

Territory Pathology is Combatting COVID-19 in Rural Australia with NGS

The public health laboratory is using Illumina's COVIDSeq™ Assay to sequence the virus and track variants in the country's Northern Territory.



DIMITRI MENOUGHOS IS THE MOLECULAR BIOLOGY SUPERVISING SCIENTIST AT TERRITORY PATHOLOGY.

Introduction

Since the pandemic began two years ago, the world has witnessed over 486 million confirmed cases of COVID-19 and more than 6.1 million deaths, according to the World Health Organization. Nations are still trying to control the coronavirus within their borders, conducting genomic surveillance and tracking variants have become a vital part of that effort. But sequencing COVID-19 cases is not always possible, especially in more remote, underserved areas that lack the technology and expertise — these areas must often send their samples elsewhere or forego genomic sequencing altogether.

Now, a public health lab has brought Illumina's next-generation sequencing (NGS) technology to rural Australia in an effort to combat the virus there. The lab, Territory Pathology, serves the Australia's Northern Territory and its staff performs all kinds of testing, including for infectious diseases like syphilis and gonorrhea. Over the past two years, the lab has handled much of the territory's coronavirus testing. Initially, Territory Pathology performed only PCR tests for COVID-19. Without access to sequencing technology, it had to send samples all the way to a Melbourne lab for genomic sequencing. But now, with Illumina technology on hand, Territory Pathology has been able to expand its COVID-19 testing capacity. "The genomic epidemiology of SARS-CoV-2 was found to be very critical," says Dimitri Menouhos, the Molecular Biology Supervising Scientist at Territory Pathology. "There was information to be given to public health organisations for responses regarding COVID-19 and lockdowns, lockouts, disease progression, and more. So we began genomic testing of SARS-CoV-2."

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In September 2021, Territory Pathology staff received training on the sequencing equipment and software from Illumina’s Field Application Scientist, and began generating SARS-COV-2 sequencing results right away. Menouhos sees NGS technology as a huge opportunity, and not just for the lab’s COVID-19 work. “Down the track, we are also going to be providing results for human genetics,” he says, “It opened up this whole new field for us. That’s what I say now—the sky is the limit for what we can do thanks to having this method and platform.”

iCommunity spoke with Dimitri Menouhos about Territory Pathology’s work on COVID-19 and other infectious diseases, the lab’s experience with Illumina’s end-to-end COVIDSeq™ Assay workflow and customer support during the pandemic, and why decentralised pathogen genomic surveillance is critical, particularly in remote areas like the Northern Territory.

Q: What services does Territory Pathology provide?

Dimitri Menouhos (DM): We are a public health laboratory, and we are the main pathology lab for the Northern Territory in Australia. We perform tests, not only for infectious diseases but also for hematology, biochemistry, and more. But primarily in our laboratory, we look for infectious diseases: hepatitis A, B, C, as well as *Neisseria meningitidis*, *Neisseria gonorrhoeae*, syphilis, and many other infectious diseases.

The Northern Territory is a substantial part of the country, and it includes a large rural area. Because of that, access to health services is difficult for people living in the Northern Territory. Sometimes we receive a sample to test as much as two days after it’s been collected. That’s how far out people live.



Q: What is decentralised pathogen surveillance and why is it important?

DM: Previously, because Territory Pathology did not have the capacity to perform sequencing, there were certain diseases that we had to send out for sequencing. We were just diagnosing patients with a positive case of a particular pathogen, and then in order to figure out what strain it was or if there was antimicrobial resistance, we had to refer it to another state. With influenza A, for example, we had to refer our samples to the WHO lab in Melbourne where they perform sequencing. *Neisseria gonorrhoeae* and *Neisseria meningitidis*, all these pathogens had to be referred elsewhere for sequencing the positive test results. But now, with the use of the Illumina sequencer, we are able to offer additional services locally, which is the targeted or decentralised pathogen surveillance.

Q: What work is Territory Pathology doing with COVID-19?

DM: Initially, we started off just performing real-time PCR tests for COVID-19. Our first PCR test was an in-house assay that we had. But then it turned out to be too laborious, so we moved on to diagnostic panels offered by another company called AusDiagnostics. And after that, the genomic epidemiology of SARS-COV-2 was found to be very critical. There was information to be given to public health for responses regarding COVID-19 and lockdowns, lockouts, disease progression, and more. So we began genomic testing of COVID-19 cases. We did have certain hurdles to overcome—the very first one was the actual platform. We didn't have a platform to perform sequencing on COVID-19 samples, and that's when Illumina came into the picture.

