

A★STAR

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Delving for insights
to reshape dermatology

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A*STAR RESEARCH

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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.

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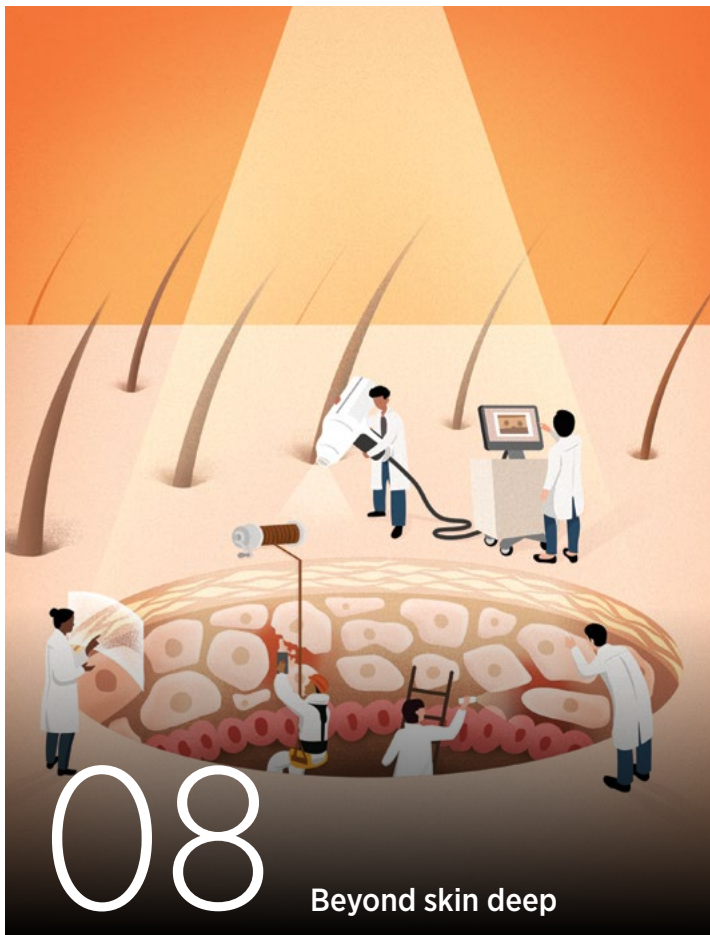
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Singapore Institute of Manufacturing Technology (SIMTech)

Singapore Institute of Food and Biotechnology Innovation (SIFBI)

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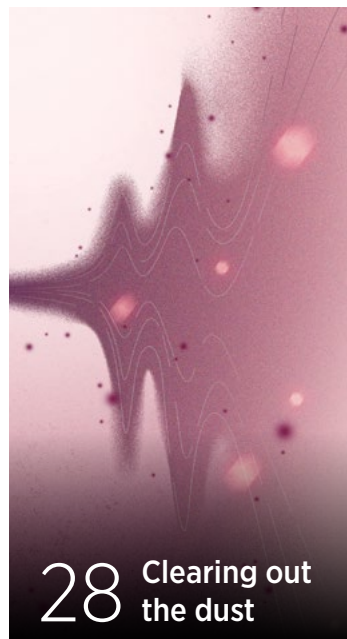
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EDITORIAL NOTES

Think of vital organs, and the heart, brain, lungs or liver likely come to mind. Compared to those, the skin may seem of secondary importance. But there's an understated value to this thin landscape of cells that envelops our bodies. It tempers heat and cold; stops invasion and poison; connects us to our world; disposes of waste; and of all organs, it is perhaps the one that matters most to our self-confidence and identity.

With its multidisciplinary expertise and close collaborations with clinicians and industry partners, A*STAR is helping to break new ground in Asian skin health. In this issue's cover story, 'Beyond skin deep (p. 08)', we dive into significant avenues of skin health research being pursued by the Skin Research Institute of Singapore (SRIS) and its partners in areas ranging from chronic wounds to the impacts of age.

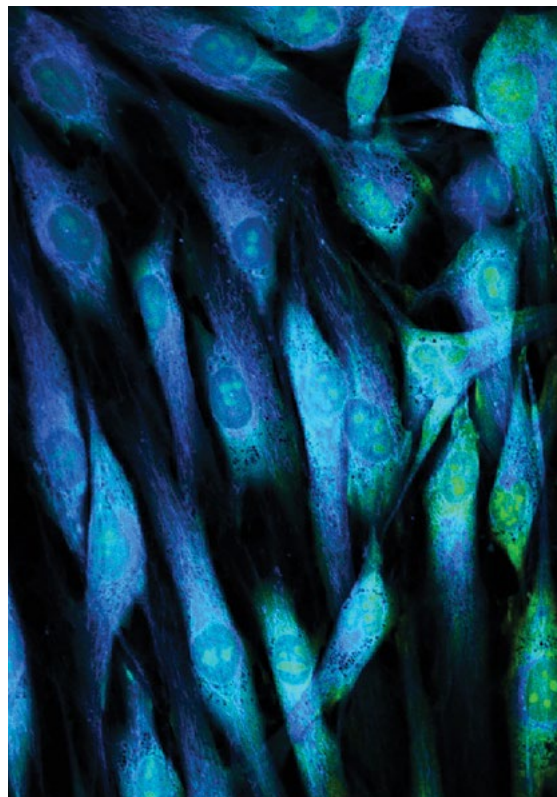
Inflammatory diseases such as eczema and psoriasis are a key research area at A*STAR as they afflict a significant portion of Singapore's population. In our first feature, 'Itching for a cure (p. 18)', Principal Investigator Kenneth Lay

considers how skin stem cells offer new insights into the root cause of this group of diseases, and how their modulation could improve patient outcomes.

Beyond genetics, our environment also affects our skin, as it responds to challenges posed by pollution. In our second feature, 'Clearing out the dust (p. 28)', A*STAR Graduate Scholar Rachel Phua discusses her work on the impact of air pollution on skin pigmentation, and shares insights from her journey as a young researcher.

Elsewhere, we feature the cutting-edge solutions being developed at A*STAR institutes for problems that range from securing pandemic healthcare data to teaching vehicles to dodge pedestrian traffic. Read more on these at 'Encrypted communications to stop the spread (p. 06)' and 'Robots gracefully weave through the crowds (p. 26)'.

For more of the latest developments from A*STAR researchers, visit our website at research.a-star.edu.sg. You can also stay up-to-date by following us on Twitter/X at [@astar_research](https://twitter.com/astar_research), LinkedIn at **A*STAR Research** and Telegram at **A*STAR Research**.



On the cover

Researchers take an illuminated look into the diverse layers of tissue that compose the human skin.



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IMMUNOLOGY

Predicting persistence, and a glimmer of hope

A two-year study uncovers potential immune biomarkers to detect long COVID, and evidence that its inflammatory symptoms may resolve over time.

Nearly four years since COVID-19 made headlines, new discoveries continue to reshape our assumptions about the disease. Siew-Wai Fong, a Senior Scientist at A*STAR Infectious Diseases Labs (ID Labs), cites the example of the populations we consider at high risk for 'long COVID': a constellation of changes to the body that can linger for months to years after infection, with potentially debilitating effects.

"Initially, the focus of long COVID research was on individuals who had severe acute illness; we now know it can also affect people who had mild or asymptomatic disease," said Fong.

Many aspects of long COVID remain a mystery: its causes, why it impacts some individuals over others, or why it manifests in varied symptoms ranging from brain fog to cardiovascular disease. Even the question of how common it is can be difficult to answer: studies report between 13 to 87 percent of patients who had COVID-19 deal with persistent symptoms.

Part of the issue is that long COVID can be difficult to diagnose. According to Fong, some patients may appear completely recovered on the outside, but show subtle signs of COVID-linked inflammation in their pulmonary, cardiac and renal systems.

