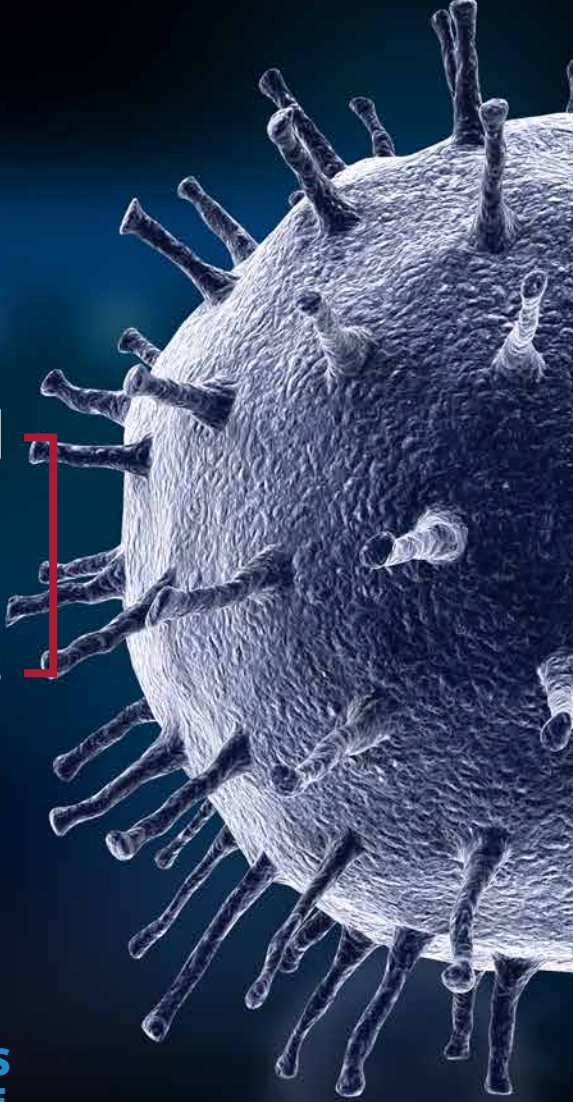



PUSHING
FRONTIERS



**INNOVATION
VS
INVADERS**

USING THE LATEST
TECHNIQUES TO OUTWIT
ANCIENT MICROBIAL ENEMIES

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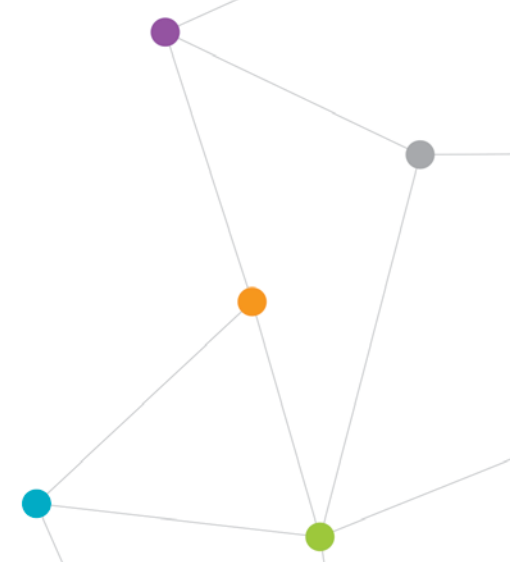
New ways to detect old foes



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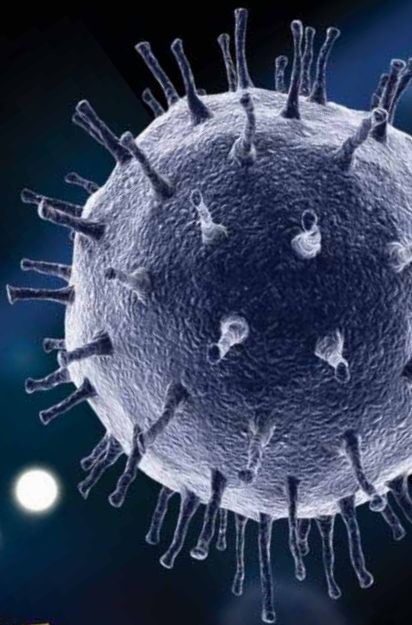


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INNOVATION vs INVADERS

USING THE LATEST TECHNIQUES TO
OUTWIT ANCIENT MICROBIAL ENEMIES



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Chief of Staff and
Vice President (Research)

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THE TROPICS: NATURE'S TREASURE TROVE



Home to nearly half of the world's population, the tropics harbour an extraordinary cultural and biological diversity amidst a wealth of natural resources. Driven by a vibrant and youthful labour force, these regions have given rise to many of today's economic powerhouses and emerging markets.

The issues relevant to the tropics—such as public health and urban development—are also increasingly important to neighbouring countries and those further afield. For instance, the emergence and spread of Ebola and Zika viruses in tropical countries have shown how important it is to control disease transmission here if we are to prevent the next epidemic or pandemic. At the same time, the tropics are a lush botanical and zoological treasure trove that may hold the key to overcoming new plagues.

As one of a handful of research-intensive campuses situated in the heart of the tropics with deep links across Asia, Nanyang Technological University is uniquely positioned to conduct scientific enquiry, find

engineering solutions and develop social programmes to raise awareness of global healthcare challenges and mitigate them.

In this issue of *Pushing Frontiers*, NTU's research and innovation magazine, we highlight the latest research into infectious diseases such as dengue, tuberculosis and malaria. We profile scientists such as malaria researcher Prof Peter Preiser from the School of Biological Sciences and others who are translating fundamental scientific findings into innovative diagnostic tools and novel therapeutics. Other reports in this issue discuss advances in 3D printing, cyber physical systems and smart transport solutions for futuristic cities.

I hope this window into NTU's efforts at combatting infection and understanding immunity will spark your interest and stimulate fruitful collaborations across scientific disciplines and geographical borders.

*Prof Lam Khin Yong
Chief of Staff and Vice President (Research)
Nanyang Technological University
Singapore*



CHALLENGES FOR SCIENCE IN THE 21ST CENTURY

The meaning of science has evolved over the centuries, from the pure pursuit of knowledge to a source of innovation that drives progress. At an event themed “Grand Challenges for Science in the 21st century”, held at NTU over four days in June this year, six eminent scientists discussed how science might be conducted in the decades to come.

Moderated by acclaimed Danish writer and thinker Tor Nørretranders, the illustrious group of scientists included Nobel Laureate (Physiology or Medicine, 2002) Dr Sydney Brenner, leading economist and complexity thinker Prof W. Brian Arthur, astrophysicist and Astronomer Royal Prof Martin Rees, computational neurobiologist Prof Terrence Sejnowski, evolutionary biologist Prof Eörs Szathmáry, and the former President of the European Research Council and NTU Visiting Professor, Prof Helga Nowotny.

Presenting their individual views and the outcomes of closed-door discussions to an audience of guests from academia and government, the six scientists stressed the need for scientists to question long-held scientific beliefs and emphasised science’s role as the best bet for the future.

Prof Arthur, Prof Sejnowski and Prof Rees noted the importance of novel technologies in unravelling the complexities of life on earth and granting access to hitherto locked or unreachable worlds—be it in our brains or in distant universes.

“Science mainly proceeds by thinking and observing, but more than anything, it proceeds by its technologies, instruments and methods,” said Prof Arthur.



1. Tor Nørretranders.
2. Terrence Sejnowski.
3. Sydney Brenner.
4. Eörs Szathmáry.
5. W. Brian Arthur.
6. Martin Rees.
7. Helga Nowotny.

Credit: Para Limes, NTU.

“Most systems in nature are non-linear, non-continuous, and not in equilibrium. The main challenge now is to explore these new worlds that don’t look mechanistic and ordered, but organic and alive.”

For Prof Rees, the hope of finding other intelligent life in the universe is what has captured his imagination. “Everybody wants to know whether there is life in any of those places,” he said. “There is probably nothing much on Mars, but things are much more exciting if we look beyond our solar system to the realm of the stars far further than we can send any probe today.”

But chasing these lofty ideals requires resources, Dr Brenner reminded the

audience. “If you ask any scientist this question, they will say the grand challenge is ‘How can I get hold of money to do science?’,” he quipped.

This point of view was also emphasised by Prof Nowotny. “We have to convince the world that investment in this kind of fundamental science—or frontier research, where you do not yet know what the outcome will be—is essential for the 21st century to continue. Science is the best invention that humanity has made to bring the future, with all its enormous potential, into the present. But it needs society and a close interaction with society to shape it,” she concluded.

TECTONICS

▶ SLOW TREMORS, LARGE EARTHQUAKES

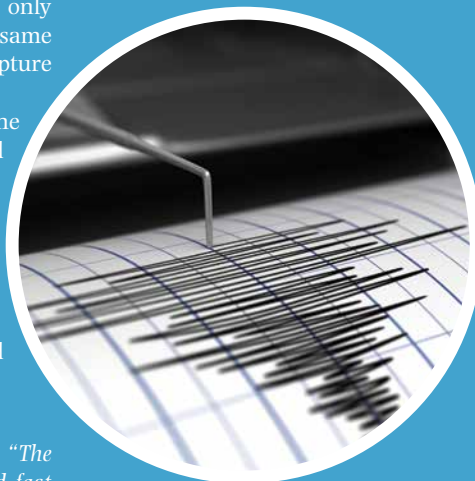
New findings by researchers from the Earth Observatory of Singapore and the Asian School of the Environment at NTU could overturn the long-held consensus that slow tremors seldom lead to large earthquakes.

In 2004, Parkfield, California, in the United States experienced a magnitude 6 quake that was preceded by unusual seismic activity. Using five years of data, Asst Prof Sylvain Barbot and his PhD student, Deepa Mele Veedu, developed a model explaining the patterns of tremors observed.

“The discovery of these vibration patterns, which are caused by alternating slow and fast ruptures occurring on the same patch of a fault, has defied our understanding of how faults accumulate and release stress over time,” explains Asst Prof Barbot.

“Our findings suggest that even if only slow movements are detected, the same area of the fault can potentially rupture in a catastrophic earthquake.”

The conclusions drawn from the Californian fault could also be used to forecast large earthquakes in Southeast Asia, he says. The area around the Mentawai seismic gap in Sumatra, Indonesia, in particular, is where scientists from NTU’s Earth Observatory of Singapore have repeatedly warned a large earthquake could strike.



—
Details of the study can be found in “The Parkfield tremors reveal slow and fast ruptures on the same asperity”, published in *Nature* (2016), DOI: 10.1038/nature17190.

THERANOSTICS

▶ MICROBUBBLES BLOW UP TUMOUR CORES

Pooling their expertise in nanomedicine and biophysics, Asst Prof Xu Chenjie from NTU’s School of Chemical and Biomedical Engineering and the NTU-Northwestern Institute for Nanomedicine, and Assoc Prof Claus-Dieter Ohl from NTU’s School of Physical and Mathematical Sciences, have invented a patient-friendly way to deliver drugs into tumours.

At the heart of the technology are micro-sized gas bubbles coated

with magnetic iron oxide and drug nanoparticles.

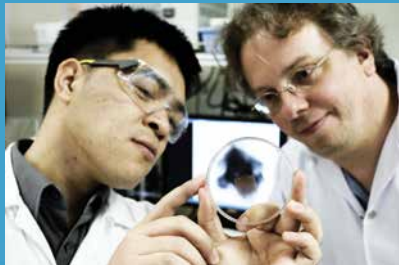
“After injection into the bloodstream, the microbubbles can be traced and concentrated around tumours using magnets—such as those already used in magnetic resonance imaging and other diagnostic machines—ensuring that the drugs don’t damage healthy tissue and organs,” explains Asst Prof Xu.

Ultrasound is then used to vibrate the microbubbles, providing the energy needed to release the drug-containing nanoparticles.

Tests in animal models showed that the particles are able to penetrate a depth of more than 50 cell layers, allowing the drugs to reach cancer cells hidden deep within the tumour core.

—
The research “Controlled nanoparticle release from stable magnetic microbubble oscillations” was published in *NPG Asia Materials* (2016), DOI: 10.1038/am.2016.37. A video produced by Assoc Prof Ohl that shows oscillations and fragmentation of microbubble droplets was featured on *New York Times ScienceTake* and won a 2015 *Gallery of Fluid Motion Award from the American Physical Society/Division of Fluid Dynamics*. The video can be viewed at <http://dx.doi.org/10.1103/APS.DFD.2015.GFM.V0029> and the recording of the video is described in the paper “Stereoscopic recording of droplet fragmentation”, published in *Physical Review Fluids* 1, 050512 (2016), DOI: 10.1103/PhysRevFluids.1.050512.

Asst Prof Xu Chenjie (left) and Assoc Prof Claus-Dieter Ohl (right) examining magnetic microbubbles on a petri dish. Credit: Lester Kok.



CELL STRUCTURE

KEEPING CELLS IN SHAPE

The cytoskeleton—a network of actin filaments that provides scaffolding for the cell—helps the cell maintain its shape and aids in cellular movement during the cell cycle.

Asst Prof Miao Yansong and Assoc Prof Mu Yuguang from NTU's School of Biological Sciences, along with researchers from the University of California, Berkeley, investigated how the dynamic assembly and disassembly of actin cables (bundles of actin filaments) are regulated during the cell cycle.

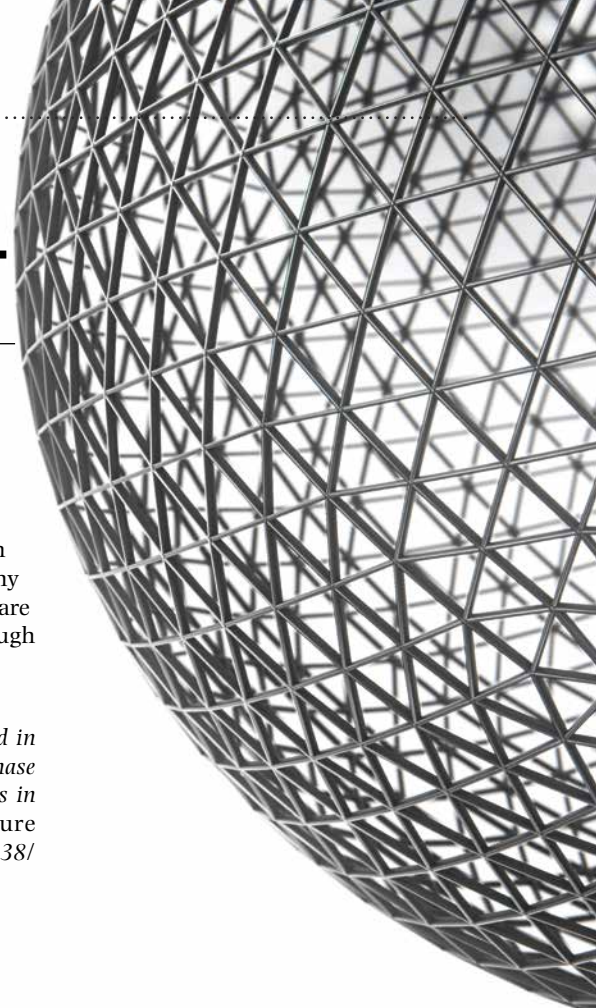
They discovered that the actin filament crosslinking protein fimbrin is phosphorylated by cyclin-dependent kinase 1, a key cell cycle regulator.

