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Colon cancer proteins show promise for blood test

Searching for less invasive screening tests for cancer, Johns Hopkins scientists have discovered proteins present in blood that accurately identify colon cancer and precancerous polyps.

Initial studies of the proteins, CCSA-3 and CCSA-4, suggest they could be used to develop a blood test to identify at-risk individuals.

"The reality is that many people are not getting regular screening colonoscopies," says cancer researcher Robert Getzenberg, Ph.D. "So, ideally we'd like to identify those with some molecular for the disease and really need them."

Current screening guidelines for healthy people call for a baseline colonoscopy - colonic cleansing, fasting and heavy sedation followed by the insertion of a flexible, optical-scanning scope through the rectum into the colon -- at age 50, followed by re-screening at least every five to 10 years. Colonoscopy is not foolproof; cancers can develop between screenings.

First discovered by Getzenberg and colleagues at the University of Pittsburgh through a protein scan, the two blood-dwelling proteins are thought to be remnants of cellular debris castoff from dead cancer cells. Although the proteins' roles are not entirely clear, the Johns Hopkins scientists say they are part of the scaffolding that supports structures within a cell's control center, the nucleus.

Alteration of such nuclear scaffolding is a hallmark of cancer cells that is easily detectable under the microscope as a misshapen and discolored nucleus. That led Getzenberg to the notion that "there must be something at the molecular level that would form a molecular flag for cancer via a blood test."

To find the flag, Getzenberg's team drew blood samples from 107 apparently healthy individuals the day before their scheduled colonoscopies, and from 28 colorectal cancer patients.

Using a particular concentration of scaffold-proteins as a marker for disease, the Johns Hopkins team - which did not know the colonoscopy results in advance -- were 100 percent accurate in identifying the 28 existing cancers. Using the same protein markers, investigators also correctly identified 51 of 53 individuals (96.2 percent) with normal colons and 14 of 18 (77.8 percent) people with advanced precancerous polyps, which Getzenberg says are the most important to detect through routine screening.

When researchers combined samples, they correctly identified 42 of 46 (91.3 percent) containing both cancers and advanced precancerous polyps. Protein levels were accurate in correctly assessing additional blood samples from 125 people with benign conditions and other cancers.

"These proteins seem very good at separating normal samples from cancerous ones and identifying other groups with pre-cancers at high risk for disease as well," says Getzenberg, who is a professor of urology and director of research at Johns Hopkins' Brady Urological Institute. Results are published in the June 15 issue of Cancer Research.

The researchers are planning larger studies at several hospitals over the next several months. It may take several years to complete the full range of testing.

Getzenberg says that storing and processing the samples are among the major hurdles in biomarker development, a field that spans ongoing research on many cancers and various body fluids. "It is difficult to get many facilities to adhere to precise storage and processing conditions important for keeping proteins stable," he says. "Different conditions could create incorrect results." Researchers also differ in the type of biomarkers they seek, with some looking for proteins, like Getzenberg, and others searching for DNA components.

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Getzenberg and the University of Pittsburgh hold a patent for the technology described above, which is licensed to Onconome Inc. Funding for the study described in this article was provided by Onconome Inc. and the National Cancer Institute. Under a licensing agreement between Onconome Inc. and University of Pittsburgh, Getzenberg is entitled to a share of royalty received by the University on sales of products described in this article. Getzenberg also is a paid consultant to Onconome Inc. which has a licensing agreement with The Johns Hopkins University covering CCSA-3 and -4 related technologies. The terms of this arrangement are being managed by The Johns Hopkins University in accordance with its conflict of interest policies.

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On the Web: http://www.hopkinskimmelcancercenter.org
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