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A*STAR
RESEARCH
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*A*STAR Research* is a publication of the Agency for Science, Technology and Research (A*STAR) — Singapore's lead government agency for fostering world-class scientific research.

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The Agency for Science, Technology and Research (A*STAR) is Singapore's lead government agency dedicated to fostering world-class scientific research and talent for a vibrant knowledge-based economy.

A*STAR actively nurtures public-sector research and development in biomedical sciences, physical sciences and engineering, and spurs growth in Singapore's key economic clusters by providing human, intellectual and industrial capital to our partners in industry and the healthcare sector.

A*STAR currently oversees the following research institutes, consortia and horizontal technology program offices, and supports extramural research with universities, hospital research centers and other local and international partners:

A*STAR Skin Research Labs (A*SRL)
Advanced Remanufacturing and Technology Centre (ARTC)
Bioinformatics Institute (BII)
Bioprocessing Technology Institute (BTI)
Experimental Drug Development Centre (EDDC)
Genome Institute of Singapore (GIS)
Horizontal Technology Programme Offices (HTPO):
- Agritech & Aquaculture (A2)
- Artificial Intelligence, Analytics and Informatics (AI^3)
- Health & MedTech (HMT)
- Infectious Diseases (ID)
- Robotics
- Social Sciences & Technology (SST)
- Urban and Green Technology (UGT)

Infectious Disease Labs (ID Labs)
Institute of Bioengineering and Bioimaging (IBB)
Institute of Chemical and Engineering Sciences (ICES)
Institute of High Performance Computing (IHPC)
Institute for Infocomm Research (I^2R)
Institute of Molecular and Cell Biology (IMCB)
Institute of Microelectronics (IME)
Institute of Materials Research and Engineering (IMRE)
National Metrology Centre (NMC)
Singapore Immunology Network (SIgN)
Singapore Institute for Clinical Sciences (SICS)
Singapore Institute of Manufacturing Technology (SIMTech)
Singapore Institute of Food and Biotechnology Innovation (SIFBI)

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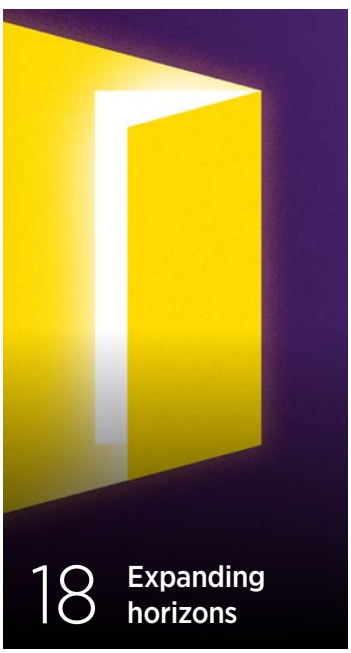

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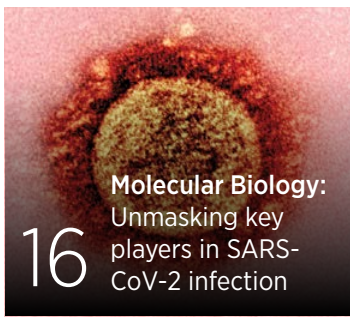
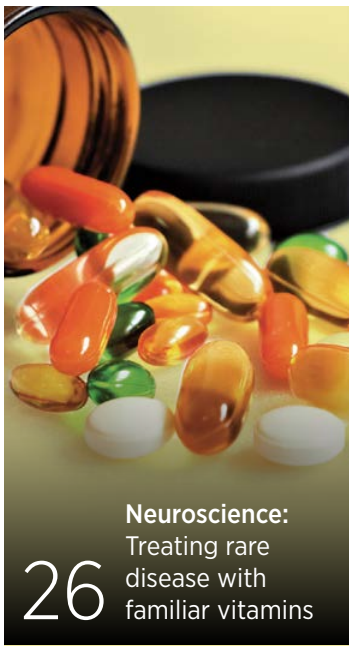
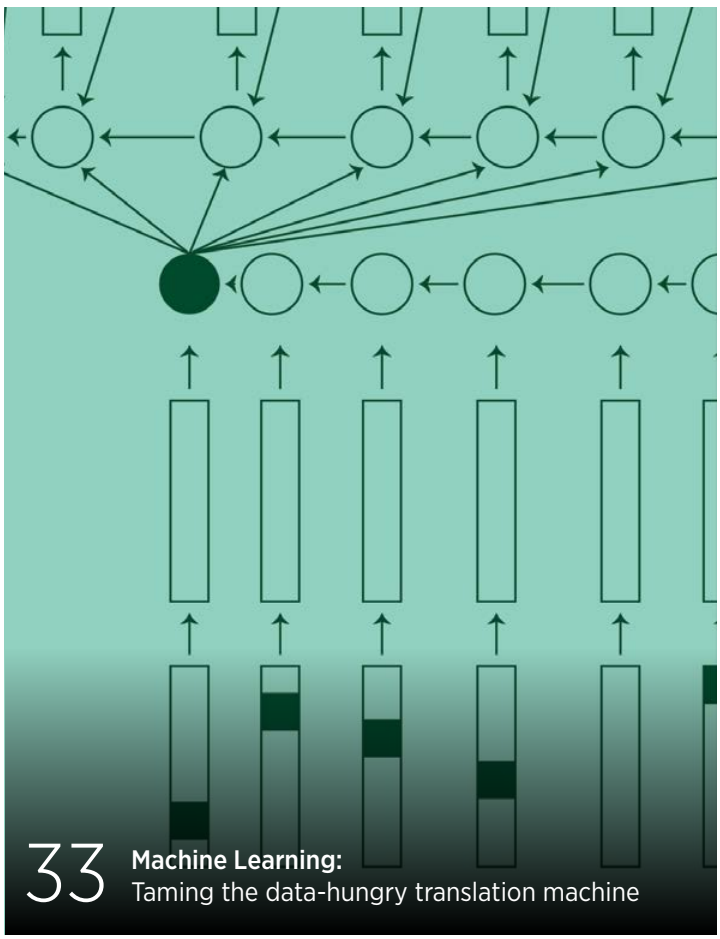
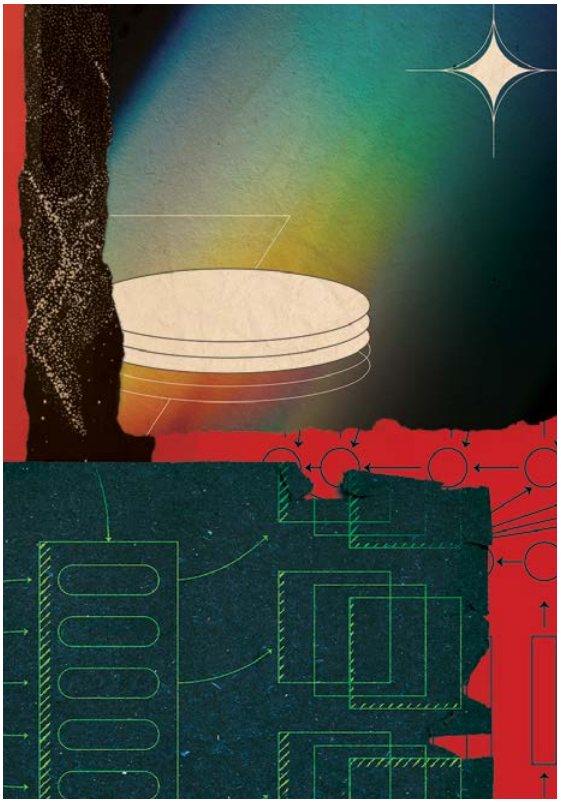






EDITORIAL NOTES



In the public eye, science is popularly associated with big breakthroughs and dazzling inventions. But for the researchers behind these advancements, science is just as much about the process as the result. It is the collective effort of generations of scientists that keeps science moving forward, from trailblazers laying the foundations to rising stars building atop decades of discoveries.

To maintain the vitality of the research and development (R&D) sector, the A*STAR Graduate Academy (A*GA) set out to secure a pipeline of talent through several scholarship initiatives. In 'Growing research talent in Singapore (p. 04),' our cover story commemorates 20 years of A*GA and describes how it supports young scientists early in their career.

Since the founding of A*GA, over 3,000 scholars have stepped beyond the walls of training institutes, equipped with a wealth of skills and character-building experiences. From research to policymaking, read about A*GA alumni in 'Expanding horizons (p. 18),' who are making waves in their respective fields while mentoring the next generation of scientific talent.

Whether studying in Singapore or overseas, these budding scientists are dedicated to addressing the complex global challenges unfolding before them. In 'Stars in the making (p. 38),' meet the 2022 cohort of A*STAR scholars who are making their first foray into the exciting world of R&D.

In the midst of the anniversary celebrations, A*STAR scientists continue to expand our knowledge with basic discoveries as well as improve our lives with practical inventions. Read about how the coronavirus interacts with human RNA for COVID-19 disease development in 'Unmasking key players in SARS-CoV-2 infection (p. 16).' Elsewhere, an Institute for Infocomm Research (I^2R) team has devised a novel method to improve the accuracy of automated translations in 'Taming the data-hungry translation machine (p. 33).'

To learn more about latest developments from A*STAR scientists, visit our website at **research.a-star.edu.sg**. Stay up-to-date by following us on Twitter at **@astar_research**, LinkedIn at **A*STAR Research** and Telegram at **A*STAR Research**.

On the cover
The A*STAR Graduate Academy celebrates two decades of supporting scientific talent to advance research and development in Singapore and beyond.

For the latest on A*STAR's COVID-19 research, please scan the QR code or visit: https://research.a-star.edu.sg/tag/covid-19/

GROWING RESEARCH TALENT IN SINGAPORE

TWO DECADES OF THE A*STAR GRADUATE ACADEMY

For twenty years, A*STAR has secured and developed a pipeline of scientific talent in Singapore through its suite of scholarship schemes.

LAI FUNG CHAN
Chairman of A*STAR

What should a scientist aspire to do with their career?

If you were to ask the late Nobel Laureate Sydney Brenner, his answer may have gone beyond making paradigm-shifting scientific breakthroughs or creating innovations that impact the world. On top of research impact, Brenner also cared deeply about nurturing young scientists and giving them the room to grow and take the lead in pushing research frontiers.

Brenner's conviction that we must groom the next generation of scientists is something A*STAR has more than taken to heart. In 2001, A*STAR established the A*STAR Graduate Academy (A*GA), the office responsible for administering a comprehensive suite of undergraduate, PhD and postdoctoral scholarships.

Now some two decades later, A*GA has given over 3,400 aspiring scientists access to top-class education in Singapore and abroad, creating a strong pipeline of scientific talent for the country in the process.

"Research and development are of strategic importance to Singapore—both in enhancing our economic competitiveness and in helping the country overcome our manpower, land and carbon constraints as well as improving food security and pandemic resilience," said Ms Lai Fung Chan, Chairman of A*STAR. "The A*STAR scholarships allow us to invest in our young people and build up a pool of scientific talent who will be able to help address not only national challenges but also complex global ones."

KHIN YONG LAM
A*GA Executive Director, 2001–2006

THE GENESIS OF A*GA

As a country that places strategic importance on research and development (R&D), Singapore is more than aware of the value of scientific talent.

"Twenty years ago, we realized that as much as we valued the contributions of international researchers to Singapore, it was also critical that we build up a core group of Singaporeans who would be the future leaders within our research ecosystem," recalled Professor Lam Khin Yong, A*GA's Founding Executive Director and current Senior Vice President (Research) at Nanyang Technology University Singapore (NTU).

A key component of A*STAR's strategy to achieve this goal was A*GA. In its early years, the A*GA office was responsible for overseeing numerous aspects of A*STAR's manpower development efforts and scholarship administration, with the main goal of producing a pool of Singaporeans with PhD degrees—1,000 of them, to be exact—in wide-ranging disciplines from biomedical sciences to materials science and sustainability engineering.

Why the emphasis on PhD degrees? "While research and innovation do not necessarily require a PhD degree, the rigorous training offered by a PhD will give researchers immense exposure and domain expertise in their chosen field," explained Lam.

With that reason in mind, A*GA designed a variety of scholarship schemes that provided students with the opportunity to study and conduct research at top universities in Singapore and abroad.

For example, the BS-PhD National Science Scholarship secures promising young Singaporeans right out of junior college, before they commit to other organizations or institutes of higher learning.

A*GA also partnered with universities both locally and abroad to bolster A*STAR's education capacities. Scholarships like the A*STAR Graduate Scheme (AGS) now allow PhD scholars to receive joint supervision by Nanyang Technological University (NTU) and National University of Singapore (NUS) faculty members as well as A*STAR scientists, while joint programs with international universities and research institutes provide scholars with international exposure.

GOING BEYOND BORDERS

Once A*GA was up and running, the focus in subsequent years shifted to adding breadth and depth. This included expanding its reach internationally and offering scholarship schemes to graduates from outside Singapore.

"Around 2007, we started the international dimension, a charge led by the Singapore International Graduate Award (SINGA) scholarships," said former Executive Director Khiang Wee Lim, who pioneered the active search for international scientific talent together with academic leaders from NUS and NTU.

The motivation was simple: to increase the diversity of the talent pool of students in Singapore.

In its early years, SINGA offered international students a chance to pursue a PhD degree in Singapore at NUS or NTU, and has since expanded the program to include the Singapore University of Technology and Design (SUTD) and the Singapore Management University (SMU).

For further flexibility, Lim and his team started the A*STAR Research Attachment Program (ARAP), a collaboration between A*STAR and partner universities that allowed scholars to complete half of their degrees in their home country and the other half in Singapore as an alternative to SINGA's full four-year stay in Singapore.

"It was a win-win solution for everyone involved. It also fostered more collaborative research," said Lim.

KHIANG WEE LIM
A*GA Executive Director, 2009–2013

ALFRED HUAN

A*GA Executive Director, 2013–2017

REMEMBERING THE HUMAN ELEMENT

This consideration for scholars and understanding their needs is something that has remained a priority for A*GA.

"In my time at A*GA, I was very cognizant of the fact that research is a human enterprise," said Alfred Huan, who served as A*GA's Executive Director from 2013 to 2017. "When we look at talent, we have to remember we are talking about human individuals with their own differences and needs."

Although it may seem obvious, A*GA is mindful to see its scholars as individuals first, with problems that require solutions with a human touch, Huan said.

From determining reasonable stipend amounts for scholars in various cities to ensuring they received the academic and emotional support they need to complete their degrees, keeping that human aspect at the forefront served as a guiding principle for Huan.

On top of the overarching goal to secure scientific talent, Huan also prioritized building relationships and trust with the scholars.

With the wide pool of scholars that joins A*GA's ranks every year, some will inevitably need a little more support from A*GA, whether in the form of advice, encouragement or counseling.

Huan, now the Assistant Chief Executive of the Science & Engineering Research Council (SERC) at A*STAR, shared that some new scholars embarking on their PhD degrees sometimes struggled to adapt to the research environment. International scholars were also prone to feeling lonely, being away from their families and friends.

"Spotting these struggles early is crucial to ensure the scholars can get the support they need," said Huan, adding that he would befriend scholars over social media to keep up with how they were settling in and provide advice on coping with their PhD training. "After all, the talent pipeline is not a factory line," he shared.

HUCK HUI NG

A*GA Executive Director, 2017–2019

THE SHIFTING SANDS OF RESEARCH

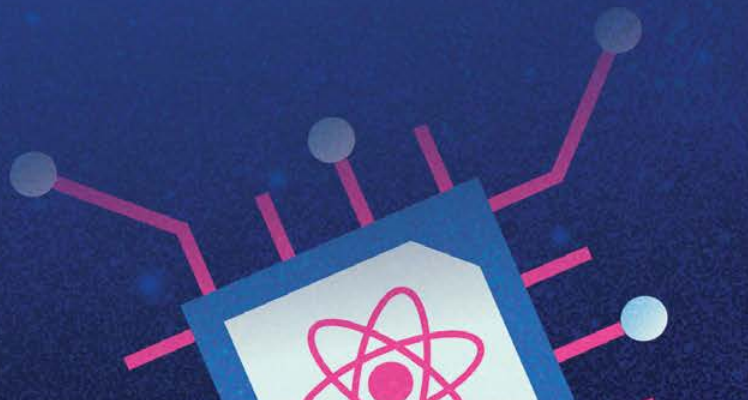
Huan's successor, Professor Huck Hui Ng, recalls that in addition to nurturing existing scholars, one of his main goals as Executive Director was to promote the scholarships and encourage bright young talent to pursue a career in Science and Technology (S&T).

