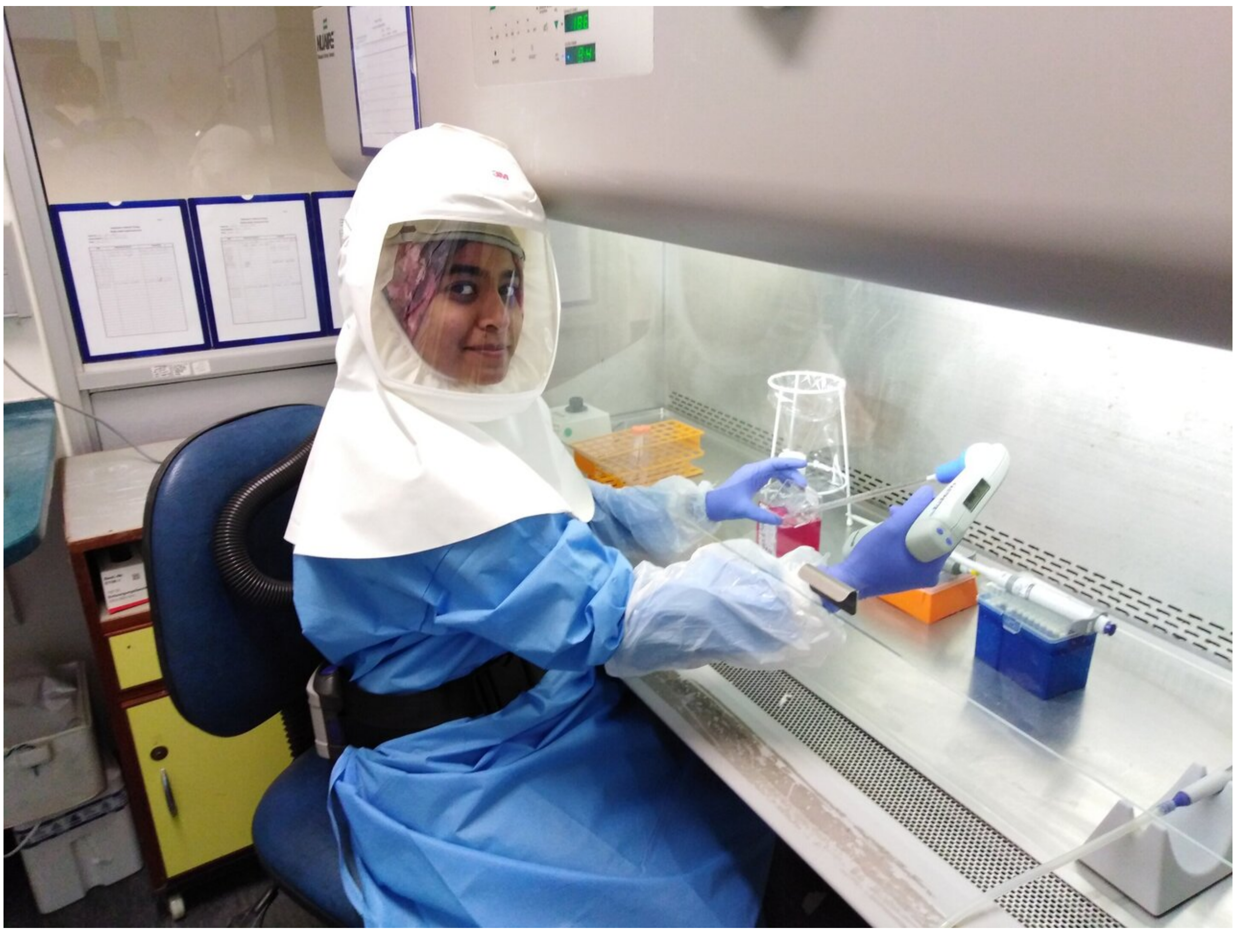
Teams isolate South Africa's first laboratory culture of SARS-CoV-2

