NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

PUSHING FRONTIERS

FACULTY ON THE FRONTLINE

COMING TOGETHER TO COMBAT COVID-19

CONNECTING THE DOTS IN A COMPLEX WORLD

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Embracing the century of complexity

THE FAMILY DOCTOR

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Catalysing change in family medicine

AT THE FRONTIERS OF A PANDEMIC

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Diagnostics, detection and social media discourse

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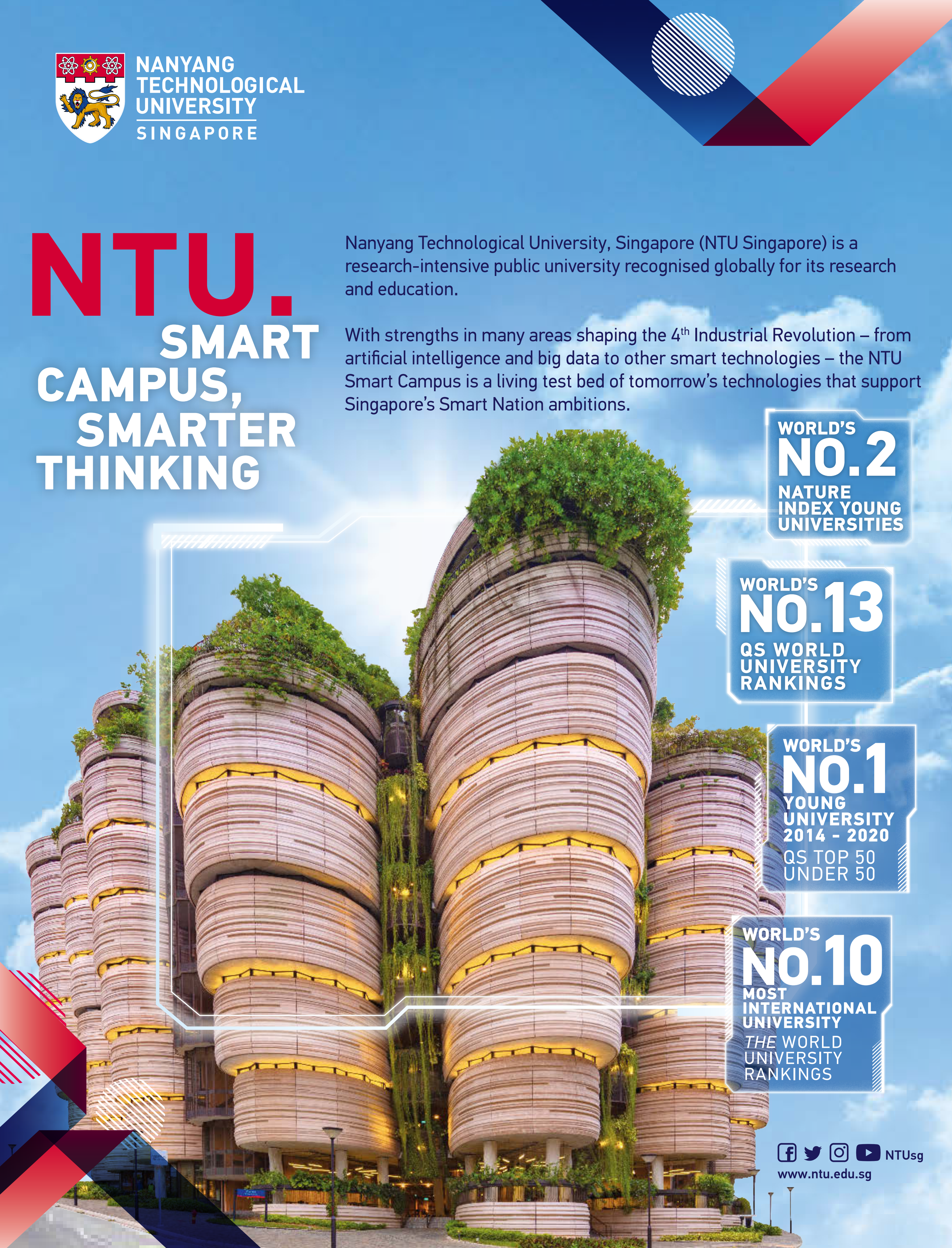
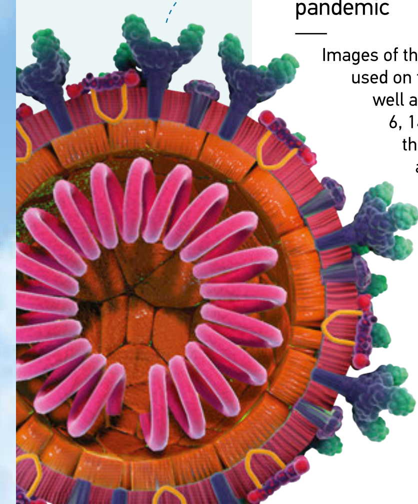


Images of the coronavirus used on the cover, as well as on pages 3, 4, 6, 14, 16, and 17 of this issue, were adapted from digital 3D models of SARS-CoV-2 developed by scientists at Fraunhofer Singapore at NTU (see also page 7).



Stories in this issue can also be found at *researchnews.ntu.edu.sg*

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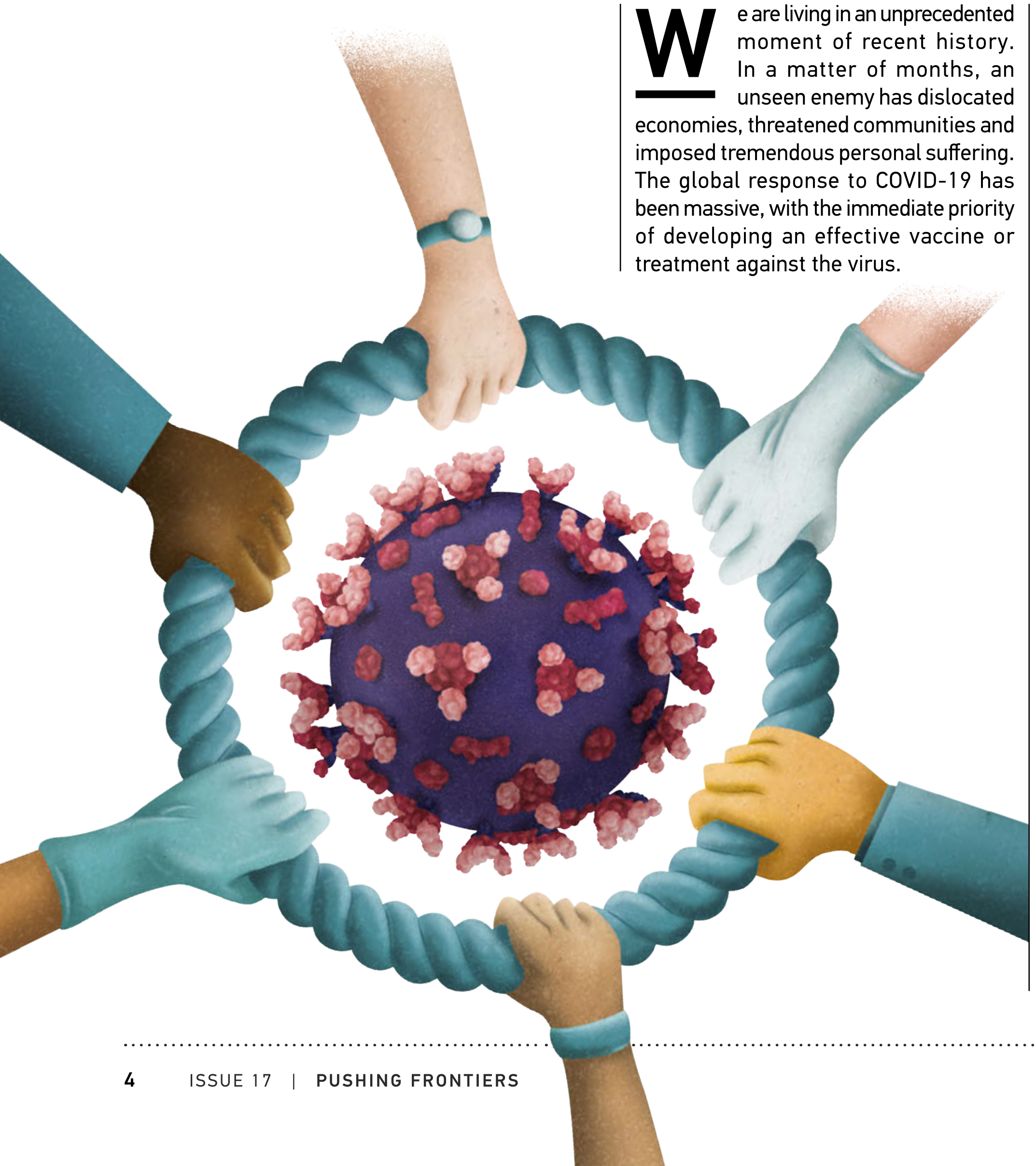
NTU UNITED AGAINST COVID-19

We are living in an unprecedented moment of recent history. In a matter of months, an unseen enemy has dislocated economies, threatened communities and imposed tremendous personal suffering. The global response to COVID-19 has been massive, with the immediate priority of developing an effective vaccine or treatment against the virus.



This edition of *Pushing Frontiers* showcases NTU's efforts to understand COVID-19 biology and minimise its impact on those infected and on society. Scientists at NTU are collaborating with local research institutions and hospitals on projects ranging from diagnostics to epidemiology, clinical disease management and healthcare delivery.

The virus is rapidly reinventing how we work and interact with one another, and its longer-term implications on society remain an open question. Therefore, NTU researchers are studying behavioural responses to lockdowns and social distancing, helping to combat fake news and shaping public policy guidelines.

As a key research institution in Singapore, NTU is committed to tackling the novel coronavirus using its deep expertise in natural sciences, medicine and social sciences. We strongly support the national strategy to contain and arrest COVID-19 and deploy our resources to prepare and protect Singapore from future pandemics.

Prof Lam Khin Yong
Senior Vice President (Research)
Nanyang Technological University
Singapore

A CAT-AND-MOUSE GAME WITH INFECTIOUS DISEASES

Backed by large grants, NTU researchers are using wastewater and molecular biology to track the spread of pathogens

In contrast to COVID-19, which appeared in humans only in late 2019, the mosquito-borne disease malaria emerged hundreds of thousands of years ago and has since accompanied humans across the globe, including in the region surrounding Singapore. Though specific species of the malaria-causing parasite *Plasmodium* typically infect only certain primate host species, cross-infections between host species—including to humans—have repeatedly occurred in the past.

Supported by a grant from Singapore's Ministry of Education over five years, a Singapore research team plans on shedding light on the molecular basis of malaria zoonoses.

"We want to understand the mechanisms by which malaria infections are restricted to certain primate species, and how these mechanistic restrictions are being breached during a zoonotic transition," says Prof Zbynek Bozdech of NTU's School of Biological Sciences, who is leading the project "Mechanisms of zoonosis of infectious diseases: The malaria model".

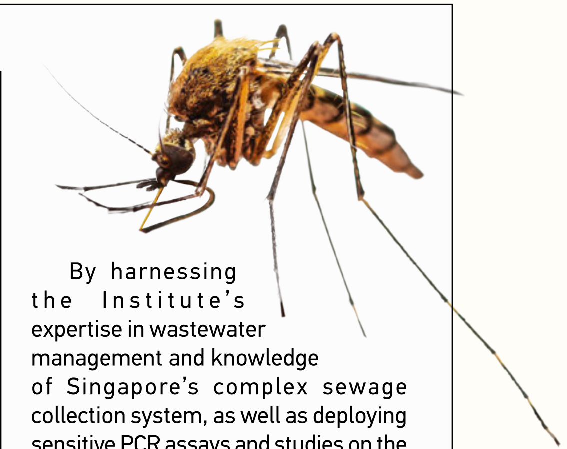
By simulating malaria adaptation across species in a laboratory model, the researchers aim to detect the biological features that normally maintain transmission barriers between species.

"These molecular factors can serve as tools for diagnosis and monitoring of malaria zoonoses, as well as targets for the development of therapeutics and vaccines," says Prof Bozdech. "Moreover, we hope to develop general concepts of zoonoses that could be applied across infectious pathogens, including viruses like SARS-CoV-2."

A key challenge for public health officials during the COVID-19 pandemic is how best to monitor the prevalence of SARS-CoV-2 infection in a population. One promising idea for the early detection of viral outbreaks at the population level is wastewater-based epidemiology.

"By monitoring sewage from various urban areas or complexes such as residential blocks, dormitories or medical facilities, we aim to rapidly identify COVID-19 outbreaks without invasive procedures involving human interactions, and in a very cost-effective manner," says Prof Shane Snyder, Executive Director of NTU's Nanyang Environment and Water Research Institute.

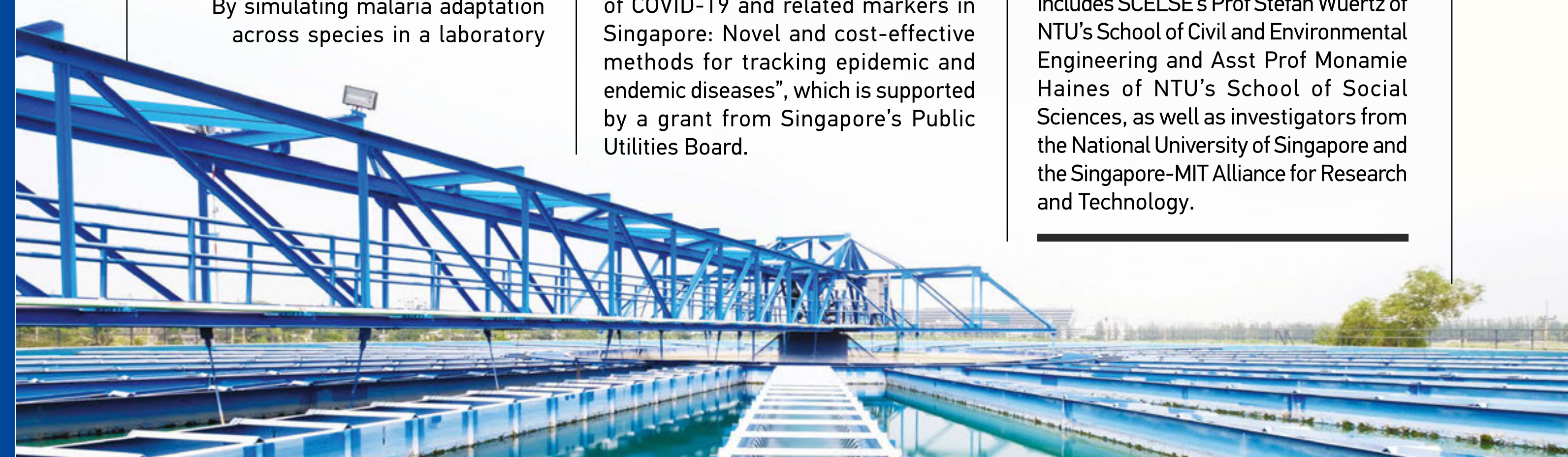
Prof Snyder is leading the project "Wastewater-based epidemiology of COVID-19 and related markers in Singapore: Novel and cost-effective methods for tracking epidemic and endemic diseases", which is supported by a grant from Singapore's Public Utilities Board.



By harnessing the Institute's expertise in wastewater management and knowledge of Singapore's complex sewage collection system, as well as deploying sensitive PCR assays and studies on the decay of SARS-CoV-2 in wastewater for model optimisation, Prof Snyder hopes to achieve a warning level for SARS-CoV-2 prevalence of 0.001% or better—equivalent to one case per 100,000 residents.

