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# Your pharmacist's secret weapon: How your DNA can help perfect your medication

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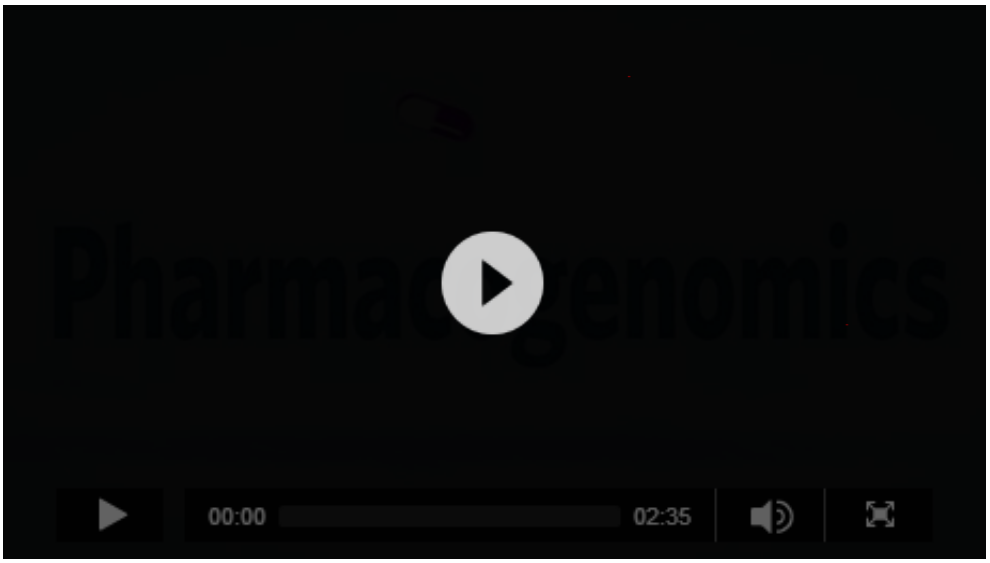
Catherine McLeod suffered one of her worst drug reactions – a minor stroke – while behind the wheel. She drove through a red light, and an oncoming vehicle totalled her car.

No one was seriously injured. But after the accident in 2005, she experienced two more minor strokes and kidney damage because of the litany of medications she was taking for bipolar disorder, diabetes and other conditions, she said. “I was overmedicated.”




Pharmco-what!? Understanding how your genes interact with medicines (The Globe and Mail)

McLeod, now 62, is working with a different psychiatrist to adjust her medications, which add up to at least 10 pills a day.

In the past year, she has endured side effects ranging from blood-pressure fluctuations to Parkinson’s-like symptoms. Finding the right medications in dosages she can tolerate is “still hit-and-miss,” she said.

McLeod is hoping to find answers in her DNA. A team of researchers at the University of British Columbia are testing patients’ saliva for genetic variations that affect how individuals respond to

medications. She said she "jumped at the chance" to participate.

The study is the largest in North America to look at whether community pharmacists can gain the skills required to collect DNA samples from patients, walk them through the consent process and explain how specific drugs may interact with the patient's genetic makeup. So far, 200 patients in 33 pharmacies throughout British Columbia have participated in the study. The next phase, expected to start in 2016, will involve 1,000 patients in pharmacies across Canada.

The goal, researchers say, is to bring personalized medicine to a pharmacy near you.

"I see genetic information as a way to prescribe less medication – and more accurately," said the study's principal investigator, Dr. Corey Nislow, an associate professor at the UBC Faculty of Pharmaceutical Sciences.

Specialists in pharmacogenomics – the study of gene-drug interactions – have linked more than 150 medications to genetic variations that affect how a patient reacts to specific drugs. The growing list does not cover every drug on the market, which number in the thousands, but it includes some of the most widely prescribed medications, such as antidepressants, cholesterol-lowering statins and blood thinners.