While A*STAR looks for applicants who display a passion for S&T, A*GA also actively identifies and engages with young talent through extensive outreach programs to ensure a vibrant and diverse community of scientists in Singapore. For Ng, this is a point of pride.

"One of my most satisfying achievements is engaging with young students and identifying the top candidates for research scholarships," he said. "Talent is the foundation for Singapore and the world to excel in R&D—without it we will not be able to build the research and innovation ecosystem we need."

Besides securing a pipeline of talent, A*GA also needs to remain flexible to anticipate and accommodate Singapore's changing manpower and research needs over time. In this vein, A*GA regularly reviews its manpower policies to ensure that they remain relevant.

For example, with Ng at the helm in 2018, A*GA launched the A*STAR Computing and Information Science Scholarship to attract and train students in the increasingly in-demand fields of computer science and artificial intelligence.



EDUCATING THE EDUCATORS

Former A*GA Executive Director Professor Lisa Ng noted that on top of engaging with the students, it is equally important to engage with educators to foster a deeper understanding and appreciation for science, technology, engineering and mathematics, or STEM.

"In the past, the focus was on the students. But we forget that educators play a very influential role in their students' lives," Ng said. "If we have a group of educators who do not feel positively about STEM, how can they transmit that same positivity and strength to their students?"

To that end, Ng spent her time as Executive Director working closely with the Ministry of Education, science teachers and other stakeholders in the wider school system to highlight the value of STEM education.

"I mainly shared the different pathways you can take with a STEM degree. They were very appreciative because even if you've been a dedicated teacher for a long time, it's not always easy to see how a career in science can lead to different success pathways."

Ng believes showing this diversity of options offered by a research degree is pivotal in attracting scientific talent.

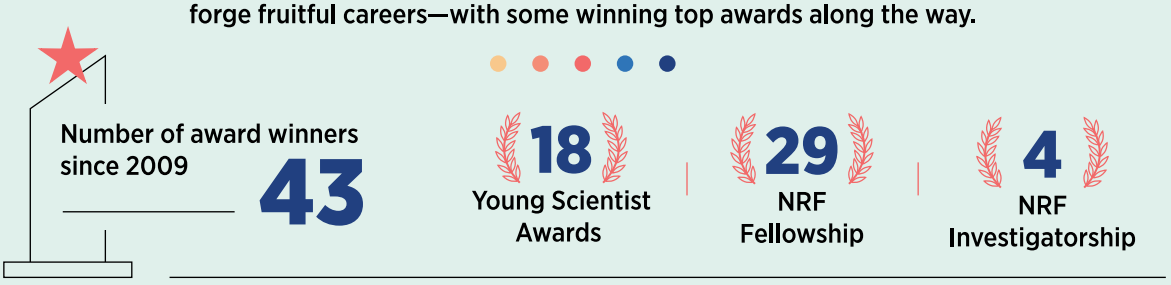
"As the whole ecosystem matures in Singapore, there are more pathways to succeed in science beyond becoming a research leader or professor," she said, adding that the skills A*STAR scholars gain in their education will remain applicable to both their professional and personal lives for years to come.

LISA NG

A*GA Executive Director, 2019–2020

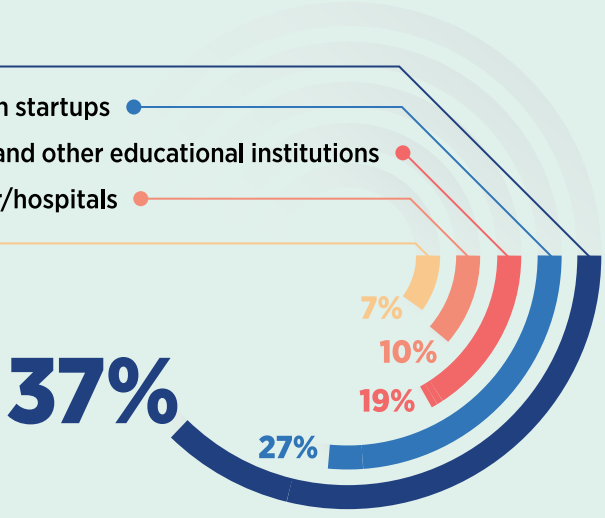
Scholars at the forefront of research and innovation

From research to startups and beyond, A*STAR scholars have gone on to forge fruitful careers—with some winning top awards along the way.



Where are they now?

A*STAR scholars* now work in:



*excluding international awards

TIMOTHY SEBASTIAN

A*GA Executive Director, 2020–current

SUPPORTING SINGAPORE'S LARGER ECOSYSTEM

A*GA is more than just a standalone suite of scholarships designed to secure a pipeline of scientific talent for the nation.

As Professor Huck Hui Ng puts it, A*GA's work does not end at the awarding of scholarships. Instead, A*GA continues to track the progress and wellbeing of its scholars as they progress in their studies and beyond.

For instance, A*GA takes care to expose current scholars to the wider research context through diverse experiences, arming them with sufficient experience to embark on their careers after graduation. Part of these efforts includes making sure scholars are given opportunities to attend conferences, organizing innovation and entrepreneurship workshops as well as mentorship from their supervisors.

In recent years, A*GA's role has expanded to cover the deployment of graduating scholars and to provide support to early career researchers, creating a complete end-to-end ecosystem for aspiring scientists in Singapore.

For current A*GA Executive Director Timothy Sebastian, the most rewarding part of being involved in A*GA is seeing how its scholars have impacted the S&T landscape in Singapore.

Many of A*GA's numerous alumni are now highly accomplished researchers themselves, leading their research groups and laboratories to make significant contributions to the research ecosystem. Other scholar alumni have become entrepreneurs, translating their research innovations to market, while some have taken on senior positions in the private and public sectors.

"The many positive contributions our scholars are making is a strong testimony to the value of the A*STAR scholarship program and to the hard work of the A*GA team over the past two decades," said Sebastian.

GOING ABOVE AND BEYOND

More than two decades since setting its sights on producing 1,000 Singaporean PhD graduates, A*GA has more than met that initial goal.

"A*GA has always focused on identifying, attracting and nurturing the best talent to create a strong pipeline of research scientists and engineers for A*STAR and the wider Singapore S&T ecosystem," Sebastian said. "As we move forward, this fundamental objective does not change."

However, to continually meet those objectives, A*GA's strategies have evolved over the years under the hands of its various Executive Directors and through the feedback and recommendations of A*STAR scholars themselves.

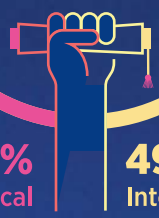
"We will continue to deepen our engagement with scholars to improve the feedback loop," said Chan, reinforcing A*GA's commitment to constant growth and improvement.

At the same time, she expressed her hopes that A*GA alumni will find meaning and fulfillment in their individual careers, and work collectively to build a robust research and innovation ecosystem in Singapore—much like Sydney Brenner wished for all those years ago. ★

Scholarships At A Glance

By fostering the next generation of scientific talent, A*GA's impact is felt across Singapore and the world.

more than **3,360** scholars and awardees *since 2001*



51% Local

49% International

1,890 Local Applicants

14,540 International Applicants

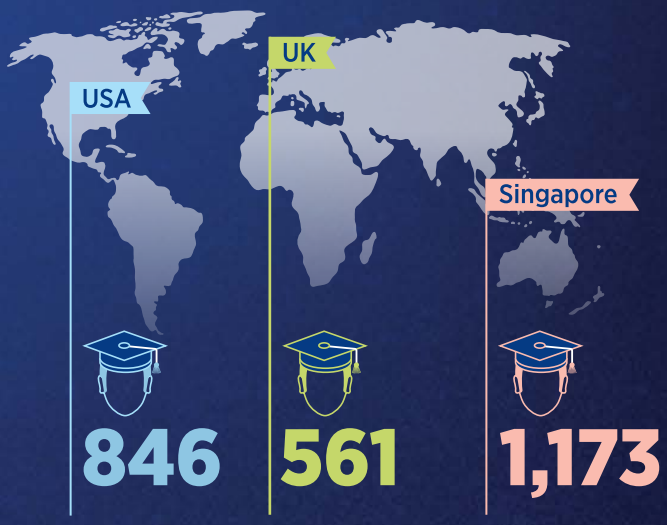
Where did they go?

106 universities across **15** countries

Universities that have hosted the most scholars

National University of Singapore, Singapore	753	Local
Nanyang Technological University, Singapore	404	Local
University of Cambridge, UK	202	International
Imperial College London, UK	201	International
Stanford University, USA	116	International
Massachusetts Institute of Technology, USA	105	International

Countries that have hosted the most scholars



MEET THE ALUMNI

HOW HAS BEING AN A*STAR SCHOLAR CHANGED YOUR LIFE?

SHAWN HOON

National Science Scholarship (PhD), 2003
Lead, Synthetic Biology Program and Director, Molecular Engineering Lab (MEL) at Institute of Molecular and Cell Biology (IMCB), A*STAR

"Thanks to the A*STAR scholarship, I was able to further my studies in the field of genetics after my previous degree in electrical engineering. More than a decade after my studies, I am still sharing ideas and collaborating with the diverse network of scholars I met then. It has also been a pleasure to try and pay it forward to my juniors as they embark on their own journey in science."

HUANQIAN LOH

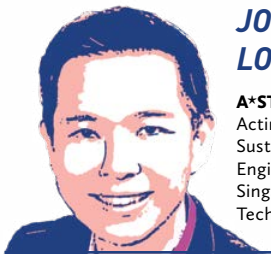
National Science Scholarship (BS-PhD), 2007
President's Assistant Professor, National University of Singapore (NUS);
Principal Investigator, Centre for Quantum Technologies (CQT)

"Being an A*STAR scholar gave me the valuable opportunity to work with some of the best scientific minds in the world. These role models mentored me and helped me grow into my current position as an independent research team leader. I also enjoy networking with fellow A*STAR scholars, which has led to collaborations that boost my current research program."

KA YI LING

National Science Scholarship (BS-PhD), 2010
Co-Founder and Group Chief Technology Officer, Shiok Meats

"Through the National Science Scholarship, I had the great fortune of working with and learning from world-renowned scientists and inspirational mentors such as Professor James Thomson, who was the first scientist to isolate human embryonic stem cells; and Professors Davor Solter and Barbara Knowles, both pioneers in epigenetic and imprinting fields. My growth as a scientist and science communicator through the scholarship has provided me with the training to be the entrepreneur-scientist I am today with Shiok Meats."



JONATHAN LOW SZE CHOONG

A*STAR Graduate Scholarship, 2009
Acting Research Division Director, Sustainability & Life Cycle Engineering Division (SLED) at Singapore Institute of Manufacturing Technology (SIMTech), A*STAR

"I've always enjoyed research and I knew that a PhD was the next step in advancing my career as a researcher. I'm extremely grateful to A*STAR for putting their faith in me, especially when my research area of sustainability and life cycle engineering was so new in Singapore back in 2010. With A*GA's generous support, I was able to fully focus on my PhD studies and build up the technical capabilities that serve me well even today."

JACKWEE LIM

A*STAR International Fellowship, 2013
Senior Research Fellow, Singapore Immunology Network (SIgN), A*STAR

"I was awarded the A*STAR International Fellowship for postdoctoral training at both the University of Pennsylvania and the European Molecular Biology Laboratory. Since joining the Singapore Immunology Network in 2016, I have applied those valuable working opportunities to building platforms and collaborating with startups in different industries: from developing animal vaccines to identifying immune irregularities present in various diseases."

ANJAN SOUMYANARAYANAN

National Science Scholarship (BS-PhD), 2002
Senior Scientist and Program Head, Institute of Materials Research and Engineering (IMRE), A*STAR; Assistant Professor, National University of Singapore (NUS)

"The flexibility provided by my A*STAR scholarship allowed me to devise a PhD thesis project across departments at the Massachusetts Institute of Technology and Harvard University. The experience of this cross-institutional effort and the networks it yielded have played an invaluable role in my growth as a scientist. It equipped me with the skills and confidence to develop interdisciplinary ideas and capabilities and enabled me to build cross-institutional programs upon returning to Singapore."

XINYI SU

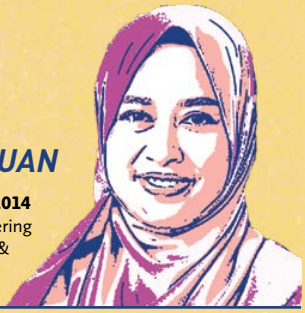
National Science Scholarship (MBBS-PhD), 1999
Senior Principal Investigator and Director of Innovative Technologies Division, Institute of Molecular and Cell Biology (IMCB), A*STAR

"As an A*STAR scholar, I had the privilege of pursuing my PhD at the University of Cambridge under the supervision of Professor Ashok Venkitaraman. I have been fascinated with cancer biology as an undergraduate student, and my PhD research allowed me to understand how genomic instability drives cancer formation. More importantly, it laid the foundation and equipped me with the scientific skills necessary for my career as a clinician-scientist."

GURPREET SINGH

A*STAR Graduate Scholarship, 2013
Founder, Respiree

"A*GA provided me the opportunity to complete my doctoral studies here in Singapore and then a postdoctoral training at the Massachusetts Institute of Technology. These opportunities, as well as financial and ecosystem support from A*STAR, cannot be understated. Not only did I gain fundamental research skills that are needed for a career in science, I was also able to engage with the broader clinical ecosystem."



SITI NURHANNA RIDUAN

A*STAR International Fellowship, 2014
Senior Research Scientist, Bioengineering Systems, Institute of Bioengineering & Bioimaging (IBB), A*STAR

"The A*GA experience for me was more than just a scholarship. By experiencing a range of research areas and roles, I was able to grow professionally and personally. It exposed me to the rigors of academic research and helped me become agile and adaptable to changes. Through my time as a scholar, I met my mentors who recognized my potential and encouraged me to push beyond what I thought were my limits."

ZHI HENG LOH

National Science Scholarship (PhD), 1997
Associate Professor, Nanyang Technological University (NTU)

"Receiving the A*STAR scholarship was truly a life-changing moment. Without it, I would not have been able to focus on pursuing my passion for chemistry while experiencing living overseas. The scholarship and the exciting career pathways it led to made me realize that it is possible to do what you love and still get paid for it."

HAO LI

National Science Scholarship (BS-PhD), 2005/2009
Assistant Professor, National University of Singapore; Research Scientist, Institute of Molecular and Cell Biology (IMCB), A*STAR

"I have gained such diverse life experiences from my scholarship, from the warmth of the American Midwest to the innovative culture of the Bay Area. Most importantly, I was able to meet other scientists who are deeply committed to their work, which inspired me in my own research. Thanks to the scholarship, I was also given opportunities to travel to conferences where I established connections with international scientists." ★

INFECTIOUS DISEASE

Boxing in the coronavirus

A new cost-effective barrier enclosure protects healthcare workers by effectively containing airborne viral particles from COVID-19 patients.

Formerly found exclusively in hospitals and laboratories, personal protective equipment (PPE) has become part and parcel of everyday life due to the pandemic. Across the globe, medical staff are scrambling to secure limited supplies of surgical masks and N95 respirators to minimize the transmission of airborne SARS-CoV-2.

Given worldwide PPE shortages, hospitals in the US to South Africa have reportedly come up with a new approach to limit COVID-19 infection: creating protective 'bubbles' around patients using barrier enclosures. Such box shields are typically mounted on the hospital bed over the patient's head. This strategy traps any virus-containing aerosol emissions produced as patients cough or talk, reducing the risk of airborne transmission to healthcare workers.

While box shields have taken various forms during the pandemic, few studies have definitively assessed the effectiveness of these enclosures. To fill this gap, a multidisciplinary team led by Dan Daniel of A*STAR's Institute of Materials Research and Engineering (IMRE) investigated whether simple, cost-effective materials could be used to create effective barriers against aerosol particles.

Daniel, an expert in droplet and aerosol physics, hypothesized that the physical barrier alone would not be enough to create a robust, sealed system—enclosures would also need to be placed under negative pressure, meaning that fresh air should be able to flow into the chamber but not out of it.

"Sufficient suction is necessary to create a negative pressure environment inside the chamber and contain the aerosol emitted by patients," explained Daniel, noting that previous barrier enclosure designs failed to take this into account.

"An important part is to improve user-friendliness so that it does not impose further burdens on healthcare workers who already have to don lots of PPE."