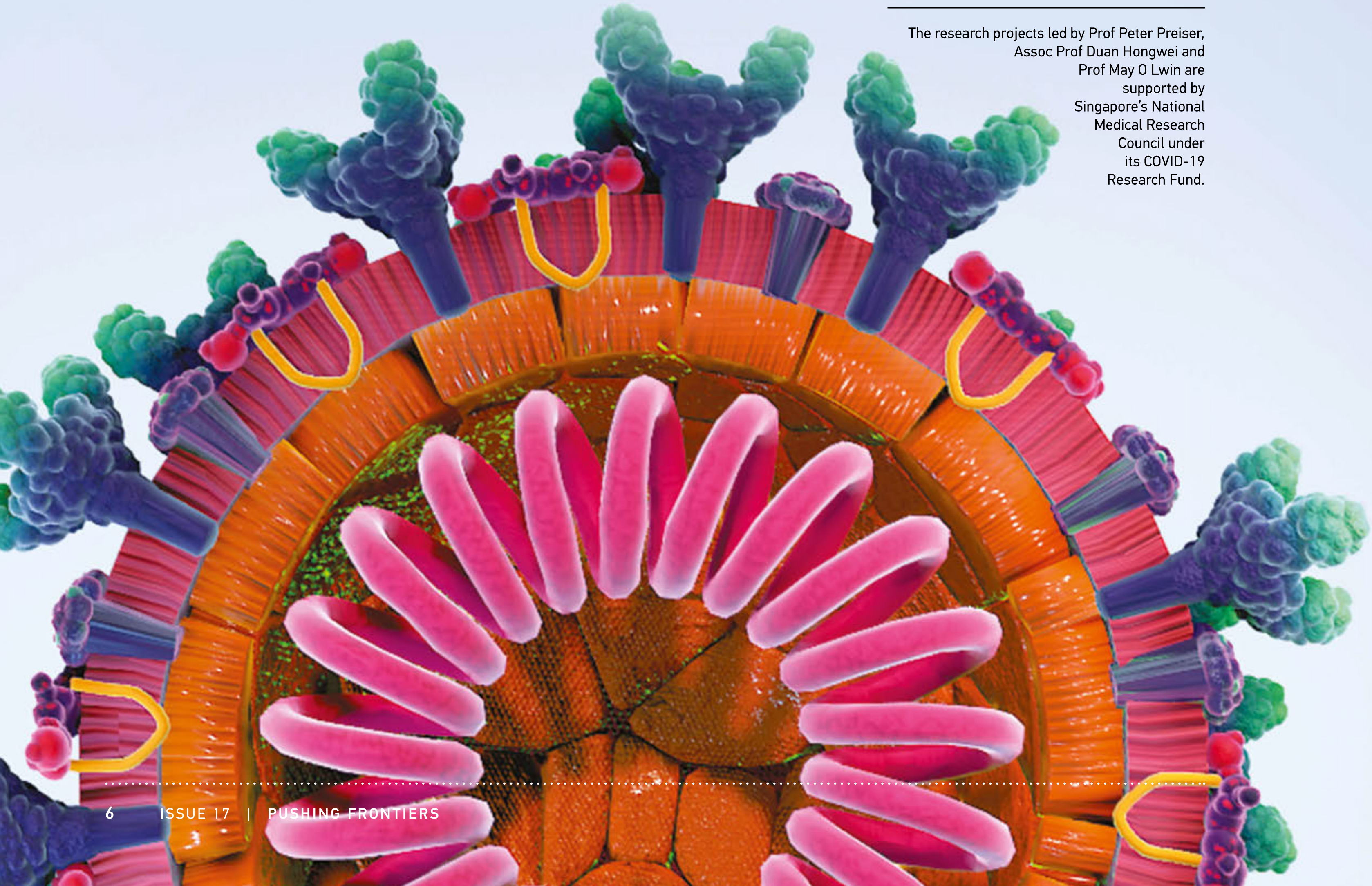
Wastewater surveillance of COVID-19 in the community is also underway at NTU's Singapore Centre for Environmental Life Sciences Engineering (SCELSE). Joining forces with Singapore's National Environment Agency, the team—led by Assoc Prof Janelle Thompson of NTU's Asian School of the Environment—helped set up surveillance methods at the dormitories of foreign workers, some of which became centres of COVID-19 outbreaks. The researchers also support community-wide surveillance at Singapore's four wastewater reclamation plants. Information from this approach has already been integrated into Singapore's COVID-19 response.

The team's new grant, "Sewage-based surveillance for rapid outbreak detection and intervention in Singapore", is supported by the National Research Foundation, Prime Minister's Office, Singapore, under its Campus for Research Excellence and Technological Enterprise (CREATE) programme. Focusing in parallel on SARS-CoV-2 and other viral pathogens, the grant includes SCELSE's Prof Stefan Wuertz of NTU's School of Civil and Environmental Engineering and Asst Prof Monamie Haines of NTU's School of Social Sciences, as well as investigators from the National University of Singapore and the Singapore-MIT Alliance for Research and Technology.



AT THE FRONTIERS OF A PANDEMIC

From effective communication in a pandemic to the development of diagnostic kits, NTU's research community is banding together to provide urgent solutions to COVID-19.



SENSITIVE TEST FOR THE NUCLEOCAPSID PROTEIN

An expert in malaria biology, NTU's Associate Vice President (Biomedical and Life Sciences), Prof Peter Preiser, is developing a rapid diagnostic test kit for the detection of SARS-CoV-2 infection.

He is working closely with Assoc Prof Hadley Sikes of Massachusetts Institute of Technology and other scientists at the Singapore-MIT Alliance for Research and Technology (SMART), where he is co-lead principal investigator of the antimicrobial resistance interdisciplinary research group.

"The ability to accurately test for the coronavirus nucleocapsid protein, which is observed from as early as day one of disease onset, in swabs or bodily fluids such as saliva or blood, could help significantly in containment efforts," he says.

The research projects led by Prof Peter Preiser, Assoc Prof Duan Hongwei and Prof May O Lwin are supported by Singapore's National Medical Research Council under its COVID-19 Research Fund.

SCALING UP COVID-19 DETECTION

The development of a high-throughput diagnostics kit for SARS-CoV-2 is the goal of Assoc Prof Duan Hongwei, who is the Associate Chair (Research) at NTU's School of Chemical and Biomedical Engineering.

In collaboration with Assoc Prof Luo Dahai of NTU's Lee Kong Chian School of Medicine and Prof Lam Yee Cheong of NTU's School of Mechanical and Aerospace Engineering, Assoc Prof Duan is devising a fully automated microbiochip assay platform for rapid high-throughput, ultrasensitive detection of SARS-CoV-2 proteins and virus-specific antibodies present in serum and respiratory specimens.

"With our multichannel system, we aim to quantify virus antigen and antibodies of multiple samples simultaneously, using microlitres of specimens," he says. The researchers are currently testing the device on COVID-19 clinical samples.

UNDERSTANDING THE EPIDEMIC POTENTIAL OF COVID-19

Clinician-scientist and infectious disease expert Prof Annelies Wilder-Smith of NTU's Lee Kong Chian School of Medicine is modelling the impact of Sweden's approach to the pandemic on the Swedish healthcare system, as well as the effects of quarantine measures on board the Diamond Princess following a COVID-19 outbreak on the cruise ship. Addressing knowledge gaps in how COVID-19 spreads through populations, she develops policy recommendations for the management of the pandemic.

She is also studying the impact of nonpharmaceutical interventions for COVID-19 such as isolation, contact tracing and social distancing. "We need to remain humble about this novel virus. There is still much to learn," says Prof Wilder-Smith, who also serves as a consultant to the World Health Organisation on issues related to COVID-19 vaccine development.

SOCIAL MEDIA BEHAVIOUR IN A PANDEMIC

Drawing on her experience in health and infectious disease communication, Prof May O Lwin, Chair of NTU's Wee Kim Wee School of Communication and Information, is examining global mainstream media and social media discourse surrounding the COVID-19 pandemic.

"Our objective is to understand how mainstream and social media are influencing public behaviour during infectious disease outbreaks, especially during the current outbreak of COVID-19," says Prof Lwin, who is also Associate Dean (Special Projects) of NTU's College of Humanities, Arts, and Social Sciences, and Director of the NTU University Scholars Programme.

In a collaboration with the National University of Singapore's Saw Swee Hock School of Public Health, Prof Lwin is developing a community-based syndromic COVID-19 surveillance system to help policymakers examine importation risk, the potential size of outbreaks and what interventions may mitigate COVID-19 spread.

A CLOSE-UP OF SARS-COV-2

To support COVID-19 research and education, computer scientists at Fraunhofer Singapore in NTU have launched Virtual SARS-CoV-2, a digital 3D model of the novel coronavirus. The resource will be made accessible to scientists and the public (fraunhofer.sg/en/covid-19), and can be run on personal computers or in immersive virtual reality scenarios using virtual reality equipment.

"With Virtual SARS-CoV-2, we are developing a tool that provides interactive visualisation, converting complex information into easily digestible visual stories," says Prof Wolfgang Müller-Wittig, Executive Director of Fraunhofer Singapore, the first Asian affiliate of Europe's largest application-oriented research organisation, Fraunhofer Society.

Using virtual reality goggles to interact with a 3D model of SARS-CoV-2. Credit: D J Saravana Kumar.

HUMAN EVOLUTION

A PEEK INTO ASIA'S GENETIC DIVERSITY

Human genetic databases have to date focused on people of European descent, which means that crucial information on a large proportion of the world's population remains lacking.

Enter the GenomeAsia 100K Project, which aims to increase the coverage of genetic diversity in Asia by sequencing and analysing the genomic DNA samples of 100,000 individuals from across Asia. It is co-led by the consortium's scientific chairman, Prof Stephan Schuster of NTU's Singapore Centre for Environmental Life Sciences Engineering, and Asst Prof Kim Hie Lim of NTU's Asian School of the Environment.

In the pilot phase, the researchers collected and analysed datasets of 1,739 individuals from 219 ethnic population groups across 64 countries, using whole-genome sequencing. The pioneering study found that Asian population groups descend from at least ten ancestral lineages—a stark contrast to European populations, which all originate from a single ancestral lineage. Ethnic groups sampled in India, Malaysia and Indonesia showed the greatest genetic diversity.

A comprehensive genetic map for Asia will guide studies of diseases unique to Asian populations and help researchers identify drugs that respond differently in certain ethnic groups, the researchers say.

The study "The GenomeAsia 100K Project enables genetic discoveries across Asia" was published in Nature *(2019), DOI: 10.1038/s41586-019-1793-z.*

(From left) Asst Prof Kim Hie Lim, Prof Stephan Schuster and GenomeAsia 100K Executive Chairman Mahesh Pratapneni led the pilot study. Credit: NTU.

INFECTIOUS DISEASES

POKING HOLES IN ANTIBIOTIC RESISTANCE

Causing tens of thousands of deaths every year around the world, antibiotic-resistant microbes are among the biggest public health challenges of our time. In particular, certain strains of gram-negative bacteria are resistant to antibiotics considered the last line of defence.

Led by Assoc Prof Kevin Pethe of NTU's Lee Kong Chian School of Medicine and Prof Mary Chan of the School of Chemical and Biomedical Engineering, an NTU team has designed a peptide that is able to overcome antibiotic resistance in gram-negative bacteria by two distinct mechanisms.

Their cationic block β-peptide not only compromises the integrity of the bacteria's outer membrane but also deactivates membrane-localised pump systems, thereby disrupting the efflux of antibiotic compounds. The peptide was effective in sensitising bacteria to multiple classes of antibiotics in *in vitro* studies as well as in mouse models of systemic infection.

Potential applications for the peptide include adjunct antibiotic therapy in difficult-to-treat infections with gram-negative bacteria, the researchers say.

"A glycosylated cationic block poly(β-peptide) reverses intrinsic antibiotic resistance in all ESKAPE gram-negative bacteria" was published in Angewandte Chemie *(2020), DOI: 10.1002/ange.201914304.*

(From right) Assoc Prof Kevin Pethe, Prof Mary Chan and PhD student Zhang Kaixi. Credit: NTU.

DRUG DISCOVERY

UNMASKING A TB SUPERHERO

Treatments for tuberculosis (TB), the leading cause of deaths from infectious diseases worldwide, often fail due to relapse and the emergence of drug-resistant bacteria.

A mainstay of anti-TB drug regimens since the 1970s, the small molecule pyrazinamide continues to be included in most new drug combinations against both drug-sensitive and multidrug-resistant TB.

However, the exact mechanism by which pyrazinamide acts on *Mycobacterium tuberculosis*, the causative agent of TB, remained a mystery until Prof Gerhard Grüber from NTU's School of Biological Sciences and Prof Thomas Dick from the Hackensack Meridian Health Centre for Discovery and Innovation in the US decided to investigate its mechanism of action.

The team found that a metabolised form of pyrazinamide, called pyrazinoic acid, binds to the bacterial enzyme aspartate decarboxylase. This binding in turn triggers a cascade of reactions that ultimately interrupt the synthesis of adenosine triphosphate, the cellular energy currency that drives essential processes in the bacteria.

Not only has the veil been lifted on pyrazinamide's mechanism of action, the research findings also validate drug-induced target degradation as a new approach in drug discovery.

The article "Pyrazinamide triggers degradation of its target aspartate decarboxylase" was published in Nature Communications *(2020), DOI: 10.1038/s41467-020-15516-1.*

VIRAL COMPLEXES MADE CRYO CLEAR

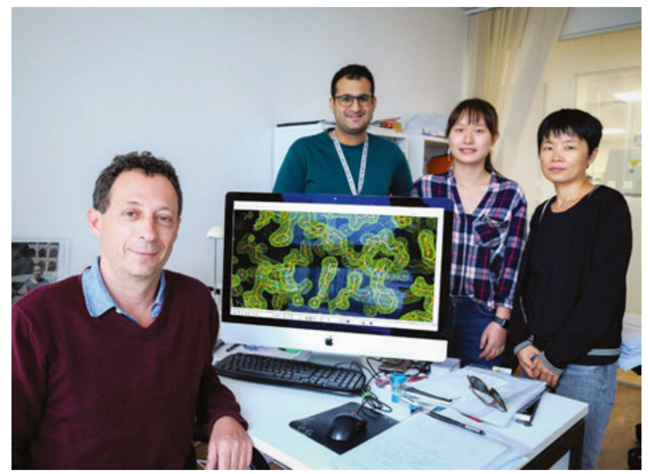
Human metapneumovirus (HMPV) and the closely related respiratory syncytial virus (RSV) can cause severe infections of the upper respiratory tract and the lungs. Particularly susceptible groups include premature babies, infants and older adults, as well as immunocompromised individuals and those with heart and lung disease.

Given that a structural understanding of these viruses may lead to new drug targets, a team of molecular and structural biologists, led by Assoc Prof Julien Lescar of NTU's School of Biological Sciences and the NTU Institute of Structural Biology, investigated a key component of HMPV's infection cycle.

During infection, HMPV releases enzymes into host cells, which form enzyme complexes and initiate viral replication and propagation. Using cryo-electron microscopy, the researchers captured high-resolution images of the HMPV enzyme complexes and built 3D computerised models of them. Analysis of the molecular structures revealed key sites of enzyme interaction that appear to be highly specific for the viruses.

Armed with new structural insights, the researchers aim to develop inhibitors that interrupt enzyme complex formation in a broad spectrum of viruses, including HMPV and RSV.

The research "Structure of the human metapneumovirus polymerase phosphoprotein complex" was reported in Nature *(2019), DOI: 10.1038/s41586-019-1759-1. Watch animated depictions of enzyme complexes at bit.ly/HMPV3Dmodel (Supplementary Videos 1 and 2).*

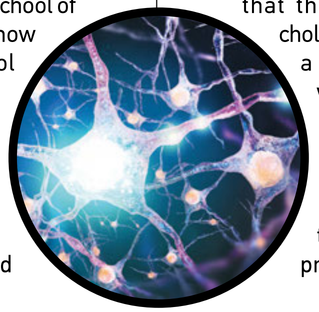


(From left) Assoc Prof Julien Lescar and team members Dr Abbas El Sahili, graduate student Ms Jia Huan and Dr Xinlei Qian. Credit: NTU.

NEUROSCIENCE

REGULATING THE HIGHS AND LOWS OF CHOLESTEROL

The plasma membrane surrounding cells of our body, including neurons in the brain, consists mainly of lipids, and in particular, cholesterol. Now, an international team, led by Nanyang Asst Prof Yasunori Saheki of NTU's Lee Kong Chian School of Medicine, has identified how cells monitor cholesterol levels in the plasma membrane.



This sentinel role appears to belong to a group of lipid transfer proteins called GRAMD1 proteins, which are located in the endoplasmic reticulum (ER), an intracellular network of membrane-enclosed compartments where cholesterol is produced.

Once the GRAMD1 proteins sense that the plasma membrane's cholesterol pool has exceeded a certain threshold—which risks membrane destabilisation—they transport surplus cholesterol back to the ER, signalling a stop to *de novo* cholesterol production.

Given that cholesterol is a major structural component of neurons, an imbalance in cholesterol metabolism might offer insights into neurodegenerative diseases such as Alzheimer's and Parkinson's, suggest the researchers.

