Makerere makes strides in HIV cure study

By Agnes Kyotalengerire

On February 28, 2005, *New Vision* reported that researchers from Makerere University had developed a model that could lead to a cure or preventive treatment for HIV.

"The scientists intend to carry out a series of experiments to see if restriction enzymes can indeed arrest HIV. If successful, another experiment will be done on monkeys and eventually human beings. This might last up to 10 years," the article read.

The research has been ongoing, and today, 13 years later, more has been achieved.

According to their latest findings published in *AIDS Research and Human Retroviruses*, a US-based international peer-reviewed journal on HIV/AIDS research, the dons used biotechnology (genetic engineering) to develop HIV-cure enzymes. Their findings were published on January 1, 2018. The study was done in a laboratory in Mulago.

What next?

Dr. Misaki Wayengera, the principal investigator and a geneticist at Makerere University College of Health Sciences, said the next step as per world research standards would be to test the enzymes in animals, preferably monkeys.

"We picked sets of human body cells. When we infected the first cell line (TZM-BL) with HIV, it gave a fluorescent protein signal, which made it easier for us to understand HIV in laboratory setting," Wayengera explained.

"The cells that were treated with (artificial) enzymes were protected against HIV. The second group of cells had HIV integrated in them; we treated them with the enzymes and they were cured. This has given us a model for studying a method of curing HIV."

The model is based on the natural method that bacteria use to resist virus invasion.

Most bacteria have an enzyme system called restriction modification system (RMS), which thwarts any attempt by a virus to invade a bacterial cell. The scientists hope that this natural system can be incorporated into human beings to clear HIV infection and other viruses.

History

At the beginning of the research in the early 2000s, the dons thought they would introduce into a human being, the genes responsible for production of restriction enzymes. However, the direction the research has taken is of producing RMS enzymes synthetically and use them as medicine. Wayengera said it was impossible to use the natural enzymes derived from bacteria to cut up HIV without causing danger to the human genes.

Misaki Wayengera during an interview about HIV at the New Vision offices yesterday. Photo by Juliet Kasirye

So, the researchers decided to proceed with the genetically engineered (artificial) restriction enzymes that recognise longer stretches of DNA and, therefore, pose little risk to the hosts' DNA.

The research saw Wayengera spend two years in Canada, where he identified bacteria enzymes that cleave HIV-1 DNA. This story is quite similar to the discovery of pencillins from fungus (notetum) by Alexander Flemming in the 1940s, to fight bacterial infections in man.

At the time they identified bacteria restriction enzymes that cleave HIV-1 DNA, teams of scientists elsewhere were working on producing more specific and efficient artificial enzymes using precursors of these bacteria nucleases or scissors.

"Similar results have been confirmed by scientists in China and the US," he said. Wayengera explained that studies in mice done in the USA showed that CRISPR/cas9 can cure mice of HIV-1.

"For us, having these results coming from our laboratory is very important as it keeps us at the frontier and in the race," Wayengera said.

This work was patented in Uganda and at the African Regional Intellectual Property Organisation (ARIPO) in 2013.

Expenses

The development of a new drug from scratch to preclinical animal studies costs about $250m (sh750b). However, given that this validation data in cells is ready, he said they might require less, $3-5m (sh10.9b-sh18.2b) to undertake the studies in monkeys in two to three years.

Wayengera explained that their unique research is based on the previous scientific discovery that HIV replicates by creating a copy of DNA in the human body. It transcribes itself in DNA before making several copies of itself.

The enzymes work by recognising short sequences that read in the same manner to and from.

The research team

The team was funded by GlaxoSmithKline (GSK), a British pharmaceutical company headquartered in Brentford, London, through the Trusting Science Funding Scheme that gave them $110,000 (about sh360m).

The initial team (before this current publication) Wayengera worked with comprised Henry Kajumbula (a virologist and chairperson of microbiology) and Wilson Byarugaba (retired geneticist from Makerere University). Currently, Wayengera is working with four other researchers Moses Okee, Fred Ashaba and Bernard Bagaya and Moses Joloba.

"It is important that people understand the economic ramifications of this work," Wayengera says. If we can show that this works in monkeys, then a bigger pharmaceutical might offer us as much as $0.6b-$1.2b. This is the market price for validated new molecular entities in the pharmaceutical industry.

Another option would be to stay our ground and develop the drug ourselves," he said.