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New method for early detection of colon cancer

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A new, highly sensitive method to detect genetic variations that initiate colon cancer could be readily used for noninvasive colon cancer screening, according to a study published in *Cancer Prevention Research*, a journal of the American Association for Cancer Research.

"Tumor cells are released into stool from the surface of precancers and early-stage colon cancers, but detecting a cancer-initiating genetic mutation among a large quantity of normal DNA from a patient's stool is like looking for a needle in a haystack," said Bettina Scholtka, Ph.D., assistant professor in the Department of Nutritional Toxicology at the University of Potsdam in Nuthetal, Germany. "By combining for the first time locked nucleic acid-based, wild-type blocking polymerase chain reaction and high-resolution melting, we were able to achieve the desired sensitivity. The extremely high sensitivity of this technique allows us to find very low amounts of different types of the cancer-initiating mutations in patients' stool samples.

"Colon precancer cells carrying these genetic variations are routinely shed in stool samples, but these cells can be detected in blood only after the cancer has advanced, so stool is better than blood if we are to catch these cancers at a very early stage," she added.

About 60 percent and 40 percent of patients with colorectal cancer have genetic variations in the genes APC and KRAS, respectively. Because these variations are also present in precancers, methods for spotting them can help detect colon cancers early. The new method described in

this study can detect a single cancer-specific gene variation among 10,000 times the amount of normal DNA, and is up to 5,000-fold more sensitive than other noninvasive screening methods.

A multicenter study is needed to validate the sensitivity and specificity of this new method in comparison with standard screening methods like colonoscopy, according to Scholtka.

Scholtka and colleagues used 80 human colon tissue samples representing cancers and precancers to detect genetic variations using a combination of two techniques: The first technique—locked nucleic acid (LNA)-based, wild-type blocking (WTB) polymerase chain reaction—suppressed normal DNA present in large quantities in the sample; and the second technique—high-resolution melting (HRM)—enhanced the detection of genetic variations.

The researchers were able to detect APC variations in 41 of the 80 samples. They were also able to detect previously unknown variations in APC. In contrast, the routinely used technique called direct sequencing could detect variations only in 28 samples.

They then analyzed 22 stool samples from patients whose colon tissues had APC variations, and nine stool samples from patients whose colon tissues did not have APC variations, as controls. They were able to detect APC variations in 21 out of 22 samples.

The researchers also detected variations in the KRAS gene using 20 human colon tissue samples to demonstrate that the WTB-HRM method can be used to detect variations in genes other than APC.

"By using our technique for examining a selection of genes that become mutated during the process of colon cancer formation, it is possible to detect the very first stage of colon cancer and even precancers in a stool

sample," said Scholtka. "It will be possible to prevent cancer in many cases by removing the precancerous lesions after early detection."

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