The article "Movement of accessible plasma membrane cholesterol by the GRAMD1 lipid transfer protein complex" was published in eLife *(2019), DOI: 10.7554/eLife.51401.*

AGEING

THE WISDOM OF OLDER GUT BACTERIA

Wrinkles and other physical changes are part and parcel of ageing. However, we age not only on the outside, but also inside, with our gut microbiota playing an influential role in the ageing process.

To investigate how changes in gut microbiota are linked to ageing, Prof Sven Pettersson of NTU's Lee Kong Chian School of Medicine and an international team transplanted gut microbiota from either 24-month-old ("old") or six-week-old ("young") mice into "young", germ-free recipient mice.

Mice transplanted with "old" gut microbiota not only experienced enhanced muscle strength and physical fitness, they also grew substantial numbers of new neuronal and intestinal cells compared to mice receiving "young" microbiota.

In particular, recipients of "old" microbiota were enriched in microbes producing butyrate—a short-chain fatty acid associated with an increase in pro-longevity hormones and other proteins with roles in energy homeostasis and metabolism. Germ-free mice treated with sodium butyrate showed increased neurogenesis and intestinal cell growth, recapitulating the phenotype found in mice transplanted with "old" microbiota.

The researchers hope that their findings may lead to innovative food products that either are supplemented with butyrate or promote short-chain fatty acid-producing microbes in our gut, which may possibly attenuate the negative effects of ageing.

The study "Neurogenesis and prolongevity signalling in young germ-free mice transplanted with the gut microbiota of old mice" was published in Science Translational Medicine*, 2019, DOI: 10.1126/scitranslmed.aau4760.*

DIABETES

HALTING THE MARCH OF PRE-DIABETES

Asst Prof Yusuf Ali has found that specialised cells in pancreatic islets may help to prevent the transition from pre- to full diabetes. Credit: NTU.

Mini organs in the pancreas called pancreatic islets are home to beta cells. These beta cells synthesise and secrete insulin, a hormone that regulates blood glucose levels.

In pre-diabetic patients, insulin resistance begins when cells in the muscles, body fat and liver start ignoring the signals sent by insulin to transfer glucose from the bloodstream into cells. To maintain regular blood glucose levels, the beta cells compensate for the reduced sensitivity by boosting insulin secretion in a process that is supported by an increase in the mass and number of beta cells called islet remodelling.

Looking for novel approaches to slow down the progression of diabetes, Asst Prof Yusuf Ali of NTU's Lee Kong Chian School of Medicine, together with scientists from NTU's School of Biological Sciences and researchers in Germany and Sweden, investigated the extent to which a particular cell type—islet resident macrophages—contributes to pancreatic remodelling.

Using diabetic mice engineered to lack macrophages, and by designing *in vivo* experiments where macrophages are specifically depleted from pancreatic islets, the researchers observed significantly reduced pancreatic remodelling and insulin secretion. Mice lacking macrophages in islets rapidly developed diabetes.

Understanding the role played by islet macrophages in pancreatic remodelling may be useful in finding treatments that halt or slow down the transition from pre-diabetes to full diabetes, the researchers say.

The study "Islet macrophages are associated with islet vascular remodelling and compensatory hyperinsulinemia during diabetes" was published in American Journal of Physiology–Endocrinology and Metabolism *(2019), DOI: 10.1152/ajpendo.00248.2019.*

DIGITAL HEALTH

DOES AN APP A DAY KEEP THE DOCTOR AWAY?

With an estimated 800,000 suicides globally each year, suicide remains one of the leading causes of preventable deaths around the world.

Mobile apps may help those at risk of depression and suicide, and there are currently many such apps for digital devices available.

In their study, Assoc Prof Josip Car and his team at NTU's Lee Kong Chian School of Medicine appraised the trustworthiness of depression management and suicide prevention apps, as well as their adherence to six evidence-based clinical guideline recommendations—mood and suicidal thought tracking, safety plan development, recommendation of activities to deter suicidal thoughts, information and education, access to support networks, and access to emergency counselling.

Out of 69 depression and suicide prevention apps assessed, only five offered all six strategies. Some apps, including those that had been downloaded more than a million times, even provided inaccurate suicide crisis helpline phone numbers.

"With the high rates of smartphone use around the world, health apps can be a crucial addition in the way users manage their health and wellbeing on a global scale," says Assoc Prof Car, who is Director of NTU's Centre for Population Health Sciences.

"However, for this to become a reality, health app development and release should follow transparent, evidence-based models and guidelines," he adds.

The study "Suicide prevention and depression apps' suicide risk assessment and management: a systematic assessment of adherence to clinical guidelines" was published in BMC Medicine *(2019), DOI: 10.1186/s12916-019-1461-z.*

Assoc Prof Josip Car's research highlights the need for responsible design of suicide prevention apps. Credit: NTU.

THERAPEUTICS

THE SECRET(OME) TO TISSUE REPAIR

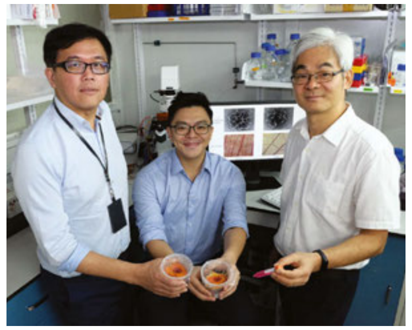
Multipotent cells in the body, called mesenchymal stem cells, secrete a cocktail of immunomodulatory and regenerative factors collectively termed the secretome. To trigger the production of the pro-healing secretome, researchers typically culture mesenchymal stem cells under oxygen deprivation, or turn to biochemicals or genetic engineering.

An interdisciplinary team of NTU researchers, led by Asst Prof Dalton Tay of the School of Materials Science and Engineering, Assoc Prof Andrew Tan of the Lee Kong Chian School of Medicine, and Assoc Prof Newman Sze of the School of Biological Sciences, has found a more efficient way to grow stem cells and enhance secretome production.

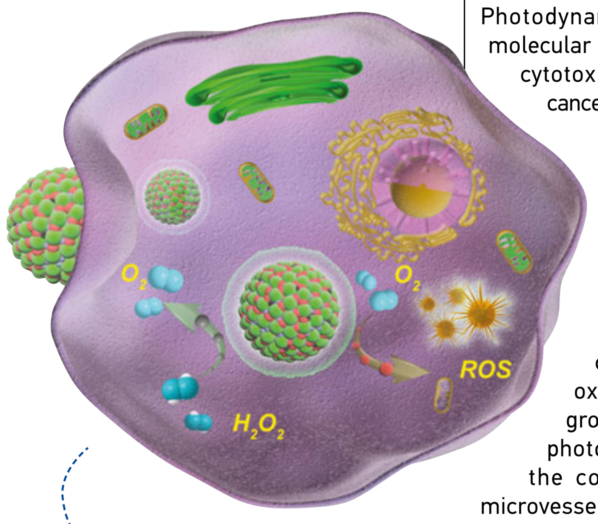
Mimicking the body's natural microenvironment, the team grew the cells on a hydrogel—3D networks of polymers with high water content. They harvested the secretome and showed improved blood vessel formation in a chicken egg chorioallantoic membrane model, as well as faster cutaneous wound repair in a mouse model, as compared to the secretome from cells grown under classical conditions.

"Going forward, we aim to further develop advanced cell culture materials to manipulate the production and therapeutic potential of the secretome, so that the same types of healing factors present in different body tissues during tissue repair can be produced in the lab," says Asst Prof Tay.

More details of this research can be found in "Materials stiffness-dependent redox metabolic reprogramming of mesenchymal stem cells for secretome-based therapeutic angiogenesis", published in Advanced Healthcare Materials *(2019), DOI: 10.1002/adhm.201900929; and in "Soft material approach to induce oxidative stress in mesenchymal stem cells for functional tissue repair", published in* ACS Applied Materials & Interfaces *(2016), DOI: 10.1021/acsami.6b09222.*



Using a chicken egg membrane model, (from left) Assoc Prof Andrew Tan, Asst Prof Dalton Tay and Assoc Prof Newman Sze demonstrated improved blood vessel formation due to healing factors produced by hydrogel-grown stem cells. Credit: NTU.



Schematic showing oxygen (O_2) generation catalysed by an enzymatic nanoagent (green-red balls) to enhance the efficiency of photodynamic cancer therapy. Credit: Zhao Yanli/reproduced from *Nature Communications* (2020), DOI: 10.1038/s41467-019-14199-7.

NANOMEDICINE

KILLING TUMOURS WITH A LIGHT, AIRY TOUCH

Photodynamic therapy, which uses molecular oxygen to generate highly cytotoxic oxygen species that kill cancer cells, is an effective clinical treatment for superficial and localised tumours. It also has fewer side effects compared to conventional radiotherapy, chemotherapy and surgery.

The efficiency of photodynamic therapy is compromised, though, if oxygen levels are low in fast growing tumours. In addition, photodynamic therapy induces the collapse of tumour blood microvessels, causing further oxygen deprivation (hypoxia).

To break the vicious cycle of photodynamic therapy-induced tumour hypoxia, Prof Zhao Yanli of NTU's School of Physical and Mathematical Sciences and his colleagues developed a self-assembled nanoagent that is able to generate oxygen inside tissues.

Serving a similar role as the enzyme catalase, the nanoagent raised local oxygen levels by catalysing a reaction between single-atom ruthenium nanoparticles and hydrogen peroxide present in tumour microenvironments.

A combination of the catalysis-based nanoplatform and photodynamic therapy resulted in the elimination of tumours in a mouse model, a result that could not be achieved by photodynamic therapy alone.

The nanoagent could also be used as a cancer theranostic to image and track tumours inside the body, the researchers say.

The research study "Self-assembled single-atom nanozyme for enhanced photodynamic therapy treatment of tumor" was published in Nature Communications *(2020), DOI: 10.1038/s41467-019-14199-7.*

ROBOTICS

A NERVOUS FEELING

Bringing us a step closer to prosthetics that can "feel" is a prototype of an artificial nerve built by NTU researchers that can detect mechanical stimulation and transmit these signals electrically.

Mimicking how nerve cells convert mechanical signals into electrical signals that get sent to the brain, Assoc Prof Zheng Yuanjin of NTU's School of Electrical and Electronic Engineering and his colleagues designed an all-in-one bionic artificial nerve that integrates the functions of perception, recognition and transmission.

The artificial nerve consists of an electrical double-layer structure that can detect external mechanical stimulation such as physical touch. Due to its architecture, it is able to integrate mechano-perception and signal transmission, as well as recognise the location of external mechanical stimulation, without requiring the integration of multiple sensing units.

The team is working on making the artificial nerve stretchable and biocompatible, with the aim of developing prosthetics that contain "feeling" nerves.

"By incorporating the function of spatiotemporal analysis and algorithmic analysis, we hope that our bionic artificial nerves will promote further development of sophisticated neuroprosthetics and intelligent robotics," the researchers say.

More about this research can be found in "A bioinspired analogous nerve towards artificial intelligence" in Nature Communications *(2020), DOI: 10.1038/s41467-019-14214-x. Watch a video of the artificial nerve playing a virtual piano at bit.ly/ANVirtPiano (Supplementary Movie 1).*

GETTING A GRIP ON HUMANOID HANDS

For humanoid robotic hands to serve as prosthetics, they must rely on a tendon-driven transmission system to transmit an actuation force to the joints. However, currently available tendon fibres have low toughness and stretchability, and many of them are non-conductive, which means that wires must be integrated into the robotic hands to transmit electrical signals from sensing systems.

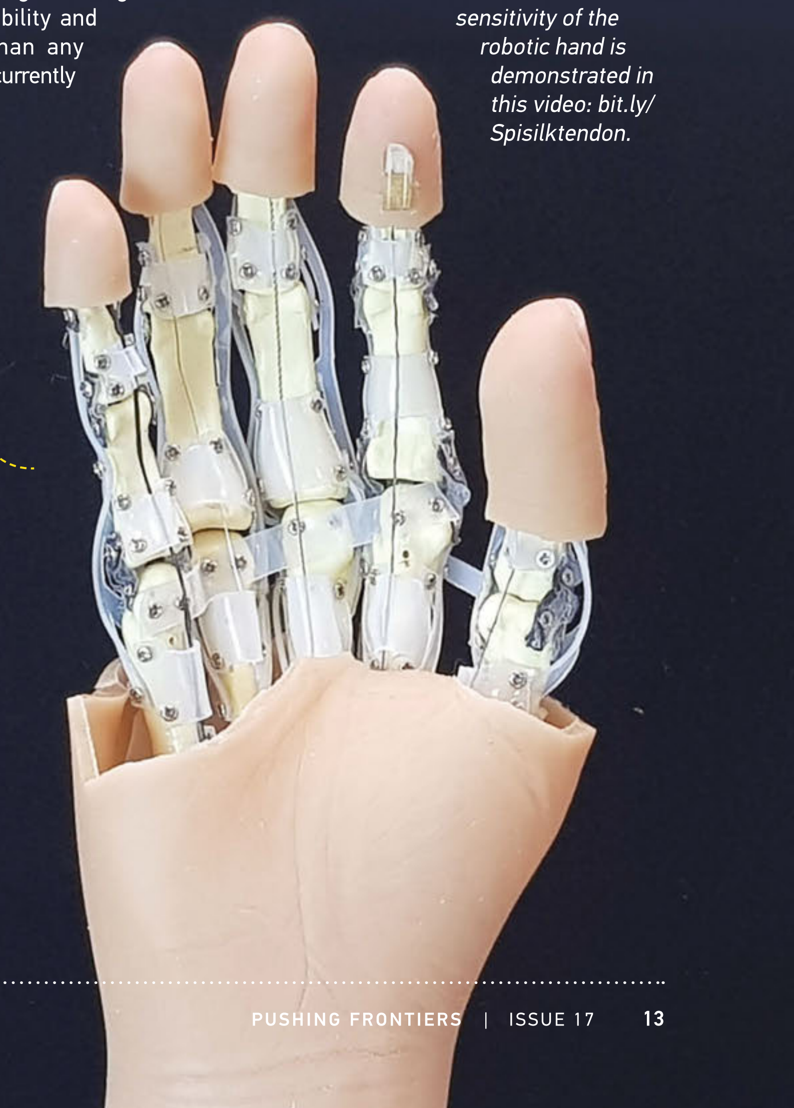
A research team from Singapore and China, led by Prof Chen Xiaodong of NTU's School of Materials Science and Engineering, has now created an "electro-tendon" from spider silk that resembles human tendons.

In more than 40,000 cycles of bending and stretching, the electro-tendon exhibited considerably higher toughness, durability, flexibility and conductivity than any other material currently available.

"A single electro-tendon fibre enabled our robotic hand to capture fragile objects, such as an inflated balloon, without damaging them, thus eliminating the need for additional wires or circuit components," says Prof Chen, who is also Director of the Max Planck-NTU Joint Lab for Artificial Senses.

Besides robotics and prosthetics, other potential applications for the electro-tendon fibres include durable anti-static cables as well as electrodes for tough and flexible electronic circuits.

The article "A supertough electro-tendon based on spider silk composites" was published in Nature Communications *(2020), DOI: 10.1038/s41467-020-14988-5. The tactile sensitivity of the robotic hand is demonstrated in this video: bit.ly/Spisilktendon.*



A 3D-printed humanoid robotic hand incorporating an electro-tendon made of spider silk and a pressure sensor mounted on the index finger. Credit: Pan Liang/Chen Xiaodong.

FACULTY ON THE FRONTLINE

COMING TOGETHER TO COMBAT COVID-19

By combining their expertise for a singular goal, health experts from NTU's Lee Kong Chian School of Medicine are helping Singapore tackle COVID-19 on all fronts.

In a matter of months, SARS-CoV-2, the virus that causes COVID-19, has wreaked havoc across the globe. Although its impact is still being tallied, it is becoming clear that this is an outbreak that is on a scale not seen in over a hundred years.

For many people living in Singapore, life has slowed down tremendously. Circuit breaker measures meant to curb the spread of COVID-19 forced a bulk of the population to temporarily retreat into their homes. As the economy gradually reopens, the silent war being waged against the coronavirus by the nation's top doctors and researchers continues to be stepped up.

The battleground? Hospitals and research laboratories, including those at NTU's Lee Kong Chian School of Medicine, or LKCMedicine, Singapore's third medical school, set up with Imperial College London. Despite having only accepted its first cohort of students in 2013 and officially opened in 2017, LKCMedicine's talented roster of clinician-scientists has ensured its capacity to contribute to the nationwide COVID-19 response.

