Predicting Immunotherapy Response in Colon Cancer Patients

Researchers hope to easily identify which colon cancer patients are unlikely to benefit from immune checkpoint inhibitors (ICIs).

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For many patients with colon cancer, the advent of immune checkpoint inhibitors has substantially improved their treatment options. Immune checkpoint inhibitors (ICIs) work by removing the "brakes" from immune T cells, unleashing them on cancer cells.

Unfortunately, however, ICIs do not work for everyone, and they can have life-threatening side effects for some patients. Given these factors, ICIs should only be used in patients who have the potential to benefit from them—the problem is, clinicians are often unable to predict who those patients will be.

At Columbia University, former Damon Runyon-Rachleff Innovator Piero Dalerba, MD, and his colleagues are working to find a way for clinicians to shine a light in the dark. In a recent study, the team identified one group of colon cancer patients for whom ICIs are less likely to be effective: a relatively large fraction of patients with a subtype of colon cancer called colon cancer with microsatellite instability (a term that refers to a high number of mutations in short, repeated sequences of DNA known as "microsatellites").

In 10% of these patients, the cancer cells contain a recurrent mutation in two genes, HLA-A and HLA-B, that are crucial for activating the immune system. The proteins encoded by these genes bind antigens and present them to T cells. When they don't function, tumor cells can slip by unnoticed, even when T cells are unleashed by ICIs.

This discovery means that clinicians may soon be able to identify, with a relatively simple genetic test, patients who should be prioritized for different kinds of treatment because they are unlikely to benefit from ICIs. Though this may seem like bad news, for patients on the search for the right treatment, it helps to have even the wrong turns well-lit.

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