

Cancer test shows promise for bringing the benefits of immunotherapy to more patients

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Immunotherapy is a highly effective treatment for patients whose cancers harbor mismatch repair deficiency, and a new study identifies more cancer patients who could benefit from this form of therapy. Investigators from Brigham and Women's Hospital, a founding member of the Mass General Brigham health care system, found that nearly six percent of endometrial cancer patients and one percent of colorectal cancer patients with mismatch repair deficiency were missed by immunohistochemistry, the current standard of care test for this condition. In these missed cases, the condition was instead detected by next-generation sequencing, which researchers estimate could identify 6,000 additional patients in the U.S. who would otherwise not be offered immunotherapy. Results are published in the journal *Cancer Cell*.

"In colorectal cancer and [endometrial cancer](#), which are the two types of cancer where mismatch repair deficiency is most commonly seen, immunotherapy is not the [standard treatment](#) unless a patient has this condition," said first author Elias Bou Farhat, MD, a postdoctoral research fellow in the division of Pulmonary and Clinical Care Medicine at Brigham and Women's Hospital. "But in patients with this condition, even in late-stage cancer, those who receive immunotherapy can live for years and in some cases be potentially cured. Including [next-generation sequencing](#) as a complimentary testing practice could benefit patients in all phases of cancer, from pre-treatment to advanced stages."

More than 150,000 people are diagnosed with colorectal cancer and more than 65,000 people are diagnosed with endometrial cancer in the United States each year. In these two types of cancer, patients often have high rates of mismatch repair deficiency, a genetic state where errors in DNA occur due to a lack of certain repair proteins. This state impairs DNA's ability to repair itself and can lead to many types of cancer. Previous research has shown that [cancer patients](#) with this condition

typically respond well to immunotherapy treatment, which uses a person's own immune system to fight cancer.

In this study, the researchers looked at a cohort of 1,655 patients from Brigham and Women's Hospital and Dana-Farber Cancer Institute who either had colorectal or endometrial cancer and who received both immunohistochemistry and next-generation sequencing tests. The researchers observed that nearly six percent

of the patients with endometrial cancer and one percent of the patients with [colorectal cancer](#) were missed as being mismatch repair deficient by immunohistochemistry but caught by next-generation sequencing. These patients responded better to immunotherapy than other treatments and their survival and treatment outcomes were the same as those who were found deficient by both tests.

Immunohistochemistry only detects mutations that affect the antigen; next-generation sequencing is a more sensitive test because it looks for more mutation characteristics. While the current work suggests that next-generation sequencing will be a more sensitive diagnostic tool in these cases, further studies are needed to confirm and generalize this study's findings.

The study's data also showed that in patients with the same cancer type at the same stage, those who did not receive immunotherapy had worse outcomes than those who did.

"We don't want to miss these patients or we could be depriving them of a treatment that can have long-term benefits," said senior author Amin Nassar, MD, a member of Yale Cancer Center who did much of the work while he was a resident at Brigham and Women's Hospital. "We also want to avoid giving patients treatments that could be more toxic and/or less effective—we want to treat [patients](#) with the appropriate

therapy."

Next, the researchers would like to see if these findings apply to other sequencing panels and other [cancer](#) types. They also plan to investigate the potential role of other genetic deficiencies involved in the condition of mismatch repair deficiency.

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More information: Elias Bou Farhat et al, Benchmarking mismatch repair testing for patients with cancer receiving immunotherapy, *Cancer Cell* (2023). [DOI: 10.1016/j.ccell.2023.12.001](https://doi.org/10.1016/j.ccell.2023.12.001)

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