

Strong science foundation key to Singapore's Covid-19 efforts

Swift response to pandemic builds on broad base of capabilities built up over years: NRF

Cheryl Tan

Even before Singapore's first Covid-19 case was detected on Jan 23, the local research community was moving to pivot quickly to Covid-19 research, developing a response on all fronts: from manufacturing test swabs to building the country's testing arsenal. This was possible only because of a strong foundation in science. Said Professor Low Teck Seng,

chief executive of the National Research Foundation (NRF): "Our national response to Covid-19 builds on the broad base of scientific capabilities that Singapore has built up over the years." He added: "For instance, our capabilities in infectious diseases and diagnostic test kit development have supported our national testing and virus surveillance efforts. "This has enabled the RIE (research, innovation and enterprise) community to swiftly pivot and scale up its response as needed."

To support research efforts, the Ministry of Health and NRF launched a \$45 million Covid-19 research fund under the RIE plan for this year. It has gone towards research areas such as the modelling of viral transmission, developing novel therapies and translating research outcomes into products and solutions. Singapore's efforts have paid off. A vaccine is now in the pipeline, with the first shipments expected in the first quarter of next year. Dubbed Lunar-Cov19, it is co-developed by Duke-NUS Medical School and American pharmaceutical firm Arcturus Therapeutics. Preliminary findings from early-stage trials indicate positive re-

sponses in both safety and human immune response. So far, no serious side effects have been observed, and phase three clinical trials should start this month. As at the end of last month, local researchers have contributed more than 1,100 scientific publications to an international pool of knowledge on Covid-19, with research beginning as early as in January. Duke-NUS Medical School announced on Jan 30 that its team of scientists had successfully cultured the virus from an infected patient's sample, making the Republic the third country in the world outside of China to do so. In February, the first made-in-Singapore diagnostic kit, Fortitude,

which can detect the Covid-19 virus with high accuracy, was rolled out locally. It is now in use at 13 hospitals and laboratories here, as well as internationally. Other scientists, too, have pivoted from their areas of expertise to develop diagnostic test kits. Professor Peter Preiser, associate vice-president for biomedical and life sciences at Nanyang Technological University, redeployed his platform technology, initially used to differentiate between types of malaria parasites, to detect proteins produced by the Sars-CoV-2 virus. This helped him develop two test kits: an antigen rapid test and a serology test.

To meet local testing demands, researchers from the National University of Singapore linked up with Temasek Foundation and produced three different swab designs through 3D printing and injection moulding. A total of 7.5 million 3D-printed swabs and around five million injection-moulded swabs have been produced this year. The team is on track to meet the demand for 60 million injection-moulded swabs, which they will deliver throughout next year. Therapeutics research into Covid-19 is also showing promising results. Last Friday, local biotechnology company Tychan announced that it is conducting the final phase of clinical trials for its antibody T027, which could help Covid-19 patients recover faster. Even as work continues at full throttle, more is being planned. Part of a \$25 billion RIE plan for the country over the next five years includes investment in a national effort to guard against future threats from infectious diseases.

tansuwen@sph.com.sg

Research efforts on Covid-19

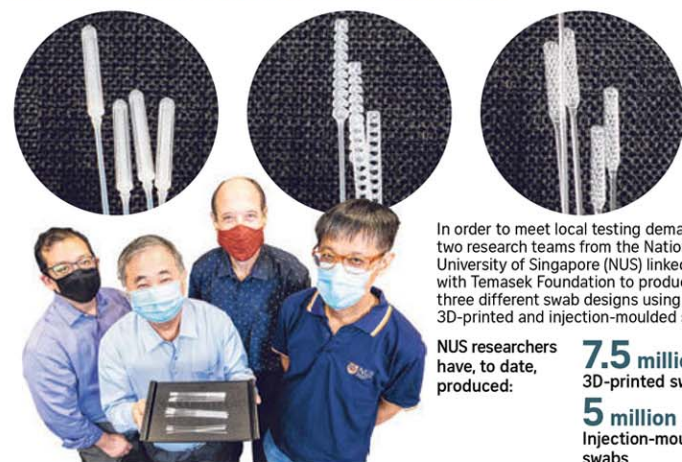
Local researchers have played a critical role in Singapore's response to Covid-19 by contributing to a pool of international knowledge on the virus, developing novel test kits and therapeutics to combat Covid-19, and beginning trials on our own vaccine. Cheryl Tan and Shabana Begum highlight some of these contributions.