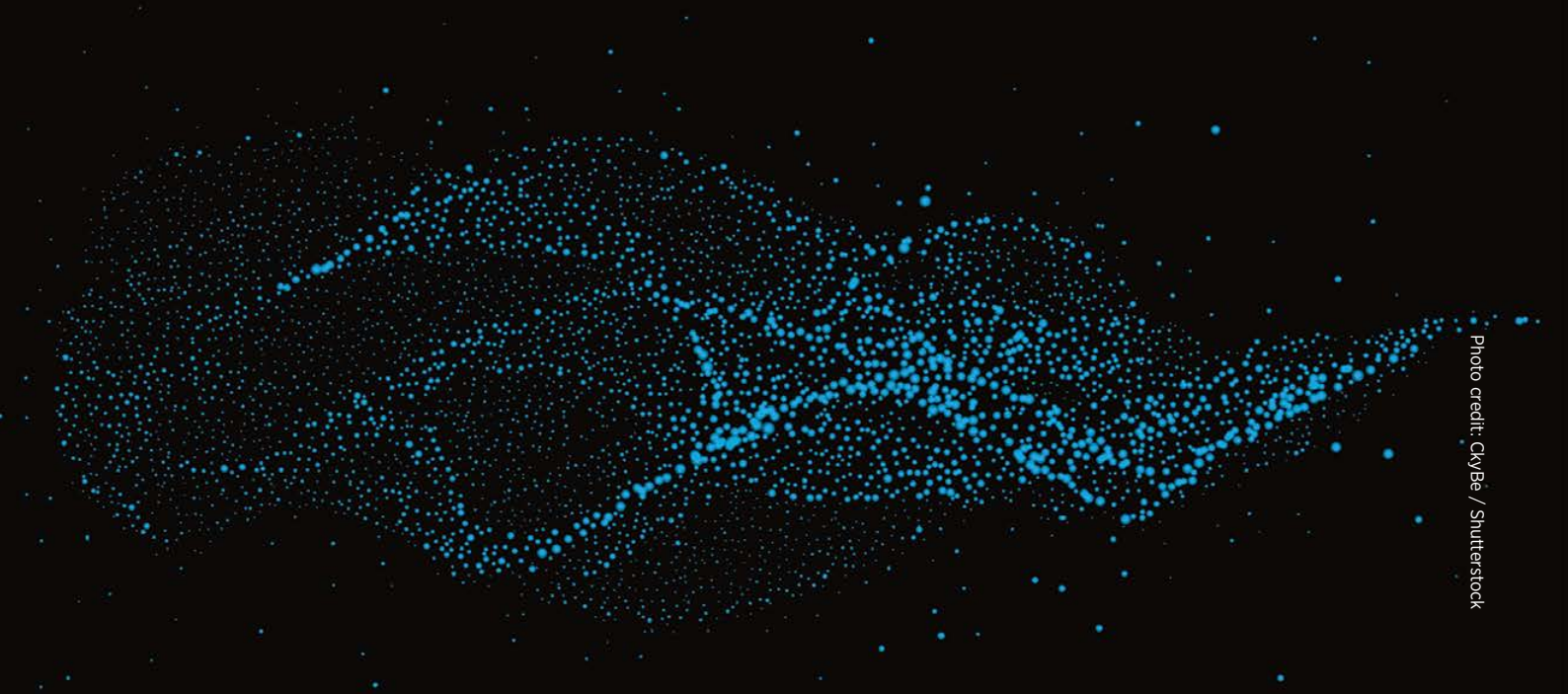
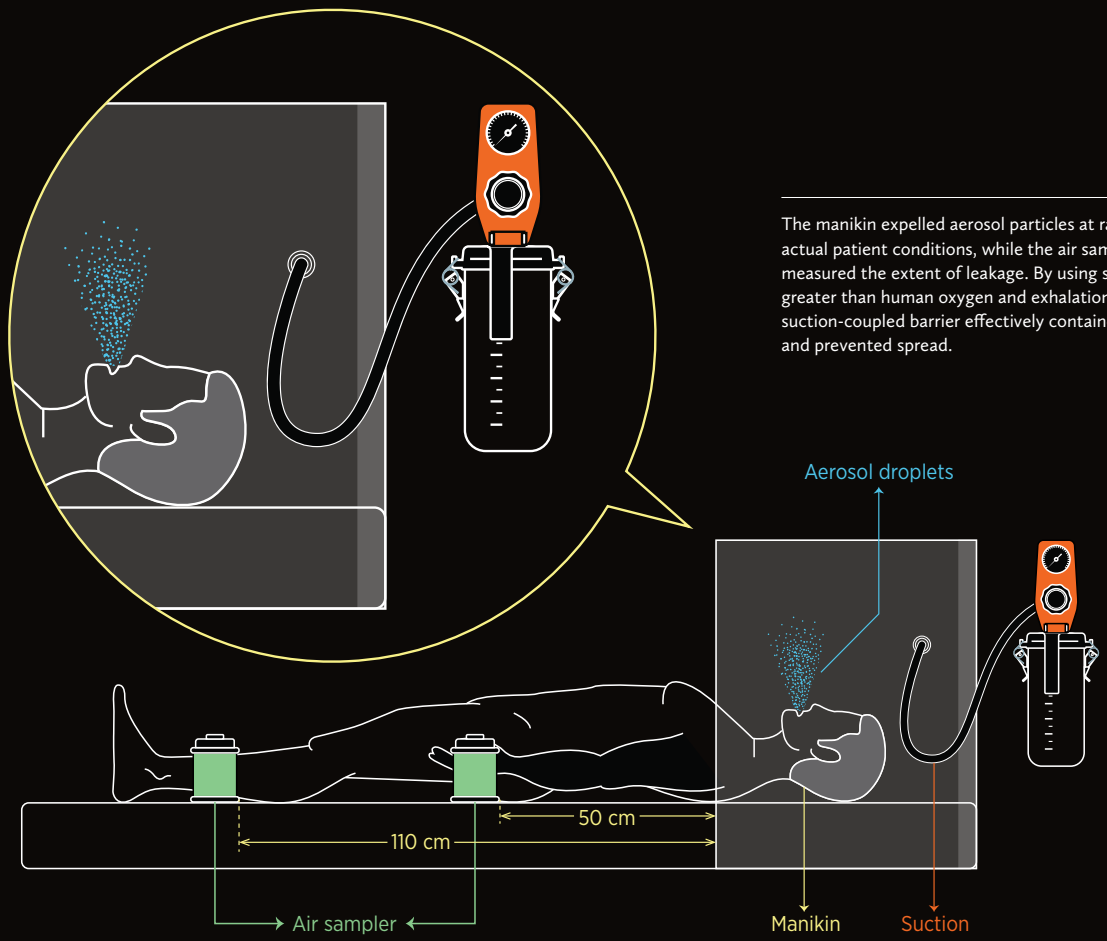


Photo credit: CkyBe / Shutterstock



The manikin expelled aerosol particles at rates simulating actual patient conditions, while the air samplers measured the extent of leakage. By using suction forces greater than human oxygen and exhalation rates, the suction-coupled barrier effectively contained the aerosol and prevented spread.

Collaborating with researchers and clinicians from Ng Teng Fong General Hospital, Nanyang Technological University, Singapore and Ngee Ann Polytechnic, Daniel and the team first designed and constructed a model suction-powered box shield using readily available materials like acrylic and plastic draping. Suction was then provided by two wall units typically found above hospital beds.

To simulate real-life conditions, the researchers custom-built a special manikin that generated and exhaled aerosols much like a COVID-19 patient would. The team then placed the manikin in the box shield, visualizing and measuring the presence of any leaking aerosols.

As hypothesized, the box shield coupled with suction reduced the leakage of exhaled aerosol by over 99 percent. In comparison, a passive enclosure with no suction only achieved about 60 percent protection. These findings demonstrate how relatively simple medical engineering solutions can make a difference in protecting healthcare workers, particularly in resource-limited settings.

Daniel and colleagues plan to further their research by finding the best way to scale up the production of their barrier enclosures and to work with doctors in promoting the widespread adoption of the technology. "An important part is to improve user-friendliness so that it does not further burden healthcare workers who already have to don lots of PPE," said Daniel. "This requires significant input from clinicians." ★

Researcher
Dan Daniel, IMRE

LEFT
If not contained, SARS-CoV-2 particles emitted by patients can linger in the air and infect others in the area.

1. Daniel, D., Lin, M., Luhung, I., Lui, T., Sadovoy, A., *et al.* Effective design of barrier enclosure to contain aerosol emissions from COVID-19 patients. *Indoor Air* **31**, 1639-1644 (2021).

IMMUNOLOGY

Cracking the code of long COVID

Elevated levels of inflammatory factors may be linked to persistent COVID-19 symptoms, researchers find.

For most COVID-19 patients, the infection resembles a sprint, with mild symptoms that typically subside in a couple of weeks. But for those with 'long COVID,' it's more of a marathon. Even months after initial symptoms have waned, these individuals are plagued by serious and ongoing health problems. Unfortunately, it remains unclear why some are predisposed to persistent symptoms and how best to address these lingering complications.

"Much is still unknown about why some patients with COVID-19 continue to show symptoms for months," explained Lisa Ng, Executive Director at A*STAR's Infectious Diseases Labs (ID Labs). "Long COVID has greatly affected patients' quality of life and has had a huge impact on healthcare costs and resource utilization."

Taking a closer look at the biology behind this mysterious phenomenon, Ng and colleagues studied a cohort of nearly 300 Singaporean COVID patients for up to six months after the onset of the disease. The researchers tracked and analyzed participants' levels of circulating inflammatory cytokines in search of patterns linking particular immune responses with persistent symptoms.

The team discovered that patients with long COVID had elevated levels of two key inflammatory biomarkers previously associated with chronic respiratory conditions: a molecule called MCP-1 and PDGF-BB, a growth factor responsible for blood vessel formation.

Interestingly, it wasn't just those affected by persistent COVID symptoms who had these tell-tale markers of chronic inflammation—the COVID 'sprinters' did too. "Our longitudinal analyses of cytokine responses in recovered patients revealed subclinical changes potentially underpinning the development of post-COVID-19 complications even in those who did not have persistent symptoms," said Ng.

Additionally, their investigation revealed fascinating insights into the complex, multi-dimensional nature of long COVID. Ng's team found that while prior studies conducted in Europe had indicated a 55 to 87 percent incidence rate of persistent COVID symptoms, only 10 percent of the Singaporean patient cohort was affected. "The differences in demographics and ethnicity may explain this discordance in the frequency of persistent symptoms," suggested Ng.

Together, these findings contribute to our understanding of the long-term consequences of COVID and unlock new possibilities in the hunt for clinical interventions to slow or even stop the progression of persistent symptoms. Speaking on ongoing efforts by the team, Ng said, "We are still monitoring COVID-19 patients longitudinally to appreciate the dynamics of cytokine responses and study their associations with recovery trajectories and long-term outcomes of COVID-19." ★

Researcher
Lisa Ng,
ID Labs

ABOVE
The dynamics of how SARS-CoV-2 attacks human cells and the resulting systemic inflammation may hold clues to long COVID symptoms.

1. Ong, S.W.X., Fong, S.W., Young, B.E., Chan, Y.H., Lee, B., *et al.* Persistent symptoms and association with inflammatory cytokine signatures in recovered coronavirus disease 2019 patients. *Open Forum Infectious Diseases* **8** (6), ofab156 (2021).

Photo credit: NIAID / Flickr

COVID-19

Is it safe to breastfeed after the COVID-19 vaccine?

Research reveals the safety of mRNA COVID-19 vaccines for breastfeeding mothers and the potential of passing immune protection to the baby.

The arrival of mRNA vaccines against COVID-19 marked the most important turning point in the pandemic. Though beset by supply chain and deployment issues at first, the global vaccination drive has now hit its stride, saving countless lives worldwide and allowing millions more to enjoy some degree of normalcy.

However, the ramped-up vaccine rollout has also highlighted some gaps in our understanding of this new vaccine technology. For example, experts know that seasonal flu vaccines can be safely given to breastfeeding mothers. The vaccine may also be beneficial for the baby, as protective antibodies can be passed via breast milk, priming the young immune system to fight off pathogens.

Unfortunately, there was no such certainty during the mRNA vaccine's early days, which led to some nursing women feeling reluctant to get their shots. While guidelines have now been updated to be more unequivocal about the safety of vaccines during pregnancy and breastfeeding, initial doubts may have lasting consequences where vaccine confidence is concerned.

To improve the understanding of mRNA vaccines during breastfeeding, a team of researchers led by Liang Wei Wang, a Fellow at A*STAR's Singapore Immunology Network (SIgN), measured levels of IgG and IgA antibodies, key components of the immune system's response to COVID-19, in the breast milk of women who received the Pfizer-BioNTech jab.

"We are interested in how vaccine-elicited antibodies secreted into breast milk perform against SARS-CoV-2 variants of concern."

While other studies measured the relative ratio of IgA and IgG levels in the samples, Wang and his team looked at the absolute concentrations of each antibody type for a more direct and accurate comparison of how mRNA vaccines affect the immune system.

"We discovered that IgA and IgG were in fact produced at comparable levels, rather than IgG being the dominant antibody type as reported by others," he said.

According to Wang, this was a significant discovery. The presence of the more stable IgA antibodies in breast milk suggests that breastfeeding after COVID-19 vaccination could also pass on some degree of immune protection to the baby.

On the other hand, traces of the vaccine itself were virtually absent in breastmilk, with only four samples testing positive for very low levels of vaccine mRNA. The team also observed no concerning side effects in the breastfed infants.

Moving forward, the researchers hope to further deepen the understanding of mRNA vaccines and breastfeeding to better inform maternity vaccination guidelines. "We are interested in how vaccine-elicited antibodies secreted into breast milk perform against SARS-CoV-2 variants of concern and how mRNA boosters given to previously infected lactating women affect protective antibody titres in milk," Wang said. ★

Researcher
Liang Wei Wang, SIgN

BOTTOM
Mothers vaccinated against COVID-19 were found to produce protective antibodies in breast milk with no concerning side effects in breastfed infants.

1. Low, J.M., Gu, Y., Ng, M.S.F., Amin, Z., Lee, L.Y., *et al*. Codominant IgG and IgA expression with minimal vaccine mRNA in milk of BNT162b2 vaccinees. *npj Vaccines* **6**, 105 (2021).

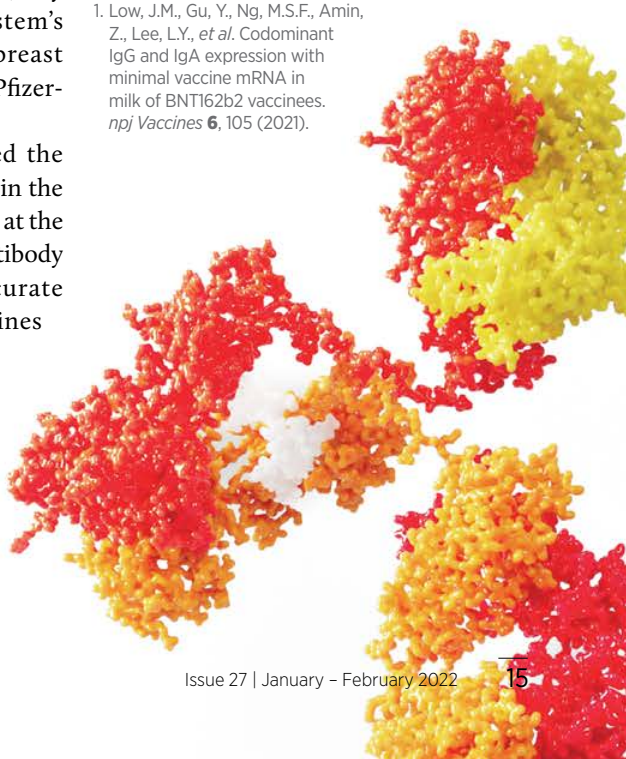


Photo credit: ANIRUDH / Unsplash

MOLECULAR BIOLOGY

Unmasking key players in SARS-CoV-2 infection

SARS-CoV-2 genome structures and their interactions with human RNA are shown to be important in virus survival and pathogenicity.

COVID-19 has taken the globe by storm and completely disrupted the world's norms. As a disease with such a huge effect on people's quality of life, researchers across the world have been racing against time to understand the infectious mechanisms of SARS-CoV-2, the virus that causes COVID-19.

So far, a lot of research has gone into how antibodies interact with SARS-CoV-2 proteins and the genome, with little known about how the virus interacts with human RNA once it infects a cell. Filling this knowledge gap is the aim of Yue Wan, Associate Director of Epigenetic and Epitranscriptomic Systems at A*STAR's Genome Institute of Science (GIS).

"SARS-CoV-2 is known to degrade many host proteins to facilitate its replication and translation," explained Wan. "Emulating our previous work on the dengue virus and the Zika virus, we mapped the SARS-CoV-2 genome to identify structural elements important for its growth and survival."