“Our findings suggest that phosphorylation of fimbrin regulates

the assembly and stability of actin cables in cells,” says Asst Prof Miao, who holds a joint appointment at NTU's School of Chemical and Biomedical Engineering.

The study gives important insights into the mechanisms by which the cytoskeleton—and thus the many cellular processes it is involved in—are regulated during the cell cycle through kinase phosphorylation.

Details of the research can be found in “Fimbrin phosphorylation by metaphase Cdk1 regulates actin cable dynamics in budding yeast”, published in Nature Communications (2016), DOI: 10.1038/ncomms11265.



STRUCTURAL BIOLOGY

UNDERSTANDING ANTIBIOTICS AT THE ATOMIC LEVEL

Although more than half of antibiotics target the bacterial ribosomal complex, the precise role of the complex's individual components is not well understood.

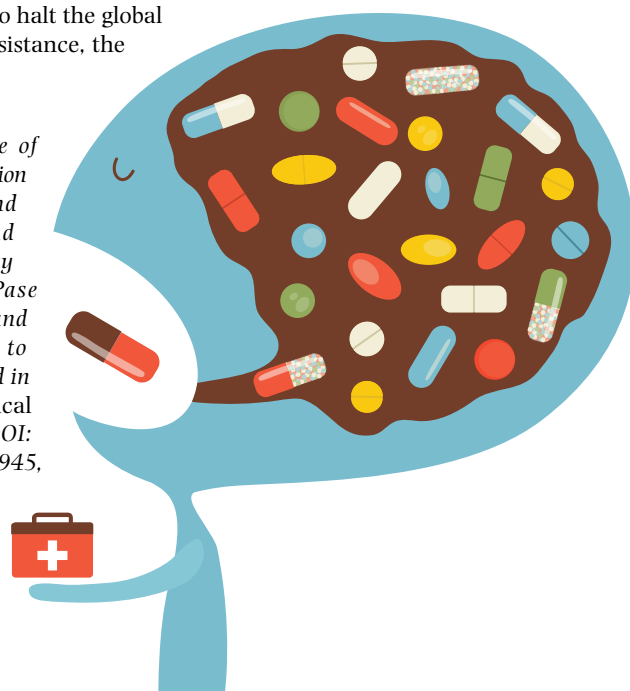
Zooming in on elongation factor 4, Assoc Prof Gao Yonggui and his team from NTU's School of Biological Sciences used cryo-electron microscopy to analyse the protein's structure at atomic resolution. Their study yielded new clues that could help to decipher the factor's controversial role in bacterial protein production.

In a separate study, the team investigated how antibiotics block protein translation in bacteria. The researchers discovered that widely-used antibiotics such as fusidic acid and neomycin block the mobility and activity of bacterial ribosomes, thereby disrupting protein production and killing the bacteria.

Deep insights into the workings of the bacterial protein production machinery

could prove crucial in designing new and better antibiotics to halt the global spread of antibiotic resistance, the researchers say.

The studies “Structure of the GTP form of elongation factor 4 (EF4) bound to the ribosome” and “Similarity and diversity of translational GTPase factors EF-G, EF4, and BipA: from structure to function” were published in The Journal of Biological Chemistry (2016), DOI: 10.1074/jbc.M116.725945, and RNA Biology (2016), DOI:10.1080/154762862016.1201627, respectively.



ENERGY

☞ BUGS + SUN = HYDROGEN FUEL

Hydrogen is a promising environmentally-friendly fuel. However, generating hydrogen requires a lot of electricity, limiting overall energy gains.

Aiming to solve this dilemma, a team of engineers, chemists and microbiologists from NTU has designed a hydrogen production system that combines solar energy and the biocatalytic activities of microbes without the need for additional electrical input.

Led by Assoc Prof Joachim Loo, the interdisciplinary team from NTU's School of Materials Science and Engineering and the Singapore Centre for Environmental Life Sciences Engineering combined electricity-producing microbial fuel cells with photoelectrochemical cells (PECs) to produce hydrogen synergistically.

"By inserting electron transfer molecules into *E. coli* membranes that improve the efficiency of charge transfer capabilities, we have modified the microbes to work in our favour," says Assoc Prof Loo.

PECs split water into hydrogen gas and oxygen with the help of solar energy. "The PEC's ability to capture solar energy has also been improved with chemically modified gold-titanium oxide photoanodes," he adds.

—
Details of the technology can be found in "Enhancement in hydrogen evolution using Au-TiO₂ hollow spheres with microbial devices modified with conjugated oligoelectrolytes", published in npj Biofilms and Microbiomes (2015), DOI: 10.1038/npjbiofilms.2015.20.

☞ POWERING BATTERIES WITH "SALT"

Millions of lithium-ion batteries are used in smartphones and other portable and home electronics. However, global reserves of lithium are scarce and often located in remote and politically sensitive areas, sparking the search for alternative elements.

A team from NTU's School of Physical and Mathematical Sciences has now discovered that sodium, an element abundantly found in ocean waters and sediments, has capacities that equal or even surpass those of lithium.

"Using ultrathin nanostructures made of layered tin sulphide, we constructed sodium-ion anodes that were able to achieve high-capacity and high-power densities," says Prof Shen Ze Xiang, who led the study.

"Moreover, these sodium-ion batteries allowed charging in as little as one minute, exceeding charging rates obtained with lithium ions," he adds.

Combining the properties of high-energy batteries and high-power supercapacitors, sodium-ion batteries might provide a low-cost and safe alternative to lithium-ion batteries and pave the way for next-generation energy storage technologies, the researchers say.

—
The study "Array of nanosheets render ultrafast and high-capacity Na-ion storage by tunable pseudocapacitance" was published in Nature Communications (2016), DOI: 10.1038/ncomms12122.



➤ PUTTING AN ULTRAFAST SPIN ON ELECTRONICS

Conventional electronics based on the charge of electrons are fast approaching a theoretical limit to their decades-long improvements in size and power.

Opto-spintronic technology—which instead relies on light and the spin quantum state of electrons—could breach this barrier, but has been hampered by a lack of semiconducting materials to effectively control the spin quantum states.

Now, a team from NTU led by Assoc Prof Sum Tze Chien from the School of Physical and Mathematical Sciences, and Asst Prof Nripan Mathews from the School of Materials Science and Engineering, might have found just the right material.

Applying ultrafast circularly polarised light pulses to layered organic-

inorganic hybrid perovskites—a material previously hailed as wonder material for highly efficient solar cells and bright light-emitting diodes—the researchers were able to selectively manipulate the spin up/down states of electrons in the perovskites.

The research is a significant step to realising the promise of opto-spintronics, which could lead to smaller, faster and more efficient electronics with low power consumption, the scientists say.

Details of the research can be found in “Tunable room-temperature spin-selective optical Stark effect in solution-processed layered halide perovskites”, published in Science Advances (2016), DOI: 10.1126/sciadv.1600477.



MOLECULAR SENSORS

➤ A RING TO CAPTURE THEM ALL

By replacing two of the six carbon atoms in the ring structure of benzene with the cheap and abundant chemical element boron, researchers at NTU have synthesised a hybrid benzene ring with unexpectedly high reactivity to greenhouse gases such as carbon dioxide.

The researchers, led by Asst Prof Rei Kinjo and Asst Prof Hajime Hirao from NTU's School of Physical and Mathematical Sciences, showed that the hybrid molecules are able to reversibly bind small molecules such as carbon dioxide and emit blue fluorescent light when irradiated by UV light in the unbound state.

According to the researchers, the hybrid benzene could be used in a wide range of catalytic reactions, including capturing the greenhouse gas carbon dioxide and converting it into valuable chemicals.

Furthermore, binding to carbon dioxide and other small molecules quenches fluorescence emission of the hybrid benzene compounds. Hence, the researchers suggest that the compounds could not only be used to capture and convert carbon dioxide and other small molecules, but also act as molecular gas detectors.

Details of the research can be found in “1,3,2,5-Diazadiborinine featuring nucleophilic and electrophilic boron centres”, published in Nature Communications (2015), DOI: 10.1038/ncomms8340, and in “Ambiphilic boron in 1,4,2,5-diazadiborinine”, published in Nature Communications (2016), DOI: 10.1038/ncomms11871.

PHOTONICS

▶ LIGHTING THE WAY FOR NEXT-GENERATION COMPUTERS

Topological insulators allow the one-way flow of electrons without backscattering, even if they encounter impurities or disorders. If photons instead of electrons can be controlled in a similar one-way manner, the technology could be used to build next-generation optical computers that transmit data in much higher density and much more quickly than current electronic computers.

“But we need to expect—and find ways to overcome—certain limitations if we want photons to do things that electrons do,” explains Asst Prof Zhang Baile from NTU’s School of Physical and Mathematical Sciences.

To explore these limitations, Asst Prof Zhang and his team constructed a model that allows investigating the behaviour of light transport under various defect conditions.

A fundamental understanding of the possibilities of using photons instead of electrons for robust data transmission could help to guide future photonics-based computing, Asst Prof Zhang says.

Details of the research can be found in “Probing topological protection using a designer surface plasmon structure”, published in Nature Communications (2016), DOI: 10.1038/ncomms11619.

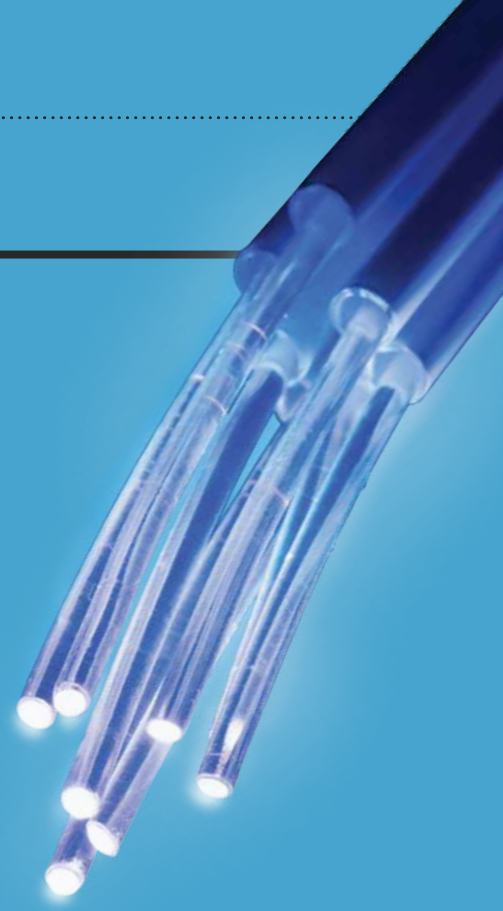


PHOTO SENSORS

▶ CAPTURING A BULLET IN FLIGHT

To prevent collisions, autonomous vehicles require precise, fast and lightweight photo sensors for safe navigation. Researchers led by Asst Prof Chen Shoushun from NTU’s School of Electrical and Electronic Engineering have developed a fundamentally new photo sensor technology that may be up to the task.

Called CeleX, the sensor does not produce pictures but features. Thanks to a special algorithm that looks only at relative change in light intensity and the speed of change, the sensor picks out moving objects and limits computation

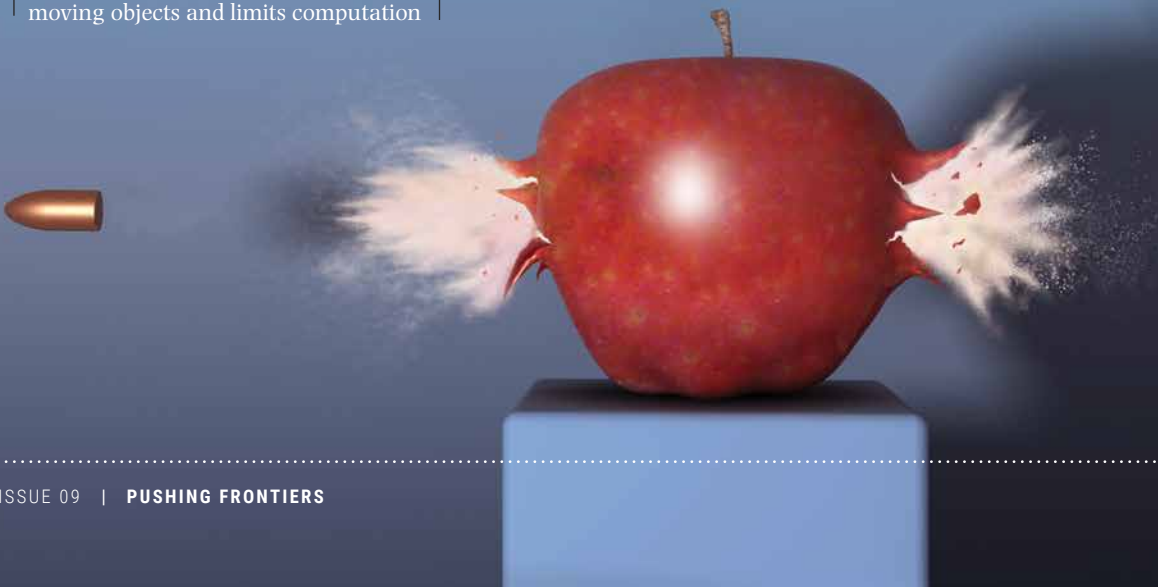
to these data points, omitting all unnecessary information from non-moving objects.

“The speed of the sensor is not limited by any traditional concept such as exposure time or frame rate,” says Asst Prof Chen. “The response time of the sensor is in nanoseconds, which is so fast it could capture a bullet in flight.”

Since the sensor is able to capture the environment in full colour, it can also be integrated with regular surveillance systems and other commercial

applications such as high-speed railways, he adds.

The CeleX camera sensor system has been patented and is being further developed and commercialised under Hillhouse Technology Pte Ltd, an NTU spin-off company founded in 2015 by Asst Prof Chen and his partners with the help of NTU’s start-up hub, NTUitive.



