Fighting the Virus Among Us

ON THE VACCINE FRONTLINES SINCE THE 1970s, VIDO-INTERVAC IS AMONG THE LEADERS IN THE FIGHT AGAINST COVID-19

BY ABIGAIL CUKIER

In January, within 24 hours of the World Health Organization (WHO) declaring COVID-19 a health emergency of international concern, the Public Health Agency of Canada gave researchers at the University of Saskatchewan's VIDO-InterVac Centre permission to work with the virus.

VIDO-InterVac (Vaccine and Infectious Disease Organization-International Vaccine) houses one of the largest and most advanced Containment Level 3 facilities in the world, with seven laboratories, including select agent and aerobiology labs, a clinical pathology lab with tissue processing and automated histology and hematology suites and 18 animal isolation rooms. The organization also includes Containment Level 2 facilities with 19 labs, a surgical suite and a 160-acre research farm for large animal studies.

In 1975, VIDO (originally, the Veterinary Infections Disease Organization) was created with a couple of employees, two trailers and a $200,000 budget. Research focused on infectious diseases in food animals and development of livestock vaccines. In 1978, staff moved into the first permanent facility on the University of Saskatchewan campus.

In 2003, the organization opened a 50,000-sq.ft. expansion of its Level 2 laboratories and offices, and extended its research focus to infectious diseases affecting both animals and humans. VIDO was renamed the Vaccine and Infectious Disease Organization; after the Level 3 facility was added in 2010, the name became VIDO-InterVac.

Today, VIDO-InterVac has about 170 researchers, technicians, trainees and administrative staff and a $20-million annual budget. The organization has spun off four companies, holds more than 100 Canadian and U.S. patents and has developed and commercialized eight vaccines, six of which were world firsts. Two more vaccines are in commercial development, one for porcine epidemic diarrhea virus (PEDV) and one for contagious bovine pleuropneumonia (CBPP).

VIDO-InterVac's director and CEO, Dr. Volker Gerdts, says the organization follows the One Health approach, which recognizes that the health of people is closely connected to the health of animals and the environment. "Serving the livestock and poultry industry has been, and will always be, an important part of our mandate," Dr. Gerdts explains. "Due to an increasing globalization and urbanization, however, the interface between humans and animals has become more and more important, as new diseases continue to emerge between the two. To remain successful, our research needs to continue to focus on both human and animal health, and the boundary between them."

Dr. Gerdts completed his post-doctoral studies at VIDO-InterVac and was hired to stay on as a scientist. He was associate director of research for 11 years before taking over as director last year. Dr. Gerdts says the focus on emerging diseases and threat of pandemics is the biggest change he has seen in his 20 years at the organization.

"We realized we needed high-containment facilities that allow us to work with emerging pathogens," he says. "The vision was that we needed an organization to translate discovery knowledge into real products. Solutions through research became our mandate."

Even before the WHO declared the Zika virus a global public health emergency in February 2016, VIDO-InterVac had begun to develop a novel animal model for the disease and to establish if there is a link between fetal infection and microcephaly. This January, the organization became the first non-government facility in Canada to gain regulatory approval to work with African swine fever. This deadly and fast-spreading viral disease is killing millions of pigs worldwide, and could devastate Canada's pork industry.

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to isolate the SARS-CoV-2 virus, using a clinical sample obtained from Sunnybrook Health Sciences Centre in Toronto. It was also the first in the country to establish an animal model for testing of vaccines, antivirals and therapeutics. By the end of February, VIDO-InterVac researchers had created a vaccine candidate and were the first in Canada to develop and test a COVID-19 vaccine in ferrets.

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Due to their susceptibility to human respiratory viruses, ferrets were thought to be a potential model for SARS-CoV-2. For this project, ferrets receive two immunizations and then researchers expose them to the virus and measure whether they develop the disease. They will also study whether they transmit the virus to other animals, to test the ability of the vaccine to reduce transmission to other animals. Manufacturing and safety testing in animal models is expected to be completed this summer, with clinical testing in humans planned for the fall.

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In April, the federal government announced a $23-million investment to support VIDO-InterVac's pre-clinical testing and two phases of clinical trials of the COVID-19 vaccine. A month earlier, the government had announced $12 million towards the organization's construction of its own vaccine manufacturing facility to Good Manufacturing Practices standards as required for human vaccine production, as well as $11.3 million for operational funding for high-containment laboratories.

Dr. Gerdts says that generating interest in funding research into a pan-coronavirus vaccine for humans has been a challenge. "We have wanted this facility for a very long time, as Canada does not have enough capacity to manufacture vaccines," he admits. "We need to be ready for the next pandemic. To ensure Canadians have access to these life-saving vaccines, it's important that we develop timely vaccines here in Canada."

Current and past research highlights

Bovine tuberculosis

Caused by Mycobacterium bovis, this debilitating disease can spread to humans and other domestic and wild animals. In fact, Dr. Gerdts says up to 10 percent of human TB is transmitted from cattle in some countries. To develop a vaccine, researchers used a genomics-based approach termed reverse vaccinology to identify candidate proteins that could stimulate a protective immune response in cattle. These proteins are being screened to determine which are expressed during infection and which can cause an immune response, and therefore are potential antigens for a vaccine.

Zika virus

VIDO-InterVac developed the first animal models in neonatal and fetal pigs to study the Zika virus. "Pigs are immunologically, physiologically and anatomically similar to humans," explains research scientist Dr. Vladi Karniychuk. The lab was the first in the world to show in animal models that Zika infection in the womb produces altered immune responses and sex-specific brain abnormalities in apparently healthy pig offspring.

Zika virus can cause severe abnormalities in fetuses, such as brain lesions and life-long developmental and cognitive impairment in children. However, most infections in pregnant women are not associated with developmental abnormalities in fetuses and newborns. "The study found that children affected in utero, even by mild Zika virus infection, can appear healthy at birth but develop immune dysfunction and brain abnormalities later," says Dr. Karniychuk. Researchers inoculated selected fetuses at the mid-stage of development, which resulted in trans-fetal virus spread and persistent infection in the placenta and fetal membranes for two months. Offspring did not show congenital Zika syndrome or other visible birth defects. However, a month after birth, some offspring exhibited excessive interferon alpha (IFN-α) levels in blood plasma in a regular environment. Most affected offspring also showed dramatic IFN-α shutdown during social stress, providing the first evidence of the impact of prenatal Zika virus exposure and postnatal environmental insult.

The lab is now using the animal models to understand the pathogenesis of congenital Zika virus infection and the long-term health effects in offspring, and to test novel interventions to prevent fetal infection and disease outcomes.

African swine fever

This virus is estimated to kill every third pig in the world, says Dr. Gerdts. "North America is so far free of it, but it is a big concern and threat," he explains. African swine fever leads to haemorrhagic fever and death of infected animals. Endemic in many parts of Africa, the disease is caused by infection with a large DNA virus. Vaccines are currently not available. The first non-government facility in Canada to gain regulatory approval to study the virus, VIDO-InterVac is working with collaborators to develop a viral vector vaccine that incorporates several African swine fever genes. BL