\$45 million Covid-19 Research Fund set up by the National Research Foundation (NRF) and the Health Ministry to support research in areas such as developing novel therapies and translating research into products and solutions

\$40 million dedicated to the National Innovation Challenge, co-organised by Enterprise Singapore, the Infocomm Media Development Authority and NRF to accelerate innovation efforts and overcome challenges in the post Covid-19 world

>1,100 Peer-reviewed papers that scientists in Singapore have published on Covid-19 (as at end-November)
156 Covid-19 test kits* that have been given provisional authorisation by the Health Sciences Authority (HSA)
NOTE: *Including PCR tests, antigen rapid tests and antibody tests.

3D-PRINTED AND INJECTION-MOULDED SWABS



In order to meet local testing demands, two research teams from the National University of Singapore (NUS) linked up with Temasek Foundation to produce three different swab designs using 3D-printed and injection-moulded swabs.

NUS researchers have, to date, produced:
7.5 million 3D-printed swabs
5 million Injection-moulded swabs

DEVELOPED COVID-19 TEST-KITS FOR LOCAL USE

HSA has given provisional authorisation to 156 test kits, including polymerase chain reaction (PCR) tests, antigen rapid tests and antibody tests.

Fortitude (Feb 8)

- First made-in-Singapore diagnostic test, which is able to detect the coronavirus with high accuracy.
- Since February, the kit has been deployed in 13 hospitals and labs locally, as well as more than 20 countries globally.
- It comprises a pre-packed mix of reagents to test patient samples, which are then fed into a PCR machine to analyse the results.



Resolute 2.0 Test Kit (July 18)

- PCR test co-developed by DSO National Laboratories and the Agency for Science, Technology and Research (A*Star) which can cut Covid-19 testing time by half (it usually takes around four hours).
- Takes about 60 to 90 minutes to get test results.



Serology Test

cPass Test to detect neutralising antibodies

- First of its kind to receive approval from the United States' Food and Drug Administration.
- Developed by Professor Wang Linfa, director of Duke-NUS' emerging infectious diseases programme, GenScript Biotech Corporation and the A*Star's Diagnostics Development Hub.
- The neutralising antibodies are thought to be preventing the coronavirus from entering the patient's cells.
- Can be used to see if vaccines are working, to check what proportion of the population has already been infected, and to assist in contact tracing.
- Can yield results within an hour.



THERAPEUTICS

MONOCLONAL ANTIBODIES

Monoclonal antibodies are immune system proteins created in the laboratory, and are specifically engineered to neutralise Sars-CoV-2, the virus causing Covid-19.

DSO National Laboratories

- Announced the discovery of five antibodies which could neutralise Covid-19, after screening antibodies from recovered patients.
- Currently working with the Experimental Drug Development Centre in the pre-clinical and clinical development of AOD01, the most promising antibody of the five.
- Antibodies from a recovered patient would stay in one's system for a month, and would help the patient to fight the infection and recover faster.



Tychan

- Currently conducting clinical trials for the final phase of its drug, an immune system protein known as TY027, after it received approval from HSA in October.
- T027 is being tested for its ability to slow down the progression of the disease and confer temporary protection against infection.
- The trial, which began last Friday, will involve 1,305 volunteers.



A*Star and Chugai Pharmabody Research in Japan

- Developing therapeutic antibodies which bind to the virus, preventing it from attacking human cells.
- They are researching this for clinical use (since May).



LUNAR-COV19 VACCINE

mRNA vaccine developed by Duke-NUS Medical School and Arcturus Therapeutics is currently undergoing clinical trials and may be available early next year. Economic Development Board pumping in some US\$45 million (S\$60 million) into the manufacture of the vaccine.