➤ FUNGI TURN FOOD WASTE INTO NEW FOOD

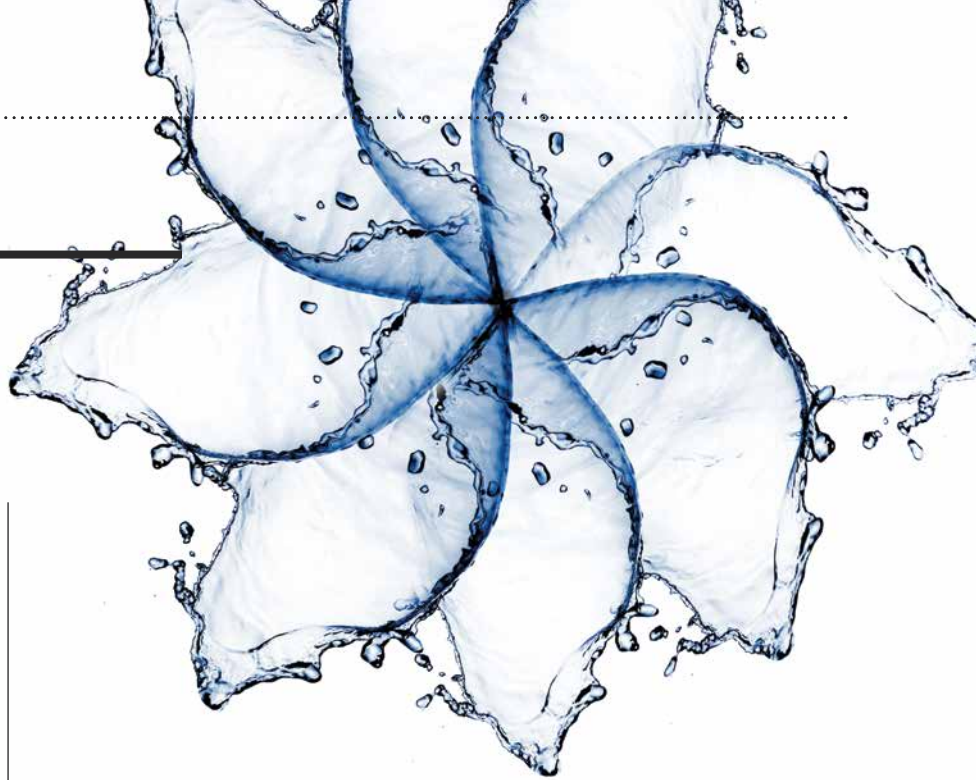
Fungi could be the solution to more sustainable food production, say researchers from NTU's Schools of Chemical and Biomedical Engineering and Civil and Environmental Engineering.

"Enzymes secreted by such fungi break down soya bean residues—typical leftovers from soya milk and tofu production called okara—into a cotton wool-like product, which, mashed up, can be further processed into yeast medium," explains Dr Jaslyn Lee, who developed the method as a doctoral student at NTU's Interdisciplinary Graduate School.

The okara-based yeast growth medium is not only much cheaper to produce than commercial yeast growth medium, but also works without the addition of peptones—soluble proteins derived from plants like potato and wheat—potentially saving these crops and agricultural land for other purposes.

"By using food production residues for the production of new foods instead of dumping them into landfills, we can help to secure sustainable food resources and reduce pollution of the environment," says research lead Prof William Chen, who, together with Dr Lee, previously developed methods to use waste cooking oil as a carbon source for microbial conversion into other high-value food ingredients.

The technology has been filed for intellectual property through NTUitive, NTU's commercialisation hub, and has already drawn interest from big food companies.



➤ LOW-PRESSURE MEMBRANE LOWERS WASTEWATER TREATMENT COSTS

The final steps of wastewater treatment typically include ultrafiltration and reverse osmosis, the latter being an energy-intensive process that requires high operating pressures.

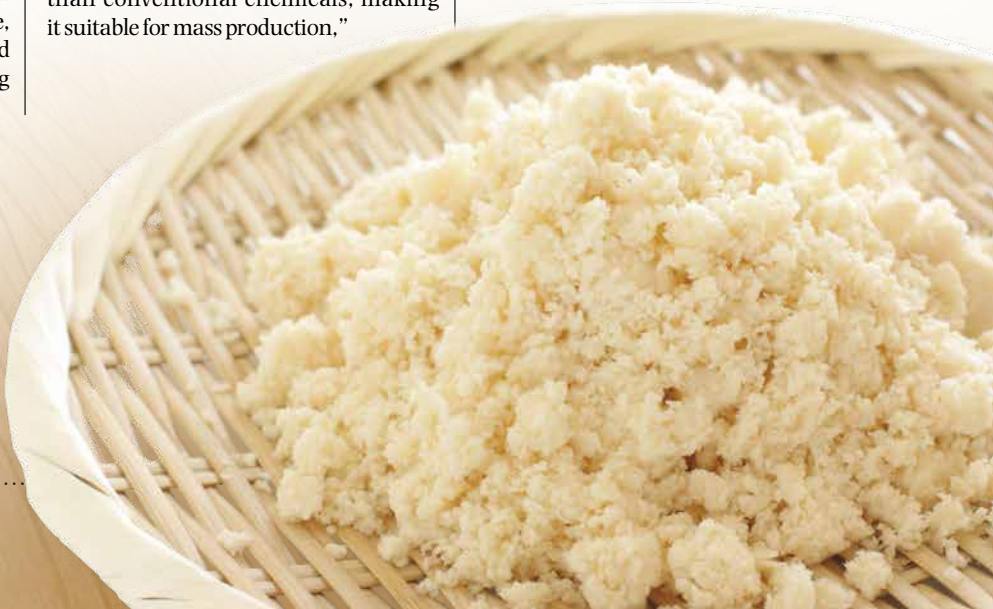
By simplifying the dual-membrane-based process into a single step, researchers have developed a low-pressure hollow fibre nanofiltration membrane that greatly reduces the energy costs of wastewater treatment while maintaining discharge quality requirements.

"Our new membrane is also easy to manufacture using low-cost chemicals that are 30 times cheaper than conventional chemicals, making it suitable for mass production,"

explains inventor Prof Wang Rong, Chair of NTU's School of Civil and Environmental Engineering and Director of the Singapore Membrane Technology Centre at NTU's Nanyang Environment and Water Research Institute.

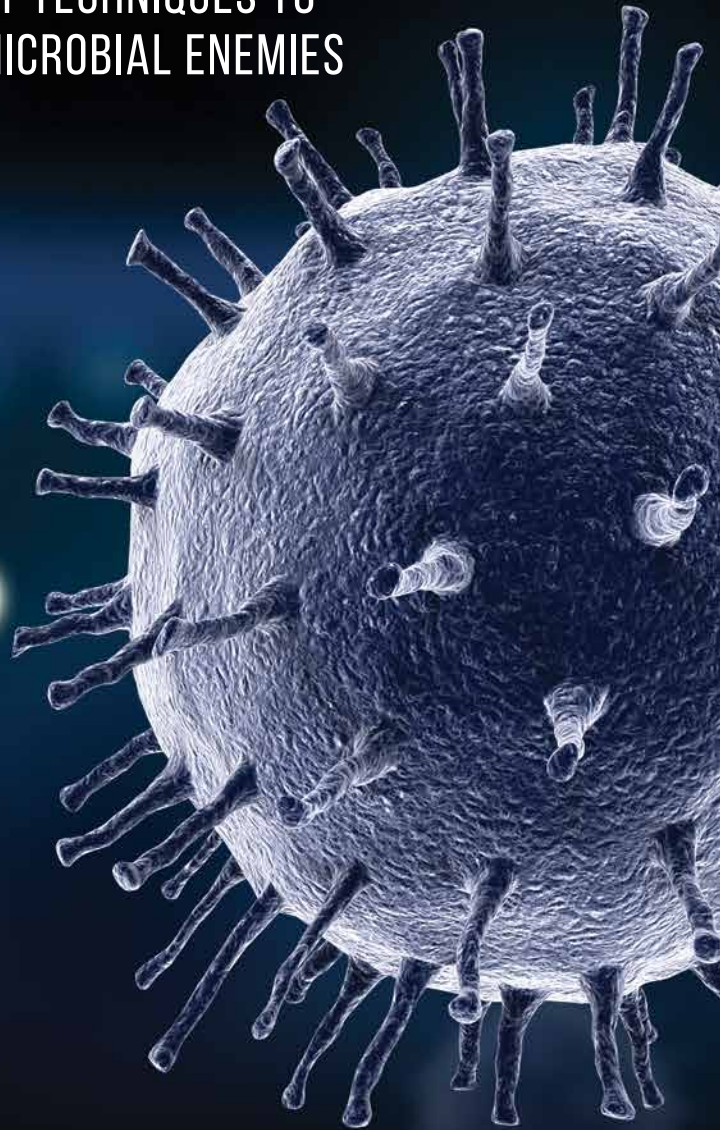
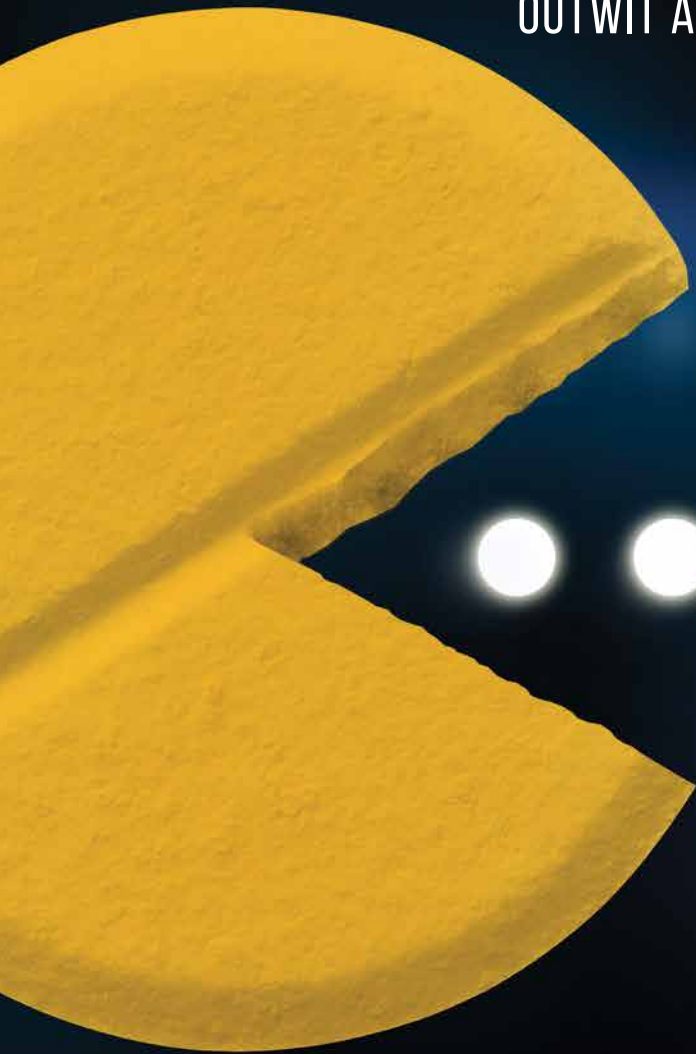
The membrane is now being commercialised through NTU spin-off company De.Mem. The company, which owns over a dozen water and wastewater treatment plants in Vietnam and Singapore, will test the real world usage of the membrane and also build a pilot production plant for manufacturing.

Okara



INNOVATION VS INVADERS

USING THE LATEST TECHNIQUES TO
OUTWIT ANCIENT MICROBIAL ENEMIES



From crystal structures to clinical studies, NTU researchers are taking a multi-pronged approach to tackling the challenges of infectious diseases.

Under the microscope, infectious pathogens—little more than tiny bags of genetic material—may seem curiously unimpressive to the untrained eye.

Yet, as outbreaks of diseases such as influenza, Ebola, multidrug-resistant tuberculosis and Zika have made clear, microbes pose significant threats to global health. Deceptively simple, they draw from an extensive repertoire of tricks, packed into genomes a mere fraction the size of ours.

The most basic of viruses encode proteins that help them evade and suppress the immune response; bacteria are constantly engaged in an evolutionary arms race to stay one step ahead of the drugs we throw at them,

while parasites keep the immune system guessing by regularly varying their coats of surface proteins.

At NTU, a diverse group of researchers are part of worldwide efforts to develop new treatments, vaccines and other transmission control strategies for a wide variety of pathogenic microbes. Key to their success: a detailed understanding of how pathogens cause disease, as well as how the human immune system fends off invaders.

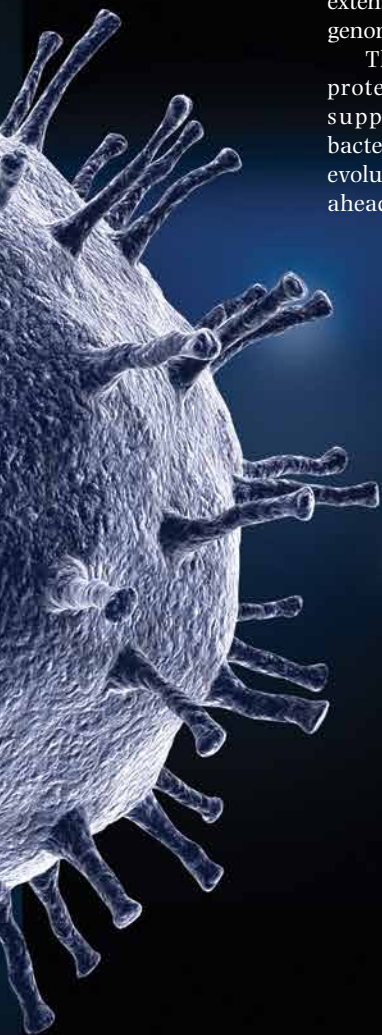
NEW WEAPONS AGAINST AN OLD FOE

Dengue is no stranger to the region—the mosquito-borne viral disease has been in Southeast Asia and most of the tropics for decades. Yet, no antiviral drugs are available, and while a vaccine has recently been approved in some countries, doubts remain about its effectiveness and long-term safety.

“Dengue virus is a difficult pathogen, with a complicated life cycle and host immune response that we have only just begun to understand,” says Asst Prof Luo Dahai of NTU’s Lee Kong Chian School of Medicine, who studies the intricate molecular dance between viruses and the cells they infect. “The more we know about the virus and the disease it causes, the better the chances we have of developing therapeutics.”

A prime target for anti-dengue drug development, says Asst Prof Luo, is NS5, the largest protein encoded by the virus. NS5 wears multiple molecular hats; besides churning out copies of the viral genome, it also carries out enzymatic reactions such as attaching a methyl group to the start of the viral genome, masking the virus from the host immune response.

Working with Assoc Prof Julien Lescar of NTU’s School of Biological Sciences, Asst Prof Luo’s group recently captured the first ever crystal structure of NS5 in the act of performing this methyl group transfer. With this molecular snapshot, the researchers can now





observe the interactions between NS5 and the viral genome in great detail—valuable information for designing drugs to disrupt the process.

Asst Prof Luo is already applying similar strategies to Zika, a closely related virus now linked, alarmingly, to microcephaly and other neurological complications in newborn babies. “It is our responsibility to use our knowledge, resources and expertise accumulated over the years on dengue to study Zika,” he says.

With effective treatments or vaccines still out of sight, Asst Prof Yeo Tsin Wen of NTU’s medical school is tackling one of dengue’s fatal complications—dengue haemorrhagic fever. He is studying the relationship between vascular leakage and the severity of dengue and developing approaches to identify those patients most at risk of developing life-threatening complications.

BREAKING THROUGH BIOFILMS

Bacteria are single-cell organisms. In nature, however, they typically exist as biofilms—complex communities of microbes held together by an extracellular matrix of secretions such as polysaccharides, nucleic acids and proteins.

There are huge advantages for bacteria to live as biofilms—they can share genetic material and divide up metabolic tasks. Meanwhile, the extracellular matrix forms an almost impervious shield against antibiotics and other antimicrobial agents.

As such, biofilms are the major culprits behind infections acquired in hospitals, where they grow on medical devices such as catheters and artificial heart valves. They are also a leading cause of chronic infections—of the lung, ear and sinus, for example.