No one disputes the data. But medical experts disagree on how health-care professionals should put this knowledge into practice – and whether routine genetic testing will result in better medication choices for patients.

The UBC test is not the same as 23andMe, the $199 "personal genome service" kit sold online with the slogan "knowledge is power." The California company has come under fire for mining genetic data from unwitting clients and violating the U.S. Food and Drug Administration's restrictions against selling an unapproved diagnostic test.

Unlike 23andMe, the UBC test does not screen for genetic variations that might reveal a patient's ancestry or the chances of developing cancer and other diseases. Using saliva samples identified only by numeric code, the researchers look solely at genetic variations involved in functions such as drug metabolism.

In theory, patients with variants linked to slower metabolism of a given drug would need a lower dose, since their bodies do not clear the drug as quickly. High metabolizers would need a higher dose. And in some cases, genetic testing may suggest that the person should avoid the drug entirely.

But in practice, the human body is more complex. Other factors besides genes can affect how a patient metabolizes medications, including age, diet, multiple drug interactions and overall health. Specialists warn that prescribing a dosage based on genetic testing alone could put a patient at risk for undertreatment or dangerous side effects.

Pharmacists are ideally suited to weigh all these factors, according to Geraldine Vance, chief executive officer of the B.C. Pharmacy Association, which is co-funding the study along with

investors Genome British Columbia. As experts in drug interactions, pharmacists are trained to advise physicians if they see any reason why a prescribed medication or dosage may be unsuitable. They already adjust medications based on liver and kidney function, and review a patient's medical and family history before filling a prescription. Genetic testing "is about adding another tool, a more precise tool," Vance said.

In the study, patients meet with a pharmacist in a counselling room at their local drugstore. After going over the consent forms, the pharmacist gives the patient a plastic test tube with a funnel attached and leaves the room while the patient spits into the vial. The test tube is sent by courier to UBC, where DNA is extracted from the sample and analyzed. About a week later, the pharmacist goes over the results with the patient using a report that includes a list of medications and their predicted impact on the patient. The results might indicate the patient has an increased risk of a specific side effect or a lower-than-normal chance of the treatment working.

The plan, Vance said, is for a stand-alone company to make this tool available through Canadian pharmacies as early as 2017. The one-time test would look at up to 150 medications at a yet-to-be determined cost.

She suggested that extended health benefits could help pick up the tab, and down the road, provincial governments could cover it. Vance added that BC Pharmacy Association members "have and will continue" to talk to private insurance companies, government and individual patients about how to divvy up the cost.

Pharmacists in the UBC study currently receive about five hours of training in handling saliva samples, addressing privacy concerns and going over test results with patients. Vance could not say whether the training duration would change for a commercial test, but she added that "the focus on ensuring each pharmacist has the same level of training to offer the same level of service will continue."

Genetic testing to predict medication response is already routine in cancer clinics and research centres such as the Mayo Clinic. But adjusting medications based on genetic testing is not as easy as it sounds, according to Dr. Richard Kim, a clinical pharmacologist at the University of Western Ontario. If it were, he said, "every hospital in North America would be doing it."

Kim opened Canada's first personalized medicine clinic in 2008, which offers genomics-guided dosing for medications including the blood-thinner warfarin, cholesterol-lowering statins and the breast-cancer drug tamoxifen. Since then, he and a co-ordinated team of physicians, pharmacists and other specialists at the London Health Sciences Centre have treated more than 3,000 patients with complex health conditions.

Kim and his team confirm that they are giving the right dosage by measuring patients' drug levels using mass spectrometry, a chemistry technique that identifies the amount and type of chemicals present in a patient's blood. Even among patients with a similar genetic makeup, he said, actual drug levels in the body "still vary a lot."

He emphasized that pharmacogenomic testing can be a useful tool. But accounting for genetic factors in treating patients with complex health problems requires specialist knowledge that pharmacists cannot acquire in a day-long training session or an introduction to pharmacogenomics in school, he said.