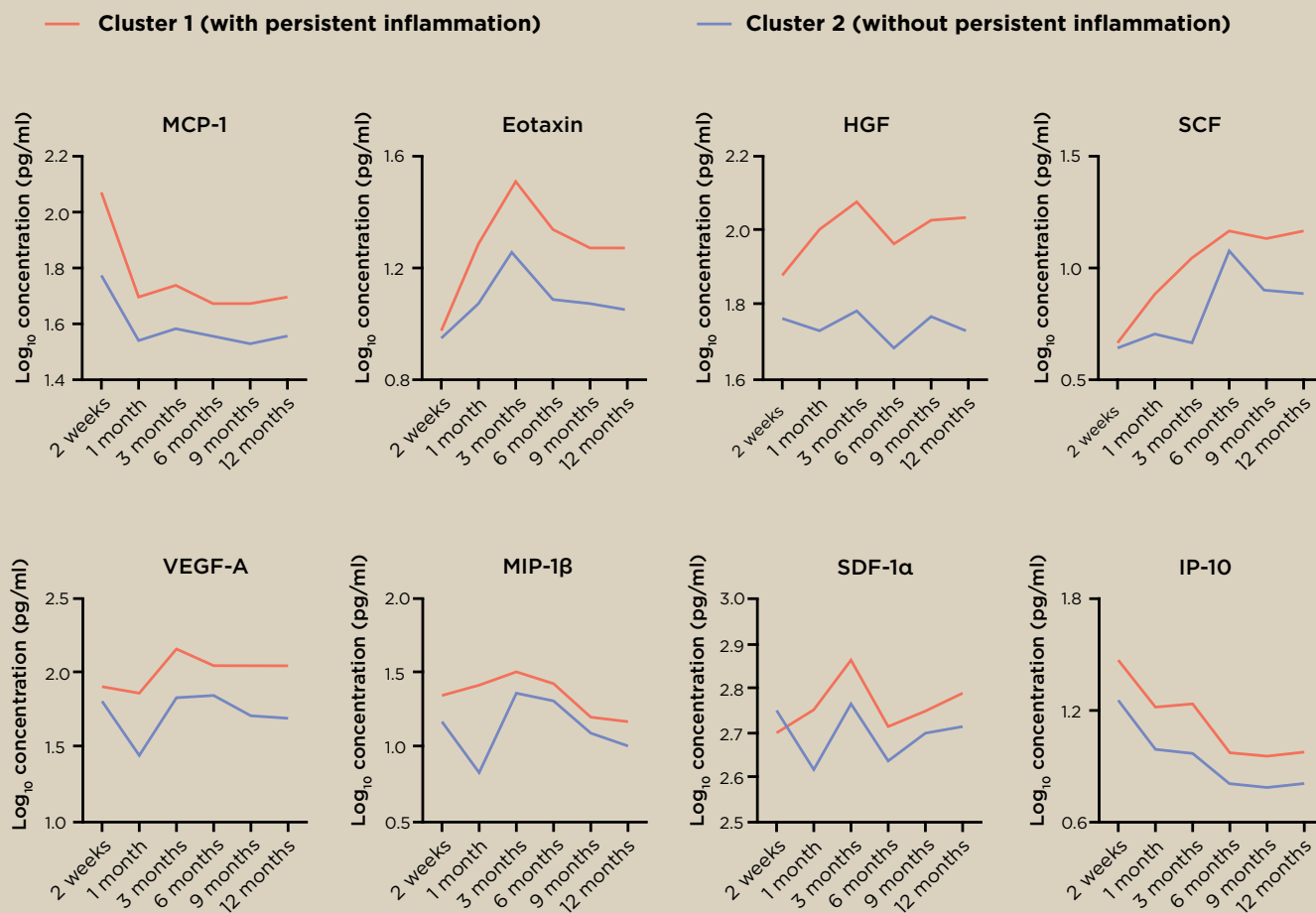
"The good news is that prolonged inflammation seen in these patients reverted to healthy levels within two years after initial infection."

"If we can detect long COVID earlier in its course, we can start treatment before it further impacts a patient's health," said Fong.

Working with the National Centre for Infectious Diseases, Singapore; National University of Singapore; Changi General Hospital; and Tan Tock Seng Hospital, A*STAR researchers tracked how post-COVID complications progressed in survivors of severe disease. They also searched for immune biomarkers that can be used to identify patients likely to have persistent inflammation.

The researchers recruited 78 patients in Singapore who were hospitalised with

Photo credit: Li Lin / Unsplash



Changes in immune mediator levels observed in a cluster of 78 patients with COVID-19 up to 12 months after their initial onset of illness. Previous studies have associated MCP-1, MIP-1β and IP-10 with chronic fatigue syndrome—a common symptom of long COVID—while other biomarkers have been linked to inflammatory effects in blood vessels and nerve cells.

COVID-19 in the pandemic's early phases. Over two years after their discharge, the researchers collected blood samples and the patients' self-reported data on any symptoms experienced.

A year into the study, 29 participants reported symptoms such as lingering cough and fatigue. Their blood samples revealed high levels of cytokines: immune mediators known to promote inflammation. The team also noted that patients with persistent inflammation showed distinctive levels of T cell differentiation and higher levels of specific IgG antibodies.

"The good news is that prolonged inflammation seen in these patients

reverted to healthy levels within two years after initial infection," said Fong, adding that the study also provided much-needed insights on lingering effects experienced by high-risk patients, who often had comorbidities like diabetes or high blood pressure.

"We believe our study offers some reassurance to affected individuals that their symptoms will resolve with time," said Fong. "Hopefully, our findings will also accelerate the search for treatments that aid recovery from long COVID. Further studies are needed to identify the mechanisms behind the prolonged inflammation and immune activation caused by COVID-19." ★



Researchers

Siew-Wai Fong and Lisa Ng,
ID Labs

IN BRIEF

Formerly hospitalised COVID-19 patients with long COVID symptoms exhibited distinct T cell differentiation signatures and elevated pro-inflammatory cytokine levels, which normalised by two years post-infection.

1. Fong, S.-W., Goh, Y.S., Torres-Ruesta, A., Chang, Z.W., Chan, Y.-H., *et al.* Prolonged inflammation in patients hospitalized for coronavirus disease 2019 (COVID-19) resolves 2 years after infection. *Journal of Medical Virology* **95** (5), e28774 (2023).

Encrypted communications to stop the spread

A novel machine learning framework enables data sharing for pandemic management while safeguarding patient privacy.

Patient data is inherently sensitive—healthcare providers are bound by ethical and legal frameworks to keep personal, diagnostic and genetic information behind confidentiality screens. However, certain exceptional circumstances may call for a delicate balance between individual privacy and the collective benefit.

Jun Jie Sim, a Senior Scientist at A*STAR's Institute for Infocomm Research (I²R), explained that although viral genome data from patient samples are anonymised for contact tracing in pandemic management, there's a chance that patient identities can inadvertently be revealed.

"During the onset of a new variant, people who were classified as having the same [viral] strain can be assumed to have had close contact," explained Sim, adding that metadata such as the geographic location of the sample may be enough to identify an individual.

Sim led a team that developed a privacy-preserving machine learning (ML) framework to help facilitate pandemic management without compromising patient confidentiality. The system, called CoVnita, was built using genomic sequence data from eight common SARS-CoV-2 strains and data-sharing simulations between multiple clinical providers.

CoVnita's workflow made use of an honest-but-curious threat model, a data security framework that protects sensitive information from database users that might try to learn more than they should from the available data. "You can think of them as the *kaypoh* (nosy) neighbour that helps keep the corridor clean, but never fails to listen in on what's happening in the block," said Sim.

CoVnita allowed multiple organisations to upload patient samples and jointly train the model while ensuring patient

information stayed private throughout the training process. The team's framework used three key technologies: Differentially Private Stochastic Gradient Descent (DP-SGD) and federated learning (FL) were used to train the model 'in the clear' (i.e., with unencrypted patient data), while homomorphic encryption (HE) was used to perform classification with encrypted data.

"Differential privacy ensures protection against model inversion attacks which try to sniff out information related to the model's inputs—in this case, sequencing data," said Sim. "In this work, we used those three technologies to ensure two things: that the original patient data stayed protected during training, thanks to DP-SGD and FL; and that new patient data was protected during classification, thanks to HE."

CoVnita provides quick and accurate classifications of SARS-CoV-2 strains which can help reduce the burden on hospital infrastructure to improve patient triage. The framework also enables secure and private data sharing for bioinformatics analyses that are crucial for managing and monitoring pandemics.

Sim said that CoVnita demonstrates the feasibility of using privacy-preserving ML in real-world healthcare settings. "We now plan to extend this framework to support other models, statistical methods and other forms of medical data, like images," Sim said. ★

Researcher

Jun Jie Sim,
I²R



IN BRIEF

CoVnita addresses privacy concerns in sharing viral genome sequencing data by using advanced encryption and machine learning techniques to securely classify SARS-CoV-2 strains for effective pandemic management.

1. Sim, J.J., Zhou, W., Chan, F.M., Annamalai, M.S.M.S., Deng, X., et al. CoVnita, an end-to-end privacy-preserving framework for SARS-CoV-2 classification. *Scientific Reports* **13**, 7461 (2023).

IMMUNOLOGY

Mixed shots hit a moving target

While the new Omicron XBB COVID-19 subvariant deftly dodges immune defences even in vaccinated individuals, researchers find that mixed mRNA vaccines may offer a vital boost of protection.

As the SARS-CoV-2 virus circles the globe, it continues to evolve as a masquerade of variants, many of which have caught even vaccinated communities off-guard. One of the latest is Omicron XBB: a 'hybrid' of the notorious Omicron variant, stemming from two different Omicron strains that traded genetic data while co-infecting the same cells.

Since its discovery in August 2022, XBB swept across Southeast Asia and became Singapore's most common SARS-CoV-2 variant, despite the country's high national vaccination rate. Matthew Zirui Tay, a Principal Investigator at the A*STAR Infectious Diseases Labs (ID Labs), led a team that examined just how effective current vaccine regimens might be in shielding people against XBB infection.

"Like many pathogens, SARS-CoV-2 has a natural tendency to mutate and escape even well-designed vaccines, which means they need to be continually updated to maintain their effectiveness," said Tay.

"SARS-CoV-2 has a natural tendency to mutate and escape even well-designed vaccines."

Working with colleagues at the National Centre for Infectious Diseases, Singapore; the Singapore Immunology Network (SIgN); and the Bioinformatics Institute (BII), researchers from ID Labs compared antibody responses to XBB versus the 'original' (wildtype) and Omicron BA.1 SARS-CoV-2 strains in individuals who had received three doses of mRNA vaccines and never been infected. The 59 study participants received two doses of the Pfizer-BioNTech BNT162b2 vaccine, then a third dose of either BNT162b2 or the Moderna mRNA-1273 vaccine.

