

More efficient tests may one day replace endoscopy

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Micrograph showing inflammation of the large bowel in a case of inflammatory bowel disease. Colonic biopsy. Credit: Wikipedia/CC BY-SA 3.0

In two journal articles, a University of Houston biomedical researcher reports a step forward in diagnosing intestinal diseases, including colorectal cancer, ulcerative colitis and Crohn's disease using stool proteins. The current gold standard for colon cancer testing measures blood (hemoglobin) present in stool, and tests for inflammatory bowel disease (IBD) measure levels of calprotectin, a protein that detects inflammation in the intestines.

"The unique aspect of both research reports is that we are looking at [stool samples](#) comprehensively, and not just at one or two favorite molecules," said Chandra Mohan, Hugh Roy and Lillie Cranz Cullen Endowed Professor of biomedical engineering in the UH Cullen College of Engineering. "We are casting a wide net, and this has never been done before."

With colon cancer, typical fecal blood tests look for hemoglobin in stool samples. In Mohan's work, hemoglobin is just one of more than a thousand proteins being hunted.

"By the time you see blood, it might be too late, and there are other proteins that appear in the stool if someone has colon cancer, and they may appear much earlier than when the blood appears," reports Mohan in *Nature Communications*.

Using aptamer-based screening, Mohan and team screened 1,317 proteins searching for precursor biomarkers of [colon cancer](#) and found

five elevated. Stool MMP9, fibrinogen, myeloperoxidase, and haptoglobin emerged as promising stool biomarkers of [colorectal cancer](#), outperforming stool hemoglobin.

Aptamers are pieces of DNA that can be selected to bind to other molecules. They serve as bait, carefully selected for each [protein](#) they will try to detect. If the protein is present in the stool, it will bind to the aptamer in the library. If the protein is not present, it will be washed away.

"Longitudinal studies are warranted to assess the clinical utility of these novel biomarkers in early diagnosis of colorectal [cancer](#)," said Mohan.

Mohan's research team includes Robert S. Bresalier, University of Texas MD Anderson Cancer Center; Nicholas Chia, Mayo Clinic; Hao Li and Kamala Vanarsa, University of Houston.

Predicting the future with markers for IBD

In the *Journal of Gastroenterology*, Mohan is reporting similar findings in early diagnosis of [ulcerative colitis](#) and Crohn's [disease](#), finding several proteins elevated in pediatric patients with the disease after screening for 1300 proteins. Those proteins are stool Ferritin, Fibrinogen, Haptoglobin, Hemoglobin, Lipocalin-2, MMP-12, MMP-9, Myeloperoxidase, PGRP-S, Properdin, Resistin, Serpin A4, and TIMP-1, all significantly elevated in both ulcerative colitis and Crohn's disease.

The team took samples from patients at four different time periods, allowing the researchers a rare window into disease progression.

"Using the new biomarkers, we can predict if the disease will become worse or if the intestines will become more inflamed. Stool proteins

assayed at baseline can predict how the disease might progress in the weeks and months ahead," reports Mohan.

The IBD study represents the first use of the aptamer-based screen of stool samples in IBD, representing the largest-ever targeted stool proteomic study in IBD.

"We demonstrate the utility of comprehensive aptamer-based proteomic screens in identifying novel disease biomarkers for IBD that outperform the current gold standard, fecal calprotectin," said Mohan.

Mohan's hope is to replace the invasive endoscopy test by finding stool markers that can predict what is happening in the intestine without having to do endoscopy. Stool tests for proteins can be done at home and through the mail.

On this paper, Mohan was joined by Subra Kugathasan from Emory University whose lab supplied the stool samples; Suresh Venkateswaran, Emory University; Sanam Soomro and Kamala Vanarsa, University of Houston.

Provided by University of Houston

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