- Around 106 volunteers enrolled in the early-stage trials observed antibody and T-cell response, with no adverse side effects that were deemed to be treatment-related.

How it works

- Delivers the spike gene of Sars-CoV-2, the cause of Covid-19, in the form of RNA or ribonucleic acid.
- This allows the body to recognise and fight the virus should it try to infect the person.

PHOTOS: KELVIN CHING, NUS, A*STAR, DSO NATIONAL LABORATORIES, GENSCRIPT BIOTECH CORPORATION STRAITS TIMES GRAPHICS

TOP PICKS

Out of the 1,100 publications, here are three noteworthy ones:

1 Serological investigation of the Covid-19 infection

Primarily led by Wang Linfa

- Using serology tests, the study showed links between three clusters of Covid-19, comprising 28 locally transmitted cases.
- They were from two churches and a family gathering.
- An individual from Church A had transmitted the virus to a primary case from Church B at a family gathering they both attended.
- All tested positive for Covid-19 except individual A, who had recovered and tested negative. The individual was diagnosed with past infection using serology testing.

2 Interventions to mitigate early spread of Covid-19 in Singapore

Using modelling by Alex Cook

- Adapted an influenza epidemic simulation model to estimate the likelihood of Covid-19 transmission in Singapore.
- Took cumulative infections at 80 days, after detecting 100 cases of community transmission, under three infectivity scenarios, with 7.5 per cent of cases assumed asymptomatic.
- Ran a model with a range of intervention scenarios and found that quarantining infected individuals and their family members, workplace distancing and school closure once community transmission has been detected could significantly reduce the number of Covid-19 infections.

3 Singapore becomes the third country in the world outside of China to culture the Sars-CoV-2 virus

Researchers from Duke-NUS Medical School

- The team successfully cultured the coronavirus from an infected patient's sample, just four days after receiving the sample in late January, in the medical school's containment laboratory.
- Singapore becomes the third country in the world outside of China to culture the virus.
- On Jan 30, Duke-NUS said the cultured virus will be used for:

- Developing new diagnostic methods
- Monitoring potential mutation
- Testing for potential vaccine and drugs

• The research was done in collaboration with scientists from institutions such as the National Centre for Infectious Diseases, Singapore General Hospital and the Ministry of Health.

ScienceTalk

Covid-19 and the coming of age of Singapore science

ChangAi-Lien
Associate News Editor

The worst of times has brought out the best in people. Particularly so on the research front, where scientists in Singapore have made their mark on the world stage.

Biotech firm MirXES, for one, switched gears as early as January, working with the Agency for Science, Technology and Research and Tan Tock Seng Hospital to shift its expertise in cancer detection in another direction – to create kits that could sniff out the virus instead. With six years of experience under its belt producing PCR (poly-

merase chain reaction) tests, the company was able to come up with its Fortitude Covid-19 test kits within three weeks. Fast and highly accurate, the PCR tests are considered to be top of the line. With the support of Enterprise Singapore's Enterprise Development Grant, the company quickly scaled up production of kits to one

million per week through automation, and these have since been deployed in 45 countries. Likewise, hundreds of doctors, scientists and researchers from all fields have thrown their weight behind the battle against the virus – with efforts ranging from 3D printing of test swabs to creating the award-winning contact tracing programme TraceTogether, as



Professor Stephan Schuster says the virus crisis proves that scientists are able to move to new fields. PHOTO: NANYANG TECHNOLOGICAL UNIVERSITY

Stephan Schuster

Analysing air and surface samples to find virus traces

Audrey Tan
Science Correspondent

Professor Stephan Schuster is an environmental detective. Like his crime-solving counterparts, the professor at Nanyang Technological University's (NTU) School of Biological Sciences looks for what is unseen by the naked eye.

This has come in useful during the Covid-19 pandemic, as humanity battles an unseen foe.

His work involves taking samples from the air and surfaces, and analysing them to find traces of genetic material of organisms like viruses.

