new data to explore why immune cells in some patients can be reactivated by immunotherapy and eradicate tumors while the same treatment fails to help other patients.

"This work follows a study our team recently published in [The Lancet Gastroenterology & Hepatology](#) reporting that immunotherapy administered before liver cancer surgery can kill tumors and likely residual cancer cells," says Thomas Marron, MD, Ph.D., head of the Early Phase Trial Unit at the Mount Sinai Tisch Cancer Center, the clinical trial lead, and co-senior author of the study.

In this follow-up study, the research team analyzed [tumor](#) samples taken from 29 patients before and after treatment with checkpoint blockade. Using single-cell technology and powerful computational platforms, the team identified distinct groups of immune cells within tumors that determined which patients responded positively to immunotherapy and which did not.

These studies represent the first developments out of Icahn Mount Sinai's TARGET "platform"—The Neoadjuvant Research Group to Evaluate Therapeutics, founded by Drs. Marron and Merad. TARGET's goal is to harness the technological capabilities of the Human Immune Monitoring Center and map the molecular changes that occur in cancer and [immune cells](#) undergoing treatment to reveal precisely how immunotherapy works.

Only through understanding the mechanisms of how these revolutionary immunotherapies work in humans and the multiple mechanisms behind treatment resistance can we further improve outcomes for all patients, say the investigators.

"Reactivation of a type of T cell called CD8 T cells by checkpoint blockade was known to be critical for clearing tumor cells. Our new study shows that killer CD8 T cells are only reactivated when in close proximity to two other immune cell types: [dendritic cells](#), which educate CD8 T cells to recognize [cancer cells](#), and helper CD4 T cells, which aid in activating the CD8 T cells," says Alice Kamphorst, Ph.D., co-senior author of the study, and assistant professor of Oncological Sciences at the Precision Immunology Institute.

These findings indicate that these specialized immune cell niches control the reactivation of CD8 T cells and subsequent tumor eradication by [checkpoint blockade](#). By deciphering the molecules pivotal to the formation of these niches within tumors, the researchers intend to

identify novel therapeutic targets to use in combination with PD1 blockade and test these treatment combinations via the TARGET platform.

The paper is titled, "Intratumoral dendritic cell-helper T cell niches enable CD8<sup>+</sup> T cell differentiation following PD-1 blockade in hepatocellular carcinoma."

**More information:** Intratumoral dendritic cell-helper T cell niches enable CD8<sup>+</sup> T cell differentiation following PD-1 blockade in hepatocellular carcinoma., *Nature Medicine* (2023). [DOI: 10.1038/s41591-023-02345-0](https://doi.org/10.1038/s41591-023-02345-0)

Provided by The Mount Sinai Hospital

Citation: Study reveals a trio of immune cells vital in response to liver cancer immunotherapy (2023, June 15) retrieved 2 May 2024 from <https://medicalxpress.com/news/2023-06-reveals-trio-immune-cells-vital.html>

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