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MEDIA RELEASE

UP chemical pathology scientists develop groundbreaking nanobodies for COVID-19 detection and therapy

PRETORIA – Researchers at the University of Pretoria (UP) are producing unique nanobodies which could be of groundbreaking use in rapid testing for COVID-19 as well as a form of therapy for some diseases.

Nanobodies can be used to design "dipstick" tests to examine saliva and produce a result in a few minutes, much like a pregnancy test. These can be used in communities and homes for COVID-19 diagnosis. "They can also be used in an airport testing centre," says Professor Tahir (TS) Pillay, Head of National Health Laboratory Service (NHLS) Pathology and the Department of Chemical Pathology at UP, who is leading the research. "For example, before flying abroad, passengers can be tested, will get the result within 30 minutes and be allowed to check in or not."

Nanobodies are one-tenth the size of conventional antibodies, which makes them easier to work with while there is an urgent need for good, cheap and sensitive rapid tests for COVID-19, according to Prof Pillay. Currently, international airports such as Heathrow and airlines like Emirates are setting up testing centres, where they will use nucleic acid testing to identify people who might have COVID-19. Another potential test is serology, which tests for antibodies; this means if you have a high level of antibodies already, you are unlikely to be carrying the virus and are therefore considered safe to travel.

Yet another test is an antigen, which detects the virus by identifying its proteins. This type of test could be cheaper to produce on a mass scale if the sensitivity is good enough. "However, antigen detection tests are not widely used because their development has been more recent and the tests might not be sensitive enough," says Prof Pillay.

He explains that all these tests use conventional antibodies, which are temperature-sensitive (they need to be kept cold), are expensive to produce, and aren't as robust and sensitive as nanobodies. "None of them use a nanobody, which is a very stable antibody and resistant to temperature changes over a wide range."

Prof Pillay has started collaborating with a Taiwanese company to build a microchip with the nanobody on the surface for an electronic biosensor for COVID-19. "This will be used to create a handheld device that could be used at an airport, for example, and would use saliva." A major advantage of nanobodies is that they are heat-stable and do not require refrigeration, so they can be easily transported.

Prof Pillay explains that nanobodies were originally discovered in the camel family as well as in sharks. Conventional antibodies (such as those used in monoclonal antibody therapy) are employed in the treatment of a variety of diseases, from cancer to inflammatory disease, but the production costs make them expensive and many are not available in South Africa.

In terms of using nanobodies as a therapy, Prof Pillay explains that "a nanobody can be produced to act against any protein antigen if you have enough of the protein". Alpacas are immunised with the

protein and the gene for the nanobody is isolated from the animal's blood. In the case of COVID-19, any of the viral proteins can be used.

"In our case, the spike protein is the specific protein antigen, which is the basis for the current COVID-19 vaccine being tested in South Africa. The idea behind the vaccine is to stimulate the body to produce antibodies against the spike protein, enabling it to block the virus from entering cells, which causes the infection." The nanobody will prevent viral particles from binding to cells. In the case of COVID-19, the nanobody can be delivered via inhalation into the lungs or intravenously. "We have been working with nanobodies to develop cheap diagnostic tests in pathology, but with the pandemic, we have focused on SARS-CoV-2."

If it is administered intravenously, it could work similarly to plasma therapy, says Prof Pillay. The difference is that nanobodies can be produced at a much lower cost and in high concentrations, and there is no limit on its production. Plasma therapy is being touted as the next big thing in South Africa and in the United States, but it requires people to become sick with COVID-19, then recover before donating plasma if they have high enough levels of antibodies. "These antibodies do not last long, so donations will dry out. Extracting them is cumbersome and expensive for the blood transfusion service," Prof Pillay explains. "Nanobodies can replace these and will be in unlimited supply because we have the gene that makes them."

However, all human-derived products carry the risk of infection. Therefore, an artificially produced antibody has much greater potential and will be much cheaper to produce, notes Prof Pillay.

His team has also identified four novel chemical compounds against one of the main COVID-19 enzymes. "We use computer models to find new drugs based on the three-dimensional structure of a protein. As we have seen with other viral diseases, like HIV, many drugs that are effective work by inhibiting enzymes in the virus. In the case of SARS-CoV-2, in collaboration with the University of Manchester, we used the main protease (a protein degrading enzyme) of SARS-CoV-2 to fish out compounds from a large compound library. This was done in partnership with Dr Ataul Islam, who worked with me as a postdoctoral fellow at UP. These compounds will be tested in viral cultures in collaboration with other institutions in South Africa."

Caption 1: UP's Prof Tahir (TS) Pillay with an analysis of bacterial cultures expressing the nanobody proteins.
Caption 2: UP's Prof Tahir (TS) Pillay with a protein analysis of one of the nanobodies where the proteins have been stained with a blue dye.

SM (FB, LI, TW + IG if we have an interesting pic – even if it's an interesting shutterstock pic)

ANTIBODY ADVANCEMENT: UP's Prof TS Pillay and his team are producing unique nanobodies that could be of groundbreaking use in rapid tests for COVID-19. Nanobodies can be used to design "dipstick" tests to test saliva and produce a result within a few minutes, much like a pregnancy test. These can be used in communities and homes for COVID-19 diagnosis. "They can also be used in an airport testing centre," says Prof Pillay. "So before flying abroad, passengers can be tested, will get the result within 30 minutes and be allowed to check in or not." Read more:

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ABOUT THE UNIVERSITY OF PRETORIA

The University of Pretoria (UP) is one of the largest contact and residential universities in South Africa, with its administration offices located on the Hatfield Campus, Pretoria. This 112-year-old institution is also the largest producer of research in South Africa.

Spread over seven campuses, it has nine faculties and a business school, the Gordon Institute of Business Science (GIBS). It is the only university in the country that has a Faculty of Veterinary Science which is ranked top in Africa, and overall has 120 academic departments, as well as 92 centres and institutes, accommodating more than 55 000 students and offering about 1 100 study programmes.

UP is one of the top five universities in South Africa, according to the 2019-2020 rankings by the Center for World University Rankings. It is also ranked among the top 100 universities worldwide in three fields of study (veterinary science, theology and law), and among the top 1% in eight fields of study (agricultural sciences, clinical medicine, engineering, environment/ecology, immunology, microbiology, plant and animal sciences and social sciences).

In June 2019, the annual UK Financial Times Executive Education Rankings once again ranked GIBS as the top South African and African business school. The University also has an extensive community engagement programme with approximately 33 000 students involved in community upliftment. Furthermore, UP is building considerable capacities and strengths for the Fourth Industrial Revolution by preparing students for the world beyond university and offering work-readiness and entrepreneurship training to its students.

As one of South Africa's research-intensive universities, UP launched the *Future Africa Campus* in March 2019 as a hub for inter- and transdisciplinary research networks within UP and the global research community to maximise 4IR innovation and address the challenges and stresses our continent and world is facing. In addition UP also launched the Javett Art Centre in September 2019 as a driver of transdisciplinary research development between the Humanities and other faculties. In 2020 UP will launch Engineering 4.0. as a hub not only for Smart Cities and Transport, but also to link the vast resources in technology and data sciences to other faculties via Future Africa. These initiatives are stimulating new thinking at the frontier of 'science for transformation'.

For more information, go to www.up.ac.za