Two key techniques were used: a cell-based surface spike-binding flow cytometric assay, and a pseudovirus neutralisation assay. The first identified how well antibodies bound to the variants' spike (S) proteins, while the second tested how well the antibodies disarmed 'mock' versions of each variant.

"Previously, it could take weeks to months to physically bring a new viral variant into the lab," said Tay. "These innovative assays now allow us to swiftly evaluate how well antibodies perform against a new variant without having to cultivate actual virus samples, which helps us get critical information sooner and mount an agile response to evolving situations."

The team found XBB-targeting antibody levels were generally low after the third dose and waned significantly

within six months compared to the wildtype and Omicron BA.1 strains. However, they also found that participants who received the mRNA-1272 booster as a third dose showed relatively higher levels of XBB antibodies at one month post-vaccination.

Tay's team posited that heterologous mRNA vaccine booster regimens—which use different mRNA vaccines for multiple doses, rather than reuse the same vaccine—induce stronger, more durable antibody responses against XBB. Different vaccines may stimulate the immune system in slightly different ways, leading it to produce a broader spectrum of defending antibodies against variant invaders.

Tay said that these results support the approach of mixed vaccine boosters as a means of boosting immunity against variants. The team is currently delving into the mechanisms of why certain vaccine strategies offer more durable protection than others, which can guide 'future-proof' vaccine designs.

"When we develop new vaccines, we need to design them not just for the viruses we see today, but also those that could arise tomorrow," said Tay. ★



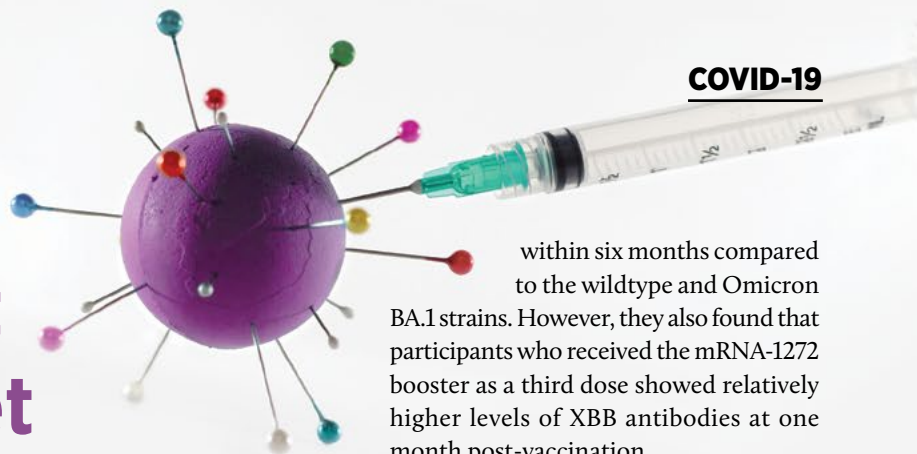
Researchers

Matthew Zirui Tay, Lisa Ng and Laurent Rénia, ID Labs

IN BRIEF

A study of individuals with no prior SARS-CoV-2 infection and who received different vaccine regimens found that heterologous mRNA vaccine boosters induced stronger and longer-lasting antibodies against Omicron XBB.

1. Tay, M.Z., Goh, Y.S., Fong, S.-W., Chang, Z.W., Rouers, A., et al. Heterologous mRNA vaccine boosters induce a stronger and longer-lasting antibody response against Omicron XBB variant. *The Lancet Regional Health - Western Pacific* **33**, 100732 (2023).





BEYOND SKIN DEEP

From molecular methods to advanced optics, scientists are combining techniques and expertise from diverse disciplines to transform skin health research and fortify the body's outermost barrier.

Whether to prepare for blazing sunshine or freezing winds, people have long turned to various methods to keep their skin in good shape. The skin's value is more than just cosmetic; it's a shield against radiation, toxins and microbes, and it's a hub of sensors that help us feel the world.

A healthy, functional skin barrier is vital to our overall wellbeing. However, some conditions can put a wrinkle in our skin's health, from irritating rashes to life-threatening wounds and cancers. As we age, our skin also naturally weakens as its component layers thin, lose their elasticity and regenerate more slowly.

Across the globe, scientists and physicians have long worked to navigate the complex frenzy of factors affecting our skin health, but humanity's diversity means major gaps remain in our understanding thereof, said Steven Thng, Chief Dermatologist at the Skin Research Institute of Singapore (SRIS).

"Asian skin types are distinctly different from European counterparts, which means data from studies on the latter

may be less relevant," said Thng. "For example, with ageing, Asian skin tends to form more age spots, while Caucasian skin forms more wrinkles. We also see distinctly different mutations and immune profiles between them in conditions like atopic dermatitis."

Aiming to fill the gaps in Asian skin health research, A*STAR is directing its multidisciplinary expertise into initiatives like SRIS. A tripartite coalition between the A*STAR Skin Research Labs (A*SRL), the National Healthcare Group (NHG) and Nanyang Technological University (NTU) Singapore, SRIS unites scientists, clinicians and engineers in high-impact, interdisciplinary skin research that translates to improved patient care.

"Skin is a complex organ with intricate functions and studying it from multiple angles is fundamental to unravelling its multifaceted dynamics in health and disease," said Sze-Wee Tan, Assistant Chief Executive of A*STAR's Biomedical Research Council. "Our ability to marry deep biological and dermatological understanding of Asian skin with engineering know-how allows us to create innovative therapies, diagnostics and skincare products for patients and consumers alike."

In partnership with other A*STAR institutes, industry and government, SRIS projects range from basic research on skin physiology to novel diagnostics and treatments. "We're bringing people together to understand the clinical challenges of Asian skin, and to use our collective understanding to produce positive impacts for patients and consumers' lives," said Rachel Watson, Executive Director of A*SRL and SRIS.



QUENCHING IMMUNITY'S FIRES

Many common inflammatory skin conditions, such as atopic dermatitis (AD) and psoriasis, are linked to issues in our immune system. Aberrant cells and molecular pathways can overreact to perceived threats, releasing a flood of molecules that can inflame the skin, impairing the skin barrier and disrupting the normal life cycle of skin cells.

“While protecting us against multiple threats such as infection and cancer, the immune system drives many inflammatory skin conditions including AD and psoriasis,” said Florent Ginhoux, a Senior Principal Investigator at SRIS and A*STAR’s Singapore Immunology Network (SIgN). “Studying its dysregulation is crucial to find new therapeutic approaches.”

AD is a key focus area at SRIS as it affects an estimated 20 percent of children and 11 percent of adults in Singapore. Also known as eczema, AD often manifests as dry, itchy skin patches and swellings which not only cause anxiety and discomfort but expose the skin to external irritants. While its exact cause remains unclear, AD has genetic components.

“The Asian filaggrin mutation spectrum differs significantly from Western populations,” said Thng.

To tackle AD holistically for Asian patients, SRIS’s National Atopic Dermatitis Programme (NADP) brings together A*STAR researchers, National Skin Centre (NSC) clinicians and industry partners to clarify AD’s burden in Asian populations; develop new diagnostics and treatments; and aid patients in disease management. NADP includes large-scale studies that combine clinical, omics and imaging data to map AD’s pathogenesis and epidemiology.

“We’re examining the molecular mechanisms of skin barrier disruption, immunity and the exposome,” said John Common, A*SRL Deputy Executive Director, who jointly established NADP with Thng and Yik Weng Yew, NSC Deputy Head of Research.

To date, NADP has produced numerous publications, garnered five industrial research collaboration agreements and drawn over SGD\$3.6 million in industry investments. Its work includes studies on cost-of-illness and quality of life for childhood AD; how inflammatory monocytes define immune dysregulation; and filaggrin gene sequencing to detect disease-associated variants.

“We are now aiming to develop our collective research findings into larger grant applications to further develop our ideas, advance our investigations of novel disease mechanisms, and apply our findings to the clinical cohorts developed within SRIS,” said Common.

Beyond NADP, SRIS also supports translational research by local biotech companies for novel AD therapeutics. These include phase 1b clinical trials for eblasakimab, a first-in-class monoclonal antibody developed by Aslan Pharmaceuticals and now in phase 2B multicentre trials.

MEETING THE SKIN'S MICROBES

Skin health isn’t linked solely to cells in our skin, but also to their closest neighbours. From body odour to dandruff, many conditions are affected by the skin’s microbial community: diverse bacteria, fungi and viruses residing on the skin’s surface which also vary widely with genetics and environment. Molecules produced by this community can modulate skin’s inflammatory response, potentially triggering disease.

To examine these tiny worlds, researchers at SRIS and A*STAR’s Genome Institute of Singapore (GIS) launched the Asian Skin Microbiome Programme (ASMP). Co-led by Common, A*SRL Deputy Executive Director Thomas Dawson, and GIS Associate Director (Genome

Architecture) Niranjan Nagarajan, ASMP initially focused on understanding healthy Asian skin, and how its microbiome was associated with health and disease.

“ASMP is driven by studies on humans using metagenomics, which provide snapshots of a whole landscape of microbial DNA,” said Nagarajan. “These not only reveal what organisms might be present, but the functional or metabolic pathways they affect in helpful or harmful ways. We’re also aiming to establish what a healthy baseline Asian skin microbiome looks like.”

