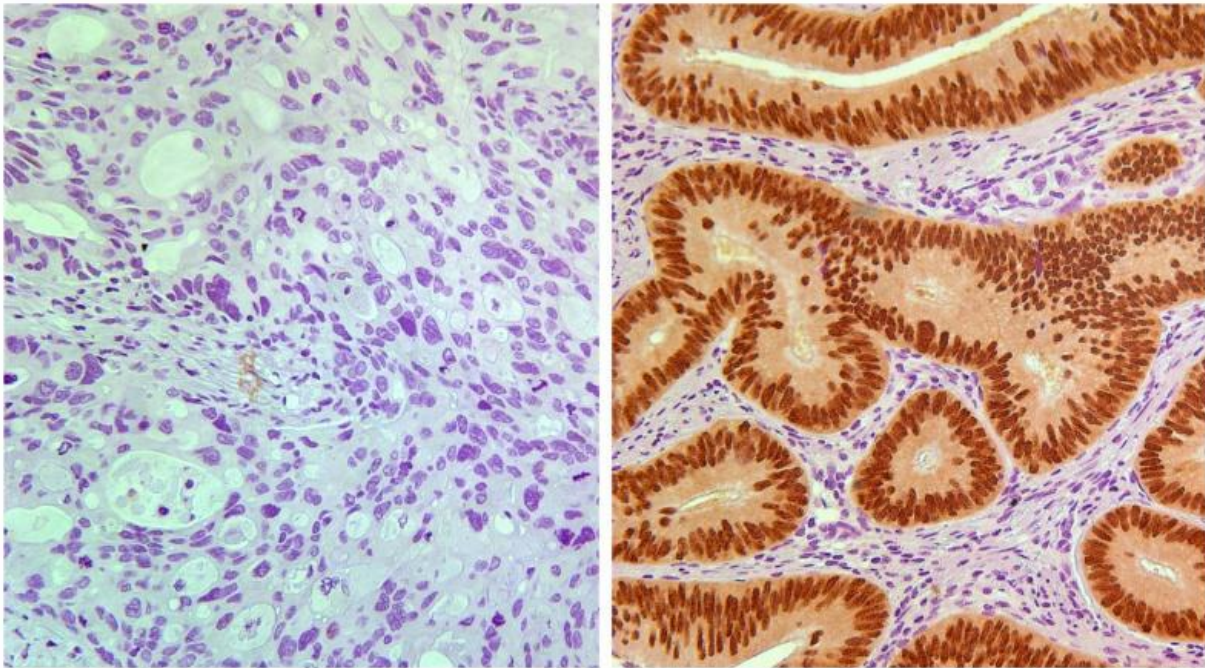


Biomarker predicts which stage II colon cancer patients may benefit from chemotherapy

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Stage II colon cancers, which are typically treated with surgery alone, were found to vary in their expression of the CDX2 gene. Those that do not express the gene (Figure 1) were found to have a worse prognosis than those that do (Figure 2). The findings provide clinicians with a biomarker that could be used to predict which patients with stage II disease are likely to benefit from postsurgical, or adjuvant, chemotherapy. Credit: Lab of Piero Dalerba, MD/Columbia University Medical Center

A multicenter research team has identified a biomarker that predicts which stage II colon cancer patients may benefit from chemotherapy after surgery to prevent a recurrence of their disease.

The study was published today in the online edition of the *New England Journal of Medicine*.

The majority of patients with stage II [colon cancer](#)—cancer that has grown into or through the outer layer of the colon but has not spread to lymph nodes or distant organs—are cured by surgery alone. However, about 15 to 20 percent of these patients eventually relapse and die of metastatic disease.

"The problem is that we don't have an easy way to single out these patients before they relapse and accurately predict who could benefit from postsurgical, or adjuvant, chemotherapy," said Piero Dalerba, MD, assistant professor of medicine, pathology and cell biology at Columbia University Medical Center (CUMC) and the Herbert Irving Comprehensive Cancer Center (HICCC), and first author of the paper.

Previous studies have found biomarkers in tumor cells that identify which stage II colon cancer patients are at higher risk for relapse after surgery. However, many of those biomarkers do not also predict which of these patients would actually benefit from [adjuvant chemotherapy](#).

The current study took a different approach to the search for potential biomarkers. Instead of looking at gene-expression patterns obtained from the random sampling of tumor cells, the researchers focused on the gene-expression pattern of cancer stem cells—the source of mature, or differentiated, [tumor cells](#)—a field of study pioneered by the paper's senior author Michael F. Clarke, MD, of Stanford University. "We reasoned that tumors containing high numbers of cancer stem cells might be associated with a more aggressive disease, and wanted to find a way

to easily find them," said Dr. Dalerba. To identify these tumors, the authors took advantage of a novel bioinformatics approach designed by Debashis Sahoo, PhD, of the University of California-San Diego, and co-first author of the study. "In essence, we asked a computer the following question: can you help us find a gene whose lack of expression is always associated with high levels of [cancer stem cell](#) markers?" said Dr. Sahoo.

By analyzing data from more than 2,000 colon cancer patients, the authors identified 16 biomarkers that fulfilled this criterion. Of these, only one—a gene called CDX2—was found to be clinically actionable, meaning that a standardized diagnostic test for detecting expression of the gene was already available. CDX2 is known to regulate cell differentiation in the layer of cells that line the colon, where the cancer begins. In the study, patients whose tumors lacked CDX2 expression had a poorer prognosis compared to those whose tumors scored positive for CDX2 expression.

"We wanted to understand if the small group lacking CDX2 expression—approximately 4 percent of the global colon cancer population—fared poorly because of an intrinsic resistance to chemotherapy," said Dr. Dalerba. "To our surprise, we found that, on the contrary, tumors lacking CDX2 expression, despite being very aggressive from a biological point of view, also appeared to benefit from early treatment with adjuvant chemotherapy."

Further analysis using data from the National Surgical Adjuvant Breast and Bowel Project revealed that this observation also held true for stage II colon cancer patients, again showing that patients with tumors lacking CDX2 expression were more likely to benefit from adjuvant chemotherapy than patients whose tumors did express the gene.

"What's exciting is that an inexpensive, simple test for CDX2 expression is already widely available," said Dr. Dalerba.

Additional clinical studies, such as prospective and randomized clinical trials, are needed before using the test as a clinical decision-making tool for colon [cancer patients](#), he added.

More information: CDX2 as a Prognostic Biomarker in Stage II and Stage III Colon Cancer, *New England Journal of Medicine*, [dx.doi.org/10.1056/NEJMoa1506597](https://doi.org/10.1056/NEJMoa1506597)

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