Prediction of chemotherapy benefit for colon cancers

CDX2 expression has been identified as a prognostic biomarker for stage II and III colon cancers that might be treatable with adjuvant chemotherapy. Traditionally, early-stage colon cancers (stage I or II) are treated by surgical resection. However, colon cancer recurs in about 20% of patients with stage II tumours.

Seeking a biomarker to identify patients with early-stage colon cancer who might benefit from adjuvant chemotherapy, investigators used bioinformatics software to screen a gene expression array database of 2115 colon cancers. 16 genes poorly expressed in undifferentiated colon cancers were identified; of these, only CDX2 encoded a protein for which a clinical diagnostic test was already available. In a validation analysis, CDX2 was measured by immunohistochemistry in colon cancer samples that had clinical and pathology data. In both stage II and stage III disease, CDX2-negative tumours were associated with lower 5-year disease-free survival than that reported for CDX2-positive tumours (48% *vs* 71%, p<0·001). Subgroup analysis showed that for patients with stage II colon cancer, those with CDX2-negative tumours had a significantly lower 5-year disease-free survival than did those with CDX2-positive tumours in an independent dataset (51% *vs* 80%, p=0·004). In addition, among all patients with stage II CDX2-negative colon cancer, the 5-year disease-free survival was significantly higher for individuals who received adjuvant chemotherapy than for those who did not (91% *vs* 56%, p=0·006).

Author Piero Dalerba (Columbia University Medical Center, New York, NY, USA) commented, "we found that approximately 4% of human colon cancers lacked CDX2 expression. These tumors appear to have a very aggressive natural history, and the patients appear to benefit substantially from adjuvant chemotherapy after surgery, in both stage II and stage III disease. We advocate for these results to be confirmed in prospective and randomized clinical trials".

Neal Meropol (University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH, USA) said, "Accurate risk stratification of patients with stage II colon cancer remains one of the holy grails for oncologists…In this paper it is notable that the proportion of patients who do not express CDX2 is quite small, and therefore the number of patients studied in this group is small. For this reason, further validation is needed before this test becomes a routine component of standard practice".

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For the **study by Dalerba and colleagues** see *N Engl J Med* 2016; published online Jan 21. DOI:10.1056/NEJMoa1506597