So we started off with just COVID-19 diagnosis, and we still do that today. Then through the use of sequencing, we are also providing epidemiological information with the genomic makeup of SARS-CoV-2—the strains and knowing which ones are linked to a given case of COVID-19.

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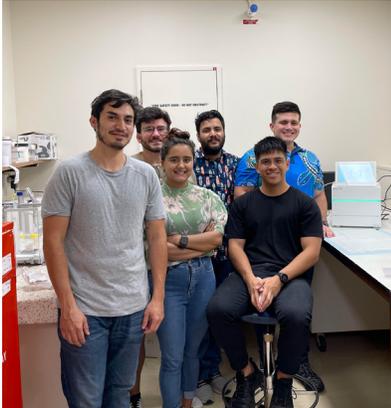
Q: What motivated Territory Pathology to set up a sequencing facility and what did that decision-making process look like?

DM: Initially, it was a mandate from the Australian Commonwealth government and the Northern Territory government that we provide genomic and epidemiological information for SARS-CoV-2. Until then, we didn't have a sequencer at Territory Pathology, or even in the Northern Territory. So, it was decided that a sequencer would be provided to us by the Doherty Institute.

We had to get the sequencer into Territory Pathology and then have staff members trained on it. We also had to increase the number of staff members in order to perform sequencing at a faster rate. As I mentioned, prior to all this, we had to refer any positive cases for COVID-19 detected at Territory Pathology to a referral lab in Melbourne. They performed the sequencing and provided the epidemiological information. But because the referral lab is responsible for all of Australia's SARS-CoV-2 sequencing, the turnaround time on tests increased. Initially, it took about 72 hours to get results back. But then because of rising COVID-19 cases and the lockdowns in Melbourne and Sydney, the turnaround time became 7 days or even 10 days. Naturally, we cannot wait such a long time for results. That was a big reason why we purchased the iSeq™ 100 system and brought sequencing capacity here to the Northern Territory.

Q: What other challenges did you encounter during the pandemic with the outsourcing model?

DM: The other issue that we had, as I mentioned, was staff member numbers. We had to allocate maybe two or three staff members to perform the send-away test (as we call it) to refer those samples. So we were running low on staff resources. There was also the associated cost of referring samples, which was much greater than the cost of performing the test locally.



Q: What was the level of NGS expertise of the lab staff when the sequencing facility was first set up?

DM: Out of all our lab staff members, the only person who had actually some prior experience with NGS was myself, due to my Honors project and my current Master's program. Other staff members had an idea of what NGS is because of their university studies or by reading research articles—but that was it. There wasn't another staff member who had previous experience with NGS or sequencing at all.

Q: How would you rate your onboarding experience with the Illumina team? What was your experience like?

DM: It was wonderful. All our questions were answered directly and immediately. In particular with Gavin Wilkie, Illumina's Field Application Scientist, who came up to Darwin and trained us all. It was quite a hurdle because of the infrastructure that we had—we didn't have a designated area for the sequencer, so Gavin told us the requirements we needed to meet. We just followed that list, found an area in Pathology, and he helped us set everything up. It was also great that Illumina provided us with the Lab-in-a-Box that they have.

There have been certain instances where, for example, the iSeq 100 connections timed out and I couldn't start a sequencing run. I immediately got on the phone and talked to Illumina's Technical Support staff; within an hour they were able to solve the issue and also guide me through steps of how to fix it myself. I'm in a rural area of Australia, which means generally it's not always possible to send an engineer to help us out. So I'd say the experience with Illumina has been great. Ten out of ten.

Q: How long did it take for you to start generating SARS-CoV-2 genome data and providing SARS-CoV-2 genome sequencing services to Northern Territory after you completed the first technical training delivered by the Field Application Scientist?

DM: The very next day. And from that moment to today, we might have had only one week of break when we were not generating SARS-CoV-2 sequencing results.

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Q: What do you like about the COVIDSeq Assay workflow and the DRAGEN™ COVID Lineage App?

DM: For the COVIDSeq Assay workflow, I adore its simplicity compared to other sequencing methods that I've used. It's simple. The instructions are very straightforward. It's very, very hard to make a mistake. I also love the fact that there are certain areas in the protocol where you can just stop and freeze the products for maybe two or three days (or even 30 days in certain parts of the protocol). This is very important because with the SARS-CoV-2 sequencing workload being so high, all our scientists are quite tired. It's very important to have the ability to take a break and resume a couple hours later or even the following day.