Both environments are ultra-low biomass environments, meaning each sample might have only a few micrograms of (genetic material), said Prof Schuster, who is also deputy centre director for facilities and capacities at NTU's Singapore Centre for Environmental Life Sciences Engineering.

"Nevertheless, the (genetic material) recovered from these sam-

ples is very complex, as they originate from many different microbial organisms," he said.

Prof Schuster and his colleagues got cracking. They found in a study pending publication that air pollution could result in negative outcomes for respiratory illnesses, including Covid-19.

The Straits Times had earlier reported that micro-organisms in the air measure between 0.5 and 10 microns and are likely to reach deep inside the lung tissue.

Those with pulmonary diseases may be unable to expel them out.

Prof Schuster said they could pivot during the outbreak because of the completion of a five-year research programme on the air microbiome, his skilled co-workers and the availability of tools like air samplers.

"This crisis has proven that scientists all over the world are able and willing to swiftly move to new fields and to apply their knowledge," he said.

audreyt@sph.com.sg



Associate Professor Tham Kwok Wai says tackling the Covid-19 outbreak requires researchers with various expertise. ST PHOTO: ARIFFIN JAMAR

Tham Kwok Wai

Fighting virus spread indoors with help of previous work

At the start of the Covid-19 outbreak, healthcare professionals and policymakers were stumped on many fronts. A key question was how the coronavirus had spread from human to human.

Researchers like National University of Singapore (NUS) Associate Professor Tham Kwok Wai leapt into action, tapping their previous work.

Prof Tham, who had researched the spread of viruses such as influenza in an indoor setting, found that the indoor environment was also a primary domain for transmission of the virus that causes Covid-19.

Because of his previous research, he knew there were measures that could control its spread indoors. For instance, increasing ventilation of a room will help to dilute the concentration of the virus in the air, reducing transmission risk. Safe distancing also works, as the viral load diminishes with distance from the infected person, he said.

Passing re-circulating air through high-efficiency filters can

help to remove viruses that usually "clump" together, said the professor from the NUS School of Design and Environment.

Before Covid-19, Prof Tham's research had focused on the impact of the indoor environment on humans, and on cooling and ventilation technologies for indoor environmental control.

"I began to see how I could apply my research on environmental intervention to Covid-19 at the onset of the pandemic, around December 2019," he said.

Prof Tham said tackling the outbreak requires researchers with various expertise.

Other than virology, for instance, knowledge in aerosol science or fluid mechanics could also help with better understanding of how expelled droplets could spread.

Prof Tham said: "This demonstrates a trans-disciplinary approach is essential in tackling the Covid-19 challenge holistically. And this constitutes the basis for policy formulation."

Audrey Tan



Professor Lim Chwee Teck with the portable polymerase chain reaction kit called Epidax. ST PHOTO: DESMOND WEE

Lim Chwee Teck

Developing a PCR test that can yield results in an hour

Shabana Begum

Professor Lim Chwee Teck has spent the bulk of his career developing microfluidic biomedical devices, which analyse tiny amounts of fluids to detect diseases such as cancer. But when the Covid-19 crisis was rapidly worsening early this year, he switched to Covid-19 diagnostics.

"We felt we had to do something despite the fact that we had not worked on flu viruses previously," said Prof Lim, director of the National University of Singapore's Institute for Health Innovation & Technology.

Since March, he and his team have developed a portable polymerase chain reaction (PCR) diagnostic system that can produce test results within an hour, and he is currently developing an antigen rapid test kit that can detect Covid-19 within 15 minutes.

The portable PCR kit, called Epidax, uses a specially designed microfluidic chip to process a

smaller amount of a nasal swab sample to detect Covid-19 faster.

A reagent is used to extract the ribonucleic acid (RNA) and amplify it on the chip so the PCR test can be done. "All these features significantly minimise sample handling and shorten the test and waiting time, so patients can get their test results in about an hour or less," said Prof Lim.

In conventional PCR tests, the nasal swabs are sent to a lab to extract the RNA before the test can be done. Those taking a conventional PCR test usually have to wait a day or two for their results.