Researchers at NTU’s Singapore Centre for Environmental Life Sciences Engineering are working to gain a fundamental understanding of the biofilm mode of life. Among them, Asst Prof Yang Liang investigates the molecular signals that bacteria use to coordinate biofilm formation and activate stress responses, while quorum sensing expert Prof Michael

Givskov focuses on developing drugs that can disrupt biofilms and enhance the efficacy of conventional antibiotics and the immune system.

However, most of what researchers know about biofilms comes from studies done in laboratory-grown models, says Asst Prof Yang. These can behave very differently from the biofilms that infect patients and contaminate hospitals.

“To understand healthcare-associated biofilms, we need ways to investigate the physiology of biofilms from infection sites,” says Asst Prof Yang.

Identifying essential matrix components and regulatory pathways from biofilms at these sites, he explains, will be essential for the development of novel diagnostic and treatment strategies, such as discovering new antibiotics that can disrupt these seemingly invincible microbial teams.

NEW TECHNOLOGIES FOR EARLY DETECTION

In addition to therapeutics and vaccines, the ability to identify pathogens swiftly and accurately is an essential part of infectious disease control.

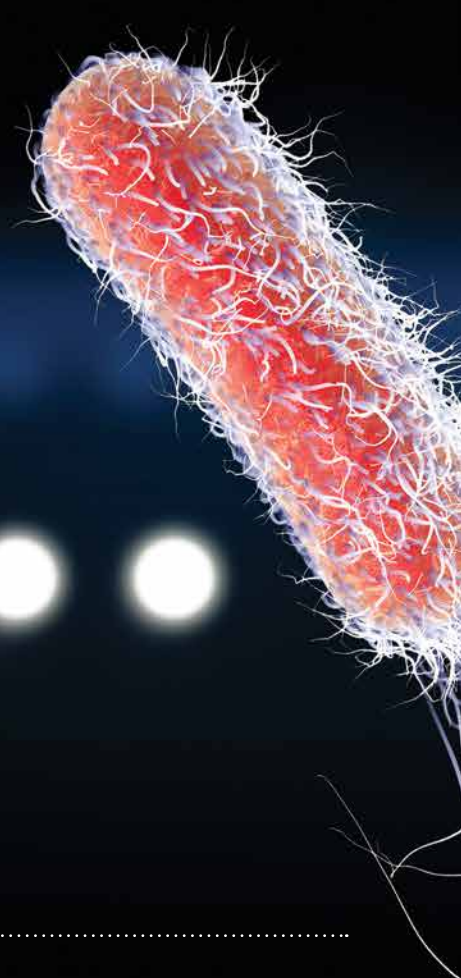
“Rapid diagnostics can give a clinician timely information to guide the choice of treatment—for instance, the class of antibiotic to use, the dose and the route of administration,” says Assoc Prof Eric Yap of NTU’s Lee Kong Chian School of Medicine. “Even if no specific drugs are available to treat emerging viral diseases, early diagnosis can help in isolating the patient to reduce transmission risk, or in providing health advice.”

However, current diagnostic methods have their limitations: microbial culture and conventional molecular biology techniques such as polymerase chain reaction (PCR) take too long, while cross-reactivity is a problem for immunological assays that rely on antibodies to recognise pathogens.

Assoc Prof Yap’s team is incorporating novel PCR, microfluidic and optical technologies into next-generation rapid diagnostics—ultrafast, automated tests that yield results in minutes, and that can be performed by healthcare workers

“We are seeking clinical collaborators who are keen to co-develop or test these assays against conventional diagnostic methods.”

Assoc Prof Eric Yap
Lee Kong Chian School of Medicine



in the clinic with the same accuracy and sensitivity as in specialised laboratories.

“While we are able to develop new assays within weeks, the rate-limiting step is to perform clinical validation trials with other centres,” says Assoc Prof Yap. “For this, we are seeking clinical collaborators who are keen to co-develop or test these assays against conventional diagnostic methods.”

WHEN THE IMMUNE SYSTEM GOES ROGUE

Most of the time, the body’s immune system effectively detects and eliminates invading pathogens. But things can go awry—if these responses fail to distinguish self from non-self, our own cells come under autoimmune attack.

The genetic and environmental triggers behind the development of autoimmune diseases such as rheumatoid arthritis, lupus and Crohn’s disease are poorly understood. In most cases, such diseases develop over long periods of time, says Asst Prof Wu Bin of NTU’s School of Biological Sciences.

To understand the early stages of autoimmunity, Asst Prof Wu studies innate immune receptors, which form part of the body’s first line of defence against infection. By elucidating how these molecules sense pathogens and activate immune responses, he hopes to identify disease markers that result in immune over-activation, for example.

“The best way to treat autoimmune diseases is to maintain the balance of our immune system before any severe symptoms develop,” advises Asst Prof Wu. “For someone with a genetic risk of autoimmune diseases, we will try to identify specific inhibitors to suppress the exact hyperactive signalling pathways, with minimum intervention.”

Such novel interventions—drugs, or diet and lifestyle changes—that prevent the onset of disease will hopefully be better alternatives to broad immunosuppressants, which doctors now use to treat autoimmune diseases, but which come with severe side effects, Asst Prof Wu explains.

FROM LAB TO CLINIC

With the aim of developing a gentler immunosuppressant, Prof George Chandy of NTU’s Lee Kong Chian School of Medicine is taking a more targeted approach. His strategy focuses on potassium channels—molecular gateways that control the flow of potassium ions in and out of cells.

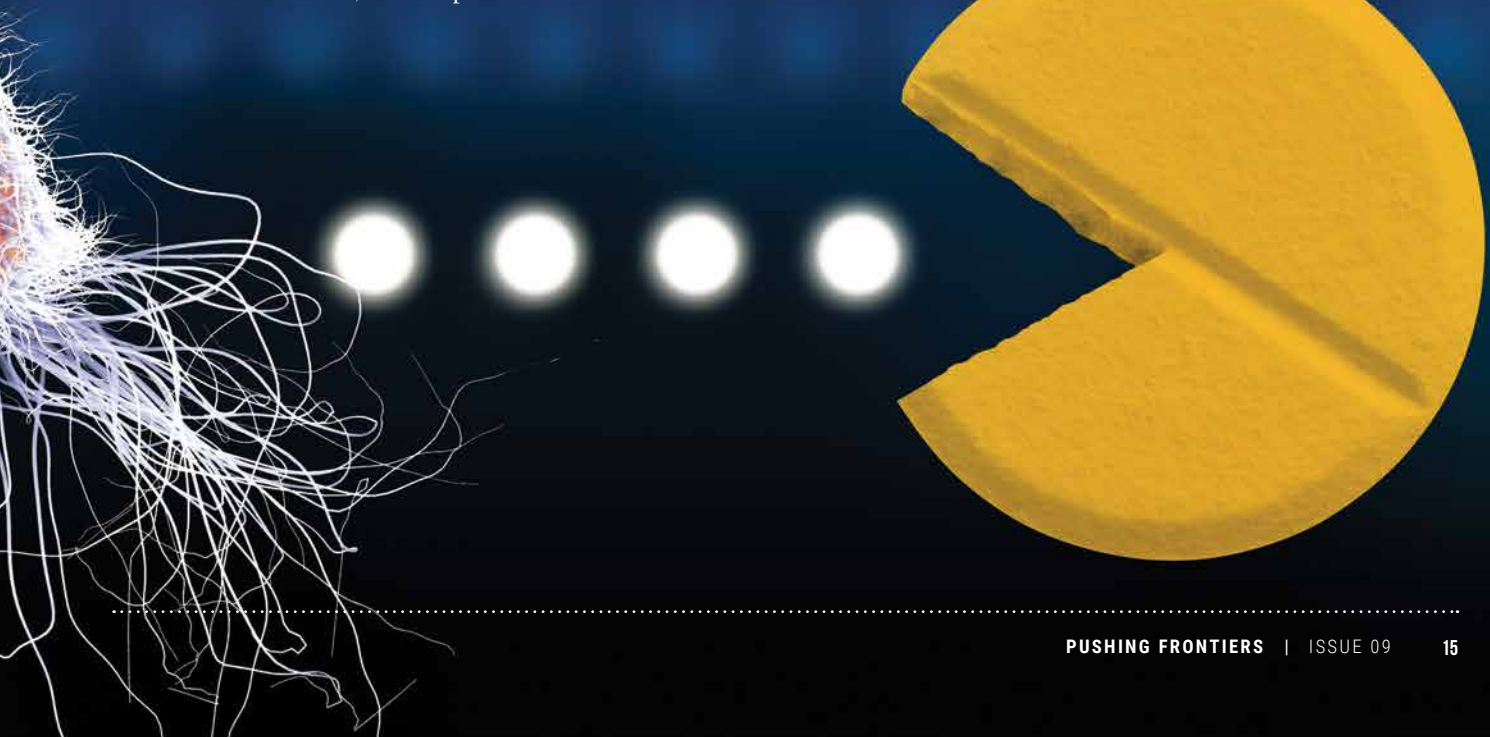
In collaboration with Prof Daniela Rhodes, a leading structural biologist at NTU, and Prof Chandra Verma of Singapore’s Agency for Science, Technology and Research, Prof Chandy’s team is designing drugs that bind to and inhibit a particular class of potassium channels required for the activation and proliferation of T-effector memory cells—

an immune cell type often hyperactive in autoimmunity.

One of their candidate molecules—a drug known as dalazatide—is currently in clinical trials, and has been shown to work in patients with psoriasis, an autoimmune disease characterised by patches of red, scaly skin. As part of a consortium of scientists, engineers and clinicians, Prof Chandy is also working with Prof Subbu Venkatraman of NTU’s School of Materials Science and Engineering and Assoc Prof Louis Tong from the Singapore Eye Research Institute to develop novel therapeutics for autoimmune diseases such as dry eye, which can cause blindness.

In other NTU-based projects close to clinical application, a Singapore-wide consortium led by Prof Annelies Wilder-Smith from the Lee Kong Chian School of Medicine aims to assess the efficacy of a locally developed influenza vaccine. In the realm of bacterial diseases, Asst Prof Guan Xue Li, also from NTU’s medical school, is studying lipid profiles to uncover new therapeutic targets and diagnostics for bacteria such as *Mycobacterium tuberculosis*.

Given the diverse, interdisciplinary nature of its biomedical research in infection and immunity, NTU is well placed to make scientific contributions towards improving global health in the tropics and far beyond.



SMART PARTNERSHIPS FOR A SMART FUTURE

TAKING THE BEST FROM
ACADEMIA AND INDUSTRY

Smart technologies created at NTU's corporate labs could be the unsung heroes of Singapore's future.

Levitating trains, rocket-packs and ubiquitous robots; nothing sparks the imagination like the thought of futuristic “smart” cities. But the technology that truly better our lives is more likely to be out of sight and out of mind. Think instead of machines quietly talking to one another to make Singapore tick, from more reliable trains to reduced manufacturing costs for small businesses.

Two new labs at NTU are reeling this smart future into the present: the SMRT-NTU Smart Urban Rail Corporate Laboratory, and the Delta-NTU Corporate Laboratory for Cyber-Physical Systems, launched in May and June 2016, respectively.

Both labs stem from the National Research Foundation (NRF) Singapore's Corporate Laboratory@University Scheme, which combines industry experience with cutting-edge research at the universities.

TRAINS THAT SELF-INSPECT

Under a US\$44 million (S\$60 million) agreement, the SMRT-NTU Smart Urban Rail Corporate Laboratory will integrate NTU's engineering research with SMRT's operating and engineering expertise. SMRT Corporation is Singapore's second largest public transport company, running three out of five of the country's metro lines.

This partnership is solving previously insurmountable difficulties faced by rail engineers in their attempts to maintain a growing and increasingly high demand network, explains the Director of the SMRT-NTU Lab, Assoc Prof See Kye Yak.

“The Mass Rapid Transit operates from 5am to near midnight, leaving the engineers very little time to inspect and maintain the railway tracks. Our lab's technologies will eventually transform trains so they double up as inspection vehicles.”

The lab's technologies will also hunt down potential problems before they happen. Prediction-analytical methods will predict wheel-rail wear and fatigue in critical rail and train components. Engineers could then repair the faults quickly, saving thousands of people from disrupted train services before the faults happen.

“Real-time condition monitoring of the trains and the railway tracks will turn the existing passive maintenance approach to a predictive maintenance one, where we can detect early signs of defects and rectify them before they become a problem,” explains Assoc Prof See.

“Our lab’s technologies will eventually transform trains so they double up as inspection vehicles.”

Assoc Prof See Kye Yak
Director of the SMRT-NTU Smart Urban Rail Corporate Laboratory

The SMRT-NTU Lab, which started operating on 1 July 2016, expects to showcase some of these technologies within two years. Promising results have already come from a project that uses radio frequency inductive coupling techniques to monitor the third rail of the railway—which supplies electrical power to the train—without direct electrical contact.

Other technologies under development at the lab include thermo-acoustic sensors that pinpoint cracks within materials through temperature fluctuations. These will help engineers detect cracks and defects lying deep within rail feet, joints and other components.

Assoc Prof See says that combining the expertise of SMRT engineers and NTU’s researchers is a great opportunity to cultivate new capabilities in Singapore. “SMRT’s test tracks and mainlines also serve as test-beds for field trials of the technologies we are developing,” he adds.

“It is a place to train good researchers and engineers for the railway industry,” he concludes, referring to the lab’s aim to train more than 100 undergraduates, 35 graduate students and 60 researchers in five years.

NAVIGATING THE FUTURE WITH CYBER-PHYSICAL SYSTEMS

Developing technologies to turn Singapore into a smart nation, researchers at the Delta-NTU Corporate Laboratory for Cyber-Physical Systems, a US\$33 million (S\$45 million) joint lab, set out to advance research into smart technologies.

Cyber-physical systems integrate complex computational applications

with physical devices to form interacting networks of cyber and physical elements, achieving competencies in advanced sensing, control, resilience and analytics.

Cyber-physical systems are becoming vital to the economy, says Prof Xie Lihua, Co-Director of the Delta-NTU Lab. “Singapore is facing the twin challenges of an ageing population and a shrinking workforce, so we need automation and Internet of Things technologies to make up for shortfalls in the workforce and improve productivity.”

Besides, daily life can also benefit from cyber-physical systems, adds Prof Xie, through seamlessly connecting smart homes with neighbourhood environments. “In the future you could walk into a mall, and your smartphone will use a shopping list compiled by your smart-home information system to direct you to the shops you need to go to.”

Delta Electronics, founded in 1971, is a global leader in power and thermal management solutions and a major player in several product segments such as industrial automation, displays and networking. Continuing the joint lab research collaborations with Delta Electronics, the Delta-NTU Corporate Lab has a good start, says Dr Tian Wei-Cheng, Co-Director of the Delta-NTU Lab and Director of the Delta Research Centre Singapore.

Early innovations include ultra-low-power and low-cost tags that can be used to track and trace items in manufacturing. Other technologies to be developed include advanced sensing, real-time data and video analytics. “Particularly exciting developments will include high-precision indoor positioning technologies, and smart warehouse

automation, smart material handling and management system technologies that will enable true smart manufacturing,” Dr Tian explains.