For the BaseSpace™ Sequence Hub and DRAGEN COVID Lineage app, I think it's probably one of the best online softwares out there for SARS-CoV-2 genomic surveillance and also in general for other applications because it streamlines the process. Even those who don't have any prior knowledge of bioinformatics—which is the case for some of my own staff members—are still able to use BaseSpace and the DRAGEN COVID Lineage App, and generate appropriate results for SARS-CoV-2 sequencing.

Q: What impact has insourcing genome sequencing capabilities had on the ability of Territory Pathology to support the COVID-19 pandemic response in the Northern Territory?

DM: Basically, the SARS-CoV-2 genomic data we generated are critical for the Northern Territory's public health response. It's very useful for tracing strains within the Northern Territory. We have a lot of rural communities and we've witnessed cases of COVID-19 from interstate travelers—some of them were linked to the rural communities, but others were not. It's very important for us to have the ability to figure out which SARS-CoV-2 strain is related to a COVID-19 cluster in a rural community. So definitely, it has had a big impact on the public health response.

Q: Can you share some examples of how genomic sequencing data was used to support COVID-19 management and pandemic response in Northern Territory?

DM: During the recent lockdown about two months ago, we used SARS-CoV-2 sequencing to relate COVID-19 clusters that we were seeing in rural communities. Another example was when the World Health Organization announced Omicron as a variant of concern on November 26th. Then, on November 28th, we detected a case of Omicron thanks to the sequencing capability that we had here. I believe we were the second state in Australia to report the Omicron variant.

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Q: With Australia ramping up vaccination efforts and adapting to an era of endemic COVID-19, what do you think the next phase of SARS-CoV-2 genomic surveillance efforts will look like?

DM: It's quite hard to predict this disease with the many strains and variants it has, and that it will likely continue to have. I believe we will follow a similar pattern to what we are currently doing. We will still follow through with the positive cases we detect and make sure we are detecting and reporting any new variants, and also see whether there's a link between clusters or not. I think that's what we'll do over the next few months and probably the year to follow. But again, it's an unpredictable virus.

Q: What is your vision for enhancing or expanding your service offerings in the future, by leveraging the NGS expertise of Territory Pathology?

DM: Because of the increasing workload with COVID-19, once again, I'm looking forward to purchasing a MiSeq™ and a NextSeq™ 2000 sequencer from Illumina. We have also had discussions with our hematology department—they would like to bring on board some of the myeloid panels that Illumina offers. We are looking at possibly establishing a genetics laboratory where you can offer both infectious disease genetic testing and human genetic testing. That's what we envision establishing in the next year or two.

Q: With the experience gained supporting SARS-CoV-2 genomic surveillance, what role will Territory Pathology play in Australia's national public health pathogen genomic surveillance going forward?

DM: I think we'll just retain our current position as we are the main lab in the Northern Territory, and also the only laboratory in the Northern Territory that can perform SARS-CoV-2 sequencing. All the Northern Territory epidemiological data that's submitted to Melbourne will come from Territory Pathology—there won't be anyone else providing the Northern Territory data to them.

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Q: Territory Pathology has had to change and adapt during the pandemic—how will that influence its work with other diseases in the future?

DM: I believe it will, in particular with *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, and *Neisseria meningitidis*. We'll start performing sequencing on these pathogens quite soon, whereas before we weren't able to and we had to refer them. Once the COVID-19 situation calms down and life returns to some sort of normality, we'll be able to focus on other pathogens as well and provide a better service for the diagnosis and genomic epidemiology of them. For example, we'll be able to detect if there are any new strains present for a pathogen, and we'll be able to detect antimicrobial resistance genes much faster and more reliably.

Q: Can you share a memorable experience you had while supporting COVID-19 surveillance?

DM: The Omicron variant is an interesting story. It happened on November 27th 2021—which was my birthday weekend, actually. I had planned to go on a fishing trip, but I received a phone call from our manager and he told me there was a possible case of Omicron. They wanted to sequence it as it had come from a South African flight, I was already on the fishing boat, but I decided to turn the boat around. Once I got to shore, I jumped off the boat, ran to the car, drove to the lab, and started sequencing. It was quite hectic.

It wasn't exactly the way that I wanted to spend my birthday, but I'm happy I did it because we were one of the very first labs to sequence the Omicron variant in Australia, and it was a good experience. There are certain moments when you have to make sacrifices to provide a better service to the public, and this was one of those moments.

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