

Microchip Diagnostic Revolutionizes HIV Monitoring In Developing Countries

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An HIV-positive woman living in a remote African village walks 37 kilometers, six-month-old baby in tow, to the nearest health clinic for a simple blood test to determine if her disease has progressed to AIDS. She will have to make the same arduous journey weeks later for her results, and if the test reveals that her immune system is weak, she'll need to return to the clinic again and again — if she's able — for antiretroviral drugs and continual monitoring.

She is just one of the millions of men, women and children living with HIV in sub-Saharan Africa that James Dou, a doctoral student at the University of Toronto (U of T), hopes to reach with his new invention: a portable lab on a chip that makes blood testing more accessible, efficient and affordable.

HIV and Sub-Saharan Africa

The World Health Organization (WHO) considers the human immunodeficiency virus (HIV) a worldwide pandemic, but

sub-Saharan Africa is disproportionately affected.

“ According to the World Health Organization, more than 22 million people with HIV live in sub-Saharan Africa, accounting for nearly 70 percent of the global total.

As HIV progresses to AIDS, the infection weakens the body's immune defenses by destroying CD4 (T-cell) lymphocytes, a group of white blood cells that help guard against bacteria, viruses and other germs. When CD4 cell levels decrease, the body becomes vulnerable to a host of opportunistic infections that invade when the body's defenses are low.

“When people are infected with HIV, they are more prone to other infectious diseases such as malaria or tuberculosis, which can become lethal,” says Dou.

A critical component of HIV care is monitoring CD4 levels and administering antiretroviral treatment when they decrease. Antiretroviral drugs help suppress the HIV virus and strengthen the immune system by inhibiting the HIV replication cycle. But such drugs must be given only when the disease progresses — and discontinued once CD4 cells return to stable levels.

Counting Blood Cells

CD4 cell counts are measured by a flow cytometer, a machine the size of a photocopier that is standard equipment in clinical labs — at least in the advanced world. Because the typical flow cytometer costs up to \$100,000 and requires both sophisticated infrastructure and trained technicians to operate, it is beyond the reach of many developing countries.

“Flow cytometers are for the most part concentrated in first world countries,” says Dou. “Many countries in the developing world simply do not have the facilities or infrastructure to offer HIV monitoring.”

The Toronto-based Dignitas International, an organization that supports people with HIV and AIDS in the African country of Malawi, has only one flow cytometer in its central health facility, which runs just 250 blood tests per week. Blood samples are collected from villages and transported to the facility for testing via an unorganized process involving motorcycles, buses and bicycles. Results can take weeks to produce and often never reach the patient at all. Dou's invention would eliminate the need for patients to travel to a central facility for blood testing or blood samples to be collected and processed elsewhere. His portable, handheld cytometer, similar to the glucose monitor developed for diabetic patients, could provide rapid, point-of care HIV monitoring in even the remotest parts of Africa. At a cost of \$5,000 to \$10,000 per device, Dou's cytometer offers the potential for affordable, efficient HIV testing, providing results in a few minutes at a cost of less than \$10 per test.

The Science of Flow Cytometry

Dou's invention grew out of his work as a graduate student in the laboratory of Professor Stewart Aitchison, Ph.D., U of T's vice dean of research in the Faculty of Applied Science and Engineering. With funding from the Natural Sciences and Engineering Research Council of Canada and Ontario's Ministry of Research and Innovation, he created — and has now patented — a multi-test particle detection and analysis platform that involves a plastic cartridge, an optical reader and software. Additional software can be easily added to the device to transmit results wirelessly to a central database.

A disposable cartridge is engineered with tiny channels, reservoirs and reaction chambers the size of a human hair. For the CD4 test, a dried reagent — an antibody designed to bind to CD4 cells combined with a fluorescent molecule — is placed in the reaction chamber. When the blood mixes with the reagent, the antibody/fluorescent compound binds to

the CD4 cells and light up. As blood flows through the channels, the optical reader and software count the CD4 cells, and an LCD on the device displays the results within minutes.

Going to Market

Dou designed his platform to be capable of executing any number of applications from counting blood cells and measuring air pollution to testing for food safety. To determine which application to pursue first — and for help bringing the invention to market — Dou and Aitchison turned to U of T's Innovations and Partnerships Office (IPO).

