Building a Better Covid-19 Antibody Test

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COMPANIES MENTIONED

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ProMIS is harnessing its unique technology platform to develop a more error-free antibody test.

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Testing has been an Achilles heel of the coronavirus pandemic, butProMIS Neurosciences Inc. (PMN:TSX; ARFXF:OTCQB) has partnered with Dr. Hans Frykman and the BC Neuroimmunology Lab to use its unique technology to create a more accurate antibody test for SARS-CoV-2, the virus that causes Covid-19.

Two main types of tests exist for Covid-19: one that detects the presence of the virus that causes Covid-19, which indicates a person has an active infection, and another that detects antibodies, showing that a person has been exposed to the virus.

The first test that was developed, a test for the presence of the virus, is used mainly to confirm diagnosis of Covid-19 in people who are showing symptoms such as a fever, a dry, persistent cough, difficulty breathing, a sense of restriction in the chest. "They are typical signs of Covid-19, but we would want to know if these are signs of the common flu or a bad cold or Covid-19. We know that Covid can progress really significantly very quickly, especially in individuals with underlying conditions," ProMIS CEO Dr. Elliot Goldstein told Streetwise Reports. "The number of tests is limited, but it's not actually the tests themselves but the reagents and systems you need to run the test that are in short supply."

"Anytime you conduct a test for the virus and get a negative response, the test indicates only that on that day at that time, the person does not have the virus. The person could have had Covid and recovered, or might have had an asymptomatic or very mild case. Or that person could get the virus tomorrow or in three days," Dr. Goldstein explained. "At any point in time the virus test helps indicate the prevalence of the virus—how many people are actually infected—if you test broadly, and at the time you do it, you can determine whether an individual is currently infected or not."

The second type of test, called serological tests or assays, is also known as an antibody test. "When a person is recovering from a viral infection, the immune system makes antibodies—also called immunoglobulins—that are specific to the virus. They neutralize the virus and help clear it out; that's part of the mechanism of why you get better," Dr. Goldstein explained.

One way to see if a person has had Covid is to test for antibodies. "A positive test means you've been exposed to the virus because, in the absence of a vaccine, that's the only way you would have the antibodies. While it's not 100% certain that antibodies neutralize the virus, based on experience with other coronaviruses, it is likely," Dr. Goldstein said. Having the virus neutralized should offer at least some protection against future re-infections.

People who have had positive virus tests know that they have Covid or had Covid and recovered, but many people are asymptomatic or may have had what felt like a light cold, and they want to know if they are at risk, or if they have some protection against the disease. "This is really important for frontline healthcare workers, people working 8-10 hours a day in intensive care or the emergency room with patients known to be very sick with Covid-19; even with protective equipment, they have significant exposure to the virus," Dr. Goldstein explained. "If someone has been through the disease and has natural antibodies, they can't infect someone else. What you want to know on an individual level is am I safe from infection and

am I safe for other people."

Generally, antibody testing is a fairly common procedure, Dr. Goldstein explained. When you spin blood in a centrifuge, it separates into three parts: red blood cells, plasma and serum. Serum is where you find antibodies. "ELISA (enzyme-linked immunosorbent assay) is a standard test that looks for antibodies, but it is not specific enough for the Covid-19 virus."

The challenge is there are multiple coronaviruses. "Four different coronaviruses are responsible for the common cold, and then there are others like SARS and MERS. They all have the same sort of halo or corona of protein around the outside of it," Dr. Goldstein said. "They look like the old naval mines used in war. The whole family of coronaviruses look like that. The amino acid sequences of different coronaviruses are not identical but very similar; they share a lot of common structures. There are only really small differences and you can't really pick them up using the usual physical methods."

Studies have shown that up to 90% of individuals in Western countries have been exposed to one or more of the common cold coronaviruses and have antibodies against them. "They look very similar to the coronavirus causing Covid-19. So in Covid-19 antibody tests, the most important thing is it has to be highly specific for the Covid-19 antibodies and doesn't test positive when it identifies a common cold antibody. That is a false positive," said Dr. Goldstein. "It's actually much safer not to have a test that has a lot of false positives because you could base a behavioral decision on faulty information."

Dr. Goldstein cited an example. "If you are testing 1,000 people and there is a 90% prevalence for the cold virus, that means around 900 people have antibodies to the common cold. If the prevalence of the Covid-19 virus is 2%, roughly 20 of the 1,000 would have antibodies to the Covid-19 virus. Let's say the serology test has 95% specificity. That means five times out of 100, it will give a false positive, indicating the presence of Covid-19 antibodies when it is really picking up antibodies against the cold virus. What this means is 5% of 900, or 45 people, will test positive for Covid when they have not had it, and are making decisions based on incorrect information. The consequences of being wrong are dramatic and highlight the need for a very good, high-quality serological test."

How does this relate to Alzheimer's and other neurological diseases that are ProMIS' core competency? "In Alzheimer's, ALS, frontotemporal dementia, Parkinson's disease and other neurological disease, we've been able to use our proprietary, unique technology to identify sites on misfolded proteins that are driving these diseases. Our core technology is the capability to understand what's special about the bad proteins that are causing these diseases and then we can make antibodies highly selective against them. Our technology allows us to identify a region, an epitopes target, which is a series of four to six amino acids where the protein has misfolded. Not only do we know where this target site is located, importantly we also determine the shape (conformation) of this site. Proteins like amyloid and alpha synuclein and TDP 43 misfold and when these proteins misfold they become toxic, they kill neurons, resulting in disease," Dr. Goldstein explained.

ProMIS has transferred that thinking to the virus causing Covid-19. "The corona is composed of the spiky protein. Remember, we want to be able to distinguish between the coronavirus causing the common cold and the coronavirus causing Covid-19," Dr. Goldstein said. "If we can distinguish between the two, we can have an antibody test that's specific for Covid-19. We are looking at a region of the virus called the receptor binding domain, the RBD, that is part of the spike protein and how it attaches to cells. We have a core competency that allows us to identify sites, and not just the location of the sites, but the shape of the sites on complex protein molecules. That allows us then to use that knowledge to create either antibodies or to create serum tests, or even quite frankly, we can use those targets to create vaccines."

Using ProMIS' proprietary technology, the company has been able to "identify a site that we believe is only present on the Covid-19 virus and not on other

coronaviruses. We are now initiating the synthesis of several different forms of that site; it's a small area," Dr. Goldstein stated. "That would then transfer to Dr. Hans Frykman's lab at University of British Columbia, a world-class serology lab. Then we will see if the targets we've identified are specific and selective antibodies against Covid-19."

When you test the serum of an individual, if they've been exposed to the virus and have the antibodies, "those antibodies should bind selectively and specifically to the target. So if the antibodies from the patient's serum are binding to the target site, we know it's a Covid-19 virus because that site is only visible in that shape on the Covid-19 virus and not the others. For the validation of our test, only in patients known to have had Covid-19 should we see binding of antibodies against Covid-19 to our target. The second validation is based on testing in serum from subjects known to have never been exposed to Covid-19 virus—such subjects have antibodies only from cold or other coronaviruses, and therefore the antibody test should be negative; there should be no binding. So we should only see binding in serum from a patient known to have recovered from COVID-19, and we should not see binding in serum from an individual known not to have been exposed to COVID-19," Dr. Goldstein explained.

"Our technology basically allows us to zero in with sniper-like precision on the structure of a protein and understand it, not only the structure overall but the shape of the regions on that protein and then that allows us to identify what is specific to that protein, in this case the spiky protein on the virus causing COVID-19," said Dr. Goldstein.

ProMIS expects to have initial results in June.

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