Scientists identify immune cells critical for immunologic memory for melanoma

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Immune-checkpoint inhibitors have become the standard of care for patients with advanced melanoma to improve survival, but only some patients respond to this immunotherapy and have long-term benefits.

The lack of a long-lasting response, researchers say, is related to failure of antitumor immunologic memory. Treatment options for advanced melanoma are limited for patients who do not respond to this type of therapy.

A new study led by Yale Cancer Center researchers at Yale School of Medicine reveals that a specific population of $CD8^+$ T-cells marked by IL-7R play an important role in better understanding antitumor memory. These immune cells also offer potential new therapeutic strategies using epigenetic therapies that often reduced tumor size.

The new research was published in the of *Proceedings of the National Academy of Sciences* on July 17.

"Identifying the immune cells that mediate antitumor memory brings us closer to understanding the immune response to melanoma and devising ways to enhance it," said first author of the paper, Goran Micevic, an instructor of dermatology and fellow in dermatopathology at Yale School of Medicine. "We are excited at the possibility of epigenetically reprograming T-cells to create better cell-based therapies for cancer."

The study investigated the formation of antitumor memory after immune-checkpoint inhibitor therapy and surgery in a model of melanoma. It found that the majority of tumor-reactive T-cells in lymph nodes expressed high levels of the receptor IL-7R, and blocking the receptor prevented formation of antitumor memory. The study revealed a potent antitumor function of this population that could be boosted by an epigenetic drug. Using the epigenetically boosted cells as a "live therapy" led to significant reduction in melanoma tumor size in 75% of cases.

Micevic was joined by corresponding authors Richard Flavell, and Marcus Bosenberg at Yale Cancer Center, as well as other Yale co-authors.

More information: Goran Micevic et al, IL-7R licenses a population of epigenetically poised memory $CD8^+$ T cells with superior antitumor efficacy that are critical for melanoma memory, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2304319120

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