At the Delta-NTU Lab, Delta Electronics and NTU will work closely to meet real market needs. The lab provides a good platform for testbed validation and verification of new technologies that monitor physical processes, create real-time adaptability and even result in smart reconfigurable shop floors. These technologies could be a boon to Singapore’s many small- and medium-sized businesses, spurring more synergies between institutes of higher learning and Singapore’s business ecosystem.

At its full capacity, the lab at NTU’s School of Electrical and Electronic Engineering will have more than 80 researchers and staff, including NTU PhD students.

“By partnering with industry, we are giving students valuable exposure in their chosen fields as well as a head start in networking with the best in the industry,” says Prof Xie.

“Singapore is facing the twin challenges of an ageing population and a shrinking workforce, so we need automation and Internet of Things technologies to make up for shortfalls in the workforce and improve productivity.”

Prof Xie Lihua
Co-Director of the Delta-NTU Corporate Laboratory for Cyber-Physical Systems

THINK IT, PRINT IT

TAKING PRINTING TO A NEW DIMENSION

In the near future, 3D printing could be used in aerospace, construction and even the food industry, thanks to efforts by researchers at the Singapore Centre for 3D Printing.

Unlike a sculptor that chips away at material to reveal the masterpiece within, a three-dimensional (3D) printer adds material exactly where it is needed, until a three dimensional object rests upon a once-empty podium.

First conceived in the 1980s, 3D printing or additive manufacturing is the construction of a 3D object by the successive addition of material according to a computer-modelled design. It was popular in manufacturing circles as it allowed product parts to be built without the need for machining, milling or moulding. This substantially reduced material wastage and saved costs for manufacturers.

Today, 3D printing is widely used outside of manufacturing and is considered one of the most dynamic innovations in recent history, allowing users to transform their thoughts into physical objects with the push of a button.

At the Singapore Centre for 3D Printing (SC3DP) in NTU, the future of 3D printing is fast taking shape. Officially launched on 17 May 2016, the centre is supported by Singapore's National Research Foundation and several other government agencies.

Advanced manufacturing technologies have been identified as a new growth opportunity for Singapore's

manufacturing sector—with the potential to make significant contributions to Singapore's gross domestic product and national security through the constant supply of essential products and services. SC3DP endeavours to keep Singapore at the forefront of 3D-printing technology, develop capabilities not yet available elsewhere in the world and position Singapore as an advanced manufacturing hub in the world.

The research centre aims to become a world leader in 3D printing and a wellspring of knowledge by attracting leading researchers and nurturing a skilled



talent pool, in addition to establishing strong links with and delivering state-of-the-art innovations to the industry.

To help Singapore-based companies ride the wave of the “third industrial revolution”, the centre has identified five key areas of research—the future of manufacturing, aerospace and defence, building and construction, marine and offshore engineering, and biomedicine and food.

FLYING HIGH, BUILDING DREAMS

Under the leadership of Asst Prof Yeong Wai Yee from NTU’s School of Mechanical and Aerospace Engineering, SC3DP’s Aerospace and Defence programme conducts research ranging from the 3D printing of lightweight unmanned aerial vehicles (UAVs) to developing new multi-functional components that integrate electrical and mechanical functions. Techniques such as selective laser melting, a method of manufacturing 3D metal parts by fusing fine metallic powder together using a laser beam, and electronic printing processes will be used.

“The aerospace industry has shown great interest in 3D printing because of its generally low production runs and ability to fabricate parts of complex geometry,” says Prof Chua Chee Kai, citing blue chip defence and engineering provider Singapore Technologies (ST) Engineering Ltd as a close industry partner.

Prof Chua is Executive Director of SC3DP and currently the most highly cited scientist in the world in 3D printing.

“Tapping the technological advancements in 3D printing made by the aerospace industry, Singapore is well-positioned to develop disruptive capabilities for UAVs in operational and industrial contexts,” he adds.

SC3DP also seeks to revolutionise the way homes are built. Imagine each storey of a building being manufactured on-site by large 3D printers, and then stacked like Lego bricks into a finished product. This scenario could become a reality with research from NTU’s Building and Construction programme led by Assoc Prof Tan Ming Jen.

The work has already sparked the interest of Sembcorp Design

and Construction Pte Ltd, the design and construction subsidiary of Sembcorp Industries, a world leader in urban development.

Similarly, SC3DP’s exploration of novel processes for the fabrication of large metal structures could benefit marine and offshore companies by developing, testing and validating proof-of-concepts. Printing-on-demand would also allow damaged parts of a ship to be replaced quickly. The Marine and Offshore programme, directed by Assoc Prof Tor Shu Beng, is collaborating on materials development with the research arm of Singapore-based marine engineering group Keppel Offshore & Marine Technology.

FOOD: THE NEXT FRONTIER

More recently, 3D printing technology has been adapted for biomedical applications. Instead of dispensing inanimate material, 3D bioprinters layer live cells to replicate the 3D structure of organs. Because 3D bioprinting uses the patient’s own cells, organ rejection and the long wait for a compatible donor could become a thing of the past.

Despite the optimism, Prof Chua cautions that 3D bioprinting is in its infancy. “There has to be a coordinated effort between engineers like myself and medical experts as we tap into each other’s field of expertise. Printing vital organs such as hearts and lungs are much more complicated than printing an ear, which does not require an extensive network of blood vessels. Research efforts have to be ongoing and we are still many years away from maturation,” he cautions.

Nonetheless, researchers at the centre have been pushing the boundaries with plans to print meat as part of their focus on food printing, a more humane and environmentally-friendly alternative to the industrial-scale rearing of livestock. Using 3D printing to customise recipes could further allow individuals with dietary restrictions or food allergies to control what ingredients go into their meal.

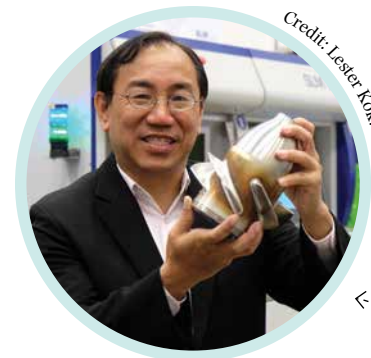
“Currently, we are working with dieticians in a hospital in Singapore to 3D-print healthy puree food that can be customised and easily consumed and

digested by elderly patients who may have various health issues and who find chewing and swallowing solid foods difficult,” Prof Chua elaborates.

ONWARD TO NEW DIMENSIONS

Even as 3D-printing applications are being developed, a new frontier in additive manufacturing is already emerging. 4D printing, whereby an object is 3D-printed from materials that respond to environmental changes, is allowing researchers to create “smart” objects that can transform to meet specific needs. For example, SC3DP has already 4D-printed a sunshade that can bend to provide shade when heated by sunlight.

Sustained industry collaboration and education are key to staying at the forefront of innovations in 3D printing technology, Prof Chua says. “At the end of the day, my wish is for our centre’s work to impact Singapore and the world. This is synonymous with SC3DP’s slogan, ‘Printing the world and beyond’.”



“There has to be a coordinated effort between engineers like myself and medical experts as we tap into each other’s field of expertise.”

Prof Chua Chee Kai
Executive Director of the Singapore Centre
for 3D Printing

Novel animal models to study infection and immunity

By Christiane Ruedl

Assoc Prof Christiane Ruedl is an immunologist at NTU's School of Biological Sciences.

The research presented here was published in *Cell Reports* (2016), DOI: 10.1016/j.celrep.2016.07.010; *Mucosal Immunology* (2016), DOI: 10.1038/mi.2015.64; *Immunity* (2015), DOI: 10.1016/j.immuni.2015.07.016; and *European Journal of Immunology* (2014), DOI: 10.1002/eji.201344359.



Transgenic mice with different levels of chimerism.

In these chimeras, the white parts come from genetically modified embryonic stem cells (ES), while the black parts correspond to the blastocysts (early embryos) in which ES cells were injected.

Animal models are important tools in biomedical research. Not only do they improve our understanding of human disease, they also help us discover and validate new drug targets for therapeutic applications.

In particular, genetically modified mice are crucial for understanding conditions ranging from infection to chronic inflammation and cancer, providing insights that cannot be obtained from cell culture alone.

At the Immunology Laboratory at NTU's School of Biological Sciences, we are developing new transgenic mouse models that would allow us to trace the origins of immune cells, understand fundamental immunological cellular mechanisms *in vivo*, and dissect the complexity of innate and adaptive immune responses involved in controlling parasite, fungal, bacterial and viral infections.

DIPHTHERIA TOXIN RECEPTOR MOUSE MODELS

One of the most efficient approaches to depleting (removing) cells *in vivo* is genetic cell ablation.

Using a system called toxin receptor-mediated cell knockout, we have generated transgenic mice that have a human diphtheria toxin receptor (DTR) gene controlled by a cell-specific promoter (Figure 1). Expression of the toxin receptor itself is not harmful but the injection of the diphtheria toxin leads to the death of the specific cell type expressing the receptor.

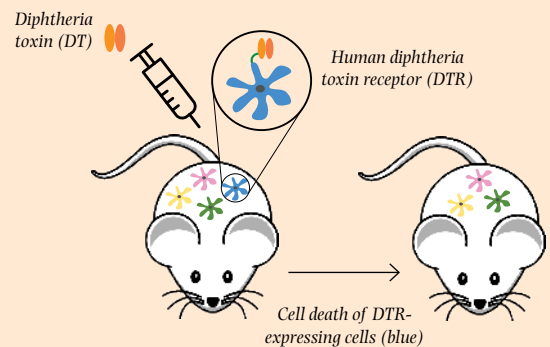


Figure 1: Toxin receptor-mediated cell knockout in diphtheria toxin receptor (DTR) transgenic mice.

Over the last few years, our laboratory has successfully generated a unique set of novel DTR transgenic mouse lines capable of specifically depleting subsets of myeloid cells such as dendritic cells and macrophages.

At the same time, we have established several experimental animal infection models mimicking viral (influenza), fungal (*Candida*) and parasitic (*Plasmodium*) infections, as well as animal models to investigate inflammatory bowel disease.

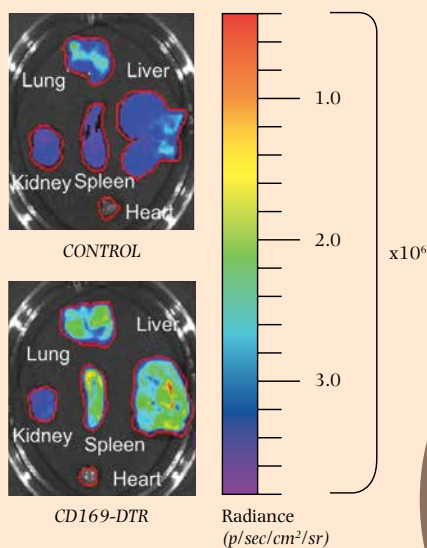
TISSUE-RESIDENT MACROPHAGES AT THE FRONT LINE AGAINST *PLASMODIUM* INFECTION

Malaria is a major health problem in the tropical and subtropical regions of the world. To date, there are no protective vaccines available; understanding the basic immune effector mechanisms of malaria immunity and pathology could lead to more effective therapies against malaria.

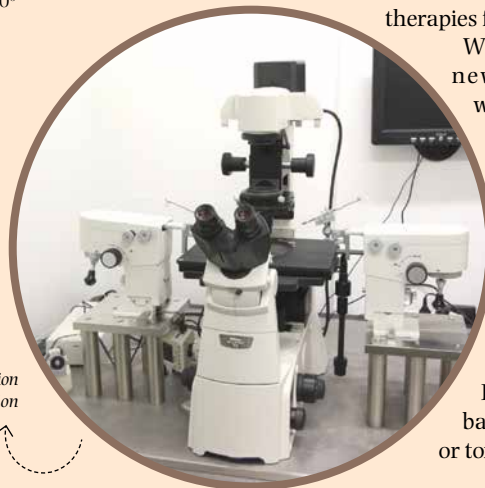
Using an animal model of malaria, we aim to understand the complex cellular interactions between different subsets of dendritic cells and macrophages in regulating immune and inflammatory responses against the parasite.

Recently, we demonstrated that a distinct innate immune cell type—the tissue-resident CD169⁺ macrophage—controls parasite propagation and sequestration, and restrains tissue/organ inflammation (Figure 2). In the absence of these macrophages, *Plasmodium* infection is lethal as a result of multiple organ failure.

Figure 2: *In vivo* bioluminescence imaging of *Plasmodium* infection in different organs collected from *Plasmodium*-infected control (top) and CD169-DTR mice (bottom). Injection of diphtheria toxin depleted the mice for CD169⁺ macrophages, leading to multi-organ failure.



Microinjection workstation



HOMEOSTASIS OF INTESTINAL EPITHELIUM CONTROLLED BY A SPECIALISED SUBSET OF DENDRITIC CELLS

A crosstalk between commensal bacteria, gut immune cells and gut epithelia is required for the proper functioning of the intestinal mucosal barrier, which protects the host against gut infections.

Testing two distinct transgenic DTR mouse strains (Clec9A-DTR and Clec4A4-DTR), we showed the role of two distinct intestinal dendritic cell subsets in controlling intestinal inflammation.

We found that Clec4A4-expressing dendritic cells have developed a functional specialisation in controlling epithelial defense and in repressing inflammation (Figure 3).

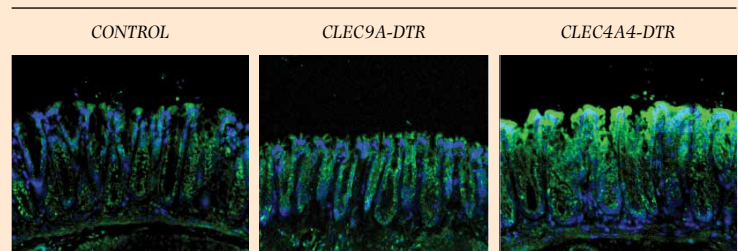


Figure 3: Enhanced production of anti-microbial peptides in colon epithelium (green) in the absence of Clec4A4⁺ dendritic cells.

ALVEOLAR MACROPHAGES CONTROL IMMUNOPATHOLOGY DURING INFLUENZA INFECTION

In addition to seasonal outbreaks, the influenza A virus can cause epidemics and even extensive pandemics, taking a toll on modern healthcare systems in the form of serious illness and death.

By exploiting one of our DTR strains (CD169-DTR), we have identified alveolar macrophages as important players in the protective response against influenza A virus infection.

These results will allow us to develop new anti-viral therapies focusing on these immune cells.

We are currently developing new mouse genetic platforms where selected target genes can be switched off by a model compound (drug equivalent) and later restored by simply withdrawing the drug.

These models give us the opportunity to temporarily perturb (in a drug-like fashion) myriads of signalling or metabolic pathways *in vivo*. In doing so, we can learn about basic biology and test the efficacy or toxicity of promising drug targets.



Breaking up bacterial blankets

Bacterial biofilms in acute and chronic infection

By Kimberly Kline

Nanyang Asst Prof Kimberly Kline from NTU's School of Biological Sciences is a Principal Investigator in the Public Health & Medical Biofilms cluster at the Singapore Centre for Environmental Life Sciences Engineering (SCELSSE) at NTU.

Parts of this study were published in Cell Host & Microbe (2016), DOI: [dx.doi.org/10.1016/j.chom.2016.09.004](https://doi.org/10.1016/j.chom.2016.09.004).

Bacterial biofilms—densely packed microbial communities encased in a self-produced matrix—are often resistant to antibiotic or immune clearance. It is thought that biofilms are associated with the majority of chronic infections, including infections of the lung, urinary tract and wounds. By contrast, biofilms have not historically been associated with acute infections.

In the lab, microbiologists often study how biofilms grow on artificial surfaces such as plastic or glass (Figure 1). However, many infection-associated biofilms require the bacteria to grow on human cells or tissues, often in environments where essential nutrients for the bacteria are in low supply. In some cases, bacterial factors that are important for biofilm formation in the lab do not appear to be important for biofilm formation during infection.

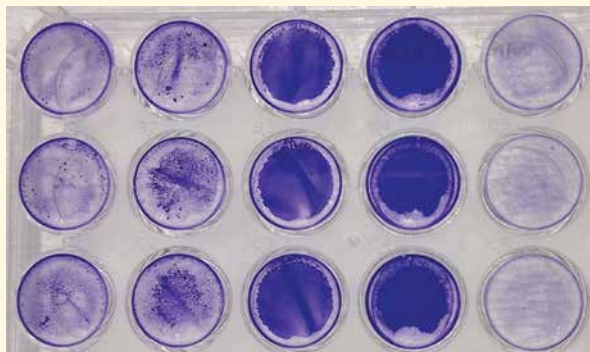


Figure 1: A typical laboratory experiment to measure biofilm formation, where dark violet staining correlates with biofilm mass when grown on plastic. Credit: Dr Artur Matysik, SCELSSE.

Therefore, we have developed new model systems to study biofilms in more realistic environments. Our hope is that if we can understand how bacterial biofilms grow during infections, we might then be able to identify new antimicrobial compounds that prevent the formation of these biofilms.

WHEN TWO BACTERIAL SPECIES MEET IN WOUNDS

Enterococcus faecalis is an important opportunistic pathogen and can be difficult to treat because it is often resistant to multiple antibiotics. *E. faecalis* causes a variety of infections—including infections of the urinary tract and blood—and belongs to the top three most common bacterial species isolated from chronic wound infections. In wounds and the urinary tract, *E. faecalis* is often found together with *Escherichia coli*.

We have shown that *E. faecalis* produces a small molecule that helps *E. coli* to overcome nutrient limitation and, in turn, promotes biofilm growth and infection in wounds (Figure 2). This work highlights how small molecule cues from one bacterial species can influence nutrient acquisition systems in another.

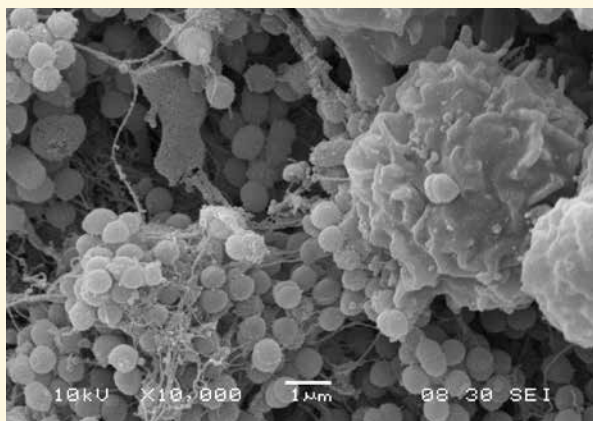


Figure 2: Scanning electron micrograph of biofilms of *E. faecalis* microcolonies (clusters of small round cells) within infected wounds, resisting clearance by immune cells (large ruffled cells shown on the right). Credit: Tay Wei Hong, SCELSE.

THE ROLE OF BIOFILMS IN NECROTISING FASCIITIS, AKA “FLESH-EATING DISEASE”

Group A streptococcus (GAS) causes a spectrum of diseases ranging in location and severity from superficial skin infections and strep throat to systemic infections like toxic shock syndrome and soft tissue infections such as necrotising fasciitis (NF).

A hallmark of NF is rapid cell death and tissue destruction affecting skin, fascia and muscle. Cell death and bacterial spread is fast, rendering early diagnosis and treatment crucial for patient survival. Although it is well-accepted that bacterial biofilms are associated with many chronic infectious diseases, little is known about the role of GAS biofilms in NF.

GAS makes several small molecules, called streptolysins, which are able to kill mammalian cells. These streptolysins induce a stress response in the host cells. We have demonstrated that toxin-induced stress within infected host cells is essential for biofilm formation on mammalian cells (Figure 3). This is because stressed mammalian cells release a factor that promotes biofilm formation.

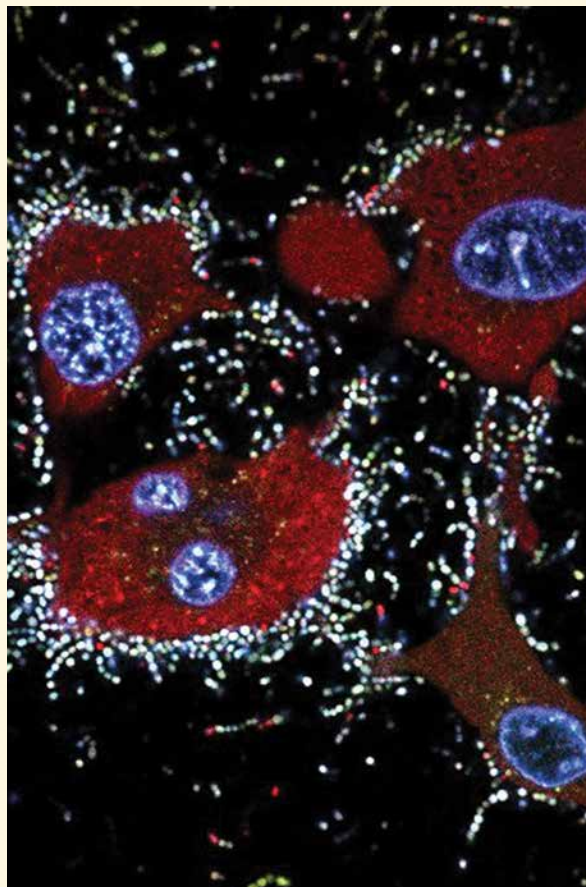


Figure 3: GAS forming biofilms (dense clusters of white dots) on and around cells found in the deeper layers of the skin, where flesh-eating infections spread. Credit: Dr Artur Matysik, SCELSE.

Using mammalian cell and animal models of biofilm-associated infection, we have discovered new pathways by which bacteria and bacterial species cue one another to promote infection and resist immune clearance during chronic infection.

In addition, we have uncovered a new host-pathogen interaction that is crucial for biofilm formation during acute flesh-eating disease.

Going forward, we will try to identify antimicrobial or antibiofilm molecules that can specifically disrupt these interbacterial or host-pathogen interactions to disrupt biofilm-associated infections.

Better drugs for bad bugs

Staying ahead in the fight against multi-drug resistance

By Kevin Pethe

Assoc Prof Kevin Pethe is an expert in antibiotic development and infectious diseases with joint appointments at NTU's School of Biological Sciences and the Lee Kong Chian School of Medicine. The former Acting CEO of Institut Pasteur Korea is internationally recognised for his contribution to the area of chemical genomics and drug discovery for tuberculosis.

The research presented here was published in Nature Medicine (2013), DOI: 10.1038/nm.3262; and Nature Communications (2016), DOI: 10.1038/ncomms12527.

With multi-drug resistant pathogens quickly outpacing the discovery of novel antibiotics, we may soon find ourselves facing the terrifying prospect of a post-antibiotic era.

Our main research interests are understanding host-pathogen interactions and identifying bacterial metabolic pathways required to establish infection, with the goal of identifying novel targets for the development of next-generation antibacterial drugs.

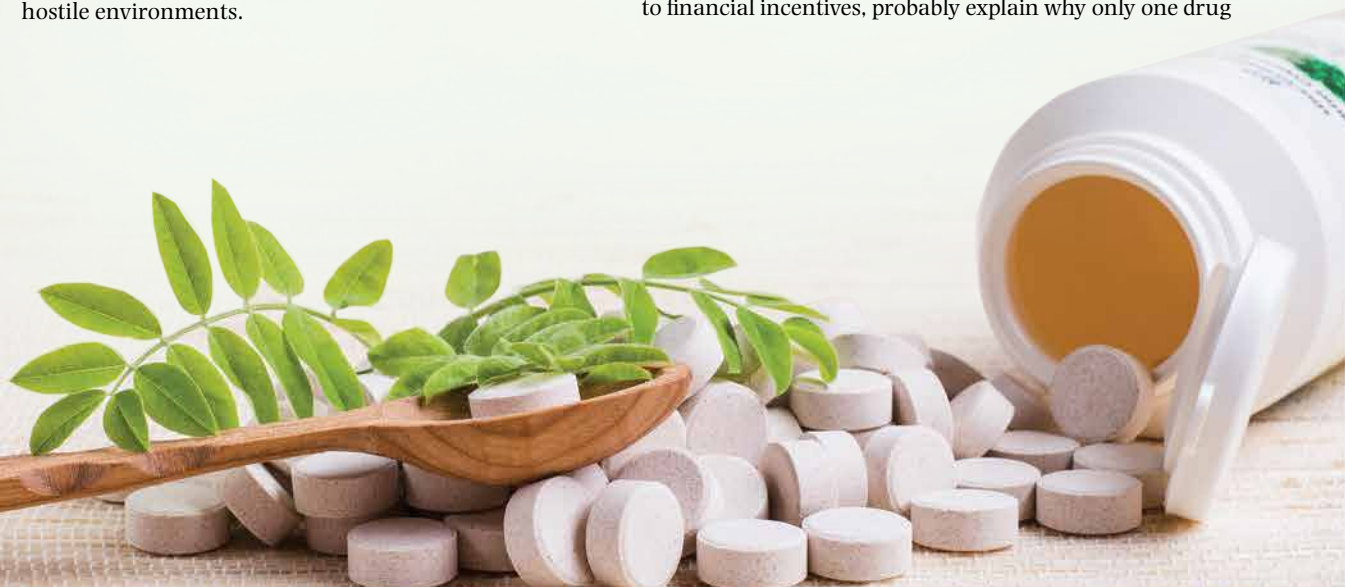
A key component of our strategy is to use high-throughput screening systems to identify essential metabolic pathways that enable pathogenic bacteria to survive in hostile environments.

NEW DRUG COMBINATIONS FOR AN OLD FOE

Tuberculosis (TB) has plagued mankind for some 50,000 years, becoming so well adapted to its human host that one-third of the human population is estimated to be latently infected with *Mycobacterium tuberculosis*, the causative agent of the disease.

To cure TB, a combination of three to four antibiotics must be administered for six months, with the treatment duration going up to 28 months for multi-drug resistant (MDR) TB. Inevitably, such a long treatment duration is associated with low patient compliance, which drives the development of further antimicrobial resistance.

Drug development hurdles, ranging from lead identification to financial incentives, probably explain why only one drug



for the treatment of drug-resistant TB was approved in the last 40 years. Moreover, clinical resistance was observed less than three years after the first use of this new drug (called bedaquiline and marketed as Sirturo), endangering 15 years of work that were necessary to bring the drug to clinical practice.

One possible reason that resistance to bedaquiline developed so quickly is the lack of appropriate companion drugs. I lead an interdisciplinary team that recently reported on a clinical stage drug candidate called Q203, which is in clinical development under a US FDA Investigational New Drug (IND) application.

Very much like cyanide in humans, Q203 blocks the ability of the bacteria to use oxygen to respire, inducing a rapid “suffocation” and death. Its molecular target is cytochrome bc1-aa3, a respiratory terminal oxidase (Figure 1).

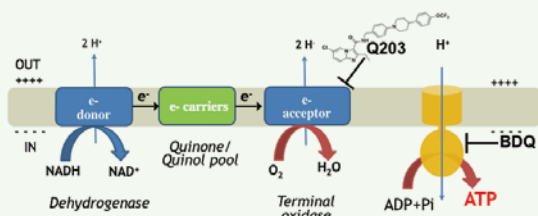


Figure 1: Q203 targets oxidative phosphorylation in *M. tuberculosis*. Q203 is an inhibitor of the mycobacterial cytochrome bc1-aa3, a terminal oxidase, whereas bedaquiline (BDQ) inhibits the ATP synthase.

We are also exploring other respiratory complexes that could be exploited for drug development, including the cytochrome bd oxidase, a bacteria-specific alternate terminal oxidase. Since the cytochrome bd oxidase is involved in persistence, inhibition is likely to result in faster clearance of the infection, significantly reducing the duration of MDR TB treatment.

Along similar lines, Prof Gerhard Grüber of NTU’s School of Biological Sciences is conducting cutting-edge research to improve bedaquiline, and to develop next-generation ATP synthase inhibitors that may be synergistic with Q203 and a drug targeting the cytochrome bd oxidase.

NEGLECTED NO MORE

In addition to TB, we are also interested in antibiotics development for neglected mycobacterial tropical diseases such as Buruli ulcer and leprosy. Both diseases are caused by bacteria closely related to *M. tuberculosis*.

Buruli ulcer is a chronic debilitating skin infection of the extremities that affects mostly children in the tropical areas of West and Central Africa, but is also endemic in Australia. Leprosy affects the skin and nerves, causing swellings on the skin and deformities in severe cases.

Studying the bacteria that cause Buruli ulcer and leprosy is complicated due to their extremely slow growth and the lack of genetic tools. Using comparative genomics and our expertise in TB, we identified central metabolic pathways

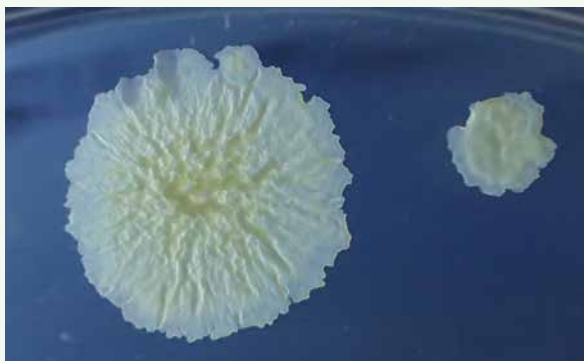


Figure 2: Colony of *Mycobacterium bovis* Bacillus Calmette-Guérin (BCG). BCG is a live attenuated vaccine for tuberculosis and the most widely used vaccine in history: four billion doses were administered worldwide since its first use in 1921. The vaccine is efficacious in infants against the most severe forms of the disease, but fails to reduce the risk of infection and development of pulmonary tuberculosis in adults.

that we predicted to be particularly sensitive to inhibitions by known anti-TB drugs.

Very recently, our predictions were experimentally confirmed in Buruli ulcer models. In collaboration with the Swiss Tropical and Public Health Institute in Basel, Switzerland, we are conducting experiments to support clinical development of some of these promising candidates.