Initially, ASMP set out to develop tools and optimise protocols, moving from marker gene-based taxonomic studies to whole-metagenome analyses. With time, it took on further technical challenges such as deconstructing the skin microbiome at increasingly higher resolutions, and reconstructing genomes of individual species from metagenomic data.

A large part of ASMP research focuses on fungal species such as *Malassezia*, their interactions with human hosts and microbial neighbours, and links to skin health and disease. Work led by Dawson recently found that *Malassezia* regulate our immune system and skin inflammatory status by producing lipid-based signalling molecules similar to human versions.

Now in its second phase of funding, ASMP is building a skin microbiome database from a large Singaporean cohort of over 2,000 individuals across 18 different skin sites. It is also collecting microbial isolates to build skin models for host-microbe interaction studies. “We’re aiming to develop our understanding of microbial functions to improve skin health and identify molecules for clinical trials,” said Common.

Working with clinicians from the National University of Singapore (NUS), National University Hospital (NUH) and NSC, ASMP also examines the skin microbiome’s links to specific diseases. These include not only skin diseases like AD—where studies show patients have perturbed microbiomes versus healthy counterparts, and an individual’s risk of severe disease can be stratified by the presence of certain microbial colonisation patterns—but also neurological conditions like Parkinson’s disease.

“In a recent study, we also found that the skin of children with recurring AD flares—despite decolonisation treatments—could be recolonised with disease-associated bacteria like *Staphylococcus aureus* through their caregivers, which means clinicians could factor them into AD treatment plans,” said Nagarajan.

“The Asian Skin Microbiome Programme is driven by studies on humans using metagenomics, which provide snapshots of a whole landscape of microbial DNA.”

— Niranjan Nagarajan, Associate Director (Genome Architecture) at the Genome Institute of Singapore (GIS)



PRESERVING SKIN INTEGRITY

The skin's layers are constantly dividing to replace old cells with new copies. In the deeper dermal layer, a complex extracellular matrix provides the skin with strength, resilience and elasticity, and is a home for blood vessels and nerves. However, these can be impaired by age or other health conditions, like diabetes or hypertension.

"Anything that compromises our skin's tissue integrity—its ability to build and maintain a strong, healthy barrier against the external environment—can lead to infections or wounds that impact quality of life," said Leah Vardy, A*STAR Research Director and a SRIS Senior Principal Investigator.

At A*STAR, chronic wounds and fragile skin in the elderly are two significant focus areas. In tropical climates, diabetic foot ulcers and bed sores are more infection-prone due to more robust microbial growth. Treatment can be challenging, with amputation a grim last resort.

SRIS's Wound Care Innovation for the Tropics (WCIT) Programme aims to transform chronic wound care and reduce its economic burden through several research areas including preclinical wound models, innovative dressings and diagnostics, a first-of-its-kind chronic wound registry, and the world's largest library of Asian chronic wound samples.

"With Singapore's ageing population, chronic wounds pose an increasing burden on the national healthcare system, affecting around 12,000 patients a year," said Yi Zhen Ng, WCIT Programme Manager. Ng highlighted a recent joint publication with the Ministry of Health, Duke-NUS and three tertiary hospitals which estimated that chronic wounds cost the nation US\$350 million annually, and its people 2,077 quality-adjusted life years.

With A*STAR's Institute for Infocomm Research (I²R) and the Diagnostics Development Hub (DxD Hub), A*STAR Senior Scientist Priya Bishnoi and colleagues are developing a digital platform that supports clinical decisions and home-based wound management. WCIT has also funded clinical projects with direct patient impact, such as the Lower Extremity Amputation Protection Programme (LEAPP), which reduced major and minor amputations in the NHG healthcare cluster by 35 and 80 percent over 18 months.

One major WCIT breakthrough is the development of the world's first perturbed wound healing *in vivo* preclinical model to successfully capture many features of human chronic wounds. Developed by David Becker, a SRIS

"Our long-term goal is to put ourselves out of a job: to solve everyday problems faced by our clinical colleagues, to fortify the skin of the elderly, to cure skin disease."

— Rachel Watson, Executive Director of the A*STAR Skin Research Labs (A*STAR) and the Skin Research Institute of Singapore (SRIS)

Senior Principal Investigator and Professor at LKC School of Medicine, and Jiah Shin Chin, an A*STAR Scientist, the model is being used to validate molecular pathways and therapeutics for wound healing and tissue repair. With this model, a unique hydrogel topical formulation was developed and validated, and will enter clinical studies at Changi General Hospital in early 2024.

Vardy, Thng and colleagues have also shown that polyamines, a family of metabolites, play a role in supporting skin barrier integrity and the wound healing response, with studies establishing links between aberrant polyamine levels and skin hyperpigmentation.

"Many complex factors—intrinsic and extrinsic—drive skin ageing," said Vardy. "We want to understand the process and develop interventions to protect and treat age-associated skin phenotypes."

DIAGNOSING AT DEPTH

The sheer diversity of skin conditions can make accurate diagnoses challenging. "Individual perceptions of skin conditions may vary; it's difficult to establish a universally applicable standard for what constitutes healthy skin," said A*STAR's Malini Olivo, Distinguished Principal Scientist at the Translational Biophotonics Laboratory (TBL).

However, advanced technologies such as non-invasive imaging and artificial intelligence are enabling a clearer view of skin health. A*STAR's work in biophotonics

and bioengineering has pioneered the development of cutting-edge devices that play a crucial role in clinically assessing skin disorders.

“Through our strategic alliance with NSC and NUH, we are gaining new insights on individual differences in skin composition, health, stress responses and therapeutic efficacy,” said Olivo. “This collaborative effort extends beyond research, as A*STAR has actively generated multiple IPs through its technological innovations, which in turn have attracted industry partners from consumer healthcare looking to validate their products.”

In groundbreaking first-in-human studies, TBL and NSC are successfully employing handheld versions of two optoacoustic technologies for dermatological applications: photoacoustic imaging (PAI) and confocal Raman spectroscopy (CRS). These innovations enable non-invasive, label-free analyses of various skin conditions including cancer, psoriasis and AD.

“The handheld PAI facilitated precise 3D tumour imaging to create dimension maps with exceptional correlation with histological data, which could simplify surgical procedures and streamline prospective cancer studies,” said Olivo. “Meanwhile, CRS played a pivotal role in evaluating skin biochemical changes—water, ceramide, urocanic acid—in AD and psoriasis patients, enabling objective assessment and treatment monitoring.”

Working with NSC clinicians, A*STAR's Bioinformatics Institute (BII) also developed machine learning (ML) models to analyse raster-scanning optoacoustic mesoscopy (RSOM) data. RSOM 3D images are derived from sound pressure waves that travel through skin tissue, collecting features about lesion sites and swollen areas. Connecting ML tools that rapidly extract patterns from these images can then help clinicians detect AD with greater accuracy and efficiency.

A*SRL not only engages with other research institutions and hospitals, but also pushes technology breakthroughs to the market through strategic partnerships with SMEs.

“These collaborative endeavours position A*STAR as a key player in advancing the diagnosis and treatment of skin disorders, while fostering innovation and commercialisation in the field,” said Olivo.

REDEFINING SKINCARE

Over the last two decades, strong collaborations between academics, clinicians and industry have driven a revolution in skin biology. “We’ve moved from draping psoriasis patients in coal tar-soaked bandages, to giving them oral drugs or injections that subdue or even resolve disease,” said Rachel Watson.

Persistent clinical gaps now guide cross-disciplinary efforts to decipher the individual differences in skin health and the aberrant molecular pathways responsible for diseases. Excitingly, researchers are gaining the technological tools to dig deeper into various layers of skin biology, from its biochemical balance and resident microbiome to inflammatory regulators and self-repair processes.

Continued support for skin research, shared knowledge databases and more effective medical devices are elevating the standard of care for both disorders and subclinical conditions, empowering people of all ages and backgrounds to feel confident in their own skin.

“There is a paradigm shift in the value placed on Asian skin health, as well as skin research in Singapore and worldwide. We can easily envision a future where advanced technologies merge with a profound understanding of individual skin biology across age groups, offering tailored solutions that prioritise not just aesthetics but holistic skin health for all,” said Sze-Wee Tan.

“Our long-term goal is to put ourselves out of a job: to solve everyday problems faced by our clinical colleagues, to fortify the skin of the elderly, to cure skin disease,” said Watson. ★



MACHINE LEARNING

A deep dive into cancer's big data

A new deep learning system outperforms traditional methods for identifying genetic mutations from DNA sequences and can be a valuable tool for improved cancer diagnostics.

Deep within the genomes of cancer cells lie subtle clues to their malignant origins. Somatic variants are genetic alterations that point to DNA replication errors or exposure to carcinogens, and are known to contribute to tumour development.

However, using automated platforms to find cancer's genetic fingerprints in patient DNA samples has been exceedingly difficult, as tumours are often highly heterogeneous and DNA sequencing is prone to errors.

Anders Skanderup, a Group Leader from A*STAR's Genome Institute of Singapore (GIS), said that breakthroughs in machine learning (ML), combined with the availability of large, multidimensional training datasets, can help realise the full potential of diagnostic technologies powered by artificial intelligence.

"The ability to generate and use large-scale next-generation sequencing data of cancer genomes can enable the training of large deep learning models," said Skanderup.

Using this approach, Skanderup worked with first author Kiran Krishnamachari and colleagues to develop a deep learning system designed to detect somatic variants in tumours. The platform, called VarNet, was trained using 4.6 million high-confidence somatic variants found in 356 tumour genomes spanning seven cancer types.

The team built VarNet using ground-truth labels (reference datasets) with an ensemble method which enabled it to

recognise genetic mutations in unlabelled genetic data. "While there are many cancer sequencing datasets available, they do not contain ground-truth mutation labels that can be used to train large models," said Skanderup, adding that they solved the issue using scale and weak supervision.

They also devised two distinct deep learning models to identify single letter DNA changes (single nucleotide variants) and insertions or deletions to the DNA code (indels). Finally, the system was engineered to generate image-like representations of mutation sites, which allowed VarNet to better 'see' mutations and make mutation probability predictions at each site.

Prior ML platforms tended to struggle with 'low purity' tumour samples containing healthy tissues that made distinguishing

somatic variants harder. However, validation tests proved that VarNet's performance often exceeded current state-of-the-art methods in these challenging scenarios.

"VarNet was shown to be more accurate than existing systems in benchmarks of low-tumour-purity settings, which improves its potential for practical use," said Skanderup. The platform was specifically designed to mimic human experts who would use visualisations of sequencing data to make side-by-side comparisons of normal and tumour samples, Skanderup added.

VarNet's unprecedented accuracy can be a game changer both in research and commercial settings, said Skanderup, who suggested that it can enhance specialised mutation detection technologies often used by medical diagnostic companies. ★

"VarNet was shown to be more accurate than existing systems in benchmarks of low-tumour-purity settings, which improves its potential for practical use."

Researcher

Anders Skanderup,
GIS



IN BRIEF

The VarNet deep learning system transforms raw DNA data from tumours and matched normal samples into image-like representations, enabling easier associations between specific DNA data patterns and somatic mutations.

1. Krishnamachari, K., Lu, D., Swift-Scott, A., Yeraliyev, A., Lee, K., *et al.* Accurate somatic variant detection using weakly supervised deep learning. *Nature Communications* **13**, 4248 (2022).

Photo credit: Tartila / Shutterstock

GENOMICS

Baring breast cancer's genetic dependencies

Researchers reveal how disrupting a key genetic control mechanism in an aggressive, difficult-to-treat form of breast cancer can significantly hinder its progression and spread.

Cancer cells defy the normal rules of biology; they possess the ability to grow and thrive in an alarmingly uncontrolled manner. These properties can be traced back to the reliance of tumours on certain transcriptional pathways to maintain their rapid proliferation, a trait scientists call 'transcription addiction'.

"Transcription addiction allows cancer cells to adapt, survive and spread," said Wee-Wei Tee, Co-Director of the Chromatin Dynamics and Disease Epigenetics Lab at A*STAR's Institute of Molecular and Cell Biology (IMCB). "However, it also creates a vulnerability that can be targeted for potential treatments."

For example, triple negative breast cancer (TNBC)—a highly aggressive cancer associated with poor clinical outcomes—typically relies on a uniform set of transcriptional programmes. This means certain therapies may be more effective for treating TNBC by targeting these essential pathways.

To delve deeper into this "Achilles' heel" in TNBC, Tee and IMCB colleagues Radoslaw M. Sobota, Manikandan Lakshmanan and Vinay Tergaonkar searched for more transcription addiction pathways specifically associated with breast cancer progression and metastasis. In previous studies, the team had identified the Negative Elongation Factor (NELF) complex as a potential target: it acts as a control switch for a metastatic process called epithelial-mesenchymal transition (EMT).

Working with Ern Yu Tan from Tan Tock Seng Hospital, Singapore; Wai Leong Tam from A*STAR's Genome Institute of Singapore (GIS); as well as collaborators from the Jiangsu Province Hospital of Chinese Medicine, China; and University of Liverpool, UK, the researchers performed a series of genomic and transcriptomic analyses in cancer cell lines and patient-derived tumour organoids. They also investigated the

effects of depleting NELF in different cell lines and mouse models.

The researchers found that deactivating the NELF complex with gene editing technologies inhibited TNBC's spread and progression. Tee described how NELF-E, a component of the NELF complex, interacted with a key EMT factor called SLUG: "Notably, SLUG emerged as one of the top interaction partners of NELF-E in the EMT state, suggesting a potential collaboration between the two proteins in driving metastasis."

NELF-E-SLUG interactions were found to functionally impact KAT2B, a histone acetyltransferase that correlates with poorer prognosis in breast cancer patients. The exciting discovery by the research team points to NELF-E and KAT2B as targets which can unlock new breast cancer treatments.

"NELF-E can be prevented from exerting its cancer-promoting effect by modulating the activities of these binding partners that play crucial roles in cellular reprogramming," Tee said.

The team is leveraging these breakthrough findings to map more of NELF-E's binding partners with crucial roles in cellular reprogramming, with the aim of one day offering hope to TNBC patients. "Despite TNBC representing only about 15 percent of all breast cancers, it stands out as a subtype with limited improvement and survival outcomes due to the lack of effective targeted therapies," said Tee. ★

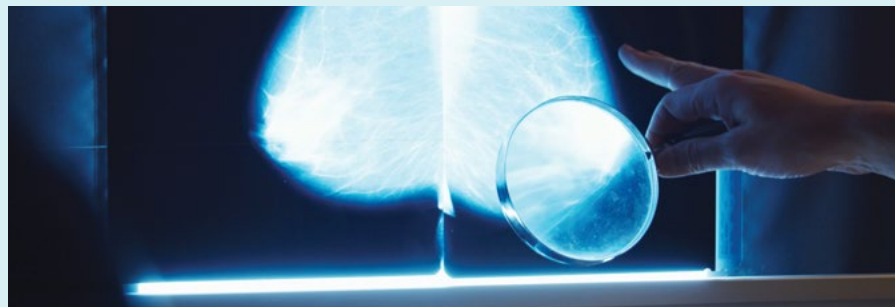
Researcher
Wee-Wei Tee,
IMCB



IN BRIEF

Targeting the NELF complex in triple negative breast cancer cells inhibits epithelial-mesenchymal transition and represents a potentially valuable therapeutic target to halt tumour progression and metastasis.

1. Zhang, J., Hu, Z., Chung, H.H., Tian, Y., Lau, K.W., et al. Dependency of NELF-E-SLUG-KAT2B epigenetic axis in breast cancer carcinogenesis. *Nature Communications* **14**, 2439 (2023).



IMMUNOLOGY

Blueprints to optimise a cancer killer

A*STAR researchers tackle the challenge of creating therapeutic antibodies that effectively kill tumours and are also easily scalable in manufacturing settings.

Think of tumours as masters of disguise. By masquerading as healthy tissues and creating a molecular shield of invisibility, cancer cells evade the immune system's surveillance. However, a next-generation therapeutic modality aims to unmask tumours, exposing them for immune destruction.

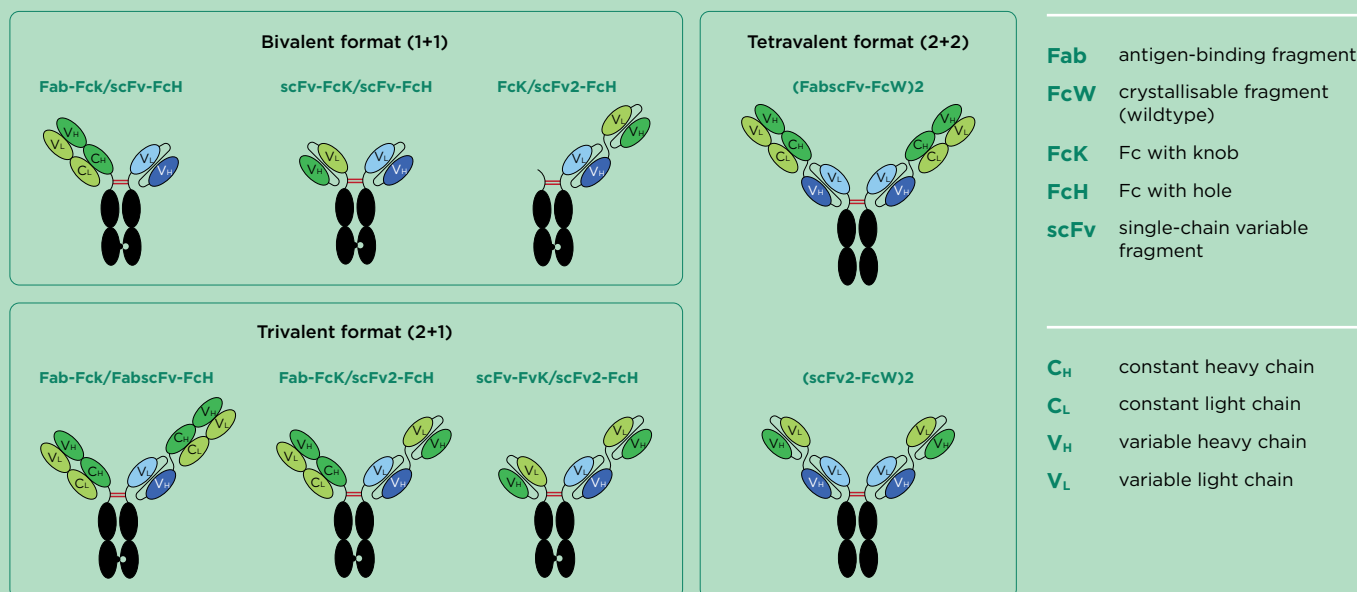
T cell-engaging bispecific antibodies (T-bsAbs) have binding 'arms' which guide T cells to tumours hiding in stealth mode. They have a molecular design space that reflects the complexity of treating diverse tumour types—their shape, size and binding properties can all be tailored to maximise their potency as antibody therapies.

"Understanding the interplay of these factors is crucial for achieving the desired therapeutic effect from a T-bsAb," said Yuan Sheng Yang, Group Leader at A*STAR's Bioprocessing Technology Institute (BTI).

However, the drug development industry has found it challenging to fine-tune T-bsAbs, as modifying antibody structures to boost their functions often also makes them more costly to manufacture.

In close collaboration with Group Leader Shengli Xu and colleagues from A*STAR's Singapore Immunology Network (SIgN), Yang's team systematically compared eight

Photo credit: Design_Cells / Shutterstock



Schematic diagrams of the eight T-bsAb antibody designs tested. The antibodies were designed to be bispecific: capable of binding to both the human CD3 receptor (blue arms) and HER2 receptor (green arms), which are key therapeutic targets in breast cancers.

commonly-used T-bsAb designs to connect the dots between molecular design, ease of manufacture and therapeutic efficacy.

To test how different antibody components—such as antigen-binding fragments (Fabs) and single-chain variable fragments (scFvs)—can affect the overall molecule, the researchers designed T-bsAbs with unique combinations thereof. They then generated specialised cell lines to mass produce their T-bsAb designs before assessing them on yield, purity, binding properties and biological activity.

“The field’s potential to provide more effective and accessible treatments across a spectrum of medical conditions holds great promise for the coming years.”

“Achieving a stable bsAb product is key to reducing production costs, as it would enhance overall product yield and quality,” said Yang.

The study demonstrated that some antibody designs, such as those with more scFv components, were highly prone to aggregation—a production flaw where antibody molecules tangle up in clusters and ruin their ability to bind targets. Too much aggregation can lead to reduced overall production yields and drive costs up, Yang added.

At the same time, therapeutic efficacy remains the paramount concern for any T-bsAb drug candidate. “We observed that some T-bsAbs behaved very differently when activating T cells and eradicating tumour cells, even when they seemed similarly highly stable and manufacturable,” said Xu.

Based on their results, the researchers homed in on two T-bsAb formats—each bearing one scFv component—that struck the balance between manufacturability and tumour cell-killing potency. According to Xu, these critical insights can streamline the development of improved, easy-to-manufacture cancer immunotherapies.

Looking ahead, Yang said that emerging technologies such as artificial intelligence and computational modelling can accelerate the rational design of T-bsAbs with enhanced therapeutic properties. “The field’s potential to provide more effective and accessible treatments across a spectrum of medical conditions holds great promise for the coming years,” Yang added. ★



Researchers

Yuan Sheng Yang, BTI

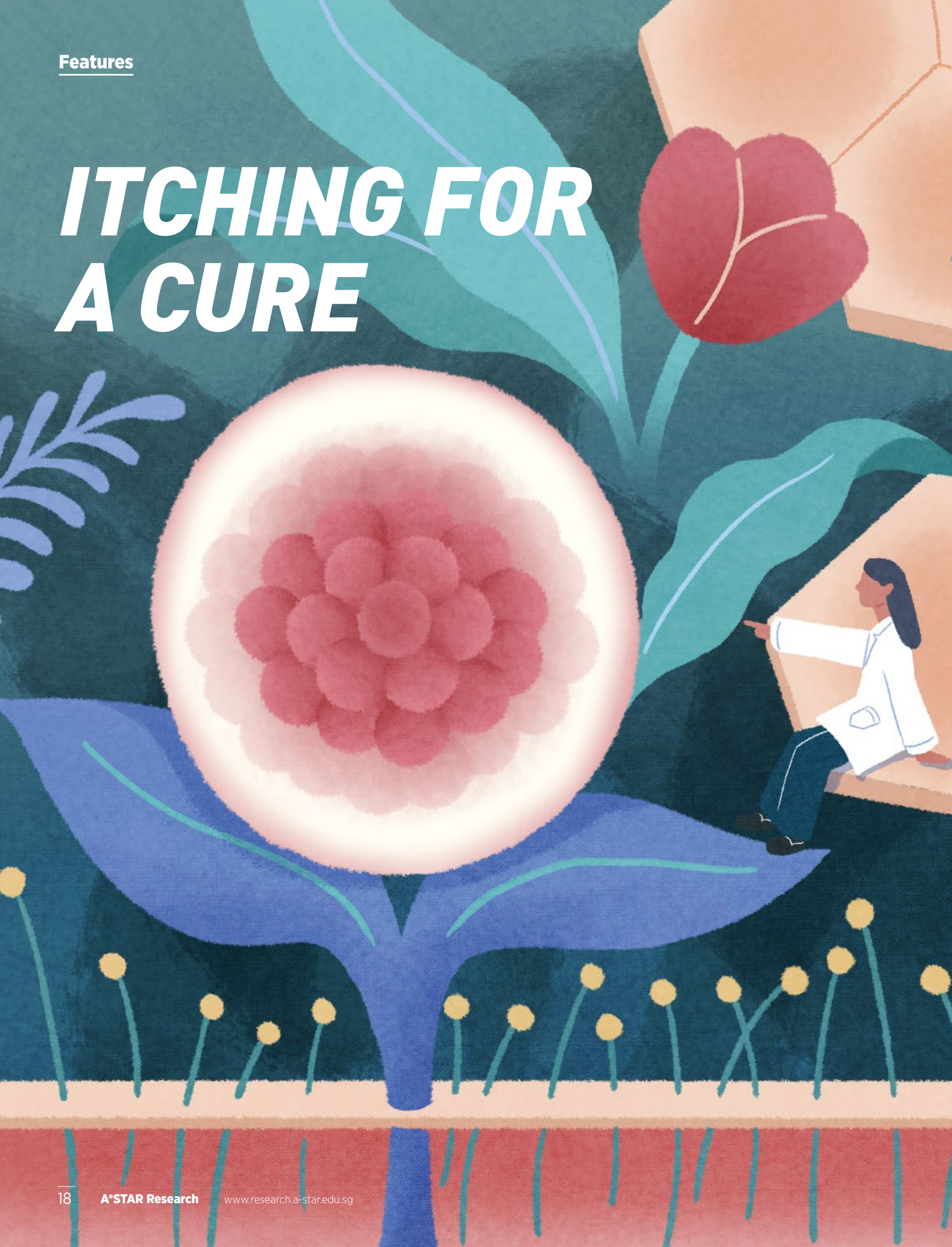
Shengli Xu and Kong-Peng Lam, SIgN


IN BRIEF

A systematic comparison of eight distinct formats of T cell-engaging bispecific antibodies reveals critical insights into their molecular design for optimal biological activity and manufacturability.

1. Loh, H.P., Mahfut, F.B., Chen, S.W., Huang, Y., Huo, J., *et al.* Manufacturability and functionality assessment of different formats of T-cell engaging bispecific antibodies. *mAbs* **15** (1), 2231129 (2023).

ITCHING FOR A CURE





The untapped potential of stem cells can lead us to new treatment avenues for inflammatory skin diseases, says Kenneth Lay.

The symptoms come and go unpredictably: persistent patches of scaly skin that shed white flakes excessively, or red and raw rashes that cause pain when clothes rub over them. When they are milder, they're uncomfortable and distressing; but when they flare, they become debilitating. Even when they're absent, they leave a constant sense of anxiety over what might trigger their return, which could be anything from a hot day or a bite of seafood, to a stressful time at school or work.

These are some of the difficult everyday realities for patients who live with inflammatory skin diseases: a group of often life-long conditions which includes eczema and psoriasis. The reasons why they come about are complex, but they often appear when something goes wrong with how our skin responds to environmental triggers. Our cellular defenders can overreact by pumping inflammation-boosting molecules in places where they're not needed, causing new problems instead of fixing old ones.

While many treatments exist for these diseases today, ranging from topical creams to small-molecule inhibitor injections that target the body's inflammatory systems, these can have their own downsides. Apart from side effects and cost, most provide only a temporary relief from symptoms as they may not fully address the root cause of disease: the dysfunctions in cellular signalling processes that agitate the skin.

At A*STAR Skin Research Labs (A*SRL), a team led by Principal Investigator Kenneth Lay is exploring the possibilities that stem cells offer to tackle inflammatory skin diseases at their root. As the basic building blocks for many other tissues in our body, stem cells have strong regenerative properties that have been used to treat brittle bones, weak hearts and other diseases linked to cellular dysfunction.

As a newly awarded National Research Foundation Fellow, Lay shares some insights from his work in stem cells, the prospects in the field, and his goals as an investigator within the wider skin research community.

Q: WHAT LED YOU TO SKIN STEM CELL RESEARCH?

I've always been interested in harnessing the regenerative potential of stem cells to treat disease, so I set out to understand the biology of various stem cell types, including mesenchymal, embryonic and induced pluripotent stem cells. During my PhD studies, I wanted to learn more about adult stem cells. They're the ones responsible for the day-to-day maintenance, renewal and regeneration of various organs of our bodies.

I chose to study skin stem cells in particular, and became fascinated by the skin as an organ: both in the important role it plays in our well-being, and the many diseases related to it that remain unresolved. I thus set up my lab with a vision to harness skin stem cell dynamics for novel therapeutics. My motivation has always been to improve lives through scientific discoveries.

There are many reasons for my focus on inflammatory skin diseases. We don't really know why we get them, and we can't really make them go away; they keep recurring despite our best attempts at treating them. Their common manifestations—pain, blisters, itch—can greatly compromise not just a person's quality of life, but their self-confidence and emotional wellbeing.

A*STAR supported my undergraduate and PhD studies in some of the best universities and laboratories in the world. They allowed me to train with mentors who played pivotal and inspirational roles in my growth as a scientist.

"Skin stem cells were the first human cells to be grown in the laboratory for clinical use. They can expand rapidly and make sheets of skin in a dish, which can then be used as grafts to save the lives of patients who have lost significant areas of their skin due to burns or genetic disorders."

— Kenneth Lay, Principal Investigator
at the A*STAR Skin Research Labs (A*SRL)

Q: WHAT THERAPEUTIC GAPS DO YOU HOPE TO ADDRESS?

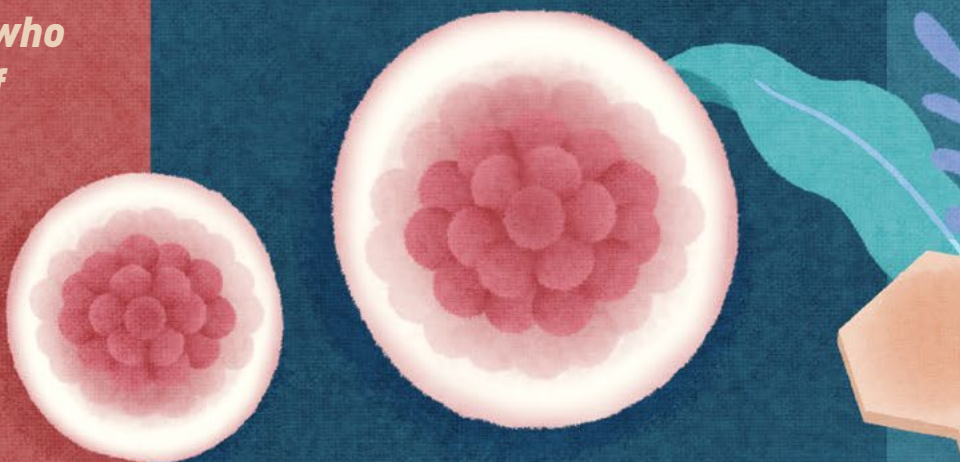
Current treatments for inflammatory skin diseases each have their shortfalls. For example, moisturisers can strengthen our skin barrier's functions, but as we shed skin cells daily, we eventually lose those improved skin layers. In patients with these diseases, the skin stem cells underlying their defective barriers will continue their aberrant crosstalk with immune cells, then differentiate into a new set of defective skin cells, which need another round of treatment... the cycle repeats itself.

On the other hand, there are immunosuppressants which are effective, but because they work by suppressing the immune system, the symptoms often return once you stop treatment, and can be worse than before. Newer immunosuppressants come in the form of costly biologics, which make administration and compliance challenging. Importantly, there are known short-term side effects to these therapies such as drug toxicity and increased risks of infections—and we still don't know what their long-term effects are.

Q: WHAT EXCITING PROSPECTS DO STEM CELLS OFFER FOR SKIN DISEASES?

Skin stem cells were the first human cells to be grown in the laboratory for clinical use. They can expand rapidly and make sheets of skin in a dish, which can then be used as grafts to save the lives of patients who have lost significant areas of their skin due to burns or genetic disorders.

Beyond these severe conditions, the regenerative potential of skin stem cells has not been fully utilised for some of the more common skin diseases that we face, such as those associated with inflammation, of which eczema and psoriasis are well-known examples. That underuse is because we still don't know how skin stem cells respond to such disease states. If we can shed more light on these mechanisms, we can start modulating them for more favourable patient outcomes.



Q: WHAT HAS YOUR LAB BEEN WORKING ON RECENTLY?

One aspect we are working on is dissecting how skin stem cells properly communicate with our immune cells. Our skin is highly potent in initiating and launching an immune attack on harmful things that have penetrated it. But when it loses control of this ability, diseases arise as the crosstalk between skin and immune cells goes into overdrive. We are now looking for ways to alleviate disease by dampening this response.

Q: WHAT IMPACTFUL EXPERIENCES HAVE YOU HAD IN THE GLOBAL SKIN RESEARCH COMMUNITY?

I was recently invited to speak at both the inaugural International Societies for Investigative Dermatology conference held in Japan, and the Gordon Research Conference on Epithelial Differentiation and Keratinization held in Spain. I shared with fellow researchers and clinicians our new insights into skin biology that we had obtained through the study of rare genetic skin disorders.

I also had the privilege to be the elected Chair and organiser of the 2023 Gordon Research Seminar, which is an international platform exclusively for postdoctorates and graduate students in skin and epithelial biology to present their work. I ran for the position as a way to contribute back to the community that has helped shape my scientific career. Raising money to run the conference was challenging, especially over the pandemic years, but fortunately the conference was a success, made possible by all the participants who presented their cutting-edge research and are stepping up to be future leaders in the field.

Attending conferences has always been a humbling experience for me. It was a privilege to share my work and get constructive feedback from the community, and also an honour to stay at the forefront of skin research by learning about the latest developments from some of the best laboratories in the world. Being able to reconnect and strengthen relationships with colleagues and friends in the skin research community after the long hiatus caused by the pandemic was an amazing feeling as well.

Q: SINCE BECOMING A PRINCIPAL INVESTIGATOR, WHAT NEW PERSPECTIVES HAVE YOU GAINED?

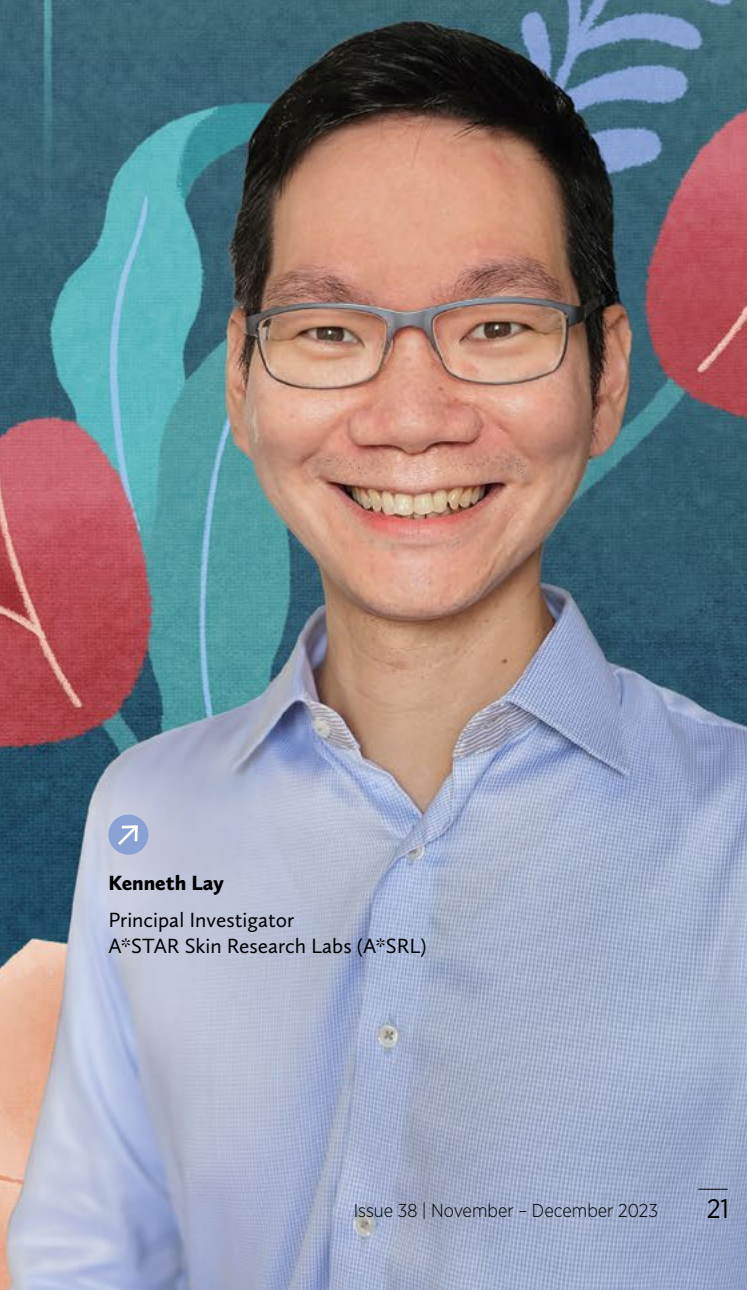
Building up a lab is like starting a new company. First, I need to have a vision; then I need to carve out different paths to realise it. Next, I need to lay the foundation for those paths, which should always rest on sound, creative and rigorous science. Finally, I need to build my team to be able to walk those paths and grow together with me as scientists and future leaders.

