

A test for targeting colonoscopies? **Yes please.**



REG JOSEPH CONSULTS WITH METABOLOMIC TECHNOLOGIES INC. EMPLOYEES, AT THE UNIVERSITY OF ALBERTA'S KATZ GROUP CENTRE FOR PHARMACY AND HEALTH RESEARCH.

In the struggle to stay one step ahead of colon cancer, an Alberta team has developed a test that uses compounds in the urine to help find individuals with pre-cancerous colonic polyps so they can be prioritized for further testing.

By Andrea Anderson + Photos by John Ulan

Colonoscopies are our main tool for catching colon cancer's creeping advance—from pesky pre-cancerous polyps to full-blown forms of the disease.

But, while a compact colonoscopy camera is the most reliable way to find and remove polyps and cancerous growths in the large intestine, the procedure is invasive and expensive. Doctors face a tricky task singling out patients who are most likely to benefit from the procedure.

A group of local researchers and industry partners hopes to change that. They're working to develop a simple urine test to screen patients before sending them for colonoscopies.

The team—which includes representatives from the Alberta-based company Metabolo-mic Technologies Inc. (MTI) and investigators from the University of Alberta—has made headway on such a test by focusing on compounds produced during the body's various metabolic processes.



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RISK FACTORS

Some of the things that affect your chances of getting colorectal cancer are simply beyond your control. Here are a few things that may put you at a higher risk for developing the disease:

- › Age
- › Sex
- › Family history
- › Personal history
- › Ulcerative colitis and Chron's colitis

**information taken from the Alberta Services Screening for Life website. www.screeningforlife.ca*

They have already tracked down a set of ten “metabolite” markers found in distinct combinations in the urine of healthy individuals, individuals with colon cancer, and those with colonic polyps. The team hopes to develop a test for these changes in the composition of urine, to help detect the presence of pre-cancerous polyps.

COMMERCIALISATION

To support its ongoing efforts to develop a commercial version of the test (dubbed PolypDx™), MTI recently secured a \$375,000 Knowledge Translation Strategic Initiative grant from Alberta Innovates-Health Solutions through the Alberta Cancer Prevention Legacy Fund.

The new funding will go towards a current trial in Lethbridge, in collaboration with Alberta Health Services and DynaLIFEDx, to hammer out the optimal strategy for using PolypDx™ in large-scale population screening.

“There are a number of protocols and procedures that we need to do for our test to make PolypDx™ robust and suitable for the commercial market,” notes MTI’s Chief Executive Officer Reg Joseph. “[AHS and DynaLIFEDx] are helping us with many of these aspects.”

If this and future studies pan out, says Reg, the urine-based test could lead to more efficient use of colonoscopies in colon cancer detection. He is also optimistic about the prospect of enhancing polyp

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screening protocols—ideally finding and removing more of the benign-but-risky polyps before they have the chance to become cancerous.

The notion of prioritizing patients for colonoscopy testing is not new. In many centres worldwide, including Alberta, healthcare practitioners screen patients by testing stool samples for traces of blood—which can signal colon problems including cancer.

Unfortunately, fecal tests are not designed to find pre-cancerous polyps, and only detect colon cancer around half the time. Moreover, many patients are either reluctant to collect their own samples or are not adept at doing so.

Consequently, many healthcare professional still rely heavily on the colonoscopy for finding polyps and colon cancers, even though most patients tested by colonoscopies are ultimately found to be polyp- and cancer-free.

In the hopes of catching more instances of the pre-cancerous polyps, the University of Alberta's Dr. Richard Fedorak and colleagues started testing urine samples from a subset of patients participating in the AHS "Stop Colorectal Cancer through Prevention and Education" (SCOPE) program.

Their idea was that the easy-to-access urine sample might contain metabolite compounds that appear or disappear in concert with colon cancer or polyps.

Sure enough, the researchers saw distinct metabolite signatures coinciding with colon cancer and with colonic polyps. By narrowing in from dozens of urine metabolites, they determined that they could distinguish between colon cancers, polyps, and healthy samples with as few as 10 metabolite markers.

And though there's some overlap between markers found in individuals with polyps and those who have progressed to colon cancer, there are also enough differences to tell them apart.

In a recent University of Alberta trial involving around 1,200 patients, for instance, Fedorak and his team found that the urine-based test could find polyps 71 per cent of the time.

Next, those developing the test want to see if it can be scaled up to screen individuals for polyps in a more routine manner in the clinic through the ongoing Lethbridge trial.

MTI is aiming for PolypDx™ tests that cost less than \$50.

SCALING UP

Collaborators on the study started collecting samples several months ago. By the time the AIHS grant ends

next year, the group hopes to have data on around 500 patients, and to gain a better idea of how the PolypDx™ test performs in a clinical setting.