NOT TO BE OUTDONE

Fifteen years ago, the Nobel laureate Joshua Lederberg wrote that “the future of humanity and microbes likely will unfold as episodes of a suspense thriller that could be titled ‘Our Wits Versus Their Genes’”.

For now, it seems that bacteria have outwitted humanity. But this is not a finality. With proper strategies, the collaborative work of large multidisciplinary teams and adequate policies to limit the overuse of antibiotics, we are in a position to extend the life of older classes of antibiotics while developing next-generation drugs.



Figure 3: Scientist working under biosafety level 3 conditions, the security level required to handle the airborne pathogen *M. tuberculosis*.

OUTMANOEUVRING MALARIA

New weapons against an ancient scourge

Prof Peter Preiser, Chair of NTU's School of Biological Sciences and an international heavyweight in malaria research, shares his views on the global outlook for malaria and his vision for the University's role in the fight against infectious diseases.



Q What is the current global impact of malaria?

A In the last ten years, there has been a big push by the world community—mainly through governments and foundations like the Bill & Melinda Gates Foundation—to reduce malaria. While these efforts have made a significant impact on the total number of malaria cases, there are still 200–300 million cases annually. Malaria kills about 500,000 people every year, significantly more than diseases like dengue or Ebola.

The decrease in total numbers of cases in some places has largely been the result of a few very good drugs, in particular the front-line drug artemisinin, which had a huge impact in terms of saving lives. But resistance against artemisinin is now spreading, particularly in Southeast Asia. The development of resistance to chloroquine a few decades ago had horrendous effects in terms of mortality and increased cases. A similar spreading of artemisinin resistance could set back the success we've seen over the last decade.

Q Researchers have been trying for more than a century to eliminate malaria from the world map of the big killers. What are the main challenges in developing effective vaccines and drugs against malaria?

A Firstly, as a eukaryotic cell, the malaria parasite *Plasmodium* is very similar to human cells, so anti-parasitic drugs can lead to unacceptable side effects. Secondly, during most of its life cycle, the parasite is hidden inside red blood cells, so it's not accessible by our immune defences or by drugs that need to cross multiple membranes to reach it.

The parasite also constantly varies—a process called antigenic variation—which means the immune system constantly has to play catch-up to deal with new immunological variants. Malaria has been a disease of humans since tens of thousands of years, which has

ensured that the parasite has developed mechanisms to cope with whatever the host is fighting it with.

The other problem is drug resistance. Using drugs in combination protects them better against resistance development, because it's more difficult for the parasite to develop resistance to two or more drugs simultaneously. But that means we need several good drugs at the same time, which all have to go through clinical studies and approval processes. Drug companies are reluctant to develop new drugs because it's not lucrative for them due to the fast development of resistance.

Ultimately, to fight malaria effectively in the long run, we need to find either a vaccine for it or alternative strategies that can effectively prevent malaria transmission.

Q Does the fact that artemisinin is derived from a herb used in traditional Chinese medicine mean that we should look more closely at traditional medicine as a source of new drugs?

A Absolutely. There is a huge amount of knowledge in traditional medicine. With traditional Chinese medicine, we have thousands of years of medical records and information on how certain herbal extracts were used and their biological or medical impact. This knowledge can be exploited to discover new bioactive molecules. We now need to move traditional Chinese medicine into the more evidence-based approaches of Western medicine, and conduct clinical studies to demonstrate what the effects are.

With collaborators across Singapore, we are screening libraries of compounds for effectiveness against malaria. We combine screening with information from traditional Chinese medicine to isolate compounds with anti-malarial activities.

The tropical rainforests of Southeast Asia harbour the biggest diversity of plants. Here at NTU, we see this as a real opportunity to identify new compounds with interesting biomedical or chemical activities.



Q What do you try to achieve in your own research and how does your work fit into global efforts?

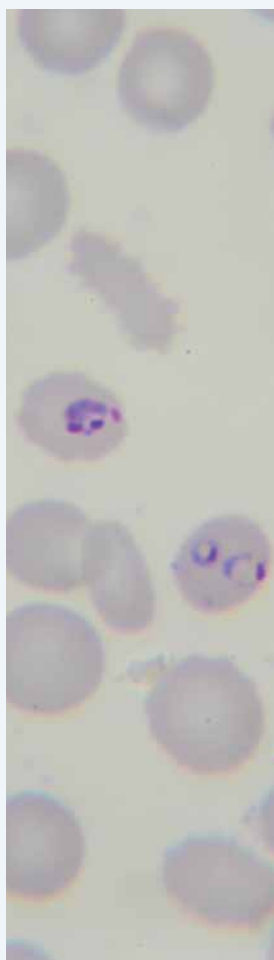
A To solve malaria in the long term, we need to have a good understanding of the biology of the parasite and how it interacts with the host in order to find its weaknesses and to develop interventions or a vaccine. My lab combines basic research with more applied and translational aspects.

One part of my research focuses on how the parasites get into red blood cells at the molecular level. This is a crucial time in the life cycle of a parasite in which it is exposed directly to the host environment and to the host's immune system. Also, once the parasite is inside the red blood cell, it produces proteins that it inserts on the cell's surface. These proteins are linked to the severity of the disease and also to the capability of the parasites to evade elimination by the immune system. So understanding the molecular details of the infection process might help to find new targets for medical intervention.

To tackle malaria, we also need good surveillance and diagnostic tools. In collaboration with other Singaporean researchers, we have developed a very sensitive tool that can detect malaria parasites in a single drop of blood. It proved to be more sensitive than standard techniques including microscopy or PCR.

I have also been involved in developing a system that allows us to test potential vaccines more cheaply using so-called "humanised" mice that express cells of the human immune system. In these mice, we can effectively study the parasite's interaction with the human immune system, in ways that would not be possible with human patients.

Globally, we work with clinical researchers in Africa and Thailand, as well as with chemists for drug development and engineers who bring in new ideas and tools that biologists might not think of.



The ring form of the malaria parasite (purple) in a blood smear.

Traditional Chinese medicine as a source of new drugs.



Q As Chair of the School of Biological Sciences, how do you think the School—and the University—can position itself to be a world leader in infectious disease research?

A At the School and NTU, we have research strengths in which we are already considered a world-leader, namely viral diseases, bacterial infections such as tuberculosis, and parasitic diseases such as malaria. Furthermore, we have fantastic capacities in terms of protein chemistry, structural biology, chemistry and drug design, as well as colleagues who are experts in the field of bacteria, such as at the Singapore Centre for Environmental Life Sciences Engineering.

By bringing people across the various disciplines together—from microbiology and computational biology to areas in engineering—the University is collectively able to come up with new concepts and ideas for better antimicrobials that can't be overcome by resistance easily.

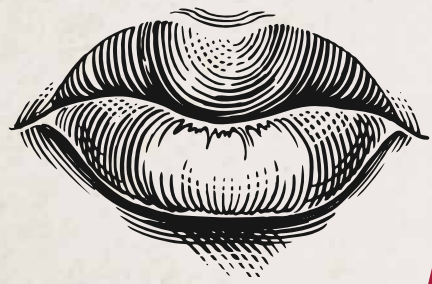
This effort would include studying traditional medicines to find yet undiscovered broad-acting antimicrobial compounds that plants produce to fight bacteria or fungi. In combination with new delivery techniques and tools that prevent resistance, I would like to see this as an avenue for the School to pursue to deliver new solutions for the global challenge of infectious diseases.

“

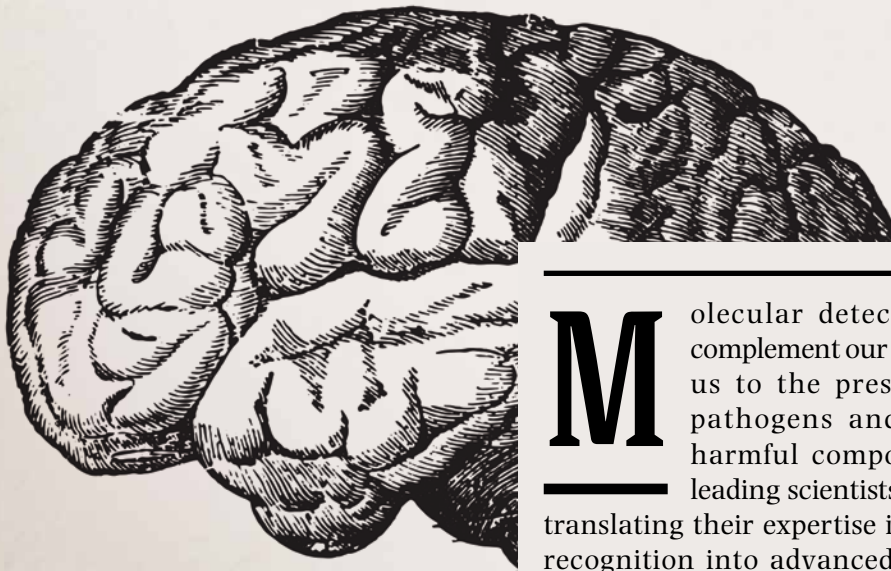
MALARIA KILLS ABOUT
500,000 PEOPLE EVERY
YEAR, SIGNIFICANTLY
MORE THAN DISEASES LIKE
DENGUE OR EBOLA.

”





SENSI AND DIAGNOSTICS



Molecular detection systems can complement our own senses, alerting us to the presence of diseases, pathogens and toxins or other harmful compounds. Meet three leading scientists from NTU who are translating their expertise in molecular signal recognition into advanced tools for sensing, diagnostics and theranostics.

NG

PROF BO LIEDBERG

Food poisoning can crop up at every step of food handling, from the time the food leaves the processing plant to the time it reaches our plate.

Prof Bo Liedberg, a world-renowned molecular physicist who joined NTU's School of Materials Science and Engineering seven years ago, is developing highly sensitive detectors for toxins like botulinum and other environmental and food contaminants, including metals and volatile organic compounds.

The Swedish scientist gained international prominence at an early phase of his career as inventor and pioneer of the science behind surface plasmon resonance, an optical detection system for the study of specific interactions between biomacromolecules. Surface plasmon resonance has been implemented and commercialised by Biacore, today GE Healthcare, and is widely used in biomedical research.

At the Centre for Biomimetic Sensor Science, where Prof Liedberg is the founding director, researchers are developing toxin sensors based on colorimetric detection, which visibly change colour to indicate the presence of toxins or other target molecules.

In collaboration with Singapore's national defence research agency, DSO National Laboratories, Prof Liedberg has also designed a sensor based on graphene nanotubes that can detect lipopolysaccharide molecules, which can cause septic shock at early stages of infection.

Other than food and environmental sensing, Prof Liedberg's work also has applications in cancer diagnostics. He has developed assays that enable early detection of a metalloproteinase that is heavily upregulated in several cancers.

"In collaboration with a Dutch clinician, we are working on colorimetric sensors that will allow surgeons to visualise in real time in the operating theatre how much of affected organs and tissues need to be cut off—a very important problem in surgery," explains Prof Liedberg, who is the leader of the Sensing and Diagnostics technology programme at NTU's Nanyang Institute of Technology in Health and Medicine. He is also the Dean of NTU's Interdisciplinary Graduate School.

In addition, he has been an advisor to two companies dealing with sensor technology—Optisense, a Dutch company, and its Singapore subsidiary, Optiqua, which develops sensor technology for water quality monitoring.



Credit: Interdisciplinary Graduate School, NTU.



Credit: NTU.

Diagnosing patients at home or in the field could hugely improve public healthcare, speeding up access to the right treatments for the sick and curbing the spread of disease.

The development of fast, cheap and portable biosensors for medical diagnostics is on top of the agenda of Assoc Prof Martin Pumera, an expert in materials chemistry at NTU's School of Physical and Mathematical Sciences, who has gained a global reputation for his research on electrochemistry in two-dimensional materials.

For his sensors, Assoc Prof Pumera uses ultrathin two-dimensional sheets of graphene or black phosphorus that can be loaded with disease-specific detection molecules like antibodies or DNA sequences.

When these sheets are immersed in solutions of body fluids such as blood or urine, the binding of disease-specific biomarkers alters the pattern of electrical currents, which are then recognised and analysed with the help of dedicated software in the portable devices.

"The idea is to make diagnostics fast, sensitive, cheap and simple and to bring it to the people's homes, which will also cut costs and time," explains Assoc Prof Pumera. "What's more, the sensors we develop are very small, which might allow them eventually to be implantable for the monitoring of diseases."

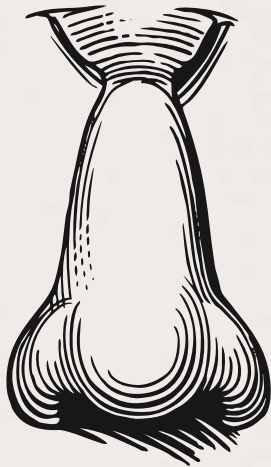
In a second, more futuristic approach, Assoc Prof Pumera is developing micro- and nano-sized robots with chemotactic properties that one day may serve as drug delivery vehicles that home in on chemicals produced by tumours or infected tissues.

Propelled by nano-sized motors, which draw their energy from compounds in their surroundings such as sugars, the envisioned nano-robots will be able to autonomously move inside the body—for instance inside the stomach or gut—and carry therapeutics to diseased cells and tissues, label cells or even remove sick cells. Made out of biopolymers, the nano-robots could then simply dissolve once their tasks have been fulfilled.

"What is exciting about these robotic devices is that they will be able to sense and act, so this will be a big step beyond just sensing and diagnosing," adds Assoc Prof Pumera.

ASSOC PROF MARTIN PUMERA





PROF WOLFGANG KNOLL

Three out of our five senses—sight, hearing and touch—have artificial sensor technologies that efficiently match or exceed the sensitivity of the human eye, ear or skin. However, technologies for the remaining two senses—smell and taste—lag behind because of the complexity of the underlying mechanisms and signal pathways.

“We can identify about 10,000 different smells with only 500 different smell receptors. It’s the combination of signals that makes it interesting, but the process is very complex,” explains Prof Wolfgang Knoll, visiting professor at NTU’s School of Materials Science and Engineering, who is a world expert in the biophysical modelling of biological membranes and surface plasmon resonance technology.

Working with the Centre for Biomimetic Sensor Science at NTU, a multidisciplinary setup with the Austrian Institute of Technology (AIT) where he is the scientific managing director, Prof Knoll is at the forefront of developing sensitive biosensors for smells and other environmental chemicals in the air.

In collaboration with NTU’s Nanyang Institute of Technology in Health and Medicine, he has also come up with scent detectors for health diagnostics to sense chemicals indicative of ailments and diseases.

His latest biomimetic smell detectors, inspired by nature and comprising smell receptors from the red flour beetle (*Tribolium castaneum*) mounted on graphene platforms, already reach a sensitivity that is only about a factor 10 below that of the beetles’ themselves.

“There is a great need for air analysis and the detection of smells in areas such as food quality control, health diagnostics, crop disease detection, indoor air management, security applications and so on,” says Prof Knoll. “The generation and detection of smells is also useful to the fragrance industry.”