“This should not be something we jump at as a broad, big-hammer approach.”

The reality, however, is that multiple research teams are looking at the feasibility of training community pharmacists in personalized medicine, including a study led by Dr. Lisa McCarthy at the University of Toronto, which aims to recruit 300 patients in the next few months.

Meanwhile, these tests are already available to anyone with access to a computer. Geneyouin, a Toronto-based company, offers an online “pill check” that looks at more than 60 medications for $500. The company stopped offering the test through primary-care clinics after learning that “physicians need a lot of education and support to be able to practise personalized prescribing,” Geneyouin’s founder, Dr. Ruslan Dorfman, said in an e-mail.

The company is now selling the test through private clinics and select pharmacies in Ontario, and is partway through a small study designed to measure the impact of its pill check service on pharmacy practice.

For patients who order Geneyouin’s PillCheck online, test results come with a warning to seek medical advice before changing medications. But what is to stop a patient from splitting a pill in half without consulting a physician or pharmacist?

Now is the time to get pharmacists up to speed so they can advise patients, Nislow said. In the age of DNA testing at the click of a mouse, “we need experts who can handle this rush of information,” he said.

McLeod, meanwhile, is reflecting on her own test results. When the researchers told her that the antidepressant she is trying is probably the best one for her, “I was thrilled,” she said.

But she was not surprised when the results suggested that she would not respond well to an antipsychotic she was on previously: “I said, ‘Yeah, it takes my brain away.’”

McLeod said the researchers were clear that she should not make medical decisions based on their report. But the consequences of paying attention to her DNA could not be worse than what she has already been through, she said.

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**The secrets in my own DNA**

In a world of seven billion people, genetic testing tantalizes us with potential answers to existential

questions: Who am I? What makes me unique? You could call it navel-gazing at the molecular level.

When University of British Columbia researchers offered to sequence my DNA for this article, I did not balk. I am not on any medication – unless you count my morning coffee – but I wondered what the test would reveal about how I might respond to drugs prescribed to me in the future.

I had no qualms about signing the rights to probe my DNA. In a counselling room at a Shoppers Drug Mart, a pharmacist explained that my saliva sample would be identified only by numeric code. Information linking me to my DNA sample would be stored in a separate computer hard drive accessible to only three researchers at UBC. My unidentified DNA sequence would be available for future research, but if I withdrew consent at any time, all data and samples collected from me would be destroyed. The researchers developed this system with help from a privacy lawyer and the office of the B.C. Privacy Commissioner.

After going over the consent process, the pharmacist handed me a plastic test tube with a funnel attached, and tactfully left the room. Generating enough saliva was tougher than it sounds – I had to massage my jaw and spit several times. But after that, I had my test results within a week.

As the pharmacist went over the two-page printout, I learned that I was unlikely to benefit from cholesterol-reducing statins. But the status of my genes involved in processing serotonin made me a good candidate for SSRI antidepressants, should I ever need them. Best of all, I discovered I had a genetic variant that reduced my risk of caffeine-induced anxiety. What a relief.

I asked whether my genetic variations were unusual. The researcher was blunt: “There was nothing remarkable about this genome.”

I knew this was a good thing, since my responses to medications were likely to be normal. But any fantasy of being a rare snowflake was definitely crushed.

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**Genome 101**

An organism’s complete set of genetic instructions, or DNA, is called a genome. A gene is a small section of the DNA string that carries instructions involved in specific aspects of heredity.

Human DNA is a tightly coiled molecule that could stretch two metres long. DNA is made of two twisting strands connected by pairs of chemicals knows as A, G, C and T. In the spiral ladder of DNA, these base pairs are the steps.

Sequencing determines the exact order of these base pairs along the entire length of a person’s DNA. Differences in this order, compared with most people, are genetic variations, or variants.

In rough numbers, there are: