The road to COVID-19 testing: The role of a Canadian biotech pioneer

July 30 2020, by John Bergeron

The polymerase chain reaction, or PCR, is used to copy strands of DNA. Credit: Pixabay/PixxlTeufel

Canadians are updated daily on the multi-faceted devastation caused by SARS-CoV-2 and on the results of COVID-19 testing from across the country. Few people may be aware that these tests are based on a method innovated by the first-ever biotech company, Cetus, co-founded in California by Canadian-born and educated Ron Cape. He was Cetus's first president in 1971, and then chairman and CEO.

Biotech was nonexistent before this. Cape obtained his Ph.D. at McGill in 1967 with John Spencer as his supervisor, who was one of the pioneers in DNA biochemistry. At the same time, Cape was president of the Professional Pharmaceutical Corporation in Montréal.

The method used globally to test for the presence of the SARS-CoV-2 virus that causes COVID-19 is known as the polymerase chain reaction or PCR. This revolutionary innovation was developed at Cetus by in-house scientist Kary Mullis. Awarded the Nobel Prize in chemistry in 1993, Mullis received the only Nobel Prize for a discovery made by a biotech company.

DNA technology was the key strategy for Cetus's business plan when the company was founded by Cape and his partners. In 1983, Kary Mullis discovered a method to exponentially amplify specific sequences of DNA in the test tube. He called it the polymerase chain reaction.

His key insight was to use an enzyme that was active at high temperature to copy DNA. This DNA-copying enzyme, known as Taq DNA polymerase, had itself been discovered by David Gelfand and Susanne Stoffel at Cetus.

Amplifying DNA

Biologist James Watson and physicist Francis Crick described the structure of DNA in 1953: two strands that are stable in a double helix structure. Each strand of DNA is aligned anti-parallel (parallel but running in opposite directions) with another complementary strand, held together by what are known as hydrogen bonds. These bonds are broken by heat.

Mullis wanted to find a way to make multiple copies of DNA that itself could be used to make the proteins that Cetus wished to commercialize

as therapeutics for cancer. His insight was to design a method to do this using Taq DNA polymerase.

Mullis designed a protocol using varying temperatures and repeated cycles to amplify DNA. He first used a high temperature to separate the double strands of DNA. Lowering the temperature allowed the Taq DNA polymerase to copy and extend sequences along the DNA strands. Once a cycle of copying was done, the temperature was raised again to re-separate the strands allowing for continuation of another amplification cycle.

With Cetus, Mullis designed a machine, the thermocycler, to enable the repeating of such cycles to make exponential amounts of DNA, much like a nuclear chain reaction—hence the term polymerase chain reaction.

PCR and SARS-CoV-2 testing

The genes in the SARS-CoV-2 virus are stored as RNA, not DNA. The standard testing protocol is to take a deep nasal swab from a patient. To detect the virus by PCR-based tests, the RNA of the virus is copied into DNA using another enzyme called reverse transcriptase. It is this copied DNA which is used for PCR amplification.

The urgency for a cure for COVID-19 has made science discoveries move at an accelerated pace. On Jan. 11, the gene sequence of the SARS-CoV-2 virus was made openly available from scientists in China. By Jan. 24, the World Health Organization made available PCR-based protocols to test for SARS-CoV-2.

The legacy of Montréaler Ron Cape and the first biotech company is the PCR test we use to detect COVID-19 disease.

Canada's National Microbiology Laboratory in Winnipeg set up the

SARS-CoV-2 test for COVID-19 based on the data distributed by WHO in January 2020 for PCR testing.

The Public Health Agency of Canada regulates the National Microbiology Laboratory. The PHAC was created in 2004 after the SARS outbreak of 2003, as a consequence of a devastating report written by David Naylor, who was then dean of medicine at the University of Toronto, regarding Canada's lack of preparedness for the lethal SARS outbreak.

Sadly, many of the detailed recommendations to prepare for another lethal virus were never implemented. The last sentence of the 2003 report on page 221 is chilling to read today: "If not now, after SARS, when?"

Advancing Canada's testing expertise

Testing is our only way to know who has been infected, where and when. The lack of coherence and standardization of tests and the communication of the results should be unacceptable today given the recommendations of the 2003 Naylor report on SARS.

Genome Canada harbors exceptionally talented scientists whose expertise is the mapping of genomes. The agency is undertaking heroic efforts to help Canada's COVID-19 response.

Using Genome Canada's testing expertise through its six genome centers could help address the gap in complete, accurate and permanent testing and reporting for the expected next SARS-CoV-2 surge, or the next pandemic.

If not now, after COVID-19, when?