"Emulating our previous work on the dengue virus and the Zika virus, we mapped the SARS-CoV-2 genome to identify structural elements important for its growth and survival."

Wan and her collaborators, Roland Huber from A*STAR's Bioinformatics Institute (BII) and Lin-Fa Wang from Duke-NUS Medical School, led their team in using different high throughput RNA and interactome techniques and observed how the virus genome interacted with itself and host RNA. Viral RNA plays a key role in helping the virus produce its proteins. As the virus' genetic material closely resembles that of human cellular RNA, the human cell is therefore 'hijacked' to help the virus to produce its proteins.

They found that the SARS-CoV-2 genome binds to *SNORD27*, a small nucleolar RNA that can both stabilize the virus and destabilize host RNAs by sequestering important cellular machinery to the viral genome and away from the host. This, along with the production of Nsp1 protein that degrades cellular RNAs, ensures a multi-pronged approach for the virus' survival.

The researchers also successfully mapped a Singapore-variant of the virus to determine its difference from the wildtype SARS-CoV-2 genome.

"These genomic maps will eventually have a therapeutic consequence as they can serve as a useful resource for understanding how the virus genome folds and how we can target it using small molecules," said Wan.

Looking ahead, Wan believes that more studies on the different SARS-CoV-2 variants should be done to understand which structural elements are functionally important and common to all variants. This knowledge is key to understanding the features that enable SARS-CoV-2 survival, such as replication, infectivity and the ability to evade host immune surveillance. ★

Researcher
Yue Wan, GIS

ABOVE
The SARS-CoV-2 genome does not only determine viral structure but also resembles human RNA, enabling the virus to hijack the genetic machinery in human cells.

1. Yang, S.L., DeFalco, L., Anderson, D.E., Zhang, Y., Aw, J.G.A., *et al.* Comprehensive mapping of SARS-CoV-2 interactions in vivo reveals functional virus-host interactions. *Nature Communications* **12**, 5113 (2021).

Photo credit: NIAID / Flickr

NANOPARTICLES

Clearer medical imaging through tiny chains

A phenomenon called superferromagnetism boosts the resolution of magnetic particle imaging.

Cancer screening is crucial for timely diagnosis and treatment but poses a slight irony. Computerized tomography and positron emission tomography scans, both valuable imaging techniques that help doctors to locate and characterize a tumor, use ionizing radiation which might induce DNA damage and, over repeated scans, could lead to a minor but non-negligible risk of cancer.

A relatively safer alternative is magnetic particle imaging (MPI), which uses non-radioactive and biodegradable iron oxide nanoparticles. A machine then externally applies shifting magnetic fields to which the nanoparticles produce a brightly-lit signal allowing doctors to easily locate the nanoparticle-labeled tumor or nanoparticle-labeled stem cells for diagnosis.

However, existing nanoparticles only react gradually, leading to image blurring in MPI scans and hence hindering its diagnostic value.

To maximize MPI resolution, lead researcher Zhi Wei Tay, a Senior Research Fellow at A*STAR's Institute of Bioengineering and Bioimaging (IBB), turned to superferromagnetism, which describes changes in the magnetic properties of iron oxide nanoparticles when they form chains.

"We believed that superferromagnetism could produce a more favorable magnetization response due to reinforcing inter-particle magnetic interactions," said Tay, who closely collaborated with the Steve Conolly Lab from University of California Berkeley and the Carlos Rinaldi Lab from University of Florida in the US.

Their hypothesis turned out to be true: when viewed through an MPI scanner, superferromagnetic nanoparticle chains reacted abruptly to an applied field, producing steep signal peaks over narrow windows of magnetic field changes.

Compared with typical MPI nanoparticles, the superferromagnetic chains yielded signal spikes that were 40 times more intense and 10 times narrower—a result that gave rise to better image brightness and spatial resolution.

Traditionally MPI could barely visualize points that were spaced 1.5 mm apart. The use of superferromagnetic particles in MPI, on the other hand, produced sharp images even when the points were 0.6 mm apart. Furthermore, 1-D magnetic measurements indicate that points 0.15 mm apart would be the actual limit for resolution improvement.

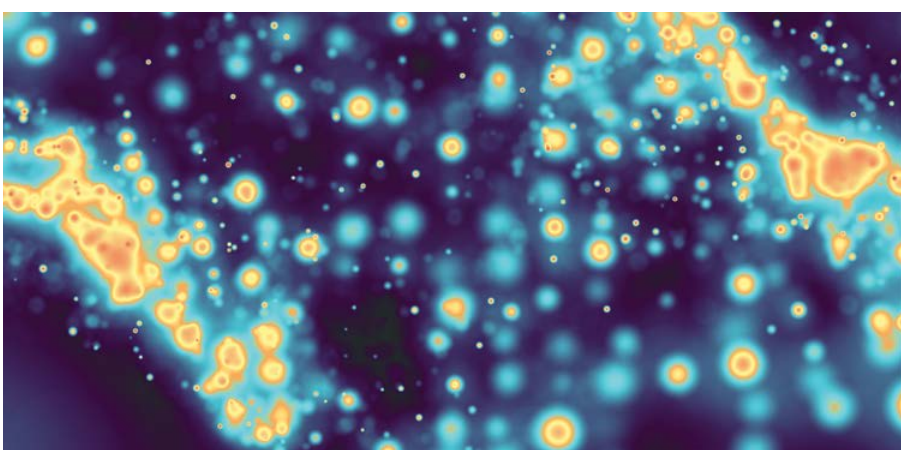
The far-superior resolution that superferromagnetism achieves could be attributed to the high stability of the nanoparticle chains due to inter-particle interactions. As a result, a stronger magnetic field is needed to initiate a reaction.

"But this is an avalanche effect because each chain member that reverses weakens the initial stability, making it much easier for the next member to reverse," Tay added.

The overall effect is that a large number of particles react very strongly in a small amount of time, producing high-resolution MPI images with very little background noise. In the future, superferromagnetic nanoparticle chains could facilitate more accurate tracking of radiation-free magnetic labels for applications ranging from cancer to stem cells. ★

Researcher
Zhi Wei Tay, IBB

1. Tay, Z.W., Savliwala, S., Hensley, D.W., Fung, K.L.B., Colson, C., *et al*. Superferromagnetic Nanoparticles Enable Order-of-Magnitude Resolution & Sensitivity Gain in Magnetic Particle Imaging. *Small Methods* **5**, 2100796 (2021).



Nanoparticles emit a bright signal when exposed to magnetic fields, paving the way for high-resolution medical imaging and diagnostics.

Photo credit: HaHanna / Shutterstock

EXPANDING HORIZONS:

A*STAR SCHOLARS THEN AND NOW

Supported by A*STAR in the early days of their budding careers, scholars recount the experiences that opened the doors to bigger successes from academia to public service.

To improve the lives of its citizens and become an economic powerhouse in Asia, Singapore recognized early on the value of a thriving research and development (R&D) scene. The city-state sprung into action to build an ecosystem ripe for nurturing diverse scientific talents through the establishment of the National Science and Technology Board (NSTB) and forward-looking research and development plans. Now, Singapore's first generation of visionary scientists has grown into mentors themselves, creating a chain reaction that continues to deepen the nation's talent pool and contribute to economic and societal progress.

To sustain this pipeline of talent, the A*STAR Graduate Academy (A*GA) launched several scholarship initiatives over the years, supporting Singapore's best and brightest in their early careers and accelerating their personal and professional growth.

While scholarship grants may come in a variety of forms, all rest on the core of providing a combination of formal education, research experience and network building. For example, recipients of the A*STAR Graduate Scholarship (Singapore) commence their PhD degrees at a local partner university while undertaking industry-focused R&D at an A*STAR Research Institute. Meanwhile, the National Science Scholarship covers a one-year research attachment at A*STAR followed by up to five years of PhD training overseas. At the same time, the Singapore International Graduate Award attracts overseas talent to study at the nation's leading academic and research institutions.

A*GA's numerous alumni continue to carry the character-building experiences from their student days that have helped shape the foundations of their careers. Many now excel beyond university hallways and laboratories, with others also making waves in industry and public service.

In this feature, seven recipients of the A*STAR scholarships reflect on the opportunities that their scholarships provided them, and how their experience as scholars empowered them to not only take their research to greater heights but also to pay it forward by nurturing the next generation of scientific talent.

XIAN JUN LOH

A*STAR Graduate Scholarship, 2002
Executive Director, Institute of Materials Research and Engineering (IMRE), A*STAR

Q: What impact did the A*STAR scholarships have on your career?

I have been well supported by A*STAR scholarships throughout my education. During my undergraduate degree, the scholarship offered an eight-week research attachment at A*STAR that opened my horizons to research. For my postgraduate studies, the scholarship provided opportunities to attend international conferences where I got to listen to renowned scientists and interact with the top researchers in my field. In my postdoctoral years, being fully sponsored by A*STAR allowed me to enhance my research training even further at the University of Cambridge in the UK.

Q: How did your training prepare you for your current career in materials science?

When I returned from my postdoctoral training in 2012, I was tasked to lead the Personal Care program in A*STAR and work with companies. This was an eye-opener for me as I had no prior training on industrial projects. I learned that practicality is as important as the scientific merit of the research project. The commercialization timeline is different for different types of products.

I also noticed that Singapore's materials science sector is rich in talent, thus providing us with many opportunities to nurture the next generation of local scientists. Doing so would not only turn Singapore into an attractive hub to draw in top international talent but also maximize the potential of our homegrown capabilities and talent.

Q: What advice do you have for aspiring A*STAR scholars?

At every opportunity I've had, I have always encouraged scholars to remain humble and continue learning. A research career is a marathon and not a sprint. Simply put, the research career is a long one. During this time, there could be numerous awards and grand accolades. However, it is important for scholars not to get carried away by the glamor and fame that comes with it.

It is important that scholars appreciate the value of hard work and be dedicated to the course. They must also stay humble and take the advice of seniors, peers and juniors at every instance.

A*STAR today is a very nurturing place for scholars. I hope that the scholars will pay it forward. Having received support, the best way for scholars to give back to society and A*STAR is to help train the next generation who can take on leadership positions in the R&D ecosystem.

JINGMEI LI

A*STAR Graduate Scholarship, 2006
Group Leader, Genome Institute of Singapore (GIS), A*STAR

Q: What did receiving the A*STAR Graduate Scholarship mean to you?

My PhD journey with A*STAR was the product of an arrangement between Singapore and Sweden, a shining example of how international collaboration is the way forward for science. My project combined the most advanced genomics technology available in Singapore at that time, with the incredible amount of clinical data available in Sweden. Each country alone would have taken a lot longer to accomplish the same results should the research have been done separately.

To put things in perspective, about 2,000 breast cancers are diagnosed in Singapore every year. During my PhD training, one project I was involved in combined data from all over the world to achieve a data pool of over 100,000 breast cancer cases. It would have taken Singapore 50 years to collect the same data set if we did not collaborate.

Q: How did your experiences as a scholar impact you?

I have matured from a scientist who was once just curious, to one who is curious but also aware of societal needs and who I am doing science for.

For my PhD thesis, I looked for genetic markers correlated with developing breast cancer. While it was scientific progress, it wasn't going to move the needle in improving public health. But my co-supervisor, now Genome Institute of Singapore (GIS) Deputy Executive Director Professor Jianjun Liu, illustrated that if we combine the effects of all the markers that we find, at some point we will make a difference. That helped me recognize the future that I couldn't see with my limited experience and exposure to science. Working in an environment with such insightful scientists opened my mind.

I asked my main PhD supervisor, Professor Per Hall, why he gave up a high-paying clinical job to take up a university position. His answer was, "As a clinician, I help one patient at a time. Doing what we do now, our results can potentially help millions of breast cancer patients." That conversation gave meaning to my research.

Q: What message would you like to share with aspiring A*STAR scholars?

For science to advance, we need to hear the voices of our young scientists! A*GA provided a safe place for me to learn from the best in the field, and to bring my ideas to life. Through the scholarship, I have found peers, friends, mentors and many of my best collaborators. I hope to welcome you to the A*STAR family!

"I have matured from a scientist who was once just curious, to one who is curious but also aware of societal needs and who I am doing science for."

— Jingmei Li, Group Leader, Genome Institute of Singapore (GIS), A*STAR

> **"Be open to new areas that you might not be familiar with or interested in and try them out. This is especially important as it is not easy to predict the future in three to five years."**
>
> — Benjamin Tee, Associate Professor, National University of Singapore

BENJAMIN TEE

National Science Scholarship, 2007
Associate Professor, National University of Singapore

Q: How did being an A*STAR scholar expand your network for collaborative research?

A*GA has been extremely helpful in building my professional network. Being an A*STAR scholar immediately connects you to a group of like-minded go-getters. Each scholar brings with them their international network, effectively growing the A*GA network exponentially. I was able to connect with top scientists, venture capitalists and many other disciplines and industries when trying to translate technologies. The A*GA network was also helpful in the early stages of company formation for a startup I co-founded, Privi Medical, which has been successfully acquired.

Q: How did the scholarship prepare you to pursue high-impact research?

With the scholarship, I could pursue topics that I have tremendous interest in with the flexibility of exploring widely. This enabled me to think big and work on groundbreaking ideas that might not have been possible if we were constrained by research topics. It also allowed me to pursue the degree at nearly any top university of my choice, and I chose Stanford University because it has a good track record of providing a mix of deep science and translational research in the heart of Silicon Valley.

There were plenty of opportunities at Stanford to develop design-thinking skills through programs at the business school or Stanford Biodesign, an ecosystem for health technology innovation. I learned how to design programs from a needs-driven perspective, while at the same time work on challenging research problems. This shaped my approach as a scientist to keep a very open mind about what could be possible.

Q: Can you share a word of advice for aspiring A*STAR scholars?

Be open to new areas that you might not be familiar with or interested in and try them out. This is especially important as it is not easy to predict the future in three to five years. Look for areas that might not be as well-studied and determine if it is a good fit for your interests. Develop a broad-based experience during your PhD and take modules outside of your comfort zone. The scholarship is an excellent platform for you to launch your career through PhD training at the highest levels.

MARVIN LEE

National Science Scholarship, 2002/2007
Vice President, Semiconductors, Economic Development Board

Q: How did the A*STAR scholarship help in your career?

The scholarship gave me a head start in my academic pursuit and provided me with the resources and the opportunity to interact with the brightest minds at Imperial College London and the University of Oxford in the UK. The deep appreciation that I have gained for science and technology laid the foundation for scientific research during my post-doctoral years and my career in public service.

Beyond lab experiments, I broadened my horizons to see how policymakers create the right kind of environment for research activities to thrive in Singapore. I am now doing investment promotion with the semiconductors team at Singapore's Economic Development Board. Compared to my previous planning and strategy portfolio where I looked across a spectrum of industries, I now dive deep into an industry vertical. The learning curve has been steep. Although the work that I do now has little relevance to my background in biomedical sciences, the new knowledge and skillsets I have picked up in my current portfolio have been phenomenal!

Q: What influenced your transition from research to public service?

While at Oxford, I always wondered about what goes on behind the scenes in research strategy. How do researchers get funding? How does Singapore decide what research areas to invest in and double down our bets on? What is our talent strategy?

A*STAR also often organizes care trips to touch base with the scholars and keeps us abreast of the latest developments in Singapore. These sessions sparked my curiosity about the key policy considerations and shifts in focus areas as the nation transitioned into the next Research, Innovation and Enterprise strategy.

"The scholarship gave me a head start in my academic pursuit and provided me with the resources and the opportunity to interact with the brightest minds at Imperial College London and the University of Oxford in the UK."

— Marvin Lee, Vice President, Semiconductors, Economic Development Board

When I joined the Bioprocessing Technology Institute (BTI), I had a coffee chat with Professor Sze Wee Tan, Assistant Chief Executive, Enterprise. We talked about how exciting things can be when you deal with policy planning day in and day out. It was a turning point for me—I decided since I've always had all these questions and a strong conviction to give back to A*STAR and Singapore, I should just jump into it myself!

Q: What lessons from your time as a scholar have shaped your approach to leadership and policymaking?

Our R&D ecosystem today is vibrant and complex with many stakeholder interests at play. This is what makes Singapore an increasingly exciting innovation hub. As an A*STAR scholar, I had the opportunity to be exposed to this wide spectrum of activities and stakeholders, but it is the authenticity in the way you manage your working relationship with people that allows you to venture further in your career and leadership journey.

