New findings may help oncologists determine effectiveness of checkpoint inhibitors

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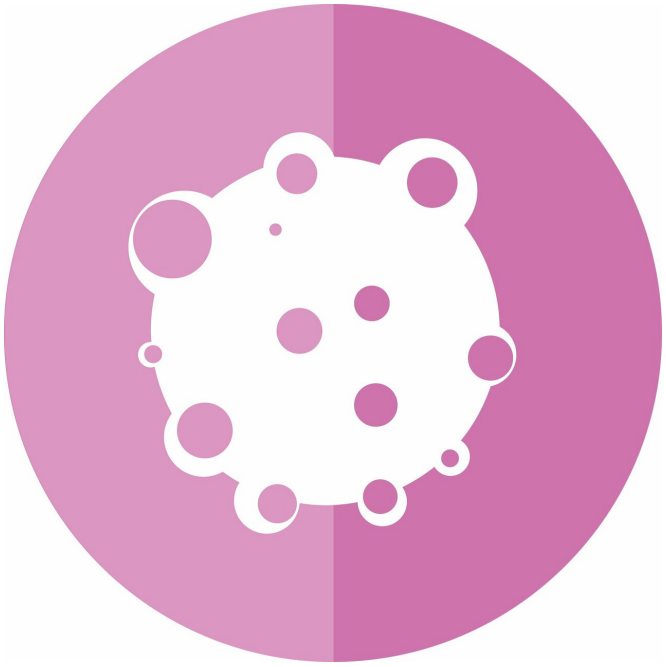

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In an article recently published in *JCI Insight*, researchers from the University of Alabama at Birmingham and Vanderbilt University have identified checkpoint inhibitor resistance mechanisms in many solid tumor cancers, including melanoma, lung cancer and breast cancer. Randall S. Davis, M.D., professor in the University of Alabama at Birmingham Division of Hematology and Oncology and senior scientist in the O'Neal Comprehensive Cancer Center, served as the paper's co-senior author.

Checkpoint inhibitors are a type of drug that patients with cancer can take to help block proteins made by certain immune system cells, such as T cells. In the normal body, the proteins help keep the immune system in check; but also, they keep T cells from attacking cancer cells that a person may have developed. CI drugs block these proteins, enabling T cells to fight cancer more effectively.

However, with patients' living longer, tumors are able to evade the therapy and alter their gene expression, ultimately tricking a person's immune system and checkpoint inhibitors from responding and attacking cancerous cells.

The published research looked at patients who had relapsed after a checkpoint inhibitor course of treatment. In the study, Davis and his team sought to determine how certain expression patterns on tumor cells could give physicians an idea of whether the patient's immune system would not respond to checkpoint inhibitors, ultimately causing a lack of response when fighting off cancerous cells.

In fact, a receptor co-discovered by the team several years ago—FCRL6—may serve as a new checkpoint target in these patients, identifying it as a potential immunotherapy option in the future.

"Our findings are significant for anyone who is a candidate for checkpoint inhibitors," Davis said. "We know that, as patients respond well to treatment and live longer, tumors are smart and will ultimately work to evade one's immune system. We're hopeful that we are closer to identifying a new mechanism that could be targeted for future therapies."

More information: Douglas B. Johnson et al. Tumor-specific MHC-II expression drives a unique pattern of resistance to immunotherapy via LAG-3/FCRL6 engagement, *JCI Insight* (2018). DOI: 10.1172/jci.insight.120360

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