Once U of T committed to Dou, the office suggested a startup company and facilitated the development of a business plan, with the help of U of T's Rotman School of Management, a commercialization plan and patent filings. "Most of our team has a technical background so adding Innovations and Partnerships brought us complementary skills in business," says Dou. "They've been very helpful in helping us make connections, complete our market analysis and apply for funding."

Engineer Meets Biologist

Director of Commercialization and Business Development Lino DeFacendis and Commercialization Manager Kurtis Scissons introduced the engineers to Rakesh Nayyar, an expert in flow cytometry who had recently become aware of the need for HIV diagnostic equipment in the developing world.

"They were initially looking at testing for leukemia/lymphoma," says Nayyar. "I advised them to look at doing the CD4 count because it's a much simpler test and the immediate need is far greater."

With valuable experience in biological testing, Nayyar joined Dou and Aitchison in forming the ChipCare Corp. to commercialize the portable cytometer.

"This is both a good business venture and humanitarian effort," says Nayyar, who was recently appointed ChipCare's CEO.

A bonus for the new company is U of T's collaboration with the MaRS center, an innovation and commercialization hub situated in downtown Toronto's discovery ecosystem. The IPO is physically housed within MaRS, which acts as a catalyst to commercialization by bringing together and supporting research institutions, startup companies, entrepreneurs and industry.

"We take a team approach and collaborate in order to leverage our complementary resources," says DeFacendis.

Getting into the Field

U of T also helped ChipCare establish partnerships with two organizations that are anxious to get the portable cytometer into the field: Dignitas in Malawi and the Camillian Social Center of Rayong, Thailand, which is dedicated to caring for orphans with HIV and AIDS.

"This proves how university research has a direct and positive impact on people's lives," says Professor Peter Lewis, Ph.D., U of T's associate vice president, research, and acting executive director of the university's Innovations and Partnerships Office. "Our team at IPO is having great success at working with U of T professors in taking their research to the marketplace for the good of society. Our work with Professor Aitchison and James Dou is an excellent example."

Dou's invention has impressed others as well: It beat out 200 entrants to win the Canadian Business magazine's Great Canadian Innovation Competition in 2009. The top prize included nearly \$90,000 in engineering and business services,

which the company used to refine its technology and develop its first prototype.

“They have de-risked the science,” says DeFacendis. “The blood flow is the tricky part. You need a clean, extremely discreet profile to count the cells.”

With additional funding, the company is set to shrink the current prototype, which is about the size of a breadbox, to the handheld version. ChipCare’s goal is to deploy 100 devices in Malawi and Thailand in 2012.

Multiple Uses in Many Countries

Dou’s portable diagnostic device also has potential applications in North America and other advanced countries, where it could help reduce health care costs. The U.S. Centers for Disease Control and Prevention recommends routine HIV screening of adults, adolescents and pregnant women — and reports that each year, nearly 22 million Americans are tested for HIV.

“The portable cytometer is a nice complement to existing flow cytometers in hospital laboratories that have a lot of bells and whistles,” says Dou. “Many of the tests that run on flow cytometers don’t need to use all of its features.”

Dou says obtaining one CD4 blood count from a flow cytometer in North America typically costs between \$75 and \$100. He expects his portable cytometer to complete the same test for approximately a tenth of the cost. But the ChipCare Corp. won’t stop with one blood test. The company has recently filed a second patent that covers the chemical processes involved in testing for other blood-related ailments, such as malaria. With one drop of blood, Dou’s device could count CD4 cells and detect malaria parasites, providing two results from one test.

ChipCare’s portable cytometer could also perform a simple complete blood count (CBC), a routine screening test used to check for anemia, infection and other diseases in patients all over the world. By performing CBCs in settings far removed from a hospital laboratory, the portable cytometer could make a huge impact on the delivery of health care.

For example, patients undergoing chemotherapy treatment for cancer must have their blood tested regularly to monitor cell counts (such as the number of white or red blood cells). The ChipCare cytometer would allow health care workers to perform blood tests in a patient’s home, eliminating the need for extra trips to the hospital or clinic.

“Our technology has the potential to revolutionize medical diagnosis by providing less expensive, accurate blood testing with timely results while saving patients pain and inconvenience,” says Dou.

ChipCare’s portable cytometer could also be engineered to count bacteria in water — an application that would eliminate the need to collect and send water samples away for analysis and instead provide immediate, onsite detection of E. coli and other dangerous microorganisms.

“It’s very meaningful and rewarding to do this work,” says Dou. “I am hoping that our efforts can allow technology to have a bigger impact on people’s health and quality of life. That is my motivation.”

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