As a strategist, it is important to not just formulate policies in an ivory tower. We also have to engage researchers, academic institutions, as well as industry players to make sure that our thinking and expectations are well-aligned so that any policy implemented would truly benefit the R&D ecosystem.

TUAN LE MAU

National Science Scholarship, 2009/2014
Scientist, Innovation Lead, Institute of High Performance Computing (IHPC), A*STAR

Q: How has being a scholar shaped your career and current research directions?

I have always been interested in how the human mind works and how we can apply this knowledge to create devices to help people. This interest drove me to pursue my undergraduate degree in Electrical and Electronic Engineering and engage in robotics projects at Imperial College London in the UK. During my PhD studies at the Massachusetts Institute of Technology in the US, I investigated brainwaves and facial movements during emotions. My PhD work led me to the Social Cognitive Computing (SCC) department at A*STAR's Institute of High Performance Computing (IHPC).

At SCC, I supported the commercial development of an emotion analytic engine called CrystalFeel, which is related to my facial emotion studies from my PhD. I also helped build the back-end system for a multi-institutional program developing brainwave systems for healthcare applications as co-Principal Investigator.

Q: How did your overseas training influence your approach to collaborative research and innovation?

Studying, working and living in three places with exposure to a diversity of cultures, ideologies and perspectives helped me grow tremendously. I brought all these learnings back to A*STAR. I applied the project management framework acquired during my studies together with different software tools into the projects that I helped manage at IHPC. This has significantly improved our R&D speed, work transparency and quality of results. I also learned to provide freedom and space for exploration to my teams to promote individuality, original thinking and productivity.

Q: What advice can you share with aspiring A*STAR scholars?

I would encourage aspiring A*STAR scholars to speak to senior scholars at different points in the A*GA journey to gain more diverse perspectives. I also strongly encourage scholars to build relationships with the A*GA team and keep in close contact with them throughout their journey.

The A*GA team is approachable and supportive, and I am especially grateful to Prof Alfred Huan, then A*GA Executive Director while I was pursuing my PhD degree. He spent time learning about my passion and encouraged me to gain experience with tech startups. He even connected me with researchers working on related projects in A*STAR for potential collaboration. This strong support system will help scholars in charting their career path and experiencing a fulfilling scholarship journey.

BENJAMIN TOH

A*STAR Graduate Scholarship, 2006
Principal Business Analyst, Technology and Innovation, Advanced MedTech

Q: What impact did the A*STAR scholarship have on your professional development?

Receiving the scholarship opened the door to a career in R&D and beyond. The scholarship was a stepping stone into the world of science and innovation which, at the time, I knew I was passionate about but did not know much about. I had the opportunity to work in a multinational team during my PhD, which equipped me with skills that were applicable not only in the lab but also in moving to public service administration.

> ***"I had the opportunity to work in a multinational team during my PhD, which equipped me with skills that were applicable not only in the lab but also in moving to public service administration."***
>
> — Benjamin Toh, Principal Business Analyst, Technology and Innovation, Advanced MedTech

Q: How did supervising students during your PhD shape your current leadership style?

Working with MSc and undergraduate students was always a fun experience because they bring a lot of energy into the team. One thing I have always said to them was that a negative result is still a result. Trying, failing and trying again is normal; what is important is the learning that takes place to plan the next experiment. The continual process of learning fostered a growth mindset in me that I have tried to inculcate in the teams I have led. Being comfortable with failure and learning from it is even more relevant now as innovation cycles shorten, meaning that we have to test and iterate new ideas more frequently.

Q: How has your scientific training and network at A*STAR benefited your transition to an industry role at Advanced MedTech?

I am privileged that A*STAR has provided me with multiple avenues for professional growth. Being seconded to Advanced MedTech was one of them and it has allowed me to experience first-hand what it is like to work in a business development role in a private enterprise.

My training at A*STAR helped me understand the science and ask the right questions when assessing the technology behind each product. The networks I have built over the years as a scientist and as Director of Planning at A*STAR's Biomedical Research Council have also served me well when I needed to ask questions and seek independent opinions. The learning curve was steep and took me awhile to adapt, but I am thankful that I was part of a great team that helped me to transition into my current role.

ASTRID IRWANTO

Singapore International Graduate Award, 2009
Chief Operating Officer, Nalagenetics

Q: How did the Singapore International Graduate Award (SINGA) help you grow?

I have always wanted to study biomedical sciences and create an impact in this field. Studying at the National University of Singapore (NUS), one of the top universities in the world, through SINGA has been such a privilege and honor. I never imagined that I could contribute knowledge by publishing in the top medical and scientific journals—all thanks to the quality of work, the extent of international collaboration and the access to state-of-the-art facilities in A*STAR and Singapore.

SINGA also provided an allowance for us to attend three overseas conferences where we could present our work. This led to my personal growth, expanding my network of scientists and key opinion leaders. Little did I know that this network would prove useful now that I am leading a startup and no longer in academia.

"The most memorable aspect would be the friendships I have built in Singapore. The community here is friendly and supportive and everyone is highly responsible. I was able to adapt easily to the culture here as it was similar to my life principles."

— Astrid Irwanto, Chief Operating Officer, Nalagenetics

Q: What were your most memorable and challenging experiences as an international scholar?

The most memorable aspect would be the friendships I have built in Singapore. The community here is friendly and supportive and everyone is highly responsible. I was able to adapt easily to the culture here as it was similar to my life principles.

The most challenging experience I faced was meeting the publication requirements at the Saw Swee Hock School of Public Health (SSHSPH) at NUS. SSHSPH required four papers as first or second authors as prerequisites for completing a PhD degree. However, if not for this prerequisite, I would not have four impactful papers, one of which led to my startup.

Q: Can you share a word of advice for aspiring A*STAR scholars?

Approach many people and talk to them about your career direction. You may not know that your discovery means a lot to the community if you do not step out of the lab. Make as many friends and engage in as many collaborations as possible.

At the end of the day, it is all about passion. If scholars network widely, work hard and publish well during their studies, they will have easier choices when advancing their careers, whether in academia or beyond. ★

NEUROSCIENCE

Treating rare disease with familiar vitamins

Metabolic changes in the neurons of patients with amyotrophic lateral sclerosis may be reversed with vitamin B3 supplements.

The health food aisles of supermarkets are typically packed with rows of vitamins and minerals, such as calcium for strong bones, zinc to stabilize blood sugar and vitamin A for eye health. But instead of just supporting optimal health, what if these off-the-shelf supplements could also help treat rare, incurable diseases?

This may someday be a reality for patients with amyotrophic lateral sclerosis (ALS), a debilitating disease that affects neural tissues and leads to the progressive loss of muscle control. Each year, around 400 Singaporeans are diagnosed with ALS, only to face limited and often ineffective treatment options. Of the two approved ALS drugs, Riluzole marginally extends lifespans, while Edaravone is only effective in a subset of patients.

At A*STAR Institute of Molecular and Cell Biology (IMCB), researchers led by Shi-Yan Ng, along with collaborators from University of California, San Francisco, are investigating novel druggable pathways involved in ALS. Ng and colleagues used lab-grown ALS motor neurons and soon made a serendipitous find.

"A very observant laboratory researcher discovered that the ALS motor neuron cultures required more frequent media changes as the media color turned yellow more quickly," explained Ng.

For the team, this observation suggested abnormalities in the ALS motor neurons' metabolic pathways—with hyper-glycolysis churning out elevated levels of lactic acid to turn the pH indicator in the cell culture media yellow.

Taking a closer look at the imbalances in mitochondrial respiration in the ALS motor neurons, the team pinpointed a mitochondrial protein called SIRT3 as the culprit. Not only were activities of the SIRT3 protein much lower in ALS neurons than healthy ones, suppressing the *SIRT3* gene in normal motor neurons made them almost indistinguishable from their diseased counterparts.

To explore potential avenues to reverse mitochondrial dysregulation, the researchers tested the effects of a Vitamin B3 derivative called nicotinamide on the ALS neurons. Upon nicotinamide treatment, the team observed striking changes in the ALS cells but not in healthy motor neurons.

"We demonstrated that nicotinamide supplementation effectively reversed mitochondrial defects and reduced disease phenotypes in the ALS motor neurons," elaborated Ng.

Their findings highlight the key role of *SIRT3* in ALS progression, and also show how common supplements like nicotinamide may help restore metabolic balance in diseased motor neurons as a novel therapeutic strategy.

To this end, Ng and the team are currently in talks with the National Neuroscience Institute in Singapore to conduct clinical trials testing the effectiveness of nicotinamide supplements in reducing ALS symptoms. Though the researchers have already filed a patent related to the project, the search for effective ALS treatments continues.

"We will continue to screen for therapeutics that can improve mitochondrial function in the ALS neurons," Ng concluded. ★

Researcher
Shi-Yan Ng, IMCB

ABOVE
Vitamin supplements could help in treating amyotrophic lateral sclerosis by reversing metabolic dysfunction in neurons.

1. Hor, J.H., Santosa, M.M., Lim, V.J.W., Ho, B.X., Taylor. A., *et al*. ALS motor neurons exhibit hallmark metabolic defects that are rescued by SIRT3 activation. *Cell Death & Differentiation* **28**, 1379-1397 (2021).

Photo credit: Saowanee K / Shutterstock

GENETICS

A closer look into the genetics of blindness

Using whole-exome sequencing, scientists have identified a gene likely linked to a common eye disorder that can lead to blindness in the elderly.

The year 1996 marked one of modern medicine's biggest milestones. For the first time, genetic screening for cancer risk became commercially available—in the form of Myriad Genetics' test for the BRCA1/2 mutations linked to breast and ovarian cancer. Similar breakthroughs have since helped save countless patients, particularly those diagnosed with inherited diseases.

But not all genetic disorders have such clear-cut diagnostic biomarkers. One of these exceptions is exfoliation syndrome, a common age-related disorder where abnormal proteins progressively accumulate in the eye's anterior chamber, causing glaucoma and irreversible blindness.

To identify these elusive genetic clues, Chiea Chuen Khor, a Senior Principal Investigator at the Genome Institute of Singapore (GIS), and his collaborators searched for potential markers for exfoliation syndrome across a dataset of protein-coding genetic variants.

The comprehensive study spanned twenty years and included over 20,000 participants across 14 countries. "Due to the rarity of disease-causing genetic variants, a large study sample size is needed to obtain enough statistical power to be certain of the results," explained Khor.

Although techniques such as genome-wide association studies (GWAS) had been deployed to demystify this disorder, such methods have so far failed to yield significant breakthroughs. This time around, Khor and colleagues adopted a more sophisticated approach—using whole-exome sequencing, which takes into account the exome, or all the genome's protein-coding regions.

By sequencing and comparing the exomes of individuals affected by exfoliation syndrome and healthy controls, the team finally found the needle in the haystack, pinpointing the *CYP39A1* gene out of a pool of over 18,000 genes predicted to have impaired protein function.

"*CYP39A1* emerged as the gene where a significant proportion of the affected individuals carried mutations compared to unaffected individuals," noted Khor.

Normally, *CYP39A1* produces an enzyme that metabolizes cholesterol into its derivatives. Because mutations resulting in the loss of *CYP39A1* function strongly correlated with an increased risk of exfoliation syndrome, the team hypothesized that the deficient gene may also impair cholesterol metabolism—likely resulting in excess cholesterol accumulating in the eye.

"The smoking gun was found when we managed to stain cholesterol within the exfoliative material, confirming that cholesterol is part of the disease process as well," he said.

As the first study to present evidence that other biomolecules beyond proteins play a key role in exfoliation syndrome, their insights propel over two decades of research forward, spurring future studies on how to treat and possibly prevent the condition. Currently, the researchers are conducting follow-up studies to determine how different *CYP39A1* variants influence the risk of blindness due to exfoliation glaucoma. ★

Researcher
Chiea Chuen Khor, GIS

ABOVE
Exfoliation syndrome, a common age-related eye disorder that can cause irreversible blindness, may be linked to a faulty gene leading to excess cholesterol accumulation.

1. Li, Z., Wang, Z., Lee, M.C., Zenkel, M., Peh, E., *et al*. Association of rare *CYP39A1* variants with exfoliation syndrome involving the anterior chamber of the eye. *Journal of the American Medical Association* **325** (8), 753–764 (2021).

Photo credit: Mikhnyuk Gallina / Shutterstock

STEM CELLS

Donor tissues provide the gift of sight

A breakthrough stem cell transplant technology uses donated cadaver eyes to restore vision in patients with retinal degeneration.

Much of how we experience the world around us hinges on our ability to see clearly. Given how vital the sense of sight is, it may come as a surprise that vision is granted by a small, delicate, single layer of cells located at the back of the eyeballs.

The retinal pigment epithelium (RPE) serves many critical functions in the eye, including absorbing light, protecting against pathogens, and nourishing the light-sensitive receptors in the retina. Injury or damage to this fragile tissue causes blurring or vision loss.

Unfortunately, cell therapy approaches using transplanted human embryonic and induced pluripotent stem cells have yielded disappointing results in experimental models, with transplants only restoring RPE function for up to a month.

Xinyi Su, a Senior Principal Investigator at A*STAR's Institute of Molecular and Cell Biology (IMCB), sought to look for alternative ways to extend the longevity of transplanted stem cells in patients with RPE damage. Collaborating with researchers at the Icahn School of Medicine at Mount Sinai, New York, National University of Singapore's (NUS) Yong Loo Lin School of Medicine, the Singapore Eye Research Institute and Duke-NUS Medical School, the team hypothesized that human RPE stem cell-derived RPE—or hRPESC-RPE, for short—holds promise as a novel cell therapy for RPE conditions.

"These stem cells, extracted from donated cadaver adult eyes, can be grown into RPE cells," explained Su, adding that hRPESC-RPE could potentially serve as a unlimited source of donor cells which could be profiled to ensure donor compatibility.

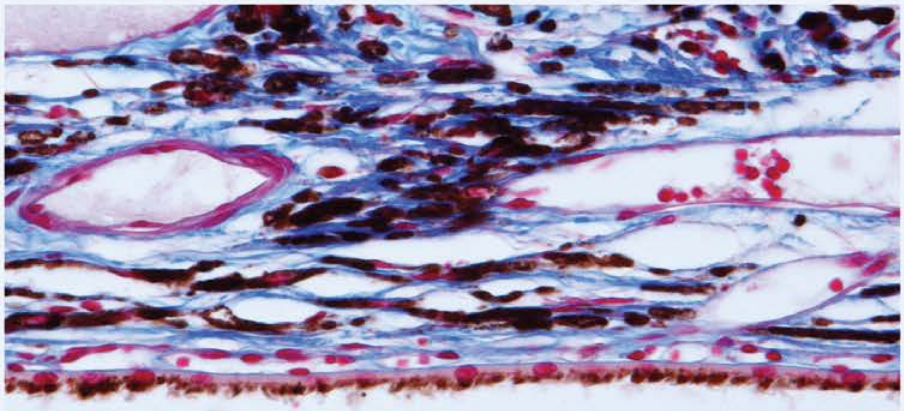
To test their theory, the team isolated hRPESC-RPE from adult cadaver eyes and maintained the cells under specialized cell culture conditions for a month. The researchers observed that these donor cells possessed stem cell-like characteristics, with the ability to divide into sheets of healthy, living RPE tissues.

Su and colleagues then tested whether these lab-grown hRPESC-RPE tissues could be used as viable therapies. Using a non-human primate model of RPE damage, they surgically transplanted hRPESC-RPE tissues into the eyes of macaques—reporting that transplanted human cells successfully integrated with the surrounding macaque tissues.

"These transplanted RPE patches were able to stably integrate for at least three months with no serious side effects," said Su. "That's three times longer than what other cell therapy approaches can achieve."

These exciting results may pave the way for life-changing therapies for the 196 million people worldwide affected by age-related macular degeneration (AMD), a disease of the RPE.

Moving closer towards the clinical translation of this technology, the team plans to demonstrate that hRPESC-RPE transplants can restore vision in non-human primate models of AMD. They are also building a preclinical data package to support an application to assess cell therapy in human clinical trials. ★



Researcher
Xinyi Su, IMCB

LEFT
The retinal epithelium plays a crucial role in vision, from absorbing light to protecting the eye against foreign particles.

1. Liu, Z., Parikh, B.H., Tan, Q.S.W., Wong, D.S.L., Ong, K.H., *et al*. Surgical transplantation of human RPE stem cell-derived RPE monolayers into non-human primates with immunosuppression. *Stem Cell Reports* **16**, 237-251 (2021).

Photo credit: Jose Luis Calvo / Shutterstock

PLASTICS

The dark side of green plastics

Mapping the life cycle of biodegradable polymers can help manufacturers make data-driven decisions on the most sustainable production practices.