So far, clinical tests with Epidax have shown 100 per cent accuracy in detecting Covid-19.

Prof Lim hopes that his faster and portable PCR system can be used for rapid screening and mass testing in places such as clinics, schools and offices.

The team has filed a patent for Epidax and licensed the technology to a local medical technology company.

nshab@sph.com.sg



Professor Marcus Ong tapped data science and simulation modelling to help cushion the impact of Covid-19 on the health system. ST PHOTO: JASON QUAH

Marcus Ong

On a data-driven mission to support health system

At the onset of the pandemic, Professor Marcus Ong realised that the unprecedented outbreak would not just impact infected patients and front-line healthcare workers.

The virus could also put the whole healthcare system, hospitals and all patients under pressure, either directly or indirectly.

To help cushion the impact of the relatively unknown virus on the healthcare system, Prof Ong – senior consultant at Singapore General Hospital's Department of Emergency Medicine – turned to his research interests in data science and simulation modelling.

Said Prof Ong: "We saw an urgent need to use data to support our health system's response to Covid-19, in order to protect our patients and our healthcare system."

He is speaking from experience, having lost some of his friends and colleagues to the severe acute respiratory syndrome in 2003.

"We realised how important a comprehensive, whole-system re-

sponse was in order to protect the health system from being overwhelmed and to save lives."

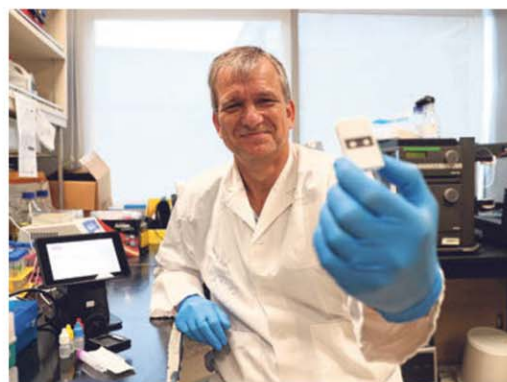
Since February, his team has been building computer simulation models based on the pandemic to improve healthcare policies in areas such as resource allocation and business disruptions.

"The virtual outbreak model can be further developed to address different disease outbreak scenarios in the future, and will also enhance our national response to future epidemics," said Prof Ong.

A recent study published by his team found that Covid-19 medical literature written in the early days of the outbreak was focused mainly on clinical elements and diagnosis.

Big-picture issues such as the outbreak's effect on the mental health of healthcare workers and how it affected the care of non-Covid-19 patients, as well as the use of novel technologies, were initially under-explored.

Shabana Begum



Professor Peter Preiser with the cellulose-based test he developed to detect proteins produced by the Sars-CoV-2 virus. ST PHOTO: TIMOTHY DAVID

Peter Preiser

Tapping malaria research to come up with Covid-19 test

Cheryl Tan

Tapping his expertise in malaria research, Professor Peter Preiser of Nanyang Technological University (NTU) came up with a paper-strip test to detect proteins produced by the Sars-CoV-2 virus.

The professor of molecular genetics and cell biology did this by adapting technology he had created to differentiate between types of malaria parasites, as he was keenly aware of the need for reliable diagnostics and rapid response in the Covid-19 crisis.

The result is a cellulose-based test that is able to recognise Sars-CoV-2 proteins in a patient's blood sample. If the viral proteins are present, the paper strip changes from white to blue in 10 minutes.

Prof Preiser produced two versions: a serology test that can recognise antibodies from past Covid-19 infections, and an antigen rapid test that can identify those who are infected with Covid-19.

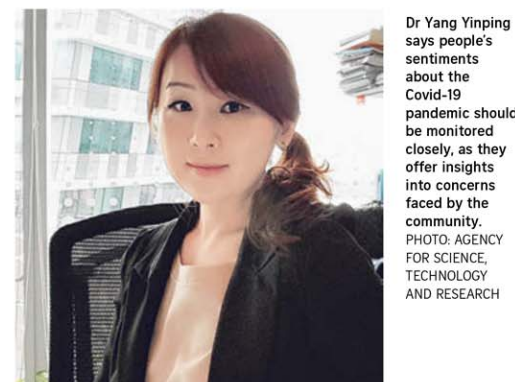
Prof Preiser, who is also associate vice-president for biomedical and life sciences at NTU, said the tests would cost only "a few dollars" each and are able to yield fast results, making them suitable for mass roll-outs.

