Identifying protein that may predict response to PD-1 immunotherapy for melanoma

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Mayo Clinic researchers have identified a protein marker whose frequency may predict patient response to PD-1 blockade immunotherapy for melanoma. An abstract of their findings was presented today at the American Association for Cancer Research International Cancer Immunotherapy Conference in New York City.

"The discovery of biomarkers of sensitivity are vital not only for informing clinical decisions, but also to help identify which patients with melanoma, and possibly other malignancies, who are most likely to benefit from PD-1 blockade," says Roxana Dronca, M.D., a hematologist at Mayo Clinic and lead author of the abstract. "This will allow us to expose fewer patients to inadequate treatments, and their associated toxicities and costs."

The marker, Bim, is a protein that helps coordinate programmed cell death. This is a natural process that occurs in many cells, including T cells, a subset of immune cells that can recognize and kill tumor cells. Interaction of a molecule called PD-1 on T cells with a molecule called PD-L1 activates Bim and can induce T cell death. Tumors can exploit this process by overexpressing PD-L1 and killing T cells that could recognize and eliminate them.

In an effort to overcome the problem of tumors evading the immune system, researchers have generated biological molecules that block PD-1 from interacting with PD-L1. These PD-1 blockers have shown promise results in some cancer patients, but not others - prompting a search for markers that could predict how patients will respond to the molecules before treatment.

"If I know that a patient has a very high likelihood of responding to anti-PD-1 therapy, I'm going to be more inclined to recommend that treatment and feel better about the choice," Dr. Dronca says.

Researchers found that metastatic melanoma patients who responded to PD-1 blockade with pembrolizumab had more tumor-targeting T cells expressing Bim and PD-1 in their blood prior to therapy than did patients who did not respond. They also observed that this trend reversed after weeks of treatment suggesting that proportions of these cells can be measured to help clinicians decide which patients should and should not be treated with PD-1 blockade.

They also discovered that responders had higher levels of soluble PD-L1 in their blood prior to treatment. This suggests that PD-1 blockade is most effective when the PD-1:PD-L1 interaction plays a major role in disease - a finding that improves scientific understanding of the therapeutic mechanism of PD-1 blockade.

  Provided by Mayo Clinic

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