The principle of reducing waste, reusing and recycling resources and products is often called the "3Rs". While it sounds simple enough, this mantra alone does not ensure a reduction in environmental footprint. Non-biodegradable polymers such as polystyrene and polyethylene, for instance, end up being the worst polluters, devastating fragile ecosystems.

Praveen Thoniyot, a Senior Scientist and Team Leader at A*STAR's Institute of Chemical and Engineering Sciences (ICES), believes that it is not only important to identify greener polymer alternatives, but also map their life cycle from synthesis to disposal. According to Thoniyot, such a sentiment is shared by key players in the plastic manufacturing industry.

"Studying the sustainability of polymer synthesis is gaining momentum due to the increased customer awareness, regulatory pressure on industry and opportunities to reduce costs," said Thoniyot. "However, there is currently a lack of understanding of the environmental footprint of polymer syntheses."

To demonstrate the feasibility of a laboratory-scale life cycle assessment (LCA), Thoniyot and his team explored the synthesis of a biodegradable plastic called polycaprolactone, or PCL. The researchers used ISO 14040 and 14044 standards, an established framework for quantifying the overall sustainability of manufacturing practices.

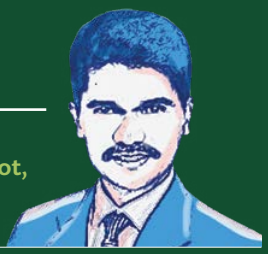
According to first author of the study Pancy Ang, a Senior Research Engineer at ICES, laboratory-scale LCA is conducted using a cradle-to-gate system boundary, which starts with the extraction of raw materials and ends with the production of PCL homopolymer.

The team's analyses allowed them to rank the three processes in terms of overall sustainability. "We found that hydrochloric acid-catalyzed ring-opening polymerization is the most environmentally sustainable route to produce PCL since it has the lowest environmental impact," said Thoniyot. In contrast, the other two processes fell short on the sustainability checklist, either requiring large amounts of power or using chemicals toxic to humans.

These findings open up possibilities for future collaborations between academia and the green plastic manufacturing industry. "Laboratory-scale LCA could serve as a preliminary tool to evaluate the environmental sustainability of different technologies across domains before scaling up or commercialization," added Thoniyot.

This approach may be useful in evaluating biodegradable alternatives with the aim to phase out current plastic materials that persist and pollute the environment. Moving forward, the researchers plan to expand their analyses to paint a more holistic picture of the sustainability of different PCL synthesis technologies.

"We need to consider both the quantitative and qualitative aspects of synthesis," said Thoniyot. "There is no current research on laboratory-scale LCA comparison of existing and emerging synthesis technologies." ★



Researcher
Praveen Thoniyot, ICES

ABOVE
Non-biodegradable plastics are major environmental polluters, prompting scientists to study the environmental footprint of alternative materials.

1. Ang, P., Mothe, S.R., Chennamaneni, L.R., Aidil, F., Khoo, H.H., *et al*. Laboratory-scale life-cycle assessment: a comparison of existing and emerging methods of poly(ε-caprolactone) synthesis. *ACS Sustainable Chemistry & Engineering* **9**, 669–683 (2020).

Photo credit: j.chizhe / Shutterstock

NANOSTRUCTURES

Microbe-busting copper surfaces

A*STAR scientists have developed self-sanitizing surfaces capable of eliminating microbes effectively within mere minutes.

One of the many aspects of our daily lives that have changed because of the COVID-19 pandemic is the way we treat surfaces. Many people across the globe have been paying significantly more attention to keeping surfaces in their living and working environment sparkling clean—a habit that is most certainly to remain.

Given that, wouldn't it be nice if surfaces are capable of self-sanitizing? Such technology would be invaluable, particularly for healthcare institutions like hospitals and nursing homes, which can be a hotbed of infections and antibiotic-resistant microbes.

For many centuries, surfaces made of copper and its alloys have been used as disinfecting agents, even before the concept of microbes was made clear. However, their efficacy is still unsatisfactory. "To break pathogen transmission over surface contact or airborne transmission, the rapid killing of microbes is crucial," said Yugen Zhang, a Senior Principal Investigator and Group Leader at A*STAR's Institute of Bioengineering and Bioimaging (IBB). "Although copper surfaces can kill 99.9 percent of microorganisms in two hours, the multifold transmission may have already occurred within this period."

In collaboration with the National Centre for Infectious Diseases (NCID) and Tan Tock Seng Hospital (TTSH), Zhang and co-corresponding author Guangshun Yi, together with their team, embarked on a quest to improve the self-sanitizing capability of surfaces. Inspired by the effectiveness of nanostructured cicada wings in physically annihilating bacteria, the research team married nature-based solutions with the intrinsic antimicrobial properties of copper to accelerate disinfection.

To synthesize this self-sanitizing surface, the researchers designed a scalable and cost-efficient chemical reaction that can be carried out at ambient conditions. The reaction initially produced sword-like copper nanostructures, but to the researchers' surprise, the morphology of the surface evolved to take the form of foam when the reaction was prolonged. To satisfy their curiosity, they decided to put both versions of the nanostructured copper to the test.

The novel surfaces were extremely efficient in eliminating a wide range of microbes, from the common *E. coli* bacteria to viral surrogates for SARS-CoV-2 and even the antimicrobial-resistant ESKAPE pathogens that evolved from the overuse and misuse of antibiotics. While the sword-like nanostructured copper surface performed better than its foam-like counterpart, both of the novel surfaces are capable of destroying microbes within mere minutes, compared to conventional copper surfaces that take hours to do the job. Together with NCID and TTSH, the team is also exploring how these work on biofilm and surfaces which form part of the clinical environment.

"Our nature-inspired antimicrobial surface works much better due to the synergistic effect of nanostructures that facilitate quicker physical cell rupture and the rapid release of copper cations due to the larger contact area," explained Zhang.

Having demonstrated the functionality of these nanostructured copper surfaces in laboratory-scale air purifiers, the team now aims to prototype their antimicrobial technology for commercialization, which shows great promise for applications in hospitals and other crowded areas—particularly relevant during these pandemic-stricken times that we live in. ★

Researcher
Yugen Zhang, IBB

ABOVE
Copper has intrinsic antimicrobial properties, opening opportunities for developing self-sanitizing surfaces.

1. Yi, G., Riduan, S.N., Armugam, A., Ong, J.T., Hon, P.Y., *et al*. Nanostructured Copper Surface Kills ESKAPE Pathogens and Viruses in Minutes. *ChemMedChem* **16**, 3553–3558 (2021).

Photo credit: NIAID / Flickr

POLYMERS

Catalyzing super energy storage

Novel polymers built with the aid of non-toxic halide salt catalysts could pave the way for high-power yet safe energy storage applications.

From the coin-like batteries that power wristwatches to the large fuel cells under the hood of electric cars, batteries play a crucial role in sustaining our technology-driven world. But as anyone who has ever owned a smartphone knows, batteries degrade with frequent usage, gradually losing their capacity to hold energy with each charge-discharge cycle.

Supercapacitors, a related class of energy storage devices, provide high power density and long life cycles and are not prone to the same rapid degradation as traditional batteries. The catch is their performance relies on charge-carrying electrolytes that trade stability for efficiency. Liquid electrolytes that efficiently conduct electrical charges pose safety risks due to solvent leakage, while solid polymer electrolytes tend to have low conductivity at room temperature.

"The electrolytes used in supercapacitors require both mechanical rigidity and high ionic conductivity," noted Jason Lim, Emerging Group Leader at A*STAR's Institute of Materials Research and Engineering (IMRE). Gel polymer electrolytes with multiple phases that share the best properties of liquid and solid polymers are a promising solution. With this in mind, Lim and fellow IMRE scientist Derrick Fam explored polyurethanes as a new class of polymer candidates for gel electrolyte applications. However, polyurethanes are typically made using catalysts containing highly-toxic metals such as tin.

To address this quandary, Lim and Fam led a team to build safer polyurethane-based gel polymer electrolytes using non-toxic tetrabutylammonium (TBA) and potassium halide salts as catalysts.

"TBA salts have better solubility in organic solvents, which facilitates easy dissociation to free up the halide ions to perform the catalysis," Lim explained. "After demonstrating that the TBA salts work, we explored the usage of potassium halide salts instead as these are a lot cheaper and much more readily available."

The researchers then devised a mixture that could dissolve small amounts of the potassium halide salts into their separate ions. By enabling efficient crosslinking among the polymer components, these catalysts could produce polyurethane gels in mere minutes.

"Despite the crosslinked nature of the polyurethanes, it still retained sufficient porosity for a liquid electrolyte to infiltrate the polymer network. This enabled the resulting gel electrolyte to possess excellent ionic conductivity while still retaining the structural properties of the solid polymer matrix," Lim added.

Given the affordable and common nature of the halide salts used, the team hopes the technique will allow for easier access to novel polymers with multifunctional properties. Besides serving as potential supercapacitors for electric vehicles, these nontoxic gel electrolytes may pave the way for biocompatible energy systems powering medical implants.

"Our research opens up avenues towards synthesizing materials sustainably and simply, and potentially lower the cost of these energy storage devices," Lim concluded. "We are also looking at expanding the use of these gels to other energy storage devices as their structural rigidity will be useful for many different applications." ★

Photo credit: Alexa_Space / Shutterstock

Researcher
Jason Lim, IMRE

LEFT
Polymer gels fabricated using the right catalysts provide exceptional charge-carrying capabilities for energy storage.

1. Chien, S.W., Tay, J.J.M., Chee, C.P.T., Loh, X.J., Fam, D.W.H., *et al*. Halide salt-catalyzed crosslinked polyurethanes for supercapacitor gel electrolyte applications. *ChemSusChem* **14**, 3237 (2021).

COMPUTER SCIENCE

Catching the culprit in electromagnetic interference

A new mathematical model quickly and reliably predicts the origin of disruptive electromagnetic interference emanating from complex electronic circuits.

We live in a tech-heavy environment, with electronic devices found almost anywhere. Unfortunately, electronic devices placed next to one another do not always get along. Radiation emitted from one device can disrupt the function of another in a phenomenon known as electromagnetic interference (EMI), which affects performance efficiency.

To this end, a collaborative team led by Richard Xianke Gao, a Senior Scientist at A*STAR's Institute of High Performance Computing (IHPC), has been developing advanced methods for detecting, identifying and diagnosing EMI sources.

Traditionally, researchers rely on mathematical models of near-field radiation to gauge energy emanating at close range from a potential EMI source. These models enable the analysis of dipoles—pairs of opposite charges across which radiation flows—and making predictions based on the number, location and intensity of dipoles in a device.

However, these conventional methods are impractical for analyzing EMI patterns as they can only be applied to a single output frequency. For example, global optimization algorithms can only predict a unique location for individual dipoles at a specific frequency. This approach fails due to the significant errors often incurred while modeling multiple dipole locations across a range of frequencies.

Seeking to overcome this challenge, Gao and colleagues explored novel ways of modeling EMI sources at a wider range of frequencies. The researchers selected three frequencies for scanning potential EMI sources and measured the magnitudes only of near-field radiation emitted at every frequency. To minimize the risk of errors while using the global optimization algorithm, they defined a spatial range within which dipoles should be located based on the size of the scanned region.

This information was then fed into a new computational framework capable of predicting the presence of dipoles at the same location—across all three frequencies. Measuring dipole moments, however, still proved to be difficult, as the intensity of radiation would vary depending on the frequency.

"To prevent this issue, we used a method called interpolation, which uses dipole moments modeled at predefined frequencies to predict values for the unmeasured ones," Gao explained.

Finally, the team validated their new modeling method in a real-world setting using devices with integrated circuits. They showed that their framework accurately reconstructed radiation patterns, even at new frequencies within the range of the predefined ones.

The study demonstrates how computational methods could measure EMI at predefined frequencies and predict a source's near-field radiation pattern across a wider band of interest. "Our method shows promise in being reliable and efficient for quickly diagnosing unknown EMI sources in a complicated environment," said Gao. ★

Researcher
Richard Xianke Gao, IHPC

LEFT
Electromagnetic energy emanating from one electronic gadget can potentially disrupt the functions of a nearby device.

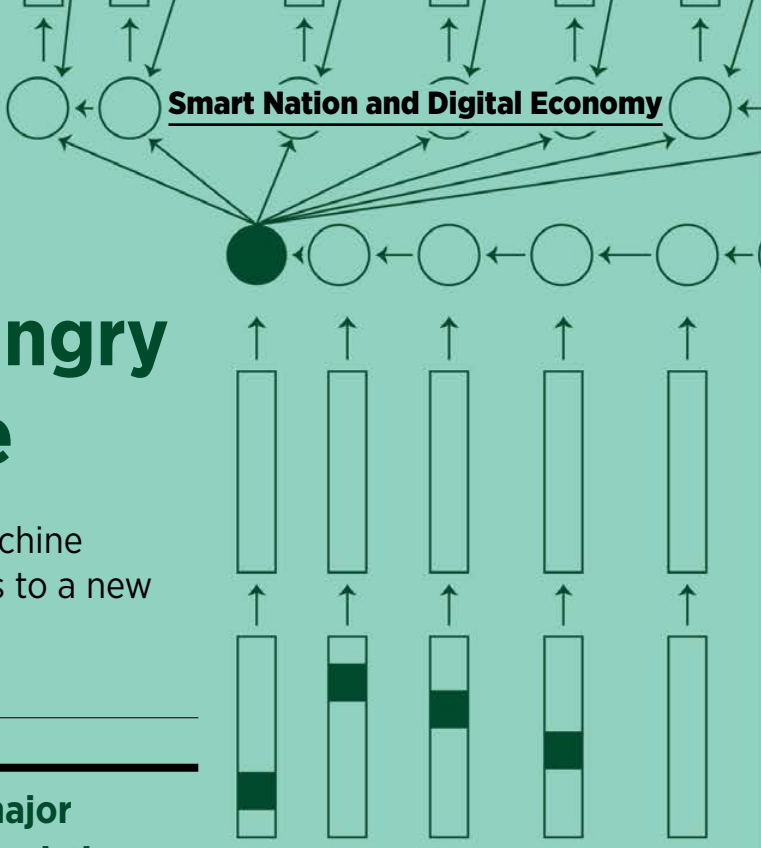
1. Song, T.H., Wei, X.C., Tang, Z.Y., Gao, R.X.K. Broadband Radiation Source Reconstruction Based on Phaseless Magnetic Near-Field Scanning. *IEEE Antennas and Wireless Propagation Letters* **20**, 113–117 (2021).

Photo credit: peterschreiber.media / Shutterstock

MACHINE LEARNING

Taming the data-hungry translation machine

Obviating the need for large datasets in machine translation models could be a reality, thanks to a new method for diversifying training data.



Anyone who has used Google Translate to decipher text in a foreign language knows that the result can often be more amusing and puzzling than informative. Artificial intelligence-based systems called neural machine translation (NMT) are here to the rescue, improving the accuracy of automated translation applications. At a time when international connections have never been more important, robust NMT systems have the potential to bring us closer together.

However, according to the experts, we're not quite there yet. "One of the major limitations of existing NMT models is that they are data-hungry," explained Xuan-Phi Nguyen, a PhD candidate at Nanyang Technological University.

For NMTs to translate accurately, they require large amounts of training data. This is a particular hindrance for low-resource languages such as Malay, Nguyen added, for which translation datasets are relatively scarce.

Nguyen and others led by Ai Ti Aw at A*STAR's Institute for Infocomm Research (I^2R) saw a novel solution to the challenge: upgrading NMT models such that they can be trained using 'synthetic data.' There are several well-established techniques for building such artificial databases, but the researchers chose to feed their original dataset into multiple forward and back translation models. The former converts text from the original to the desired language, for example, English to Chinese, and the latter from translated Chinese text back to English.

"One of the major limitations of existing NMT models is that they are data-hungry."

The team merged predictions produced by the forward and back translation models with the original data to create a larger, much more diverse dataset. "This effectively multiplies the size of the dataset by up to seven times," said Nguyen. He added that, when used to train an NMT model, the new synthetic data increases translation accuracy.

The researchers showed that their data diversification approach achieved state-of-the-art scores of 30.7 for English to German and 43.7 for English to French translation tasks. These are based on a system called Bilingual Evaluation Understudy (BLEU), which scores machine-based translations from 0–100 according to how well they correlate with human translations; scores above 30 are considered good translations.