May 12 2020, by Nicklaus Kruger



UWC's Dr Tasmin Suliman working at the biosafety level-3 laboratory at Stellenbosch University's Division of Medical Virology. Credit: UWC/SU

While much of the scientific and medical community rushes to develop therapeutic agents for COVID-19 based on clinical data, getting a better understanding of the virus remains crucial. That's why it's so important that South Africa obtained its very first known laboratory isolate of SARS-Coronavirus 2 (SARS-CoV-2) on 1 April 2020, courtesy of the collaborative efforts of the University of the Western Cape (UWC) and Stellenbosch University (SU).

"Having a pure culture of the virus opens doors for research in South Africa," says Dr. Tasnim Suliman of UWC. "Currently, much of the data that exists on this novel virus is based on detecting the genetic material, which is still possible after the virus is dead, and does not confirm whether the virus is viable and able to cause infection. Now, we can experiment on the live virus and observe how it actually behaves in the lab."

Dr. Suliman is a post-doctoral research fellow working under Professor Megan Shaw, an influenza expert who recently relocated from the U.S. to join UWC. Using the biosafety level-3 (BSL-3) laboratory at SU's Division of Medical Virology with the support of Division Head Professor Wolfgang Preiser, Suliman was able to inoculate cell cultures with samples from COVID-19 patients and succeeded in growing the virus.

"We didn't create the virus, or modify it in any way," Dr. Suliman notes. "All we have done is provided the virus with the right conditions to grow, in a space where we are able to harvest a large amount of virus to perform research. And strict safety protocols were followed."

An immediate and indispensable blessing of having an isolate is being able to supply diagnostic labs with large amounts of viral genetic material that is identical in genetic makeup and concentration. This achievement offers valuable opportunities for further research and provides an indispensable reference material for standardising diagnostic tests across multiple platforms between laboratories.

For example, the virus can be used in experiments to test new antiviral compounds in vitro, and if they show an effect against the virus without harming the cells, they could become candidates for clinical trials.

"Although South Africa is the leading African country in science and technology, we remain a resource-limited setting by developed world standards," Suliman says. "Therefore, it is a tremendous advantage for us to make this virus available and guide others on how to safely handle the virus locally."

Cultivating Coronavirus: The Art And Science of Virus Culture

Dr. Suliman obtained clinical samples from COVID-19-positive patients at Tygerberg Hospital, in Cape Town, and inoculated these samples onto live cells that were cultured in the laboratory.

If the virus is present in the clinical sample, it infects the cells and it grows. This provides a pure culture of the virus—an essential resource for all research laboratories, as well as clinical laboratories, which can use it as a positive control in their diagnostic tests.

"Virus culture was previously used routinely in diagnostic procedures, which has now been replaced with rapid, sophisticated and high-tech molecular techniques with greater capacity and accuracy, and faster turnaround times," Prof Shaw says. "Inevitably, virus culture became a dying technique, and the skill is rapidly fading from the scientific community."

Unlike bacteria that can be grown quite simply in nutrient-rich media, viruses require living cells for their proliferation. Viruses need to be able to attach to and enter cells, before redirecting the cells' machinery to produce the proteins and molecules required to assemble new virus particles. The cells themselves have their own growth requirements, and finding a combination of lab-adapted cells that are also compatible with virus growth is a highly delicate process.

"We have to literally synchronize two naturally occurring biological systems to work together to yield a desired result," Dr. Suliman explains. "Fortunately, the growth requirements of SARS-CoV-2 appear to be very similar to that of SARS-CoV-1, which gave us some sort of a roadmap."

And fortunately, she was well-equipped to follow that roadmap.

There are seven known human coronaviruses, three of which cause severe disease. As it happens, Dr. Suliman has worked with all three to varying extents, as well as one milder disease-causing CoV.

