

Researchers identify key immune checkpoint protein that operates within T cells

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A new study led by researchers at The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Solove Research Institute (OSUCCC—James) has identified a protein within certain immune cells that is required for optimal immune responses to cancer.

The findings, reported in the journal *Science Advances*, also suggest that the protein might be useful for predicting which [cancer patients](#) are less likely to respond to the form of therapy called immune checkpoint blockade.

The protein is called PCBP1, or poly(C)-binding protein 1. The researchers found that PCBP1 helps shape immune responses by ensuring that adequate numbers of activated immune T cells differentiate into cytotoxic T cells, which kill cancer cells. At the same time, PCBP1 prevents the development of too many regulatory T cells, which do not kill [cancer cells](#).

"Our findings suggest that PCBP1 is a global intracellular immune checkpoint, and that targeting it would offer a way to influence antitumor responses during immune therapy," says principal investigator Zihai Li, MD, Ph.D., a professor in the Division of Medical Oncology at Ohio State and director of the Pelotonia Institute for Immuno-Oncology (PIIO) at the OSUCCC—James. Li is also a member of the OSUCCC—James Translational Therapeutics Research Program.

"Immune checkpoint blockade therapy has revolutionized cancer treatment, especially in melanoma, non-small cell lung, and head and neck cancer," says first author Ephraim Abrokwa Ansa-Addo, Ph.D., an assistant professor in the Division of Medical Oncology and also a member of the Translational Therapeutics Research Program. "But we need better ways to identify which patients will benefit from the therapy. PCBP1 may help us do that."

PCBP1 belongs to a family of molecules called RNA binding protein. It controls gene expression when immune T cells differentiate into either regulatory T cells or into cytotoxic T cells, which carry out immune responses against infection and cancer. (Cytotoxic T cells are a type of effector T cell.)

In activated T cells, PCBP1 prevents cytotoxic T cells from converting to regulatory T cells, thereby promoting immune responses against tumors.

For this study, researchers used cell lines, tumor models, animal models, and models of diabetes and [graft-vs-host disease](#) to achieve a better understanding of the role of PCBP1 in T cells. Graft-vs-host disease is a condition in which a donor's T-cells (graft) view the patient's health cells (host) as a foreign and then attack and damage those normal cells.

Key findings include:

- In a non-cancer setting, higher PCBP1 activity promotes cytotoxic T-cell functions that inhibit tumor development and progression.
- In a cancer setting such as the tumor microenvironment, higher PCBP1 activity prevents cytotoxic T cells from expressing factors such as PD-1, TIGIT and VISTA, which produce conditions less favorable to immune checkpoint blockade therapy.
- In a cancer setting, lower PCBP1 in cytotoxic T cells triggers expression of PD-1 and other factors that suppress the T [cells'](#) [cancer](#) immune responses, producing conditions more favorable to immune checkpoint blockade therapy.

"Overall, our data indicate that PCBP1 shapes tolerance and immunity by distinctively regulating cytotoxic T-cell versus regulatory T-cell differentiation, and that it could be a marker for response to immune checkpoint blockade therapy," Li says.

More information: Ephraim A. Ansa-Addo et al. RNA binding protein PCBP1 is an intracellular immune checkpoint for shaping T cell responses in cancer immunity, *Science Advances* (2020). [DOI:](#)

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