Promisingly, the team's new method also enhanced the translation performance when it comes to Sinhala and Nepali, low-resource languages with vastly different vocabulary and grammar structures to English. Compared to the baseline NMT model, data diversification consistently increased BLEU scores by 1.0 to 2.0 points for four translation tasks: English to Sinhala, Sinhala to English, English to Nepali, and Nepali to English, achieving final scores ranging from 2.2 to 8.9.

According to Nguyen, data diversification can be applied to virtually any existing NMT model to improve translation accuracy. As a next step, the team aims to address the need to train multiple models, which can lead to consumption of more computational power and time. ★

Researcher
Xuan-Phi Nguyen, I^2R

ABOVE
Advanced data diversification algorithms can improve the accuracy of automated translation tasks.

1. Nguyen, X-P., Joty, S., Kui, W., Aw, A.T. Data Diversification: A Simple Strategy For Neural Machine Translation. *34th Conference on Neural Information Processing Systems,* (2020).

ARTIFICIAL INTELLIGENCE

Getting a headstart on predictions

By linking past observations with future possibilities, a novel framework could help computers predict human actions more accurately.

Whether watching a film at the cinema or binge-watching a series on Netflix, you've probably tried to guess how the story ends. Our ability to make predictions extends beyond our TV habits: think of how we correctly step out of the way of an oncoming pedestrian, or how tennis players estimate the direction of the ball from their opponent's movements.

While recognizing and reacting to the various future actions of other humans and objects before they happen comes naturally to us, teaching computers to do so is not as simple. However, this ability, also known as action anticipation, is critical for technologies that are involved in human-machine interactions such as virtual assistants and self-driving cars.

"Action anticipation models should be able to account for future uncertainties. For the same observations, there are numerous plausible futures and these models should be able to predict all of them accurately," said Basura Fernando, a scientist at A*STAR's Institute of High Performance Computing (IHPC).

"For the same observations, there are numerous plausible futures and action anticipation models should be able to predict all of them accurately."

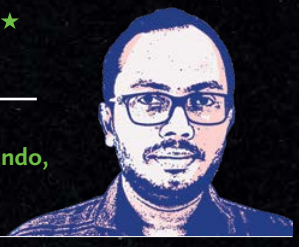
Together with Samitha Herath, a Research Fellow at Monash University in Australia, Fernando developed a framework for an action anticipation model that correlates past observations with future actions and then uses these correlations to extract predictions from current observations. Although the concept of linking past and future is not new, the researchers' framework incorporates algorithms that maximize the correlations and look for the strongest links between observed representations and future behaviors.

For their model, Fernando's team developed new similarity measures that quantify how related two objects are. For example, one function checks the similarity of cross-correlation properties between all features or dimensions, rather than just between the same features. Another evaluates the covariance of observed and future events in the data set, analyzing the relationship between their movements or trends.

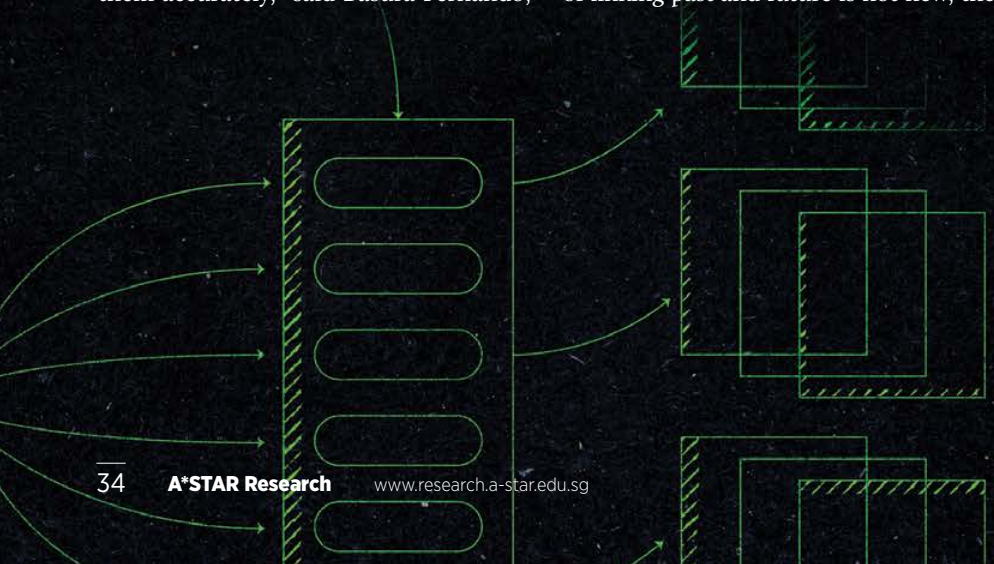
"These similarity measures look at higher-order information within a vector space," Fernando explained. "Correct similarity measures help ensure that the computer model learns effective representations of human behaviors through videos, allowing us to maximize the correlations."

The researchers' model was first trained using videos of various scenes, extracting correlation rules between the past and future events shown. When tested on another set of videos, their model was able to apply these correlations to predict future actions with higher accuracy than models using other similarity measures.

With even better algorithms in mind, the researchers aim to further study the theoretical properties of their new similarity measures and create a framework that covers risk calculations in action anticipation. ★



Researcher
Basura Fernando,
IHPC



LEFT
Effective action anticipation models must be able to use past observed data to predict future behavior.

1. Fernando, B. & Herath, S. Anticipating human actions by correlating past with the future with Jaccard similarity measures. *2021 IEEE/CVF Conference on Computer Vision and Pattern Recognition*, 13219-13228 (2021).

MATERIALS SCIENCE

Cold spray's hot potential in repairing aircraft

A new method of spraying metallic powders on the surface of worn-out aircraft components at relatively low temperatures holds promise for the aerospace industry.

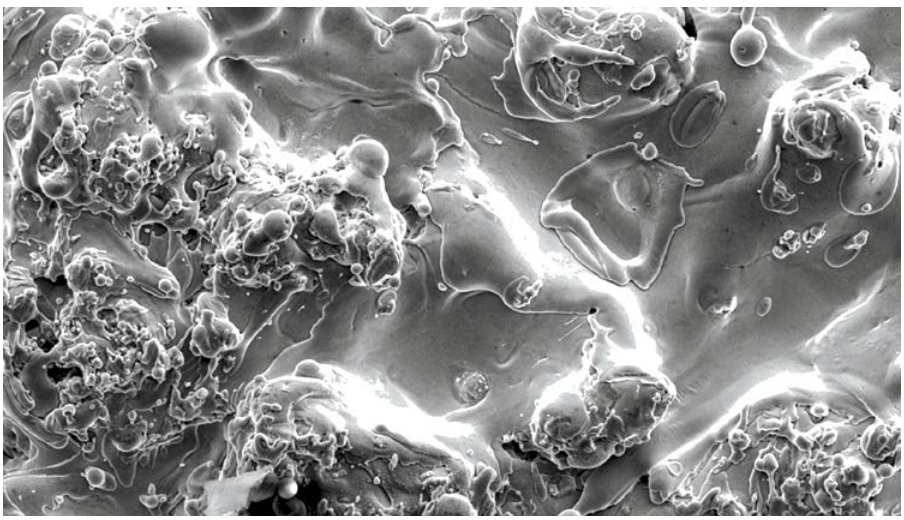


Photo credit: © A*STAR Research

Engine components in aircraft need to be built tough. Not only must these parts withstand soaring temperatures of around 650 °C, but they must also contend with mechanical forces that can lead to wear and tear over time. Regular scrapping and replacing gas turbine components, however, is an expensive and laborious process, especially when replacement parts are not readily available.

Consequently, technologies to repair metal components are in high demand by the aerospace industry. One of the most widely used materials to manufacture these components is Inconel 718, an easy-to-fabricate nickel-based superalloy with exceptional strength. Conventional methods to repair worn-out parts typically involve spraying a layer of Inconel powders on the surface, before the deposit is melted in the intense heat of plasma. This technique is known as atmospheric plasma spray (APS).

The problem, however, is that Inconel powders are often warped under plasma's extreme temperatures of around 15,000 °C, prompting materials scientists to seek alternative repair methodologies. Among these is the relatively new technique known as cold spray (CS), where Inconel powders are propelled onto the surface of a material at a fraction of the temperatures required by APS.

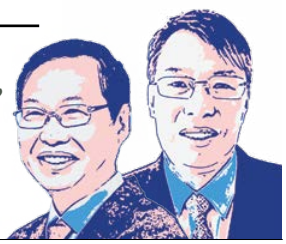
A*STAR researchers from the Institute of Materials Research and Engineering (IMRE), the Institute of High Performance Computing (IHPC) and the Singapore Institute of Manufacturing Technology (SIMTech) studied the performance of CS relative to APS, which is the current gold standard.

The team, co-led by IMRE Senior Scientist Jisheng Pan and SIMTech Principal Research Engineer Poh Koon Aw, applied Inconel powders to superalloy surfaces using both CS and APS. They then examined the physical characteristics of the resulting coatings, including their porosity, microstructure, hardness and tensile strength.

From a structural perspective, CS preserved the architecture of deposited Inconel powders, while APS altered it through heat. Promisingly, it was found that Inconel powders adhere strongly to the surface of the metal in CS—just like they did in APS. Further characterization revealed that APS coatings were stronger and more malleable than those applied with CS, which was harder but displayed residual post-coating stresses that made it more brittle. With further tweaks, the researchers conclude that CS could potentially enhance a wide range of applications, from mending aircraft carrier parts to fixing submarines.

"We hope to promote the interests in adopting CS in local industries, both for aesthetic purposes and structural repair," Pan said. Moving forward, the team plans to accelerate the technique's entry into industrial manufacturing practices. ★

Researchers
Poh Koon Aw, SIMTech
Jisheng Pan, IMRE



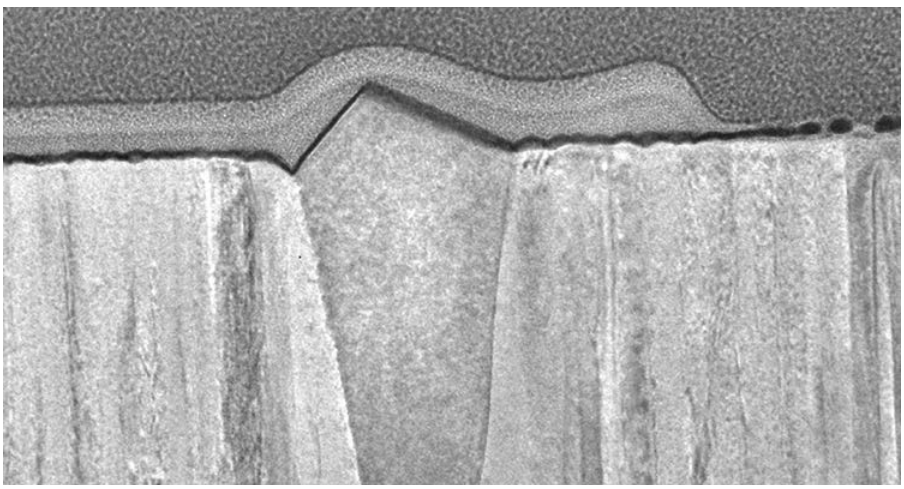
ABOVE
By using the cold spray method, Inconel powders could adhere strongly to metal surfaces without being altered by extreme heat.

1. Zhang, Z., Seng, D.H.L., Lin, M., Teo, S.L., Meng, T.L., *et al*. Cold spray deposition of Inconel 718 in comparison with atmospheric plasma spray deposition. *Applied Surface Science* **535**, 147704 (2021).

ELECTRONICS

Viewing abnormal grains in-plane sight

Revealing how abnormalities form and grow in piezoelectric films could make smart devices better at making the right connections.



Imagine the chaos if your smartphone suddenly played your guilty-pleasure song on a stranger's pair of wireless earphones. Or, in a more serious scenario, if ultrasound images were so noisy that doctors couldn't tell a tumor apart from a muscle. In an increasingly connected world dominated by radio waves and frequencies, being able to pick out only the relevant signals has never been more important.

Smart devices use radiofrequency filters to receive signals and connect accurately with each other. In turn, these filters rely on layers of thin films, typically made of scandium-doped aluminum nitride (ScAlN), that allows only the right signal to pass through while blocking out everything else.

While doping with scandium helps improve the film's filtering function, this process also often produces large, abnormal and misoriented grains on the film's surface, leading to performance inefficiencies like choppy connectivity and low data transfer between devices.

In the hopes of minimizing the risk of these abnormal grains forming, a team of researchers led by Minghua Li and Yao Zhu, both from A*STAR's Institute of Microelectronics (IME), conducted a complete characterization of the grains.

"This in-depth morphology and microstructural study aims to facilitate the understanding of how the abnormal grains form and grow," said Zhu, an A*STAR scholarship recipient.

On top of the usual scanning electron microscopy (SEM) and X-ray diffraction (XRD) imaging techniques, the team also deployed transmission electron microscopy (TEM), a technique that achieves better spatial resolution and contrast, to study the ScAlN films. Li and Zhu used TEM to obtain an in-plane, bird's-eye view of the films, allowing them to see the abnormal grains from a new angle in addition to the usual cross-sectional images.

Their SEM and XRD analysis showed that the surfaces of ScAlN films were evenly textured, and TEM revealed the normal grains to be uniform hexagonal crystals. Meanwhile, the abnormal grains appeared as pyramid-shaped spikes visibly protruding above the film's surface and exist as much larger crystals or crystal clusters.

The researchers also found that the malformed grains occupy larger area as the film grows thicker, suggesting that they grow vertically and laterally at the expense of their neighboring grains.

According to Zhu, the irregular shapes and non-uniform distribution of the grains across wafers could compromise the energy efficiency of the resulting ScAlN films, and might also cause obstacles in further ScAlN-based device fabrication.

"Moving forward, the team aims to produce high-quality ScAlN films by improving the sputtering process to significantly reduce or remove abnormal grains," Zhu said, adding that in the future, such films could lead to more efficient radiofrequency filters and better smart devices. ★

Researcher
Minghua Li and Yao Zhu, IME

ABOVE
Abnormal grains on the surface of thin films can disrupt signal transmission and interfere with the functions of electronic devices.

1. Li, M., Hu, K., Lin, H., Zhu, Y. Structural characterization of the abnormal grains evolution in sputtered ScAlN films. *IEEE International Ultrasonics Symposium 2021*, 1-3 (2021).

ADDITIVE MANUFACTURING

The pathway to printing better energy absorbers

By leveraging an alternative approach to 3D printing, A*STAR scientists have demonstrated the superior energy absorption of honeycomb-shaped functionally graded materials.

The most striking thing about the first 3D printed objects was their size. They were primarily small prototypes, a far cry from the car parts and building materials routinely manufactured today. But in the last decade, the field has evolved tremendously. Now, 3D printed objects aren't just getting bigger; they're also getting better.

A new frontier of 3D printing will enable a generation of functionally graded materials (FGM), which are objects with complex structures and compositions that impart unique functionalities. For example, FGMs might have intricate lattice pores of variable diameters or were made with a mixture of starting materials. These designs give FGM an edge over materials with uniform properties as FGM objects have both the durability of metal and the heat-resistance of ceramic.

However, the limitation is that conventional methods of manufacturing FGMs can only produce very basic outputs. "Only a few conventional methods can achieve a structural gradient. Most have limitations in controlling the precision and shape of the microstructure," explained Chen-Nan Sun, a Scientist at A*STAR's Singapore Institute of Manufacturing Technology (SIMTech).

With a vision that 3D printing could open up new possibilities in FGM manufacturing, Sun teamed up with his SIMTech colleague Pan Wang to enable the precision manufacturing of FGMs through electron beam melting (EBM). As its name suggests, EBM uses an electron beam rather than a laser to melt metal powders in a vacuum environment, reducing contaminants. EBM processes also help add stability to the lattice by minimizing residual stress even without any additional support structure. Accordingly, printing can be performed in a floating and stacking way. "EBM increases productivity and design freedom and is, therefore, suitable for mass production of FGMs and other complex designs," said Wang.

Using specialized computer software, the team designed cubic and honeycomb-shaped FGM lattice structures in two distinct orientations—one where cells were parallel to the surface and another where they were perpendicular. The researchers then gradually increased the FGM's strut diameters from one end of the structure to the other. "The densities of all structures were graded by changing the diameter of the lattice struts from 0.6 mm to 1.2 mm continuously and linearly in the z-direction," explained Sun. "With careful control, EBM can realize the FGM design accurately, reproducibly and quickly," Wang added.

Next, the team put their newly designed materials to the test. Assessing for compression stress, they discovered that the EBM-built FGMs structures collapsed in a highly ordered sequence, starting from the thinnest struts to the thickest.