In parallel with that southern Alberta validation study, MTI and its collaborators are developing PolypDx™ through other avenues, including research related to the precise set of metabolites that the test considers as well as the type of technology used to detect them.

MTI is aiming for PolypDx™ tests that cost less than \$50, according to Reg—and the company would like to eventually push that target price down even further. 



DR. RICHARD FEDORAK is a Professor of Medicine and Associate Vice-President (Research) at the University of Alberta.

An internationally recognized expert on gastrointestinal disorders, Dr. Fedorak has received some \$35 million in research fellowships and grants as well as numerous awards.



REG JOSEPH joined Metabolomic Technologies Inc. in 2010 and currently serves as the company's Chief Executive Officer. He

is also executive-in-residence in the life sciences division at TEC Edmonton, a business development group spear-headed by the University of Alberta and the Edmonton Economic Development Corporation.

Metabolomic devices for companion diagnostics and personalized medicine

By Omar Mouallem + Illustration by Kelly Schykulski

When former US President Bill Clinton announced the completion of the Human Genome Project in 2000, one commentator heralded it as “the biological equivalent of the moon landing,” and it was widely considered the gateway to locating—and presumably curing—our most complex medical conditions.

The Human Metabolomic Project, Canada’s quieter biological voyage launched in 2006 to catalog chemical compounds, and has made enormous gains. The project’s founding director, Dr. David Wishart, hopes to display its power with a prototype gadget he expects to see in your hand within a decade.



Billions of these tests are done in North America every year, but they need these big instruments that cost \$2 million and could fill up a boardroom.

Because the gadget's name is a mouthful—Metabolomic Device for Companion Diagnostics and Personalized Medicine—Dr. Wishart has nicknamed it the “Metabolomic Tricorder,” after the fictional Star Trek device that provided instant medical diagnosis and analysis with the wave of its wand.

Wearing a polo shirt, khakis and bent ball-cap, the University of Alberta researcher bears little resemblance to Dr. Leonard “Bones” McCoy, and his gadget doesn't look much like a Tricorder. Instead of being waved outside the body, the portable device analyzes blood, urine and saliva samples for their metabolites—chemical compounds produced within the body. In addition to aiding diagnoses, it's also predictive, opening the possibility of treating predispositions to illnesses such as colorectal cancer, diabetes and pre-eclampsia (the number one killer of expectant mothers).

Metabolites are molecular biomarkers that, in various patterns, tell a more accurate story of our health than DNA because they reveal environmental changes. Think of each metabolite as a musical note and each disease as a song. “If someone played only one note from a song, you wouldn't recognize it, but if you can play 30 notes, the highs and the lows, in the right sequence, you can make out a song,” says Wishart. He thinks his technology can recognize up to 40 songs (or disease signatures) with the 40,000 compounds catalogued thus far. “It's an emerging field, with little competition, so that means there's a lot to discover.”

Much of the required technology, such as mass spectrometry, has existed for years. For example, a trace of blood from every newborn in Alberta goes to labs where mass spectrometers measure chemicals to identify genetic disorders or metabolite errors. Colon cancer screening uses a similar process. “Billions of these tests are done in North America every year, but they need these big instruments that cost \$2 million and could fill up a boardroom,” says Dr. Wishart.

Dr. Wishart and his team aim to make these screenings cheaper, faster, and more efficient. Initially this will take the form of easy-to-use kits. But, eventually, Dr. Wishart hopes it will be done with a metabolomics device that fits in your pocket just like Dr. McCoy's Tricorder.

The \$8 million project is funded by AIHS, Pfizer Genome Canada and, until recently, the National Institute for Nanotechnology, to which Dr. Wishart is cross-appointed. It began two years ago in two phases: mastering the technology and miniaturizing it. Dr. Wishart says the kits could be in research labs within a year, and in clinical labs within three. The tricorder devices could be in your G.P.'s office within five to eight years.

The project had a head start because Dr. Wishart himself is a pioneer in the field of metabolomics. “If you're the only kid in the sandbox, you've got it to yourself,” observes Dr. Wishart, who in 1999 co-founded Chenomx (as in “chemical genomics”), a software company that measures metabolic data. At the time, the field was so cutting-edge that the word “metabolome” had only just been coined.

Today there are more kids in the sandbox, thanks in part to Dr. Wishart's research, but Alberta remains a world leader. “Metabolomics could be a uniquely Albertan industry,” says Dr. Wishart. “A lot of the know-how literally exists right here in Edmonton.” 



DR. WISHART receives funding from Alberta Innovates - Health Solutions. He is an professor at in the Department of Biological Sciences and cross-appointed with the Department of Computing Science and the National Institute for Nanotechnology at the University of Alberta.