Identifying a novel target for cancer immunotherapy

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Targeting a molecule called B7-H4—which blocks T-cells from destroying tumor cells—could lead to the development of new therapies that boost the immune system's ability to fight cancer, according to a review published in the journal Immunological Reviews.

"Targeting B7-H4 itself, or in combination with the current therapies, may lead to more effective treatments for a variety of cancers," said Stephen Miller, PhD, the Judy Gugenheim Research Professor of Microbiology-Immunology and of Dermatology, the lead author of the paper. Joseph Podojil, PhD, research associate professor of Microbiology-Immunology, was the first author.

Immunotherapy is a type of cancer treatment that stimulates the patient's own immune system to attack cancer cells. One immunotherapy approach involves targeting a group of proteins, called immune checkpoints, that normally prevents the immune system from attacking tumor cells. By employing antibodies that specifically block the checkpoints, these drugs unlock the "breaks" on the immune system, freeing T-cells to detect and destroy tumor cells.

"Cancer therapy has recently been revolutionized with this approach," said Miller, also director of the Interdepartmental Immunobiology Center. "However, the two checkpoint-inhibitor blockers currently used only work in a minority of patients with a particular cancer, and not at all in other forms. Additional checkpoint inhibitors need to be identified and blocked in order to enhance the therapeutic response rate in cancer immunotherapy."

In the review, Miller and Podojil highlight the potential of targeting B7-H4, a more recently discovered immune-inhibitory protein.

Miller's lab had previously studied B7-H4—and the mechanisms by which it thwarts the immune response—in the context of a treatment for multiple sclerosis, an autoimmune disease. Other research has also shown that B7-H4 is overexpressed in many types of tumors, and high levels are linked to adverse outcomes in cancer patients.

While blocking B7-H4 has not yet been clinically tested—and its actual effectiveness in cancer treatment is not yet known—the authors note that much of the existing data point to B7-H4 as a promising target for new immunotherapies that may treat a wider range of cancers.

More information: Joseph R. Podojil et al. Potential targeting of B7-H4 for the treatment of cancer, *Immunological Reviews* (2017). DOI: 10.1111/imr.12530

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