Besides his scientific work in smell detection, Prof Knoll has initiated the International Graduate School Bio-Nano-Technology. Under this graduate student exchange programme, a partnership between NTU, AIT and Austrian universities, PhD students are trained as future global leaders in science and technology and earn a joint PhD degree. Prof Knoll is also leading another initiative, the Programme on Advanced Biomedical Imaging, which involves NTU’s Lee Kong Chian School of Medicine, the Medical University of Vienna and the AIT.



Credit: Wolfgang Knoll.

THE ART OF EXPLAINING SCIENCE

A documentary produced by a team of NTU filmmakers and scientists is making waves at top international film festivals across Europe, Asia and the Americas, bagging a prestigious Remi Award at the 2016 WorldFest-Houston International Film Festival, the Sierra Nevada Award at the 2016 Mountain Film Festival and the 2016 Rochester International Film Festival's Certificate of Merit.

Called "**The Ratu River Expedition**", the documentary features the months-long expedition of a team of geologists from NTU's Earth Observatory of Singapore (EOS)—led by Asst Prof Judith Hubbard—to the foothills of the Himalayas.

Filmed by pioneering digital artist and independent filmmaker Prof Isaac Kerlow from NTU, the documentary sheds light on one of the biggest fault lines in the world, which caused the devastating magnitude 7.8 earthquake in Nepal in 2015, and explains how studying the geometry of faults with new technologies could help anticipate future earthquakes.

Present your innovative idea, research project or social initiative in just three minutes—that was the challenge 17 early-career academics from NTU faced at the inaugural **Falling Walls Lab Singapore**. Organised by Global Dialogue @ NTU, a unit at the University that facilitates high-level interdisciplinary discussions and global exchange of ideas, the contest invited participants to give inspirational talks on topics ranging from nano-sized machines to the conservation of resources and the environment and innovative night vision devices.

PhD students James Moo from the School of Physical and Mathematical Sciences and Sow Wan Ting from the School of Materials Science and Engineering came in top and will represent Singapore at the international Falling Walls Lab Finale on 8 November 2016 in Berlin, Germany. They were chosen by a jury of six academics and industry leaders chaired by NTU Visiting Professor and former President of the European Research Council, Prof Helga Nowotny.

Watch the documentary at <https://vimeo.com/168022576>.



13 international film screenings and counting: "The Ratu River Expedition" is an interdisciplinary success story by an NTU team of filmmakers and earth scientists, led by (from right) digital artist Prof Isaac Kerlow and structural geologist Asst Prof Judith Hubbard. Credit: Amin Shah.



(Left) Propelling nanomachines with bubbles: James Moo's off-the-wall idea won him the top prize. (Right) Making paper with human hair: Second prize winner Sow Wan Ting's ingenious plan. Credit: Global Dialogue @ NTU.

A different three-minute challenge was posed to all NTU graduate students in August 2016. At the **2016 Three Minute Thesis—3MT Final** (a research communication competition developed by the University of Queensland), ten graduate research students from across NTU's schools took on the task of effectively explaining their thesis' topic and significance in just three minutes. After making their way through a series of heats and semi-finals, the ten finalists wowed the judges and audience with their powerful presentations and communication skills.

The winner of this year's competition, Robbie Lee Sabnani from NTU's National Institute of Education, represented NTU at the 2016 Asia-Pacific 3MT Competition at the University of Queensland, Australia, on 30 September 2016.

EVENTS

CONFERENCE: EAST OF WEST, WEST OF EAST

Organised by NTU's Para Limes

17 – 19 October 2016

Venue: Mandarin Orchard Hotel,
Singapore

[www.paralimes.ntu.edu.sg/NewsnEvents/
Pages/Upcoming-Events.aspx](http://www.paralimes.ntu.edu.sg/NewsnEvents/Pages/Upcoming-Events.aspx)

INTERNATIONAL CONFERENCE ON THE MODERNISATION OF CHINESE MEDICINE

**Jointly organised by NTU's
Institute of Advanced Studies
and The Academy of Chinese
Medicine Singapore**

23 October 2016

Venue: Suntec Convention and Exhibition
Centre, Singapore

ntu.edu.sg/ias/upcomingevents/TCM16

ASIAN WAVE AND TIDAL ENERGY CONFERENCE SERIES (AWTEC)

**Co-organised by the Energy
Research Institute @ NTU and
Sustainable Energy Association of
Singapore**

24 – 28 October 2016

Venue: Marina Bay Sands, Singapore
awtec.asia

ASIAN CONFERENCE ON ENERGY, POWER AND TRANSPORTATION ELECTRIFICATION (ACEPT) AT ASIA CLEAN ENERGY SUMMIT (ACES)

**Organised by the Energy Research
Institute @ NTU**

25 – 27 October 2016

Venue: Marina Bay Sands, Singapore
accept.asia

WORKSHOP: BIG DATA IN ASIAN SOCIETY

**Organised by NTU's College of
Humanities, Arts and Social
Sciences**

27 – 28 October 2016

Venue: School of Humanities and Social
Sciences, NTU, Singapore
bigdata-in-asia.com

2ND INTERNATIONAL INSTITUTES FOR ADVANCED STUDY FORUM

**Organised by NTU's Institute of
Advanced Studies**

1 – 2 December 2016

Venue: Nanyang Executive Centre, NTU,
Singapore
ntu.edu.sg/ias/upcomingevents/iiasf16

CONFERENCE: DISRUPTED BALANCE—SOCIETY AT RISK

Organised by NTU's Para Limes

5 – 7 December 2016

Venue: Mandarin Orchard Hotel, Singapore
[www.paralimes.ntu.edu.sg/NewsnEvents/
Pages/Upcoming-Events.aspx](http://www.paralimes.ntu.edu.sg/NewsnEvents/Pages/Upcoming-Events.aspx)

2ND INTERNATIONAL CONFERENCE IN SPORTS SCIENCE & TECHNOLOGY (ICSST)

**Organised by NTU's Institute for
Sports Research**

12 – 13 December 2016

Venue: Nanyang Executive Centre, NTU,
Singapore
icsst.sg

CONFERENCE ON 90 YEARS OF QUANTUM MECHANICS

**Organised by NTU's Institute of
Advanced Studies**

23 – 26 January 2017

Venue: Nanyang Executive Centre, NTU,
Singapore
ntu.edu.sg/ias/upcomingevents/QM90

CONFERENCE ON COSMOLOGY GRAVITATIONAL WAVES AND PARTICLES

**Organised by NTU's Institute of
Advanced Studies**

6 – 10 February 2017

Venue: Nanyang Executive Centre, NTU,
Singapore
ntu.edu.sg/ias/upcomingevents/cosmo

COMING YOUR WAY

1 Advances in self-driving vehicles are gaining speed worldwide but international standards and regulations for large-scale deployment of these vehicles are largely missing. Spearheading the development of testing requirements and standards, NTU, together with Singapore's Land Transport Authority and the country's leading agency for urban development, JTC

Corporation, launched the **Centre of Excellence for Testing & Research of Autonomous Vehicles – NTU (CETRAN)**. Using a dedicated 1.8-ha test circuit that provides a simulated road environment, researchers at the centre aim to safely integrate self-driving vehicles with existing road traffic and Singapore's plans for urban mobility and transport concepts.

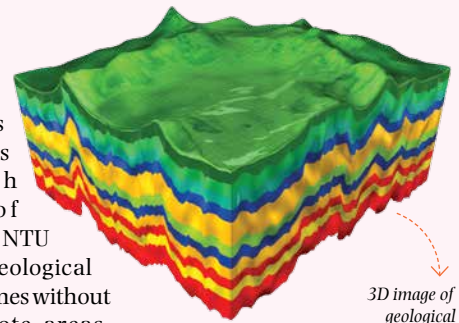


2 NTU is leading an alliance to help Asia be better insured against natural catastrophes.

Involving multinational and regional companies in the insurance industry, such as Aon-Benfield, Mitsui Sumitomo Insurance Group, Renaissance Re, Risk Management Solutions and PERILS AG, the **Natural Catastrophe Data and Analytics Exchange**

(NatCatDAX) Alliance is led by NTU's Institute of Catastrophe Risk Management and executed by a Singapore-based consortium. The alliance will work towards generating quality-assured databases covering exposure and loss for governments in Bangkok, Jakarta, Manila and Taipei due to earthquakes, wind storms and floods. It also supports market analytics and product innovation.

3 Researchers and students at the Earth Observatory of Singapore (EOS) at NTU can now explore geological processes and fault lines without travelling to remote areas. Turning complex datasets into visuals of topographic landscapes or underground rock formations, the new **EOS 3D Visualisation Laboratory** sheds light on the structure of large-scale or subsurface geological features. Powered by a high-resolution digital projector system that works in active stereo mode and requires users to wear special powered glasses, the state-of-the-art laboratory enables the brain to construct 3D images of geological structures above



3D image of geological structures.

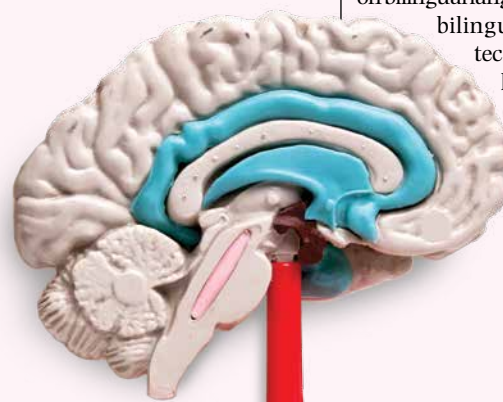


Credit: Cheryl Han, EOS

or beneath the Earth's surface and can be used to replace or complement real-life field trips.

4 More professionals in Singapore can benefit from the top-quality education offered at NTU to meet new challenges and stay relevant. The **College of Professional and Continuing Education (PaCE College)** leverages NTU's expertise in established and emerging education technologies to offer adult and continuing education through undergraduate- and graduate-level courses as well as executive, personal development and enrichment courses.

5 Two top universities in education—**NTU and Johns Hopkins University**—have joined forces to support scientists from disciplines such as language neuroscience, neuroimaging and neuro-engineering in research into the science of learning. Under the direction of NTU's Centre for Research and Development in Learning (CRADLE@NTU) and Johns Hopkins University's Science of Learning Institute, and supported by seed funding of US\$2.2 million (S\$3 million), the partnership will begin with projects on bilingual language acquisition, bilingual reading and technology-enabled learning.



6 Seawater desalination already meets up to 25% of Singapore's water needs and is of increasing importance to coastal states with low fresh water resources worldwide. To develop and commercialise innovative separation and filtration technologies to remove salt and other contaminants from seawater, the **Separation Technologies Applied Research and Translation (START) Centre** was set up as a one-stop facility to link academia to industry. Supported by NTU, Singapore's Economic Development Board, national water agency PUB and Singapore's National Research Foundation—the first of its kind in the Asia-Pacific—will explore novel

membranes and processes that can help to lower energy costs and increase yields of desalinated water.



7 High-profile online hacker attacks have highlighted the need for better cyber security and management. The **Cyber Risk Management (CyRiM) Project**, located at NTU's Nanyang Business School, will facilitate new areas of research in cyber risk, security and insurance, and help businesses and institutions defend themselves against increasingly sophisticated cyber-attacks. The three-year

pioneering project—launched by NTU and supported by the Monetary Authority of Singapore and Cyber Security Agency of Singapore together with five industry partners, Aon Centre for Innovation and Analytics, Lloyd's, MSIG Insurance, SCOR and TransRe—will work with insurers and academics in North America and Europe to drive cyber security improvements and develop affordable and effective cyber insurance products.



8 Singapore's vision of becoming a zero waste nation is getting a boost with a US\$29.3 million (S\$40 million) **Waste-to-Energy Research Facility** that will be set up by NTU in collaboration with Singapore's National

Environment Agency. The facility, the first of its kind in Singapore, will enable demonstration and test-bedding of technologies that, for example, turn waste and biomass into synthetic gas, and also provide manpower training.

9 With an estimated 1.5 billion cases of food-borne diseases globally, food safety is a key issue in sustainable food production. Turning agricultural raw materials into high-value food ingredients and reducing food wastage are other aspects that will be tackled by students from NTU and the **Netherlands' Wageningen University** under a **joint PhD programme in food science and technology**. Leveraging the two universities' expertise in nanotechnology, biomedicine and food science, the programme's two-fold aim is to innovate sustainable food production and processing technologies and to nurture talents in food microbiology and food safety.



10 Real-world case studies and interactions with leading industry experts in valuation are key parts of a new programme targeted at employees of the accountancy, financial and legal sectors. Launched by the Institute of Valuers and Appraisers of Singapore and NTU's Nanyang Business School, the 18-month **Chartered Valuer and Appraiser programme** aims to promote high standards of ethics and professionalism in the practice of business valuation and will be Asia's first professional business valuation certification programme.



THE HONOUR ROLL

ROYAL HONOURS

Prof James Best, Dean of NTU's Lee Kong Chian School of Medicine, was appointed Officer of the Order of Australia at the 2016 Queen's Birthday Honours. It is one of the highest honours in the Australian honours system. Prof Best was recognised for his distinguished service to medicine, medical education, and rural and indigenous health.



Credit: Australian High Commission.

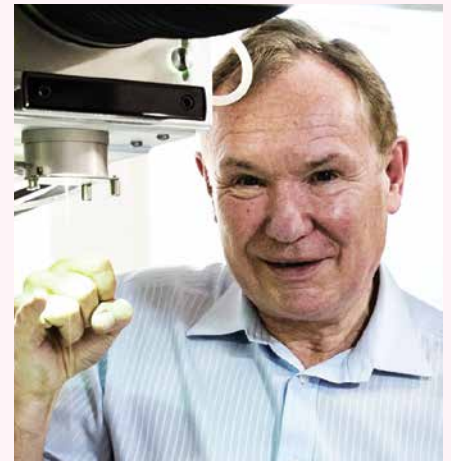


TRANSFORMING EDUCATION

Honoured as one of the world's leading educationists, **Prof Lee Sing Kong**, NTU's Vice President (Alumni and Advancement) and Director of NTU's Centre for Research and Development in Learning, was conferred an Honorary Doctor of Literature from University College London. Prof Lee, who served as Director of the National Institute of Education at NTU for eight years, was honoured for transforming the Institute into a major international education powerhouse and for pioneering a wide range of educational innovations.

HIGH HONOUR FOR INTERNET PIONEER

In the 1980s, **Prof Sir David Payne** gained international fame for developing optical fibre technology that formed the backbone of the Internet. For his revolutionary work in optoelectronics, Prof Sir Payne, who is the Director of Southampton University's Optoelectronics Research Centre, Co-Director of NTU's The Photonics Institute and Visiting Professor at NTU's School of Electrical and Electronic Engineering, was conferred an Honorary Doctor of Engineering from NTU.



PLATINUM STANDARD FOR GREEN BUILDINGS

NTU is the inaugural winner of the Green Mark Platinum Star Champion award, the highest accolade from Singapore's Building and Construction Authority for outstanding commitment to sustainable design. Over the years, NTU has won a record number of 51 Green Mark Platinum awards, the national benchmark for the design, construction and operation of green buildings with high energy-efficiency and other eco-friendly features.





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organizations capture new
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