Medical Xpress

Activation of biomarker linked with improved survival among obese patients with colorectal cancer

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Among obese patients, activation of the protein biomarker CTNNB1 was associated with better colorectal cancer-specific survival and overall survival, whereas post-diagnosis physical activity was associated with better colorectal cancer-specific survival among patients negative for CTNNB1, according to a study in the April 27 issue of *JAMA*.

Activation of the WNT signaling pathway (a network of proteins known for their roles in cancer) and cadherin-associated protein beta-1 (CTNNB1; [beta-catenin]) plays a critical role in colorectal carcinogenesis. Accumulating evidence indicates a role of WNT-CTNNB1 signaling in obesity and metabolic diseases, according to background information in the article. Considering the dual roles of CTNNB1 in carcinogenesis and energy metabolism, the authors hypothesized that activation of WNT-CTNNB1 signaling might confer proliferative ability to cancer cells. "In addition, epidemiological evidence suggests causal effects of obesity or excess energy balance on colon cancer incidence and mortality. Notably, physical activity (exercise) has emerged as a modifiable lifestyle factor that may improve cancer survival," the authors write.

Teppei Morikawa, M.D., Ph.D., of the Dana-Farber Cancer Institute, Boston, and colleagues conducted a study to examine whether CTNNB1 activation in colorectal cancer modified prognostic associations of body mass index (BMI) and level of postdiagnosis physical activity. The study

included data from 2 U.S. prospective cohort studies (Nurses' Health Study and the Health Professionals Follow-up Study) to evaluate CTNNB1 among 955 patients with stage I, II, III, or IV colon and rectal cancer from 1980 through 2004. A model was used to compute the risk of death, adjusting for clinical and tumor features.

During follow-up through June 2009, there were 440 deaths, which included 266 colorectal cancer-specific deaths. Analysis indicated there was a significant modifying effect of BMI. In obese patients (BMI 30 or greater), positive status for nuclear CTNNB1 was associated with significantly better colorectal cancer-specific survival (5-year survival: 0.85 for patients with positive nuclear CTNNB1 status vs. 0.78 for those with negative status) and overall survival (5-year survival, 0.77 for patients with positive nuclear CTNNB1 status vs. 0.74 for those with negative status). In contrast, among nonobese patients, positive status for nuclear CTNNB1 was not significantly associated with cancer-specific survival or overall survival.

The authors also found that for patients with negative status for nuclear CTNNB1, high level of postdiagnosis physical activity was associated with significantly better colorectal cancer-specific survival (5-year survival, 0.97 vs. 0.89). However, for patients with positive status for CTNNB1, physical activity was not associated with colorectal cancer-specific survival or with overall survival.

"These results provide evidence for a possible interactive effect of tumor CTNNB1 signaling and patients' energy balance status in determining tumor cell behavior. Our data support the hypothesis that progression of a tumor with an inactive WNT-CTNNB1 signaling pathway might be influenced by energy intake and expenditure, whereas a tumor with an active WNT-CTNNB1 signaling pathway might progress independent of energy balance status. Although our data need to be confirmed by independent data sets, tumor CTNNB1 status may serve as a predictive

biomarker for response to a prescription for physical activity (exercise) in clinical practice. Because physical activity is a modifiable lifestyle factor, our data may have considerable clinical implications," the authors write.

More information: *JAMA*. 2011;305[16]1685-1694.

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