Protein may predict response to immunotherapy in patients with metastatic melanoma

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A protein called Bim may hold the clue to which patients may be successful on immunotherapy for metastatic melanoma, according to the results of a study by Mayo Clinic researchers led by senior author Haidong Dong, M.D., Ph.D., and published online in the May 5 edition of *JCI Insight*.

"Immune checkpoint therapy with PD-1 blockade has emerged as an effective treatment for many advanced cancers," says the study's lead author, Roxana Dronca, M.D., an oncologist at Mayo Clinic. "However, only a fraction of patients achieve durable responses to immunotherapy and, to date, we have had no means of predicting which patients are most likely to benefit."

PD-1 blockade is a type of immunotherapy that helps make cancer cells more vulnerable to attack by T cells in the body's immune system by blocking the activity of a molecule called PD-1. PD-1 prevents T cells from recognizing and attacking cancer cells.

Dr. Dronca and her colleagues found a higher frequency of immune cells, called T cells, that expressed the protein Bim among patients who responded to immunotherapy for metastatic melanoma than among patients who were treated immunotherapy but whose disease had progressed.

"Our previous research demonstrated that Bim is a downstream signaling molecule in the PD-1 signaling pathway, and that levels of Bim reflect the degree of PD-1 interaction with its ligand PD-L1," says Dr. Dong.

A signaling pathway is a group of molecules in a cell that work together to control one or more cell functions, such as cell division or cell death.

"We hypothesized that the increased frequency of CD8+PD-1+Bim+T cells in patients who respond to immunotherapy reflects an increased number of target T cells for PD-1 blockade with pembrolizumab, which may explain the positive clinical outcomes in these patients," Dr. Dong says.

"A great advantage of this approach lies in the ease of serial peripheral blood testing, compared with repeated invasive tissue biopsies," says Dr. Dronca. "We are currently validating these results in a larger prospective cohort of patients with metastatic melanoma and in patients with lung cancer using multiple serial peripheral blood samples and standardized tumor assessment."

For the study, Dr. Dronca and her colleagues collected peripheral blood from patients at the initiation immunotherapy (baseline) and again at the time of first radiographic tumor assessment (12 weeks). They collected additional samples at each subsequent radiographic tumor evaluation for patients continuing on immunotherapy.

"The potential discovery of a way to predict a patient's response to pembrolizumab would help inform clinical decision-making," said Dr. Dronca. "It would not only help clinicians identify which patients would be most likely to benefit from the drug, but also prevent patients not likely to respond to the therapy from being exposed to unnecessary toxicities and costs."

Provided by Mayo Clinic