From improving diagnostics to creating mini lungs-in-a-dish, LKCMedicine's faculty and students are collectively wielding their expertise to take on the coronavirus on different fronts. Here, we explore three ongoing research efforts from faculty members at the school.

REINVENTING DIAGNOSTICS

The gold standard for COVID-19 diagnosis is the reverse transcription polymerase chain reaction (RT-PCR), which detects sequences specific to SARS-CoV-2 in genetic material from patient samples. But its accuracy comes with several caveats. First, it is slow. A single run can last up to six hours. Second, it requires specialised equipment and reagents, which is why samples are generally shipped to centralised laboratories. This adds to the turnaround time, lengthening the excruciating wait for a test result to 24 hours or more.

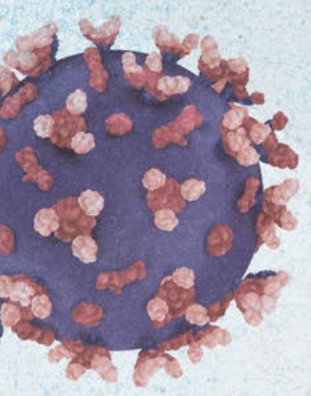
Assoc Prof Eric Yap, who heads the Medical Genomics Laboratory at LKCMedicine, wants to overhaul PCR testing. He and his team are doing this by integrating RT-PCR's many steps, a key reason why it takes so much time. Currently, a big bottleneck in the workflow is the RNA extraction step, where RNA is separated from other components in the patient sample. Not only is the process laborious, but it also requires reagents that are now in short supply.

What Assoc Prof Yap and his team have done is eliminate this step entirely. Instead, sputum or nasal exudate from patients is directly placed into the RT-PCR set-up, after which it is ready to run. "We normally can't just take a sample and put it in a PCR because there are reaction inhibitors present. If you do that, the PCR assay will fail," explains Assoc Prof Yap. "We've made the RT-PCR resistant to inhibitors." Using their method known as direct PCR, the team shortened the process into 36 minutes from start to finish.

To make PCR testing more accessible, Assoc Prof Yap and his team are also hoping to reinvent the PCR machine, also called a thermocycler. Their goal is to build a thermocycler that costs ten times less than commercially available counterparts. "Thermal cycling is essentially just heating a sample up to near boiling point and then cooling it down. If you think about it, this happens in every kitchen," Assoc Prof Yap points out. "When I make coffee or tea, the kettle goes up to near 100°C, then cools down. It is effectively carrying out one PCR cycle."

Technically, anything that boils water could be used for PCR, says Assoc Prof Yap. His team is therefore trying to convert household appliances into potential low-cost thermocyclers. Meanwhile, the costly optics that detect genetic material during PCR could be miniaturised into a tiny spectrometer chip, like the one in our smartphone. By combining these two

> **"Research is harder work than clinical work, but it is vital to drive good care."**
>
> Assoc Prof David Lye
> *Lee Kong Chian School of Medicine, and Director of the Infectious Disease Research and Training Office at the National Centre for Infectious Diseases*



innovations, Assoc Prof Yap hopes to take PCR testing out of conventional laboratories into the low-resource settings that need them the most.

Such efforts wouldn't have been possible without NTU's support. "A lot of what I'm doing is more engineering than biology. I have to credit my engineering colleagues who have taught me about optics and electronics," he shares. "NTU provides a great milieu for this cross-disciplinary work."

MISSION: PROTECT

Biological samples from patients reflect the ongoing battle against the coronavirus raging within their bodies. Analysing these samples gives scientists and physicians alike valuable insights into the inner workings of the virus—and the potential keys to its defeat.

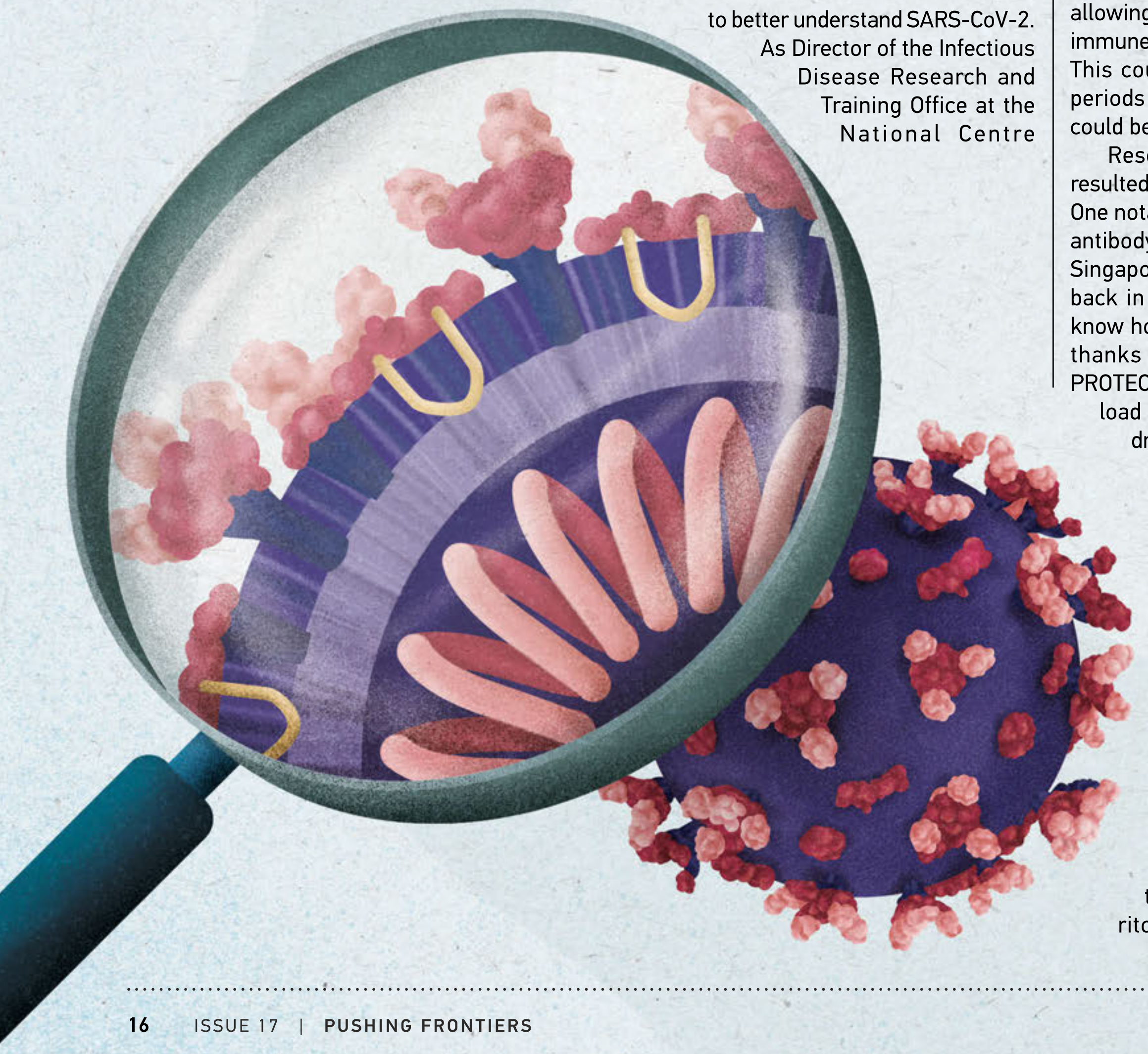
LKCMedicine's Assoc Prof David Lye is at the forefront of nationwide efforts to better understand SARS-CoV-2. As Director of the Infectious Disease Research and Training Office at the National Centre for Infectious Diseases, Assoc Prof Lye coordinates an outbreak protocol that enables Singapore's top scientific institutions to study the coronavirus in greater detail.

Known as PROTECT, the protocol was developed in 2012 and was applied during the Zika and monkeypox outbreaks in 2016 and 2019 respectively. The protocol was immediately activated after Singapore reported its first COVID-19 case on 23 January. As of mid-April, 381 patients have been enrolled in the research effort.

As the patients progress through COVID-19 infection, additional biological samples such as nose swabs, blood, urine, stool and even tears are continuously obtained and sent to approved biosafety level 3 (BSL3) laboratories at Duke-NUS Medical School and DSO National Laboratories, Singapore's national defence research agency, for further analysis. The samples are then compared to the disease's clinical progression, allowing researchers to map the body's immune response to the virus over time. This could help clinicians identify the periods when life-saving interventions could be best applied.

Research at PROTECT has already resulted in several successful outcomes. One notable example is the world's first antibody-based test that linked two of Singapore's largest COVID-19 clusters back in February. Clinicians also now know how to better manage COVID-19, thanks to information gleaned from PROTECT. "We know that COVID-19 viral load is higher early in the illness and drops towards the end of the week, so a five-day medical certificate from the family doctor makes sense," says Assoc Prof Lye. "The virus is present in stool more than 50% of the time, so toilet hygiene is vital."

In addition, findings from PROTECT have helped guide treatment options. As seen in their March 2020 publication in the medical journal *JAMA*, Assoc Prof Lye and his colleagues witnessed early on the lack of clinical effect of the anti-HIV cocktail lopinavir-ritonavir on COVID-19 patients.



With the recent uptick in local cases, the PROTECT team is now working to improve the triage process in community isolation facilities. For instance, they've been able to preliminarily identify blood markers that could distinguish among different disease manifestations in patients. The team has also evaluated the usefulness of chest X-rays as a screening tool, finding that those with normal X-rays have a low risk of developing severe COVID-19.

"This is a new virus and a new disease. There are many urgent research questions," says Assoc Prof Lye. From host-virus interactions to antiviral treatments, clearly both medicine and science still have more to learn about COVID-19. "Research is harder work than clinical work, but it is vital to drive good care," he shares.

LESSONS FROM THE LUNGS

Despite the quickened pace of science triggered by COVID-19, many aspects of the disease still perplex the best researchers and doctors worldwide. Until now, we don't know why some infected people are asymptomatic, while others develop severe symptoms and require intubation.

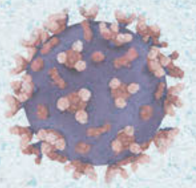
"If you have impaired immunity, you're likely to get very sick because you have no immune system to fight the virus. But if you have a robust immune system, you may also be at risk of getting a very severe disease," says Asst Prof Sanjay Chotirmall, Provost's Chair in Molecular Medicine and Principal Investigator of the Translational Respiratory Research Laboratory at LKCMedicine.

The latter effect, known as a cytokine storm, occurs when the body mounts such a strong immune response to the virus that it becomes damaging in itself. This could be why some young, otherwise healthy, COVID-19 patients suddenly deteriorate—and even die.

To better understand the disease's progression, Asst Prof Chotirmall is turning to tiny, three-dimensional versions of the lungs called lung organoids. All Asst Prof Chotirmall and his team need is a lung biopsy or nasal swab from the patient. From this, the team can recreate the diversity of cell types found in the individual's lung.

"A disease like this helps us to identify gaps in technology. In filling those gaps, we would actually be improving the way science is practised."

Assoc Prof Eric Yap
Principal Investigator of the Medical Genomics Laboratory, Lee Kong Chian School of Medicine



Lung organoids allow the team to analyse viral progression within a patient's lung in a more personalised and systematic manner. The team can even study an individual's susceptibility to coronavirus infection based on his or her cell receptors. Take, for instance, the ACE-2 receptor that mediates the cellular entry of SARS-CoV-2. Individual variations in the number of ACE-2 receptors could influence a person's likelihood of contracting COVID-19, he says.

Asst Prof Chotirmall is also using the organoids to identify key differences between the new coronavirus and its relative, SARS-CoV-1, the causative agent of severe acute respiratory syndrome (SARS) that emerged in 2003. Other aspects of his research include leveraging multi-omics approaches to investigate how viral infection changes genes on an individual cell level and to identify new diagnostic biomarkers for COVID-19. Asst Prof Chotirmall is now collaborating with Prof Stephan Schuster, Deputy Centre Director (Facilities & Capacities) and Research Director (Meta-'omics & Microbiomes) at the Singapore Centre for Environmental Life Sciences Engineering (SCELSE), to assess the impact of air quality on COVID-19 patients.

Examining air samples from a number of countries globally, the team found that pollution was associated with high case fatality rates. "Exposure to PM2.5 particulate matter is known in animal models to upregulate ACE-2 receptor expression in the airways. Populations that are primed by exposure to PM2.5 will have higher numbers of ACE-2 in the airways and be more susceptible to the virus and severe outcomes," says Asst Prof Chotirmall.

Another reason for the poorer health outcomes, he adds, is that polluted environments tend to be dominated by harmful bacteria. COVID-19 patients from such areas therefore not only have increased ACE-2 receptor expression, but are also potentially more susceptible to secondary bacterial or even co-infection. These findings, in the process of being published, could be of enormous interest especially to those living in countries with the poorest air quality.

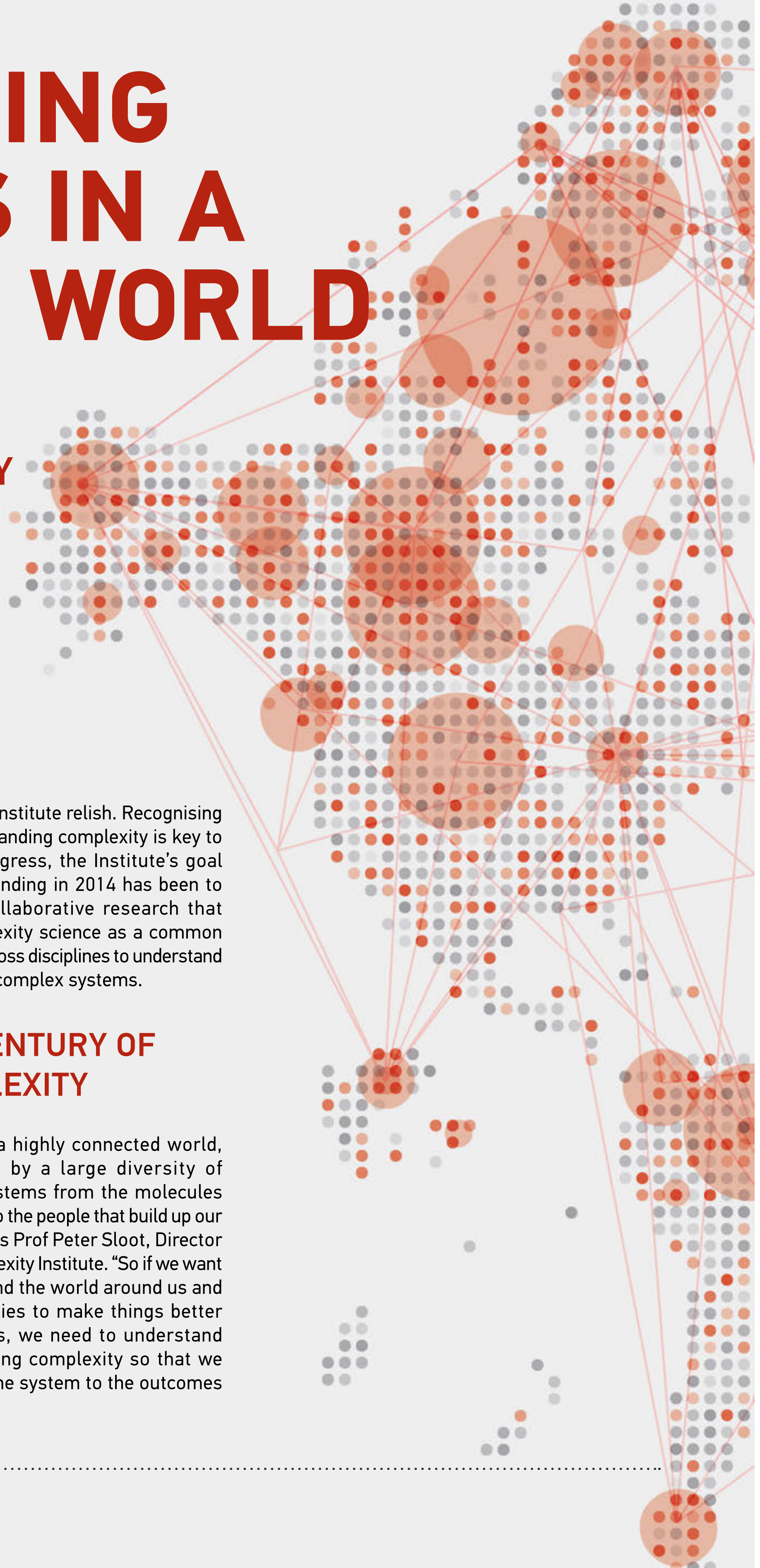
FILLING IN THE GAPS

Amid the global focus on COVID-19, there's an understandable worry that it could result in research on other pressing health concerns being neglected. Assoc Prof Yap, however, believes otherwise.