The serology test could potentially be used pre- and post-vaccination, to ensure that priority is given to those who have not been infected before, and that the administered vaccine has been effective.

Conventional serology tests can take two to 24 hours when performed in a lab, Prof Preiser noted. His team is now looking at the possibility of a "finger prick method" for blood collection, and a saliva test for convenience.

"The success of the Covid-19 tests has given us a lot of confidence in (our) technology and provided us with a lot of information on how we can use the same approach to detect other biomarkers (for other) infectious diseases," he said.

tansuwen@sph.com.sg



Dr Yang Yingping says people's sentiments about the Covid-19 pandemic should be monitored closely, as they offer insights into concerns faced by the community. PHOTO: AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH

Yang Yingping

Analysing Twitter trends surrounding outbreak

Social technologist Yang Yingping has a passion for building and applying technology to advance human communications.

She has conducted research in areas such as sentiment analysis and emotion recognition, which have useful implications on public health.

For instance, in 2013, she co-led a project to examine social network activities during the H7N9 bird flu outbreak, in collaboration with the Ministry of Health.

Most recently, the principal investigator and group manager at the Agency for Science, Technology and Research's Institute of High Performance Computing started examining people's sentiments during the Covid-19 pandemic, using an algorithm system which examines social media posts on Twitter.

To date, more than 124 million worldwide tweets have been collected and processed.

They are analysed according to four emotions – fear, anger, sadness and joy, along with the

course of events contextualising these feelings.

For instance, "fear" was observed as the global sentiment when the virus first surfaced, followed by "anger" which peaked on March 12, a day after the World Health Organisation declared the Covid-19 outbreak a pandemic.

Dr Yang said these feelings should be monitored closely, as they offer insights into concerns faced by the community.

But sentiments often vary across countries, perhaps owing to each government's response to the pandemic, among other factors, added Dr Yang.

In Singapore, for instance, "joy and other positive emotions" had overtaken initial feelings of "fear" from March 30 onwards, suggesting a sense of pride, gratitude and relief, she noted.

In the coming days, Dr Yang anticipates stronger sentiments of joy, in response to positive news of a vaccine and other treatment developments.

Cheryl Tan

well as coming up with treatments and a possible vaccine.

Indeed, Singapore was only the third country outside of China to successfully culture the coronavirus, and local researchers have contributed more than 1,100 papers on Covid-19 and Sars-CoV-2, which causes the disease.

When it comes to Covid-19 research, Singapore is punching

above its weight, and others are taking notice.

All this is a far cry from even a decade ago, when researchers here lamented that the pressure to deliver economic returns took precedence over more intangible long-term gains in say, healthcare or education.

There was also a widespread belief, even from within, that local sci-

ence was not up to scratch, and criticism that groups worked in silos, with little collaboration among teams and disciplines.

Concerted efforts throughout this pandemic have put many of these worries to rest, underscoring the impact of local research, and the community's crucial ability to work together and change tack during an emergency, something that

has been possible only because of many prior years of research and experience.

People have also been able to see, at first hand, the value of science in saving not just lives but also livelihoods.

The billions of dollars pumped into research and innovation have been a worthwhile long-term investment.

Last Friday, the Government endorsed the efforts of researchers at the forefront of the pandemic fight, and again pledged its support for research and innovation.

It announced a \$25 billion plan to chart Singapore's research landscape over the next five years, including a critical investment to shore up its defences against future infectious disease threats.

In many ways, 2020 has marked the coming of age of Singapore science, a milestone more than two decades in the making.

It is science which will help the Republic emerge from the grip of Covid-19, and to survive and even thrive, in an increasingly uncertain world.

ailien@sph.com.sg