During her Ph.D., supervised by UWC coronavirus expert Professor Burtram Fielding, she investigated viral proteins of SARS-CoV-1 from the 2002-2003 outbreak. Cloning and culturing of this potentially dangerous virus made up a large portion of her work, for which she spent four years at the University of Bonn, Germany, with Professor Christian Drosten, a world-renowned coronavirus expert.

She subsequently joined SU's Division of Medical Virology for a post-doctoral research fellowship hosted by Professor Wolfgang Preiser. There, she researched coronaviruses found in bats and their potential transmission to humans while also managing the division's BSL-3 lab. As of this year, Dr. Suliman had begun to expand her virology experience to the field of influenza viruses in the Shaw Lab, when COVID-19 took everyone by surprise.

"Since I have worked extensively with SARS-CoV during the 2002/3 outbreak, and given the similarities between SARS-CoV-1 and -2, I was already familiar with what other non-virologists and virologists outside of coronavirology may need time to figure out," Suliman says. "And with a pandemic like this, time is of the essence."

Lockdown in the Lab: Working With a Live Killer

On 11 March 2020 coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO), a week after the first infection with SARS-CoV-2—the virus that causes COVID-19—had been diagnosed in South Africa. Two weeks later, South Africa entered a national lockdown to attempt to flatten the curve, with stay-at-home orders for all non-essential personnel.

That's when Dr. Suliman emailed an inundated Prof Preiser, saying, "Prof, you know what I can do. Do you need help?"

One of the greatest limitations in growing SARS-CoV-2 is the absolute requirement of a BSL-3 lab, and the scarcity of these labs and trained personnel throughout the country. In South Africa, most BSL-3 labs lack the setup for dealing with respiratory viruses, as they are often directed towards tuberculosis, which is caused by bacteria.

Dr. Suliman is the only known South African who has ever grown a BSL-3 coronavirus, and is arguably the best-trained person to undertake the isolation of the virus responsible for COVID-19, so it was an obvious decision for her to take on this task. She is now training other scientists from the University of Cape Town.

"It was scary at first," Dr. Suliman says. "I was acutely aware that all it would take is a suit malfunction and a badly timed mishap to become infected. But with training and regularly working in the BSL-3 lab, an automatic sense of hyper-alertness develops. You get used to it."

Access to the workspace of the BSL-3 is via through three doors in succession—each preparing researchers for the next phase. The multiple doors, together with negative-pressure outward airflow, prevent any aerosols from escaping into general spaces.

"After the first door closes behind you when entering the BSL3, the door to stage 2 is released—a room where protective gear is worn: two pairs of gloves, boots, a back-closing gown or overalls, sleeve covers, and my personal favorite, the powered respirator that filters the air you inhale," Dr. Suliman says. "The battery pack and filter are worn around the waist, and a pipe connects it to the headpiece that fits snugly around the head and face. You are now ready to enter the third door to slay coronaviruses."

And slay them she did. "I worked day and night, and struggled with the lack of some essential materials, because by then, South Africa had entered lockdown and there were airfreight bottlenecks," Suliman recalls. "Finally, two weeks after I began, I looked through the microscope and saw dead cells—a sign that my virus was growing. I sat smiling in that isolated high-security lab, with only the whirring of the respirator to punctuate the silence, as I considered the potential of what I held in my hands."

The team has already begun sharing the isolate with multiple researchers and institutions for diagnostic and research purposes. They're also sharing their expertise with TB research groups, who have the infrastructure to study respiratory infections on a molecular and clinical scale, but are not skilled in handling a virus of this nature.

"This disease is very new, and despite amazing progress on many fronts, so much is still unknown. So new aspects emerge every single day, and that's why it's so important that we conduct as much research as we can," Prof Preiser says. "Because of the urgency, much of what normally happens behind the scenes is playing out in the open, and it may feel overwhelming. But this is a wonderful example of how we can work together to achieve what anyone on their own would not have been able to—and in a time of great need. That's something to be proud of."

Provided by Stellenbosch University South Africa