"Some people may see this as a distraction, that it's now taking money and time and attention away from other important diseases like cancers and chronic diseases," he explains. "But I'd say, conversely, a disease like this helps us to identify gaps in technology. In filling those gaps, we would actually be improving the way science is practised."

COVID-19 may be a trial by fire for scientists and clinicians around the globe, but with LKCMedicine's dedicated researchers working together on new innovative technologies to quell the outbreak, there's no question that NTU's medical school—and Singapore as a whole—will emerge better positioned to face future viral threats.

CONNECTING THE DOTS IN A COMPLEX WORLD



EMBRACING THE CENTURY OF COMPLEXITY

Researchers at NTU's Complexity Institute are modelling diverse outcomes in everything from pandemics to economic inequality.

What do a flock of birds, global financial markets and your immune system have in common? Each one is an example of a complex system, where the interaction of multiple components gives rise to interesting behaviour that is greater than the sum of its parts.

Take for example the immune system, which is made up of networks of molecules and cells that interact among themselves and with their environment in unpredictable ways. The difficulty of understanding such a system lies in the fact that its collective behaviour is often impossible to predict, since the interactions and relationships between its elements behave differently than each element would individually.

The late Stephen Hawking once predicted that this century would be one of complexity, which is precisely the challenge that researchers at NTU's Complexity Institute relish. Recognising that understanding complexity is key to societal progress, the Institute's goal since its founding in 2014 has been to promote collaborative research that uses complexity science as a common language across disciplines to understand a myriad of complex systems.

THE CENTURY OF COMPLEXITY

"We live in a highly connected world, surrounded by a large diversity of complex systems from the molecules in our body to the people that build up our society," says Prof Peter Sloot, Director of the Complexity Institute. "So if we want to understand the world around us and design policies to make things better on all fronts, we need to understand the underlying complexity so that we can nudge the system to the outcomes we want."

But one can hardly predict what a system will do after such a nudge, as the intervention itself would have turned it into a completely different system, Prof Sloot points out. A good illustration of this idea is the human brain, where neurons interact in a slew of dynamically changing networks.

"At what point in time does a thought emerge out of the interactions in a network of neurons? Which neurons would you trigger, and at what point in the system would you intervene to generate a particular thought? The short answer is, we don't know. We have no clue how changes in the constituting elements of a complex system affect the system's emerging properties."

What complexity science needs to focus on, Prof Sloot says, is new ways to assess the possible outcomes of these interventions. Currently, the most promising approaches for that come from non-linear out-of-equilibrium dynamics and information theory, he explains, noting that this is something researchers at NTU's Complexity Institute and the Institute for Advanced Study at the University of Amsterdam in the Netherlands have been working on.

MODELLING A PANDEMIC

Prof Sloot's own work at the Complexity Institute has tried to make sense of virology and the epidemiology of infectious diseases. For example, he has developed a predictive outcome system for HIV infection.

After receiving financial support from NTU and the European Union to study the pathways of HIV transmission, Prof Sloot was faced with a question: To stop a pandemic, would the money be better spent on better medical treatments or on changing behaviour?

For Prof Sloot, it all went back to the search for ways to capture the fundamental rules and processes that drive a pandemic. "It is clear that any answer to such a question requires an in-depth study of all the connectivity and feedback loops from molecule to mankind," he says.

To gauge the effects of medical and social interventions, Prof Sloot used an approach that took novel insights from complexity science. Together with his colleagues, he developed computational models that captured the infection and transmission processes across time and space before checking that model against historical data to generate a suite of hypothetical scenarios.

"Like a telescope that opens up a vista to the stars, computers have opened up amazing new ways to analyse different levels of complexity and unravel connections between them," he says. "Whatever idea I wanted to explore about these connections, there was always an algorithm I could design to improve my understanding of it."

LOOKING INTO THE FUTURE

The models designed by Prof Sloot to study HIV infection and transmission show promise of being used for other virus outbreaks. The SARS-CoV-2 novel coronavirus, for example, is an RNA virus like HIV. Although the subsequent infection, transmission and disease progression patterns are completely different from those of HIV, Prof Sloot believes both complexity science and the Complexity Institute's cross-disciplinary approach can help.

"One of the hardest things to capture in models are the behavioural aspects related to hygiene, distancing and quarantine because of cultural and religious aspects that we hardly understand," Prof Sloot says. "So we need social and behavioural scientists next to immunologists and epidemiologists. I am convinced that the only science that can connect the dots of this horrible pandemic is complexity science."

In collaboration with the Centre for Urban Mental Health at the University of Amsterdam, Prof Sloot is using a complexity approach to understand the impact of the COVID-19 pandemic on people living in dense urban areas. By integrating previously unconnected theories about urbanisation and mental health, Prof Sloot and his team hope to understand why some individuals thrive in urban settings whereas others end up developing mental problems.

With everything complexity encompasses, could a better understanding of it predict future pandemics?

"As we speak, in many places in the world, complexity scientists are building predictive computational models that help governments assess possible intervention strategies," Prof Sloot says. "Prediction is difficult, especially when it is about the future, but we need to give it a shot. I don't think there are other theories and methods that can do the job."

And even if it is difficult to predict the future, Prof Sloot is sure of one thing: We have an exciting journey ahead. And that journey, if Stephen Hawking is right, will be full of complexity.

"Like a telescope that opens up a vista to the stars, computers have opened up amazing new ways to analyse different levels of complexity and unravel connections between them."

Prof Peter Sloot
Director, Complexity Institute

TELEMEDICINE GOES VIRAL

DIGITAL HEALTH INNOVATION IN THE TIME OF COVID-19

Researchers at NTU's Centre for Population Health Sciences (CePHaS) are advancing the digital future of medicine and population health.

Large economies have slipped into a downturn, workplaces are shut, and once busy streets are now eerily empty. The novel coronavirus, SARS-CoV-2, if anything, has changed overnight the way we communicate, work and live.

In a time when hospitals are overwhelmed with patients, and visiting a clinic presents a genuine health risk in itself, people are turning towards an alternative that allows them to visit a doctor or renew their prescriptions from the safety of their homes—digital health.

"The beating of the digital drum has been going on for a long time, but only recently are we seeing major uplifts in its potential for healthcare," says Assoc Prof Josip Car, Founding Director of the Centre for Population Health Sciences at NTU's Lee Kong Chian School of Medicine (LKCMedicine).

"Not only does digitalisation give us the reach, but the insights and interactivity it provides are equally important, especially in a time like this."

SHAPING DIGITAL HEALTH RESEARCH

While COVID-19 has indeed changed the way we access healthcare services, it is not possible to re-wire the behaviour of an entire population overnight. Therefore, it is timely that a centre exists for research and education on the use of digital tools for health. "Digital technology will shape our public health for the better—in fact, it already has," says Assoc Prof Car.

Designated as a World Health Organisation (WHO) Collaborating Centre for Digital Health and Health Education, the Centre for Population Health Sciences aims to shape the transformative impact of digital tools in healthcare.

One area that the Centre works on is how digital health can be used to alleviate the impending global shortage of healthcare professionals, which WHO estimates to reach 18 million by 2030. Digital technology in the form of telemedicine, like teleconsultations or online pharmacies, offer an alternative venue for the public to receive medical aid and advice.

Telemedicine conducted on mobile devices—one of the many applied technologies of the mobile health (or mHealth) movement—has been particularly useful during the COVID-19 pandemic. For instance, contact tracing applications like TraceTogether, which was developed by the Government Technology Agency of Singapore, use Bluetooth Low Energy signals to log contacts with other users in close proximity.

"From patient education to public health services and now even disease management, we turn to these digital tools as a means towards or even as health solutions in and of themselves," Assoc Prof Car says. But for digital health technologies to be implemented on a wider scale, more innovation, research and evidence will be required to win the support of health policymakers and regulators, he notes. This is where researchers like his CePHaS team come in.

> **"Not only does digitalisation give us the reach, but the insights and interactivity it provides are equally important, especially in a time like this."**
>
> Assoc Prof Josip Car
> *Founding Director, Centre for Population Health Sciences*

A DOSE OF DIGITAL MEDICINE

As a practising family physician, one of the key areas in digital health that Assoc Prof Car works on is teleconsultation. Specifically, he aims to help physicians navigate their medical practice using digital tools.

"In many countries, consultations in both primary and specialist care are switching to a policy of video consultation first and physical consultation second," he says. "Therefore, we should look into equipping both physicians and patients with the skills to navigate this digital health terrain and building up evidence for using these tools."

For example, Assoc Prof Car says that most younger patients with COVID-19 can be managed remotely with self-isolation, remote monitoring and advice on how to manage their symptoms. He advises physicians to opt for video consultations instead of phone calls for patients where both the patient and the doctor have ready access to the technology, as visual cues can provide valuable diagnostic information.

Beyond teleconsultation, Assoc Prof Car and his team are also working on creating digital tools to manage chronic diseases such as diabetes. In particular, they are developing a mobile application that will enable people with Type II diabetes and their carers to better manage the disease at home, using an automated computer dialogue system.

"Our work can augment the current model of care for many patients, empowering them to be more proactive and informed about their condition," Assoc Prof Car explains. "We hope this can reduce their reliance on hospitals and potentially lower their healthcare costs as well." As digital health becomes the new norm, it will help to relieve the manpower burden on public health systems everywhere, especially during a crisis like COVID-19.

CATALYSING CHANGE IN PUBLIC HEALTH

Beyond convincing regulators and healthcare professionals to embrace digital health, issues such as insurance and medicolegal matters will also need to be addressed. "There is still much more to be done, but with the current pandemic, I foresee that the introduction of digital technologies will speed up from years to months or even weeks," Assoc Prof Car says. "It is a special time for digital health that must be seized."

While it may still be too early to draw any conclusions from the ongoing crisis, the novel coronavirus will undoubtedly bring about changes in public health policies. "The COVID-19 situation, if anything, has taught us that communication via digital technologies, such as video consultations and remote monitoring, can play a critical role in protecting health, reducing the risk of infection, and supporting chronic disease management at a much broader scale than most ever imagined," says Assoc Prof Car. "True, these interactions will never be the same as face-to-face meetings with a human touch, but digital health is proving critical in fighting the pandemic and keeping patients, nurses and doctors well," he adds.

Zooming in on viruses

Identifying key pathogen-host interactions to find new antiviral targets

By Richard Sugrue

Assoc Prof Richard Sugrue of NTU's School of Biological Sciences is an expert on the infection biology of respiratory viruses. More details on the research described here can be found in Virology *(2018), DOI: 10.1016/j.virol.2018.05.012;* Virology *(2015), DOI: 10.1016/j.virol.2015.05.014;* Antiviral Research *(2013), DOI: 10.1016/j.antiviral.2013.08.012; and* Molecular & Cellular Proteomics *(2010), DOI: 10.1074/mcp.M110.001651.*

Respiratory disease represents the most important cause of mortality worldwide, of which a significant portion is due to infectious agents. My lab mainly conducts research on respiratory-borne viruses, with a current focus on respiratory syncytial virus (RSV), human metapneumovirus (HMPV), and human and avian influenza viruses.

In collaboration with local hospitals and diagnostic laboratories in Singapore, which provide critical access to clinical and veterinary virus isolates, my research aims to identify and characterise essential pathogen-host interactions that occur during viral infection. Due to the complex nature of these questions, the projects undertaken involve a significant degree of multidisciplinary work, including imaging, functional genomics and bioinformatics, proteomics and standard molecular and cell biology techniques.

RESPIRATORY SYNCYTIAL VIRUS—A GLOBAL HEALTH CONCERN

Epidemiological data from the World Health Organisation indicates that RSV is responsible for 64 million infections per year and 160,000 deaths, mainly involving young children. It is the leading cause of viral pneumonia in young children, and this situation is exacerbated by the absence of licensed vaccines and the limited availability of cost-effective drugs.

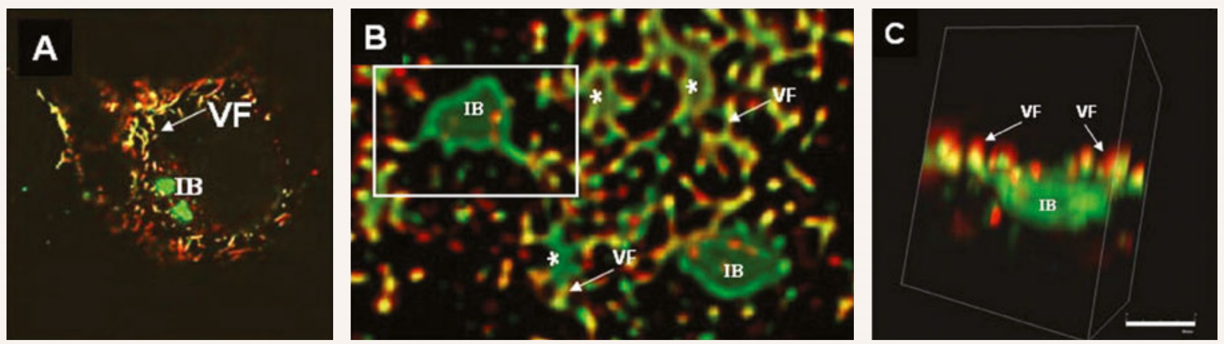


Figure 1: Images obtained by confocal microscopy of a virus-infected cell labelled using antibodies to the virus phosphoprotein (green) and virus fusion glycoprotein (red), highlighting the association of virus filaments and inclusion bodies in virus-infected cells. (A) Two-dimensional micrograph of the cell obtained at a single focal plane. (B) A series of images of a region near the surface of the same cell at different focal planes—processed and visualised in 3D—showing inclusion bodies (IB) labelled by anti-phosphoprotein and virus filaments (VF) labelled by both anti-phosphoprotein and anti-fusion glycoprotein. (C) A rotated and tilted projection of the cell's interior at higher magnification, showing an individual inclusion body and its associated virus filaments. Credit: Reproduced from *Molecular & Cellular Proteomics* (2010), DOI: 10.1074/mcp.M110.001651.

A better understanding of RSV's replication cycle could help identify novel drug targets and aid in vaccine development. Therefore, my research focuses on the identification and characterisation of essential pathogen-host interactions that occur during RSV maturation and transmission. Using light microscopy (Figure 1), we can identify virus filaments—special filamentous projections generated by virus particles to attach to and assemble at specific surface regions of cells in the respiratory tract. Another structure, known as inclusion body, contains the virus nucleocapsid—a complex of the virus genome and associated viral proteins including the nucleoprotein, phosphoprotein and large polymerase protein.

VIRUS FILAMENTS AS TARGETS FOR ANTIVIRALS

To examine RSV replication, we used a nasal epithelial organoid cell model, which closely resembles the cells in the nasal airways that are the primary site of viral infection in humans.