This phenomenon was strikingly different from how uniform-density materials behaved under pressure; they collapsed randomly and unpredictably. This property of the new EBM-built FGMs points toward the potential application as shock absorbers.

Notably, one of their honeycomb structures achieved an average specific energy absorption of 33.3 J/g, outperforming other designs previously described in the literature. "Superior performance can be achieved for FGM in applications in lightweight structures, thermal barriers and biomaterials compared to conventional uniform materials," said Sun. Given the promising results, the team is currently looking to partner with industry to launch these materials in the market. ★

Researchers
Chen-Nan Sun and Pan Wang, SIMTech

BOTTOM
Researchers are exploring novel 3D printing techniques to produce materials capable of enhanced energy absorption.

1. Choy, S.Y., Sun, C.N., Sin, W.J., Leong, K.F., Su, P.C. *et al*. Superior energy absorption of continuously graded microlattices by electron beam additive manufacturing, *Virtual and Physical Prototyping* **16**, 14-28 (2021).

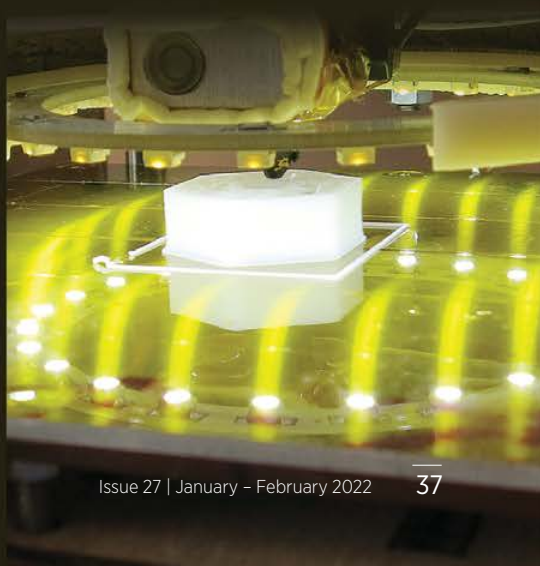


Photo credit: Enrique Dans / Flickr

STARS IN THE MAKING

PURSUING A CAREER IN STEM IN 2022

In the pursuit of scientific excellence, the current scholars of the A*STAR Graduate Academy hope to harness their education to contribute to Singapore's scientific ecosystem.

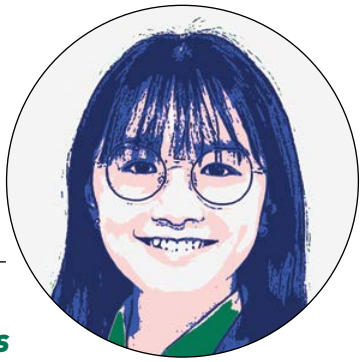
Over the last decade, science has progressed by leaps and bounds to tackle challenges posed by climate change, food insecurity, an aging population and—perhaps most urgently—a global pandemic.

With advanced artificial intelligence (AI) algorithms being used in vaccine development and supercomputers being used to simulate weather models, it is clear that scientific developments continue to be motivated by the world's greatest problems.

Since its launch in 2001, the A*STAR Graduate Academy (A*GA) has nurtured generations of scientists and researchers dedicated to solving such major issues and advancing Singapore's position as a global scientific hub.

Two decades on, scores of young talents carry on the flame of A*GA's vision. Fueled by modern challenges and dispersed across the globe in world-class universities, each aspiring scientist is striving to develop solutions that improve lives or pave the way for further discovery.

Hear from 20 of A*STAR's current scholars and discover the motivations and opportunities behind Singapore's scientific stars in the making.

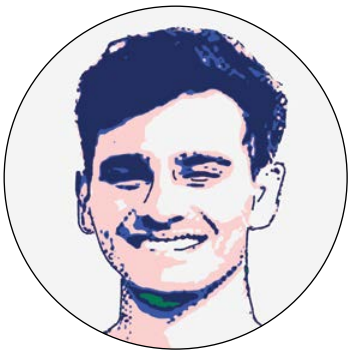


DAWN LOK

National Science Scholarship (BS), 2021
Imperial College London, UK

"I hope to bring the good practices and insights learnt from my time abroad back to Singapore and help develop technology that is useful for the community."

Now in the first year of her undergraduate degree, Lok's research interests lie in pharmaceuticals and food science. As a chemistry major, she seeks to understand and design molecules that play a part in improving lives.



ROHAN THOMAS

National Science Scholarship (BS-PhD), 2015
University of California, Santa Barbara, USA

"Traditional chemistry is often energy- and solvent-inefficient. I want to create green processes as they are almost always cheaper and more efficient."

Thomas, a second year PhD student, develops novel environmentally friendly tools for industrial applications. Working with pioneers in green chemistry, Thomas hopes to integrate their work and create new biocatalysts and processes.

TANGSHENG ZOU

National Science Scholarship (BS-PhD), 2015
ETH Zürich (Swiss Federal Institute of Technology), Switzerland

"I believe that sustainable reaction engineering in the chemical industry can show the way forward and push efforts in other industries to meet climate targets."

With the goal of achieving sustainable chemical processes, second-year PhD student Zou develops catalysts in the hydrogenation of carbon dioxide to methanol and aims to understand the reaction from the molecular scale upwards.

HUI TING ZHANG

National Science Scholarship (BS-PhD), 2014
Heidelberg University, Germany

"I hope to bring back the knowledge and skills I have learnt during my studies and apply them in the Singaporean context."

Fascinated with the complex processes that take place during embryonic development, Zhang's PhD research project uses new methods to study the regulation of embryo size—a long-standing question in the field.

ASHWIN SRINIVASAN KUMAR

National Science Scholarship (BS-PhD), 2014
Massachusetts Institute of Technology – Harvard University, USA

"The unique complexities and poor overall outcomes of this disease prompted me to delve more into this area. I am very lucky to have great mentors who have helped guide and shape my professional journey in this space."

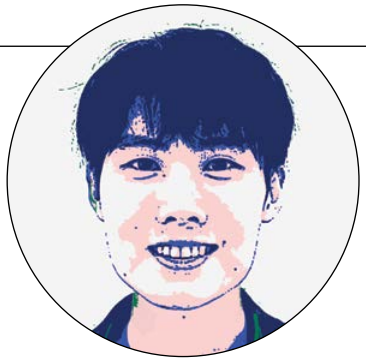
Hoping to effectively translate his research from bench to bedside, Kumar is currently working on treatment strategies for pediatric medulloblastoma, one of the most common and deadly brain cancers for children.

MICHELLE LIM

National Science Scholarship (Masters), 2021
Wageningen University & Research, Netherlands

"I hope to be able to contribute to the research efforts in A*STAR, and to advance science and create a positive impact on society."

The opportunity to study overseas and experience different learning and teaching styles appealed to Lim. She is excited to continue her food science education at the top university in the field and seeks to contribute to Singapore's growth as a food and nutrition hub.



DING XIANG CHEW

National Science Scholarship (Masters), 2021
Wageningen University & Research, Netherlands

"I choose to study food because food is human-centric, especially in Singapore where it is part of our identity. This field is relevant to our lives, and is something that interests people."

Eager to do his part to develop Singapore's food ecosystem, Chew is learning all he can from his university's expertise in this area as well as the Netherlands' established alternative protein market.

CHAITANYA KRISHNA JOSHI

National Science Scholarship (PhD), 2021
University of Cambridge, UK

"I am excited by how AI can accelerate and augment scientific discovery, from novel medicine to energy-efficient materials."

Joshi, a first-year PhD student, hopes to develop a research path with the potential for long-term impact on global challenges. In particular, he is interested in deep learning models and how they can contribute to data-driven solutions in biomedicine and materials discovery.

SIDNEY SUEN

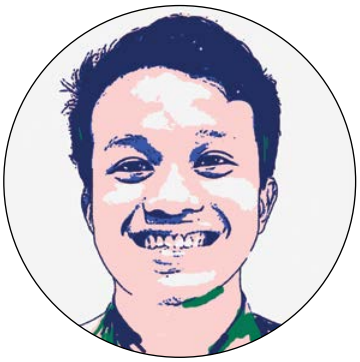
A*STAR Computing and Information Science Scholarship, 2021
Nanyang Technological University, Singapore

"Acquiring common-sense knowledge used in social interactions and structuring it in a form that machines can use will help develop AI systems that can effectively interact with people and serve their needs."

Looking to change the face of AI, Suen is harnessing social and cognitive science to understand the factual knowledge behind cultural common sense and encode it into AI systems.

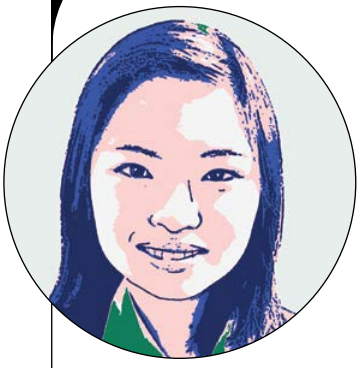
UMAR BIN MOHAMAD SAHARI

A*STAR Graduate Scholarship (PhD), 2021
National University of Singapore, Singapore



"Despite the lack of traction in pharmaceutical companies, I believe patients suffering from rare genetic disorders should be entitled to the same quality of treatment as any other patient."

Umar's research focuses on advancing therapeutics and diagnostics for rare genetic disorders. Over the course of his PhD studies, he hopes to gain the skills required to impact lives and inspire more people to pursue science.



UMA TAY

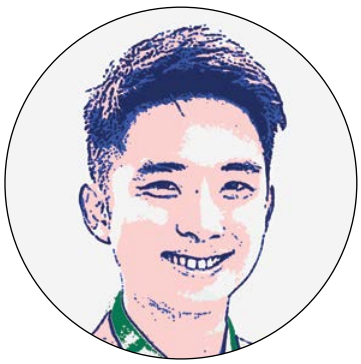
A*STAR Graduate Scholarship (PhD), 2021
National University of Singapore, Singapore

"The A*STAR scholarship empowers me to work towards fulfilling my research ambition of developing sustainable gelatin alternatives under the guidance of esteemed researchers from both NUS and A*STAR."

Practical and forward-looking, Tay noticed the burgeoning gelatin market and the ingredient's unique biocompatibility before choosing to focus her research interests on identifying plant-based gelatin alternatives.

SAM OH

A*STAR International Fellowship, 2021
University of California, San Diego, USA



"I hope to take advantage of the opportunity provided by A*STAR to enhance my research experience and bring the knowledge back to Singapore."

Oh, who had been interested in energy research since he was a polytechnic student, began developing a solid-state electrolyte that could replace current flammable organic electrolytes while pursuing his PhD studies. He continues to work on this technology as a postdoctoral scholar, in the hope that it will eventually power Singapore.

JASMIN OMAR

A*STAR Research Attachment Program, 2021
King's College London, UK

"Pursuing a PhD program as an A*STAR Scholar enables me to answer the previously unmet questions of my project and pursue my philanthropic vision."

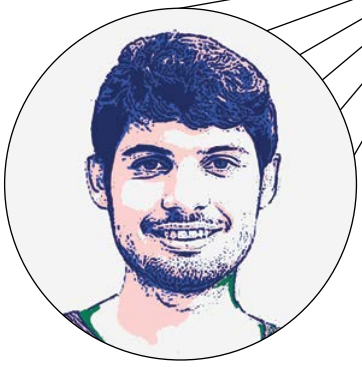
Omar is working to create novel hydrogels that can benefit patients whose retinas have pulled away from their normal position—the fifth leading cause of blindness.

LIAM JAMES SARGISON

A*STAR Research Attachment Program, 2021
Victoria University of Wellington, New Zealand

"The experience of completing my work in a space dedicated to addressing biological problems of the time has been inspiring."

To address the needs of Singapore's aging population, Sargison is researching therapeutic materials that promote natural healing—in particular, modifying pharmaceutical-grade polysaccharides to improve wound and bone repair.



MATHEUS EDUARDO GARBELINI

Singapore International Graduate Award Recipient, 2019
Singapore University of Technology and Design, Singapore

"My goal is to acquire the skills and experiences required to become a leading researcher, and to make improvements to the current state of wireless and IoT security across industry and academia."

As more Internet of Things (IoT) devices are introduced each year, Garbelini works to keep such smart devices safe and secure. He currently designs software algorithms that automatically discover vulnerabilities in wireless devices.

RUOQI DANG

Singapore International Graduate award Recipient, 2021
Nanyang Technological University, Singapore

"The world now faces the problem of carbon reduction and is in search of a suitable and environmentally friendly hydrogen energy source. How to store and transport hydrogen and what materials to choose to do this are worthy of study."

Looking to develop a sustainable method for storing and transporting hydrogen, Dang's research revolves around designing hydrogen-resistant alloys that remain strong in complex and extreme environments.

JOEL TONG

National Science Scholarship (PhD), 2021

"During my PhD degree, I hope to learn about innovative strategies, platforms and techniques that are integral to modern interdisciplinary research—skillsets I hope to later apply in A*STAR."

As a research officer at the Singapore Immunology Network (SIgN), Tong hopes to harness his background in chemistry and chemical tools to make sense of the immune system. He is working on the development of antibody-drug conjugates and engineered cytokines for cancer immunotherapy.

HIA MING

National Science Scholarship (PhD), 2017

"With a growing molecular understanding of biology, we have developed interdisciplinary tools and a systematic discipline to engineer organisms, leading to advancements in both bioproduction and therapeutics."

Ming's research on biosynthesis at the Singapore Institute of Food and Biotechnology Innovation (SIFBI) sees him working on two exciting projects: researching new technologies for creating DNA strands with enzymes and synthetically producing the main flavor molecule of hazelnuts.

JIAFEI DUAN

National Science Scholarship (PhD), 2021

"I am particularly interested in reverse-engineering human cognition to create embodied machines capable of human-level cognition and social intelligence."

As the current chair of the A*STAR Scholars Network, Duan has witnessed firsthand the peer-to-peer support and interdisciplinary collaboration between scholars. Duan's research focuses on creating artificial intelligence-enabled machines that can supplement the workforce and care for the vulnerable.

CLARE YIJIA XIE

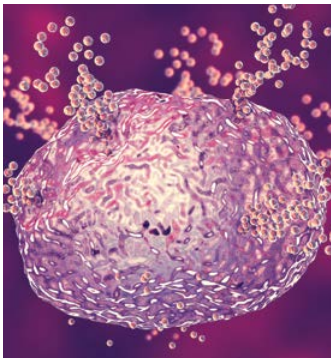
National Science Scholarship (BS-PhD), 2018

"With increasingly sophisticated simulation techniques and faster computers, I believe there is a new materials science revolution in the making. I wish to be part of the shift to accelerate materials discovery and develop innovative technologies."

At the Institute of High Performance Computing (IHPC), Xie is developing an automated workflow for high-throughput screening of heterogeneous catalysts and applying it to the analysis of alloy catalysts for ethanol dry reforming. ★

NEXT ISSUE

Here's a sneak peek of the material covered in the next issue of *A*STAR Research*



IMMUNOLOGY

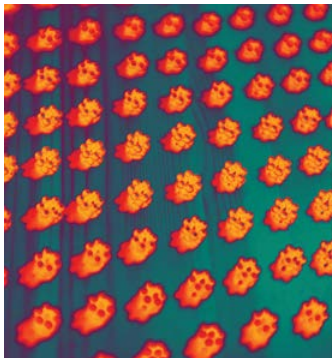
WHEN ALLERGIES PASS FROM MOTHER TO CHILD

Maternal antibodies can cross the placenta and pass on a mother's allergies to her unborn child, an A*STAR study found.

CARBON CAPTURE

CARBON-TRAPPING MINERALS PROMISE A GREENER TOMORROW

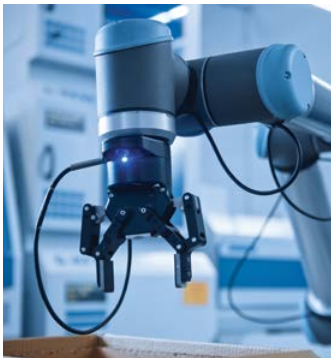
A technology for capturing waste carbon dioxide and turning it into sand could help Singapore reduce its carbon emissions.



PHOTONICS

SEEING BIOLOGICAL SPECIMENS IN A NEW LIGHT

Scientists have developed a technique for performing advanced infrared microscopy using off-the-shelf cameras built for visible light.



ROBOTICS

GUIDING HAND-EYE COORDINATION IN ROBOTS

A novel machine learning framework makes it faster and easier to train robots that can perform tasks with unprecedented precision.

Agency for Science, Technology and Research

SINGAPORE

REIMAGINE RESEARCH

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