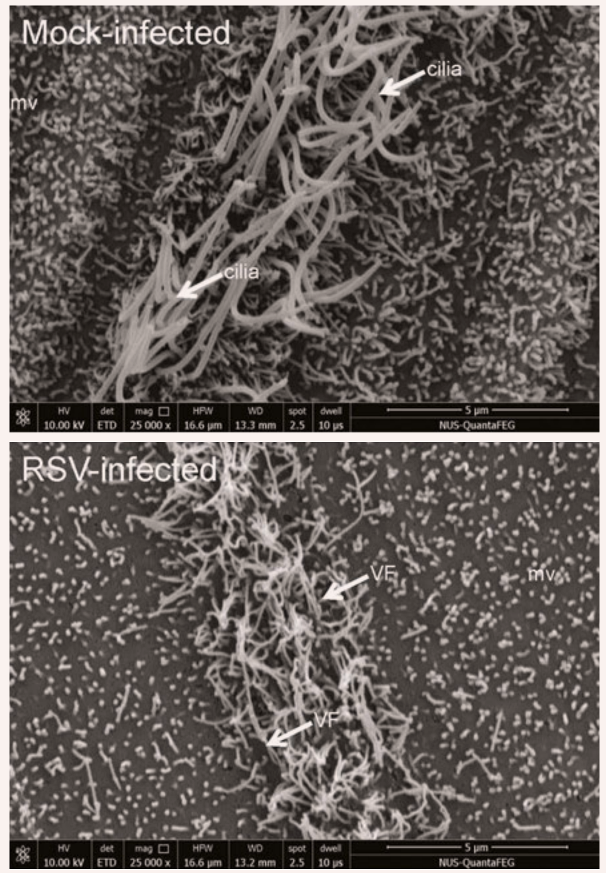
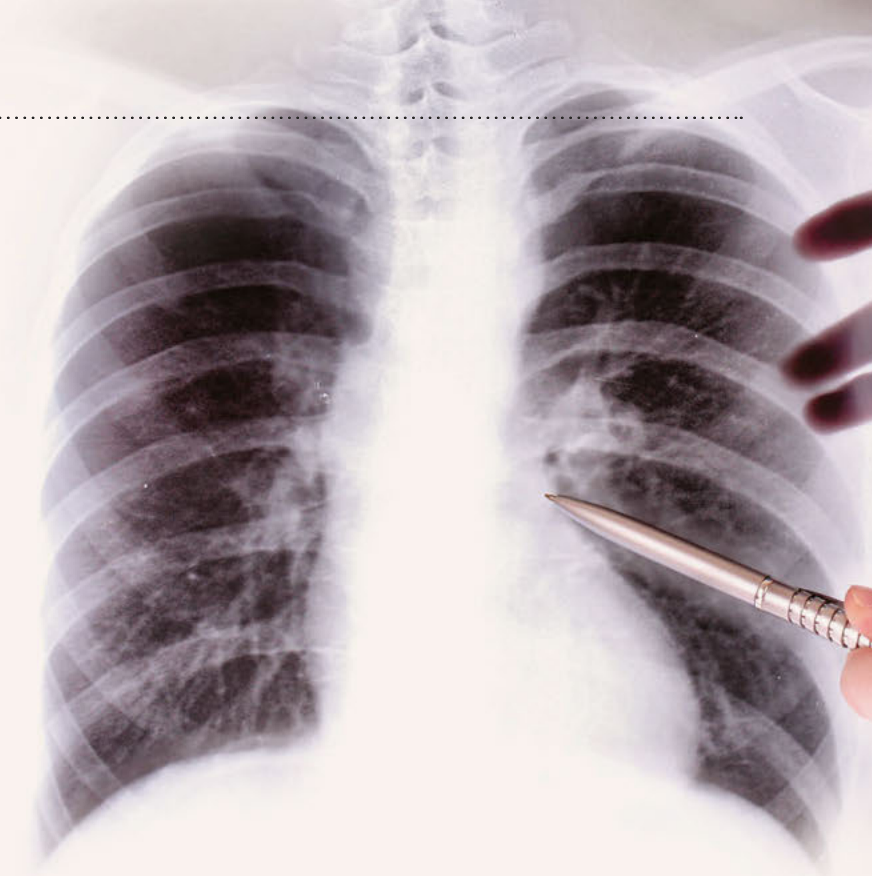


Figure 2: Scanning electron microscopy of mock-infected and RSV-infected cells. Cilia, microvilli (mv) on non-ciliated cells, and virus particles (VF) are labelled. Credit: Richard Sugrue.



Use of this cell model has allowed us to demonstrate virus filament formation during RSV infection (Figure 2), highlighting the physiological relevance of these structures in the development of antivirus strategies.

The formation of virus filaments also correlates with the degradation and dysfunction of cilia—projections of epithelial cells in the respiratory tract that clear mucus and dirt out of the airways. Destruction of the cilia contributes to the damage caused by the virus in our lungs.

NEW AVENUES TO PREVENT VIRUS PARTICLE BINDING

My lab was able to demonstrate that an enzyme called 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) is highly expressed during RSV particle formation. HMGCR is a key enzyme in the mevalonate pathway, which regulates the formation of small hydrophobic molecules. These molecules are important in the anchoring of certain cellular proteins to membranes where they are exploited by the virus to build virus particles.

We also demonstrated that a cardiovascular drug—lovastatin—is able to block virus filament formation and virus transmission. The antiviral activity of lovastatin supports our hypothesis that the mevalonate pathway is involved in the assembly and formation of virus particles on the surface of infected cells.

Our findings of virus-induced changes in cellular signalling and metabolic activities underline the complexity of the virus particle formation process. Understanding this process in greater detail may lead to the development of novel drugs to treat infection with RSV and related virus species.

Action, not reaction

A toolkit to stay ahead of evolving viruses

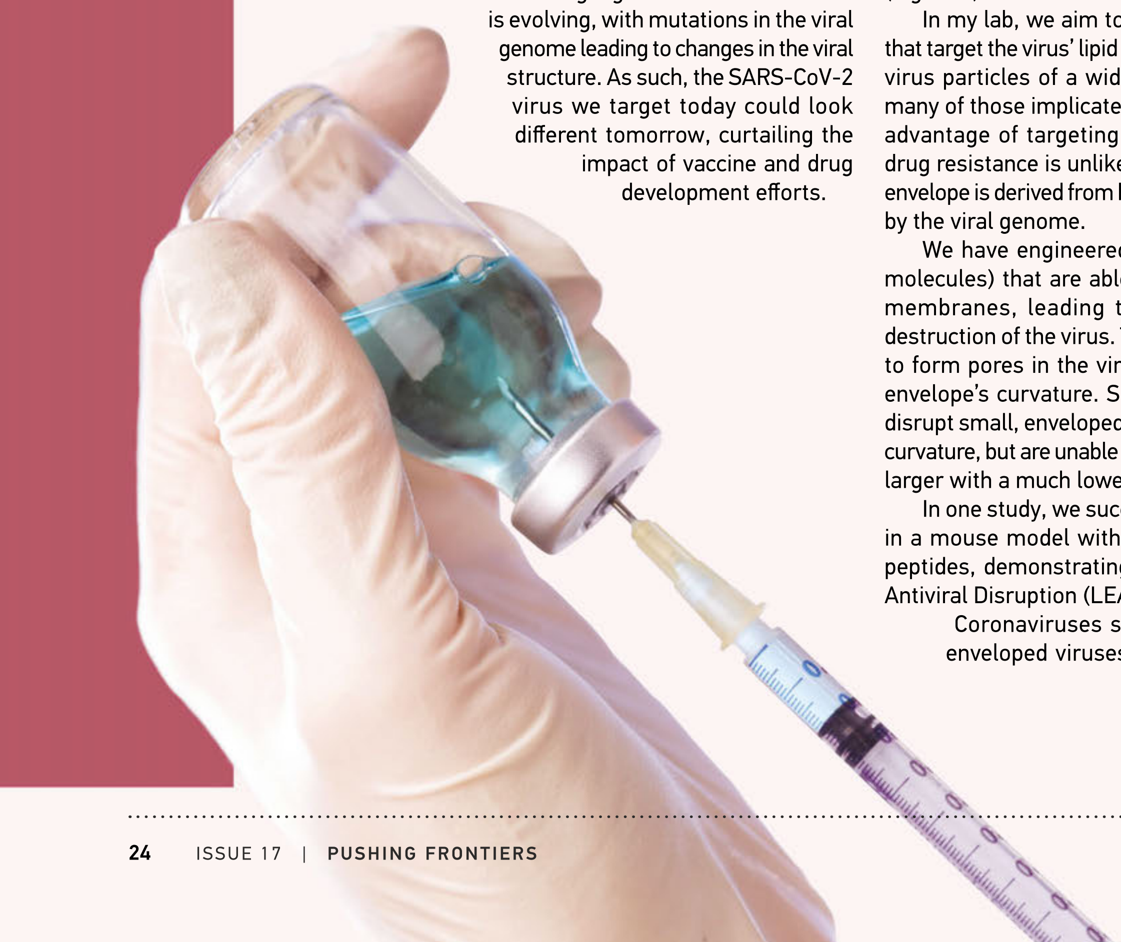
By Cho Nam-Joon

Prof Cho Nam-Joon of NTU's School of Materials Science and Engineering is the Materials Research Society of Singapore Chair in Materials Science and Engineering and an affiliated principal investigator in NTU's Singapore Centre for Environmental Life Sciences Engineering.

Parts of the research presented here have been published in Nature Materials *(2020), DOI: 10.1038/s41563-020-0698-4;* Nature Materials *(2018), DOI: 10.1038/s41563-018-0194-2;* ACS Infectious Diseases *(2018), DOI: 10.1021/acsinfecdis.8b00286;* Small *(2016), DOI: 10.1002/smll.201500854; and* Gastroenterology *(2015), DOI: 10.1053/j.gastro.2014.11.043.*

As SARS-CoV-2 spreads globally, scientists around the world are racing to develop a vaccine. However, it is estimated that it will take many months and perhaps years to develop, test, validate and deploy an anti-SARS-CoV-2 vaccine, and eventual success is not a given.

What's more, analyses of SARS-CoV-2 infections highlight the risk that the virus is evolving, with mutations in the viral genome leading to changes in the viral structure. As such, the SARS-CoV-2 virus we target today could look different tomorrow, curtailing the impact of vaccine and drug development efforts.



TARGETING TODAY'S AND TOMORROW'S PANDEMICS

While viruses can have very distinct structural features, medically important viruses often share key features that can provide the basis for broad-spectrum antiviral targeting (Figure 1).

In my lab, we aim to develop broad-spectrum antivirals that target the virus' lipid membrane—a coating that envelopes virus particles of a wide range of virus species, including many of those implicated in recent outbreaks. An important advantage of targeting virus membranes is that antiviral drug resistance is unlikely to emerge because the viral lipid envelope is derived from host cell membranes and not encoded by the viral genome.

We have engineered bioactive peptides (small protein molecules) that are able to selectively form pores in virus membranes, leading to a rupture of the envelope and destruction of the virus. The ability of these antiviral peptides to form pores in the viral membranes is dependent on the envelope's curvature. Specifically, the peptides are able to disrupt small, enveloped virus particles with high membrane curvature, but are unable to damage human cells that are much larger with a much lower membrane curvature (Figure 2).

In one study, we successfully treated Zika virus infection in a mouse model with engineered pore-forming antiviral peptides, demonstrating that the so-called Lipid Envelope Antiviral Disruption (LEAD) concept is effective *in vivo*.

Coronaviruses such as SARS-CoV-2 belong to the enveloped viruses and thus are potentially excellent targets for the LEAD strategy. As proof of concept, we tested the activity of engineered peptides against murine hepatitis virus, a species of coronavirus that infects mice, and found high antiviral activity. We are currently developing peptides with the ability to disrupt other coronavirus species, including SARS-CoV-2.

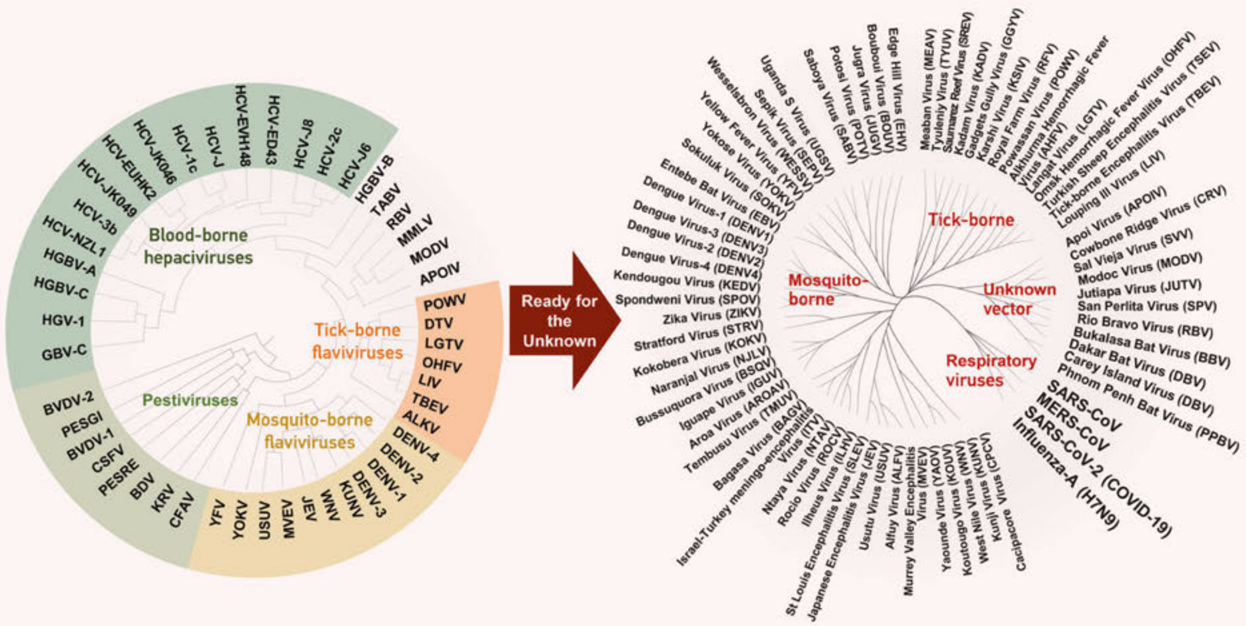


Figure 1: Broad-spectrum antiviral strategies that work against a wide range of viruses have excellent potential as first-line countermeasures against not only known but also currently unknown and understudied viruses. Credit: Reproduced from *Nature Materials* (2020), DOI: 10.1038/s41563-020-0698-4.

MAKING THE HOST INHOSPITABLE

Another strategy to decrease the potential for the emergence of resistance as well as increase the potential for broad-spectrum activity is to use small molecule inhibitors or similar means to target host cell functions important for viral infection or replication.

Not only does targeting host proteins that are not under genetic control of the virus make it more difficult for a virus species to develop resistance through mutation, many different virus species depend on access to the same host cell function. Thus, a single drug inhibiting a key host enzyme can target multiple viral pathogens, not just those that are currently known but also related viruses that might emerge in the future.

BEING PREPARED FOR THE FUTURE

Being prepared to confront future viruses with broad-spectrum antiviral countermeasures—such as the LEAD concept and other mechanistic approaches—could significantly boost our ability to ward off pandemics and reshape the landscape of antiviral drug development, including what we view as "druggable" biological targets.

Most importantly, the above approaches would allow us to be proactive, instead of reactive, to emerging viral threats.

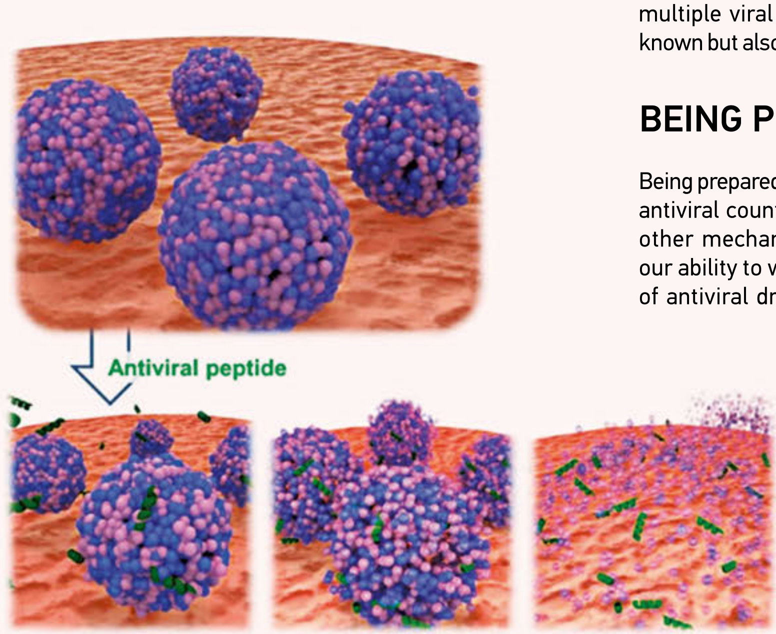


Figure 2: Precision-engineered peptides (green spirals) can selectively disrupt high-curvature membranes of enveloped viruses (blue-pink balls), effectively inhibiting viral entry into human cells. Credit: Cho Nam-Joon.

When fake news goes viral

Seeking information during the COVID-19 pandemic

By Edson Tandoc Jr

Teaching and researching on news production and consumption, Assoc Prof Edson Tandoc Jr of NTU's Wee Kim Wee School of Communication and Information (WKWSCI) is also the secretary of the journalism studies division of the International Communication Association and an associate editor of the academic journal Digital Journalism.

The research described in this article is part of Assoc Prof Tandoc's Information Integrity Initiative (IN-cube), a project that focuses on studying information quality. You can find more details on this initiative in blogs.ntu.edu.sg/in, and on his related research in Sociology Compass *(2019), DOI: 10.1111/soc4.12724; and* Journalism *(2019), DOI: 10.1177/1464884919868325. Assoc Prof Tandoc has also written extensively for newspapers and other news outlets, including [1]* Channel NewsAsia *(bit.ly/cnaETfakenews).*

Uncertainty over the COVID-19 pandemic, coupled with stay-at-home policies implemented in many cities around the world, has led to an increase in media consumption everywhere.

News outlets, which have long complained about losing audiences to social media platforms, have seen spikes in television ratings and site visits as audiences seek information on the pandemic.

Social media platforms have also seen heavier traffic than ever before, while video streaming sites have had to cut down on video quality in some places to accommodate a surge in demand.

Through a series of surveys and focus group discussions, my team has been keeping an eye on the media use patterns and information behaviours of Singaporean residents during this pandemic.

SURVEYING THE INFORMATION-SEEKING BEHAVIOUR OF SINGAPORE RESIDENTS

To find out how young adults are navigating the uncertainty brought about by the outbreak, my project officer, James Lee Chong Boi, and I conducted eight focus group discussions involving 89 young adults in Singapore who were recruited from the NTU student population in February 2020.

By the time we completed the focus group discussions, Singapore had 74 confirmed cases of COVID-19. Back then, the young adults we interviewed had already expressed uncertainty about the nature of the virus, whether to wear a mask, and how long the outbreak would last.

While uncertainty reduction theories assume that individuals seek to reduce uncertainty by seeking more information, we found that most young adults we interviewed engaged in information scanning behaviour—they did not actively seek information about the outbreak but they also did not avoid information about it.

By signing up for alerts on messaging apps such as Telegram and WhatsApp, which were set up by news outlets and the Singapore Government, our survey respondents could be alerted when a new update was ready but also control exactly when they attended to these messages.

TRACKING COVID-19-RELATED INFORMATION SEEKING

Social media and messaging apps have long been used for news-related purposes, but more so during this pandemic. We observed this in a three-wave national survey my WKWSCI colleague Asst Prof Kim Hye Kyung and I conducted between February and April 2020.

In the first survey involving 1,000 residents in Singapore conducted between 25 February and 10 March 2020, we tracked, among other topics, information seeking and scanning in relation to COVID-19.

We found that local television news was a significant source of COVID-19 information for about 57% of our respondents, but we also found significant increases in the use of digital platforms over the span of two weeks in a second survey conducted between 12 March and 1 April 2020 (Figure 1).

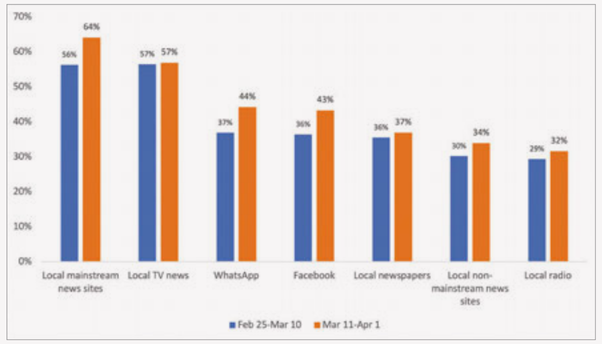


Figure 1: Percentage of participants who indicated they use the news source for COVID-19 "frequently" or "very frequently." Of the 1,000 Singaporean residents who took part in the survey conducted between 25 February and 10 March 2020, 767 participated in another survey carried out between 12 March and 1 April 2020.

Some 56% said they used mainstream news sites frequently or very frequently—this number increased to 64% after two weeks. Similarly, WhatsApp news use increased from 37% to 44% while Facebook news use increased from 36% to 43% over two weeks.

SPREADING ONLINE FALSEHOODS

Increased social media and messaging app use has its dark side, as it also increased the risk of users being exposed to misinformation about the virus.

Since January, my student Mak Weng Wai, who is a history major at NTU's School of Humanities, and I have been analysing COVID-19-related messages being forwarded on WhatsApp.

Over the span of three months, we were able to collect 153 forwarded messages—messages that were not originally created by the sender. Through our own fact-checking, we found that 35% of the forwarded messages about COVID-19 were false. Examples include several versions of a message claiming that gargling saltwater protects one from COVID-19 (Figure 2).

Figure 2: (left) An example of a message on protective measures against COVID-19 being forwarded on WhatsApp by some users in Singapore; (right) A message created by the World Health Organisation to debunk viral messages like the one shown on the left. Credit: (left) social media screenshot; (right) World Health Organisation.

While 28% of the forwarded messages were based on accurate information, some 20% of the messages mixed true and false information. For example, one forwarded WhatsApp post included a video of a Malaysian student in London recording a message for his parents. The post claimed the student contracted the virus at a party and died of COVID-19. While the video recording is real, the student had to later clarify in a Facebook post that he is very much alive.

In a news commentary for *Channel NewsAsia* [1], Mak Weng Wai and I wrote: "Online falsehoods work like viruses. They need to infect one vulnerable host who can then spread them to other hosts."

Indeed, this pandemic has exposed many of our vulnerabilities, and one of them is our susceptibility to spreading and believing in problematic information, aided by the ease and speed of information flow facilitated by social media and messaging apps.

Fighting misinformation is particularly crucial in a time like this, to protect not just ourselves but also others in the community. This is why it is important for us to keep an eye not only on the public's information behaviour, but also on the quality of information flowing through various channels—an effort that the work my colleagues and I are doing at WKWSCI seeks to contribute to.

THE FAMILY DOCTOR

Catalysing change in family medicine

In the coming decades, Singapore will be faced with significant healthcare challenges, including the twin threats of infectious diseases and a rapidly ageing population. As Singapore's first academic in family medicine, Prof Helen Smith plans on taking on some of these big research challenges.

Based at NTU's Lee Kong Chian School of Medicine (LKCMedicine), where she is Professor of Family Medicine & Primary Care and Director of the School's Primary Care Research Network, Prof Smith is studying novel ways of delivering primary healthcare, using pharmacological or psychological methods or those relating to service organisation.

As Co-Director of the Centre for Primary Health Care Research and Innovation, Prof Smith is leading a collaboration between LKCMedicine and the Singapore National Healthcare Group (NHG) to provide seed funding for research into chronic diseases and health promotion, among other initiatives.

In this interview, Prof Smith shares her views on the integral role of community-based medical services in a national healthcare system, which has become ever more essential during the COVID-19 pandemic.

Q What is the role of family medicine and primary care in a healthcare ecosystem?

A Primary care is usually the first point of contact that people have with healthcare services. When organised well, it provides comprehensive community-based care throughout life, sometimes described as "cradle-to-grave" care.

As generalists, family doctors do not focus on one organ or system but on the whole person. Patients can present with any condition—from minor or acute to severe or chronic—and the majority of a person's healthcare needs are managed very well in primary care. However, for help with a difficult diagnosis or an investigation or procedure only available in a tertiary facility, the family doctor will refer the patient to a specialist colleague, in a triage role often spoken of as "gatekeeping".

Family physicians and general practitioners take a holistic approach to problems; they are attentive to the psychosocial impact of ill health on the person as well as its physical impact. There is good international data showing that family medicine and primary care improve the quality of healthcare and patient outcomes in cost-effective ways.

Q What were some of the challenges faced by family medicine and primary care doctors during the COVID-19 outbreak, and how did they respond?

A In the very early stages of the outbreak, many patients presented at clinics with symptoms such as a cough or a higher-than-normal temperature, which might be caused by COVID-19 but are also symptomatic of many other frequent illnesses, including the common cold. Some patients presented with concerns generated by fake news or misleading information.

Very quickly, referral pathways were established and initiatives such as SASH—swab-and-send-home, a testing programme with clear criteria for eligibility—were initiated. Over 800

Public Health Preparedness Clinics (PHPCs) trained and equipped to deal with respiratory illnesses, which had been established in previous years to deal with the haze (a recurrent air pollution crisis caused by regional forest fires) and the 2009 H1N1 influenza pandemic, were re-activated to work with the polyclinics.

Clinics also adopted new ways to manage and monitor patients with other illnesses, including those with chronic problems. For instance, doctors reverted to telephone consultations to protect patients from being exposed to COVID-19-positive patients—an approach that appeared to be valued by patients for its convenience and cost-effectiveness. Thus, the novel coronavirus might become a catalyst for practice redesign, with in-person healthcare becoming the second rather than the first option for patient care.

In addition, doctors developed professional groups for information sharing and hotlines to support stressed healthcare workers.

Q How will your appointment as the first professor of family medicine and primary care in Singapore support the advancement of this specialty?

A Traditionally, research has taken place in teaching hospitals and specialist centres. However, we increasingly recognise that such research does not always address the questions that are important in family medicine: management of minor illnesses, multi-morbidity and preventive healthcare, as well as the organisation of public healthcare. Such topics need to be investigated in real-world settings.

Research can improve service delivery and the health of our patients, while at the same time benefitting healthcare providers. Participating in research encourages us to reflect on our practice and explore questions arising from patient care. In addition, developing new skills, discussing ideas and collaborating with colleagues is fun and provides another dimension to the lives of professionals.

"The novel coronavirus might become a catalyst for practice redesign, with in-person healthcare becoming the second rather than the first option for patient care."

Q What are your current research interests?

A I have evaluated novel ways of delivering health services and "new technologies" in primary healthcare over many years, using pharmacological or psychological methods or those relating to service organisation.

In one example of my current research, we are completing an evaluation of a tele-dermatology service aimed at improving the management of skin problems in primary care. The service allows patients with skin problems that cannot be diagnosed by a primary care physician to have an immediate virtual consultation with a dermatologist at Singapore's National Skin Centre. Patients benefit from timely advice delivered in an environment they are familiar with, and from being able to start their treatment without delay.

Another evaluation project aims to assess the benefits of pharmacogenetics testing in primary healthcare settings. Adverse drug reactions are a common cause of hospital admissions and it would be preferable if patients underwent pharmacogenomic testing prior to prescription rather than after developing the adverse reaction. As doctors in primary care are well placed to conduct pharmacogenomic testing, we are evaluating the potential and patients' acceptability of a medical support system that guides drug prescriptions in primary healthcare.

Q How has your appointment at LKCMedicine supported your research?

A I very much enjoy being part of a young medical school where I have been able to build research collaborations without being bound by tradition. LKCMedicine recognises the importance of translational research and partnerships between academics and clinicians to bring together different skills and perspectives in the design and execution of excellent research.

I have a long-standing interest in respiratory disease, and one of the LKCMedicine initiatives I am delighted to be part of is TARIPH, The Academic Respiratory Initiative for Pulmonary Health. TARIPH aligns academic expertise across Singapore to better understand the local respiratory disease burden and improve lung health, and I can contribute with my expertise in understanding patients' journey to seeking healthcare and patient-related outcome measures.

Excellence in research goes beyond academics and clinicians. Patient and public involvement in medical research is also important, and is an area that is still in its infancy in Singapore, but my team has been developing a novel way of engaging patients in discussions about research. I am currently planning to establish a Lived Experience Group—a patient group willing to contribute to the projects within my research group and beyond.

Q You are the Director of the Primary Care Research Network and Co-Director of the Centre for Primary Health Care Research and Innovation at the medical school. Tell us more about the network and centre.

A The Primary Care Research Network I established in the south of England in the 1990s was the first of its kind and was cited as an example of good practice in the UK Department of Health's Strategic Review of Primary Care. Subsequently, similar research networks were replicated throughout the UK, and I became the Foundation Chair of the UK Federation of Primary Care Networks and later co-founded the International Federation of Primary Care Networks, an organisation under the umbrella of the World Organisation of Family Doctors.

Similar to the UK networks, the Primary Care Research Network initiative at LKCMedicine aims to develop research capacity amongst family doctors who deal with a mix of cases that are quite different in terms of diagnoses and severity-level from diseases addressed in hospital- and specialist-based research.

Setting a different focus, the Centre for Primary Health Care Research and Innovation promotes innovative research and evaluation to strengthen the contribution of family medicine and primary healthcare to the well-being of patients and their carers. Among other initiatives, the Centre provides seed funding for research into chronic diseases and multi-morbidity, and new ways of promoting health and self-management. The Centre, which is a tie-up between LKCMedicine and NHG, also enables collaborations and the development of pilot data to justify bids to external research funding bodies.

Q Could you share with us your vision of how family medicine and primary care should be practised in Singapore?

A Efforts led by the College of Family Physicians Singapore and the Ministry of Health have already achieved much in family medicine and primary care in Singapore, but there are some major challenges ahead.

To provide good care for our rapidly ageing population, we need to move from reactive care to more integrated and proactive care for individuals with multiple chronic conditions. This transition requires family doctors to develop new clinical skills and calls for changes to the way healthcare is organised, funded and delivered. Formal evaluation of new approaches to primary healthcare delivery will not only benefit Singapore but would also be of interest to other countries facing similar challenges.

I hope to contribute to the development of a robust evidence base for high quality care in the generalist setting in Singapore, and also help train a cadre of family medicine and health service researchers. My wish is to see the professional standing of family medicine increase, aided by the introduction of mandatory postgraduate training and organisational changes including patient empanelment, use of a universal electronic patient record and the development of multidisciplinary teams even in the smaller practices.

#WorldUnited

NTU SCIENTISTS JOIN GLOBAL COVID-19 EFFORTS

Science is our best shot at a solution to the ongoing COVID-19 pandemic. Much needed vaccines and novel diagnostic approaches and therapies would not be possible without research and scientific innovation.

Here we profile three experts from NTU in the fields of virology, structural biology and bioengineering. As part of a global effort to stop the virus in its tracks, they are providing us with critical insights into molecular drug targets for SARS-CoV-2 and developing diagnostic tools to help us rapidly and accurately detect new cases of COVID-19.

Assoc Prof Julien Lescar

Credit: NTU.

Trained in both biochemistry and crystallography, Assoc Prof Julien Lescar of NTU's School of Biological Sciences is giving us a glimpse into life at the nanoscale.

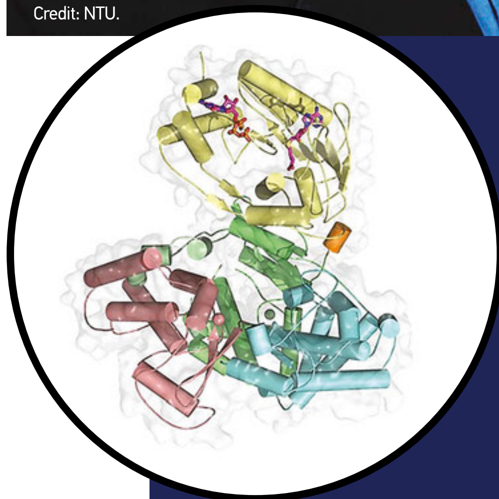
Using X-ray crystallography and cryo-electron microscopy facilities at the NTU Institute of Structural Biology, Assoc Prof Lescar and his team have determined the 3D structures of key proteins of major human viruses. These structural insights provide clues to designing new antiviral drugs, vaccines and therapeutic antibodies.

A decade-long collaboration with the Novartis Institute for Tropical Diseases in Singapore to determine the structure of key dengue virus proteins paid off handsomely when the protein structures helped scientists identify homologous structures of the Zika virus, a closely related RNA virus that emerged in 2015.

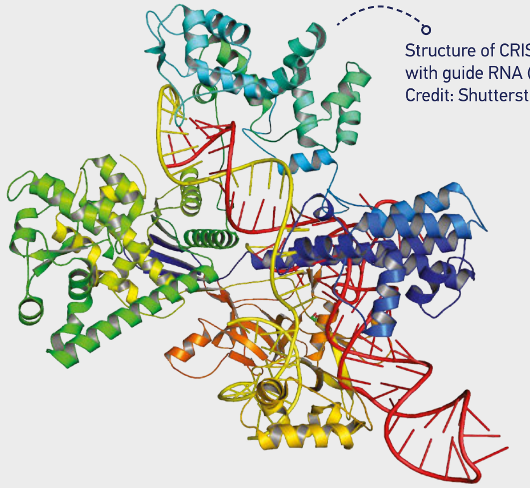
In the same vein, the molecular structures of important coronavirus proteins, resolved by Assoc Prof Julien Lescar and colleagues at the French National Centre for Scientific Research 15 years ago, now provide crucial information for the identification of molecular drug targets against SARS-CoV-2.

Assoc Prof Lescar co-founded the biotech start-up Epitoire in 2018 together with colleagues from the United States and NTU's Prof James Tam and Assoc Prof Liu Chuan Fa, with the support of NTU's commercialisation arm, NTUitive.

Epitoire develops products based on peptide ligases—molecular precision tools that have applications in medicine and biotechnology—and investigates treatments for diseases caused by dysregulated gene expression, including cancer, autoimmunity and neurodegenerative disorders.



Structure of the dengue virus non-structural protein 5, resolved by a team led by Assoc Prof Julien Lescar and Assoc Prof Luo Dahai (see also page 35). Credit: *PLoS Pathogens* (2015), DOI: 10.1371/journal.ppat.1004682.



Structure of CRISPR/Cas9 in complex with guide RNA (red) and DNA (yellow). Credit: Shutterstock.

"Extensive testing in the population is key to successfully tackling the spread of the COVID-19-causing virus," says Asst Prof Tan Meng How of NTU's School of Chemical and Biomedical Engineering.

Joining the global fight against COVID-19, Asst Prof Tan is using precision genome engineering, including CRISPR-Cas gene editing technology, to develop rapid diagnostic assays for SARS-CoV-2.

He previously designed a special enzyme for the CRISPR-Cas system, called iCas, that can be used to temporally control genome editing activity in developmental and stem cell studies.

"Understanding the functions and regulation of RNA editing—which naturally takes place in all cells during the body's development—will help to address myriad diseases in which RNA editing processes go wrong, including cancer, neurological disorders and autoimmune diseases," says Asst Prof Tan.

Currently, he is working on a CRISPR-mediated editor to correct mutations underlying genetic skin diseases such as epidermolysis bullosa and eczema. "Children with epidermolysis bullosa have fragile skin that blisters easily. Their quality of life is terrible as they are constantly in pain and often suffer from opportunistic infections," says Asst Prof Tan.

His studies on RNA editing are possible with the use of genomic, transcriptomic and nanopore RNA sequencing platforms, in combination with machine learning and computational methods designed by his lab members.

Asst Prof Tan was one of nine life scientists selected for the EMBO Global Investigator Award 2020, a career award from the European Molecular Biology Organisation (EMBO). He has a joint appointment with the Genome Institute of Singapore under Singapore's Agency for Science, Technology and Research.

Credit: NTU.

Asst Prof **Tan Meng How**

"Viruses are amazing species, simple yet difficult to understand," says Assoc Prof Luo Dahai, NTU Provost's Chair in Medicine and Principal Investigator of the Molecular Mechanisms of Viral Infection & Host Defence Laboratory at NTU's Lee Kong Chian School of Medicine.

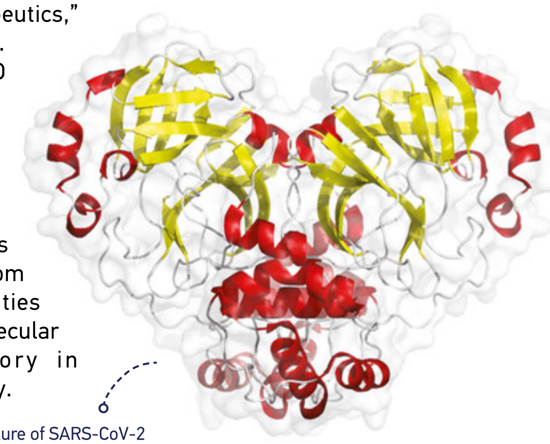
Driven by a curiosity for how viruses replicate and how our immune system defends us against them, the infection and immunity expert studies the molecular events involved in the neverending battle between host and pathogen.

In particular, he has a keen interest in flaviviruses—a class of important mosquito-borne RNA viruses that include dengue, chikungunya and Zika—and is developing dengue- and Zika-specific inhibitors and other antiviral drugs with colleagues from NTU, Singapore's Agency for Science, Technology and Research, and Duke-NUS Medical School.

During the COVID-19 pandemic, Assoc Prof Luo is leveraging his expertise in RNA viruses to characterise the SARS-CoV-2 virus replication process. He is also studying SARS-CoV-2 viral proteins for the development of rapid diagnostics with Assoc Prof Duan Hongwei, Associate Chair (Research) of NTU's School of Chemical and Biomedical Engineering.

"The more we know about the molecular biology of the SARS-CoV-2 virus, the mechanisms of infection and the host immune response, the better the chances we have of developing therapeutics," says Assoc Prof Luo.

Named an EMBO Young Investigator by the European Molecular Biology Organisation (EMBO) in 2018, Assoc Prof Luo's research benefits from access to core facilities at the European Molecular Biology Laboratory in Heidelberg, Germany.



Structure of SARS-CoV-2 coronavirus main protease. Image credit: Luo Dahai.

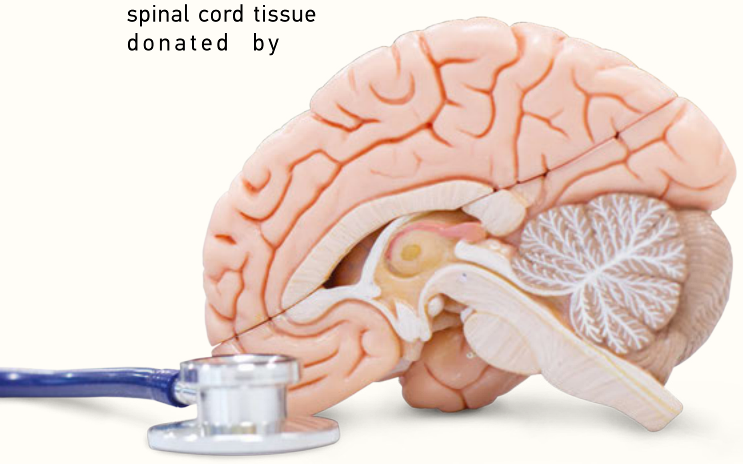
Assoc Prof **Luo Dahai**

Credit: NTU.

[COMING YOUR WAY]

1 Teaming up with NTU's Lee Kong Chian School of Medicine to establish and host the **Brain Bank Singapore** are Singapore's National Neuroscience Institute and National Healthcare Group.

The bank will serve as a national resource on post-mortem human brain and spinal cord tissue donated by patients and healthy individuals. The collection of diseased and normally-aged tissue will be used in ethically approved research into neurological and neuropsychiatric conditions, with the aim of identifying new drug targets and treatments.

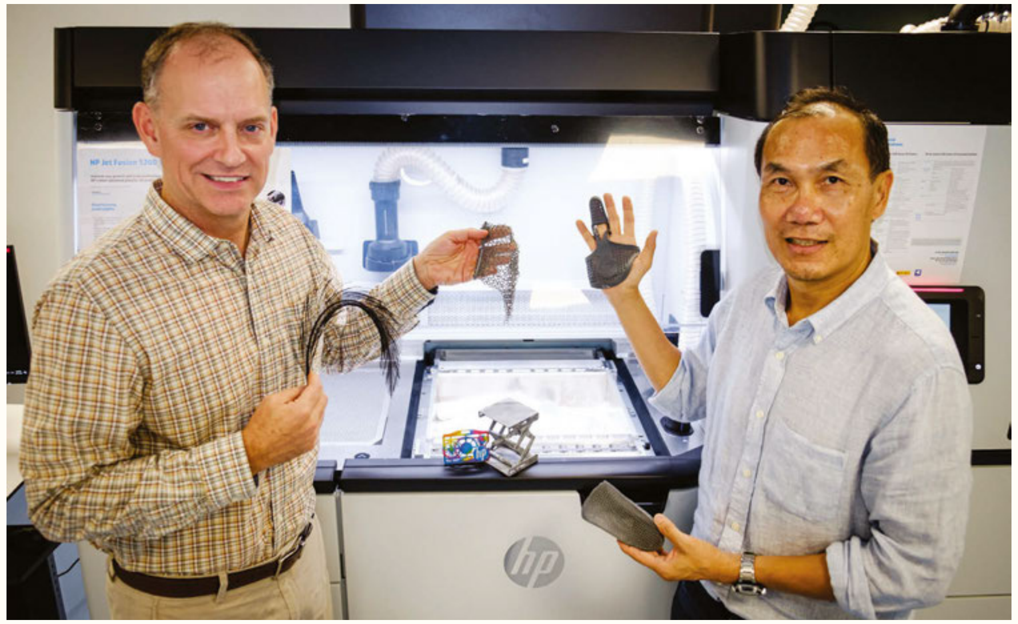


Prof Richard Reynolds of NTU's Lee Kong Chian School of Medicine (centre), Director of Brain Bank Singapore, with Dr Adeline Ng (right), a Consultant Neurologist from the National Neuroscience Institute, and Dr Jimmy Lee, a Senior Consultant from Singapore's Institute of Mental Health. Credit: NTU.

2 Intelligent design software tools incorporating machine learning were among digital manufacturing technologies showcased at the official opening of the **HP-NTU Digital Manufacturing Corporate Lab**.

Established jointly by NTU, HP Inc and Singapore's National Research Foundation, the lab is studying how to make manufacturing and supply chain operations more efficient, cost-effective and sustainable.

It will also host a new skills development programme—set up under Singapore's SkillsFuture initiative—to support the training of talent in additive manufacturing, digital product design, data management and automation.



The Co-directors of the HP-NTU Digital Manufacturing Corporate Lab, (from right) NTU's Prof Tan Ming Jen and Dr Mike Regan, with flexible 3D-printed products fabricated by the HP Multi Jet Fusion 3D printer. Credit: NTU.

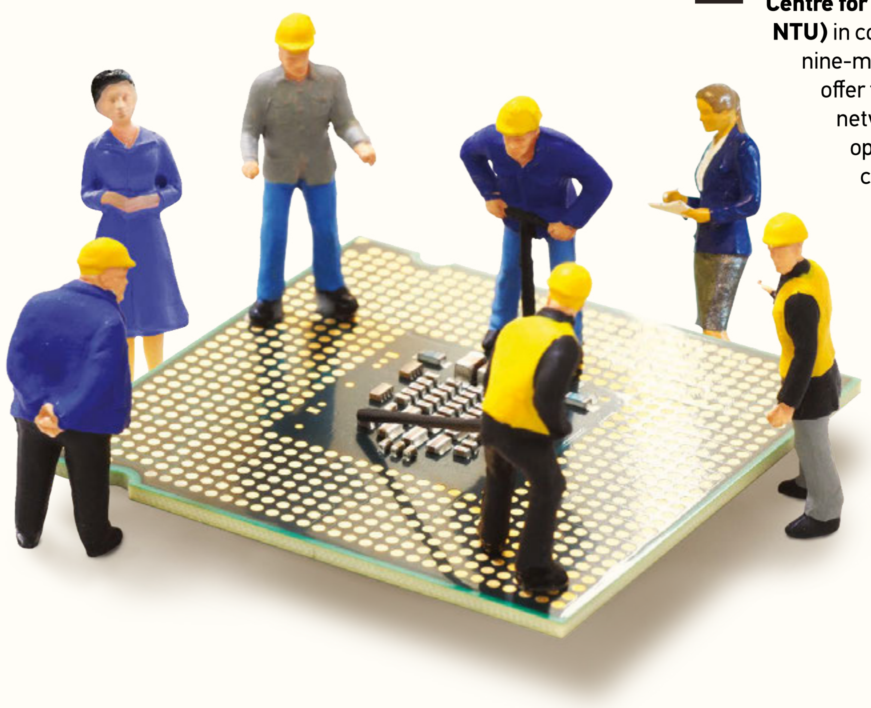
3 At the new **SERI-NTU Advanced Ocular Engineering (STANCE) Laboratory** on campus, ophthalmologists, biomedical engineers and research scientists come together to develop advanced ocular imaging technologies and drug delivery systems.

Jointly launched by NTU, the Singapore National Eye Centre, and the Singapore Eye Research Institute, the lab will build systems based on optical coherence tomography, a medical imaging technique that captures two- and three-dimensional images from the eye in micrometre-resolution. These systems will allow for early detection of eye conditions such as age-related macular degeneration, glaucoma and diabetic retinopathy.

4 To groom talent in the data centre sector, NTU has tied up with **Facebook** for a new pilot programme. Developed by **NTU's Centre for Professional and Continuing Education (PaCE@NTU)** in conjunction with NTU's College of Engineering, the nine-month pilot programme starting in August 2020 will offer four specialist certificates—in design engineering, network engineering, site operations, and facilities operations—and a graduate certificate in international construction management.

Supported by Singapore's national SkillsFuture initiative, the courses will help to train local engineering talent to meet the growing demand for data centre specialists—including in Facebook's first Asia-based data centre located in Singapore, slated to be operational in a few years' time.

Successful applicants of the pilot initiative will receive data centre-specific training and career path advice from CBRE Data Centre Solutions, a leading Singapore-based data centre facilities management provider. Following the pilot phase, PaCE@NTU plans to progressively introduce more courses in subsequent phases of the collaboration, potentially involving other data centre industry players.



[THE HONOUR ROLL]

Knowledge prize

NIE Director Prof Christine Goh, who accepted the award on behalf of the institution. Credit: NIE.

NTU's **National Institute of Education** (NIE) was presented the 2019 Mohammed Bin Rashid Al Maktoum Knowledge Award, an annual honour established by Sheikh Mohammed bin Rashid Al Maktoum, Vice President and Prime Minister of the United Arab Emirates and ruler of Dubai. It is presented to a person or institution for outstanding contributions to the production and dissemination of knowledge. The monetary prize of US$1 million is shared among the year's three winners.

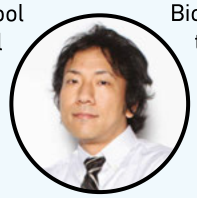
Security pioneer

NTU President Emeritus **Prof Su Guaning** has been elected as a foreign member of the US National Academy of Engineering for his academic leadership and contributions to regional security and defence. This is among the highest professional distinctions accorded to an engineer.

Distinguished membership

Lauded for his outstanding scientific contributions to computing, **Assoc Prof Li Mo** of NTU's School of Computer Science and Engineering has been selected to join the 2019 class of Distinguished Members of the Association for Computing Machinery.

Outstanding young chemist



For developing novel ways of synthesising inorganic chemical compounds, **Assoc Prof Rei Kinjo** of NTU's School of Physical and Mathematical Sciences has received the 2019 Distinguished Young Chemist Award from the Federation of Asian Chemical Societies.

World's most influential researchers

Thirty-three NTU scientists are on Clarivate Analytics' 2019 list of **Highly Cited Researchers**. Ranked among the top 1% of global scientists in their fields by citations and year, the honourees include (from top left) **Prof Huang Guangbin** (computing), **Prof Xie Lihua** (electrical and electronic engineering), **Prof Chen Peng** (cross-field), **Prof David Wardle** (environmental and ecological sciences), and **Prof David Lou** (chemistry and materials science), alongside NTU academic leaders **Prof Subodh Mhaisalkar**, **Prof Lee Pooi See**, **Prof Nikolay Zheludev** and **Prof Sum Tze Chien** (all cross-field).

Mechanobiology don

NTU Vice President (Alumni and International Affairs) **Prof K Jimmy Hsia** has been inducted into the College of Fellows of the American Institute for Medical and Biological Engineering. Prof Hsia, who is the President's Chair in Mechanical Engineering, was elected for his contributions to cellular mechanics and mechanobiology research, as well as his outstanding leadership in interdisciplinary research and education.

Career award

Nanyang Asst Prof Miao Yansong of NTU's School of Biological Sciences has been selected as one of nine life scientists to join the inaugural Global Investigator Network of the European Molecular Biology Organisation (EMBO). Aiming to groom the next generation of scientific leaders, EMBO offers leadership training and financial support to foster connections with scientists across continents.

Productive prototype

Associate Dean (Research) of NTU's College of Engineering **Prof Wen Yonggang** and his team, together with collaborators at Microsoft Research Asia (MSRA), were recognised with the MSRA Academic Day 2019 Increasing Productivity Award. The group had leveraged artificial intelligence technologies to build a video streaming prototype that offers users a better personalised viewing experience.

Terahertz science innovator

Assoc Prof Ranjan Singh of NTU's School of Physical and Mathematical Sciences has been elected as a Fellow of the Optical Society, which studies optics and photonics. He was honoured for his pioneering contributions to terahertz science and technology.

Young innovator

Final-year PhD student **Stephanie Yap** of NTU's School of Electrical and Electronic Engineering is among 20 young talents on *MIT Technology Review*'s 2020 list of Innovators Under 35 Asia-Pacific. She developed a portable device to measure water quality.