To young researchers looking to become Principal Investigators themselves, I would say: train well, build a strong scientific foundation, create a vision, and enjoy the journey. ★



Kenneth Lay

Principal Investigator
A*STAR Skin Research Labs (A*SRL)



ELECTRONICS

Sniffing out solutions for climate change action

New gas sensing technologies offer improved environmental monitoring to address climate change and improve safety.

As 2023 is poised to break records as the hottest year in recorded history, the urgency for addressing climate change has never been more palpable. Doris Ng, a Research Scientist based at A*STAR's Institute of Microelectronics (IME), said that to tackle the problem, we have to be able to accurately measure it.

"Sensing is the first step before mitigation can come into play," said Ng.

"We need to monitor greenhouse gases (GHGs) and identify areas where there are increased emissions before we can come up with plans to protect the environment."

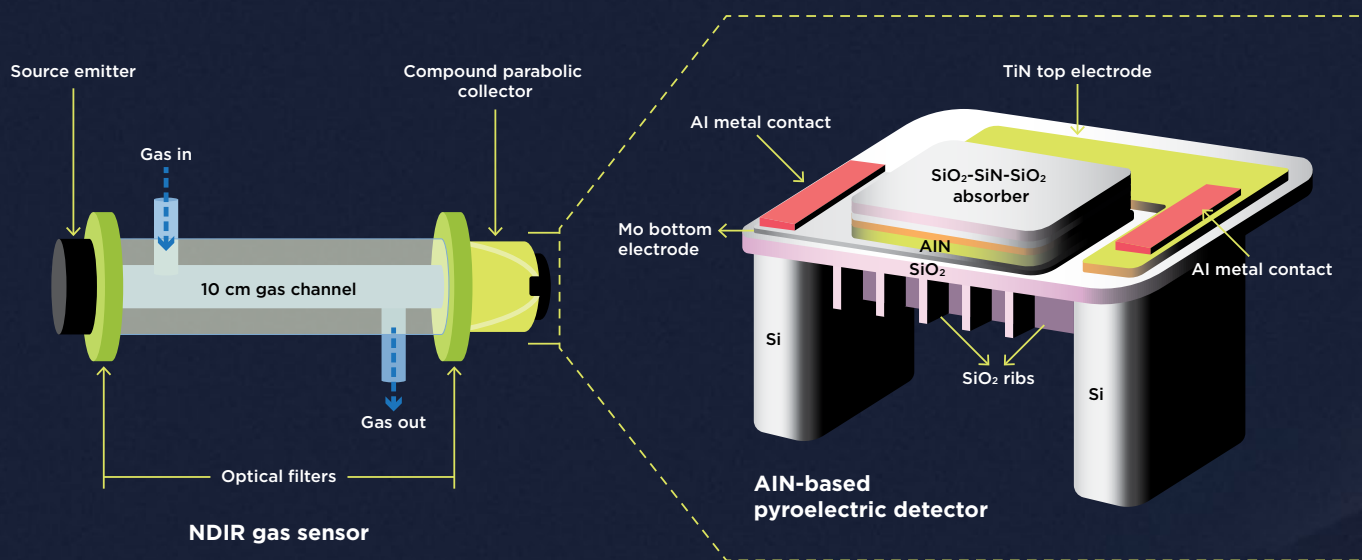
That said, it's challenging to monitor GHGs such as carbon dioxide (CO_2) and methane (CH_4) accurately—they are present at very low concentrations and their atmospheric levels can vary widely based on environmental conditions,

requiring advanced sensor technologies to track them consistently, Ng explained.

In some cases, Ng added, it may even be a life-or-death situation. "A lot of gases are toxic, flammable and explosive, but odourless," said Ng. Here, detectors that use complementary metal-oxide-semiconductor (CMOS) electronics may be advantageous as they can pick up gas concentrations rapidly, work well indoors and have low energy requirements.

In their study, Ng and colleagues developed pyroelectric detector technologies using CMOS-compatible aluminium nitride (AlN) and scandium aluminium nitride (ScAlN). Pyroelectric detectors operate on the principle of pyroelectricity, where subtle changes in temperature (when infrared light passes through a sample of gas) generate warning signals.

The researchers tested the ability of their AlN- and ScAlN-based sensors to monitor indoor air quality and ensure safety in environments prone to high CO_2 and CH_4 levels. They also integrated a compound parabolic collector into the



A schematic of the nondispersive infrared (NDIR) gas sensor prototype and its configuration. The aluminium nitride (AlN) pyroelectric sensing layer can be replaced with 12% scandium AlN (ScAlN), a doped counterpart which retains its magnetic properties at higher temperatures.

“Sensing is the first step before mitigation can come into play. We need to monitor greenhouse gases and identify areas where there are increased emissions before we can come up with plans to protect the environment.”

Photo credit: Yogesh Phuyal / Unsplash

gas sensor of the device as a means of amplifying the signal.

Testing revealed that the ScAlN detectors demonstrated superior sensitivity over the AlN-based ones, with a 40 percent increase in voltage. The detectors responded to CO₂ concentrations as low as 100 ppm and had response times of about one second, making them much faster than commercially available detectors.

CMOS-compatible pyroelectric thin films for gas sensing can make cost-effective detector technologies more widely accessible in a range of industrial settings. Additionally, the team hopes that these promising results might inspire further advancements in the field, particularly around enhancing sensitivity and shrinking detectors while maintaining high performance.

For now, Ng and team are building a prototype of their detector and working on miniaturising the sensor onto a chip.

“We’re looking at building multi-gas sensors, where we try to integrate sensors for multiple gases into a single sensor. We’re also talking to different end users across industries to integrate our sensors into their systems,” said Ng. ★

Researcher

Doris Ng,
IME



IN BRIEF

New complementary metal-oxide semiconductor electronic sensors use infrared light to quickly and accurately detect changes in carbon dioxide and methane gases in indoor settings.

1. Ng, D.K.T., Xu, L., Fu, Y.H., Chen, W., Ho, C.P., *et al.* CMOS AlN and ScAlN pyroelectric detectors with optical enhancement for detection of CO₂ and CH₄ gases. *Advanced Electronic Materials* **9** (8), 2300256 (2023).

CATALYSIS

Atomic secrets of a green plastic catalyst

New high-resolution chemical insights reveal novel opportunities for making plastic production greener, more cost-effective and more efficient.



Avoiding plastics altogether is a more sustainable choice, but given the pervasiveness of fossil-fuel derived plastics in our everyday lives, it's a tough ask.

Wen-Qing Li, a Research Scientist at A*STAR's Institute of High Performance Computing (IHPC), gave the example of light olefins such as ethylene. A simple molecule often derived from petroleum or natural gas, ethylene can be found in applications that include packaging, textiles and automotive components.

Thankfully, there are cleaner options to make light olefins from. Organic food waste and sewage produce hydrogen and carbon monoxide as they decompose. Known as syngas, this mixture can be transformed into light olefins via specific catalyst-driven chemical reactions.

Sustainability research efforts are currently centred on optimising syngas-to-light olefin reactions by boosting efficiency and preventing the release of unwanted by-products such as methane.

Li and Jia Zhang, the corresponding author of the study, noted that finding the best catalysts for these reactions can have far-reaching industry benefits: "Companies with optimised ethylene production processes can operate more cost-effectively and improve product quality, giving them a competitive edge in the market."

Teaming up with collaborators from A*STAR's Institute of Sustainability for Chemicals, Energy and Environment (ISCE²), Li and colleagues studied subtle and relatively unexplored chemical changes

in iron carbide catalysts and how these impacted ethylene formation reactions.

Taking an out-of-the-box experimental approach, the researchers used density functional theory simulations to examine the chemical dynamics on the surface of iron carbide at a high resolution. They were particularly interested in the hydrogenation and mobility of surface carbon atoms during ethylene formation.

The study revealed unprecedented insights into the intricate catalytic processes involved, including the observation that increasing the positive charge of iron atoms enhances their activity and selectivity for ethylene formation over methane. Li and colleagues also discovered that the movement of partially hydrogenated carbon intermediates on the iron carbide surface improved the overall reaction efficiency.

Li said that these findings contribute to broader efforts in making chemical processes more sustainable and less dependent on fossil fuels. Given the complex reaction scenarios on the iron carbide surface, the team has planned extended simulations which will incorporate advanced computational techniques to delve deeper into the catalyst's reaction behaviours. ★



Researchers
Wen-Qing Li and Jia Zhang,
IHPC

IN BRIEF

Using advanced computational simulations, A*STAR researchers unravelled the intricate mechanisms of iron carbide catalysts to enable sustainable and efficient ethylene production workflows for plastic synthesis.

1. Li, W.-Q., Arce-Ramos, J.M., Sullivan, M.B., Poh, C.K., Chen, L., *et al.* Mechanistic insights into selective ethylene formation on the γ -Fe₅C₂ (510) surface. *Journal of Catalysis* **421**, 185-193 (2023).

BIOCHEMICAL ENGINEERING

Manufacturing nature's sweet smells

In a breakthrough study, researchers identify how an enzyme found in fungi produces a natural chemical commonly used in cosmetics, fragrances and medicines.

Alongside visual cues like bright colours, plants send sweet-smelling signals to keep their 'friends' close—scented organic chemicals called terpenoids attract pollinators such as bees and butterflies. These fragrant molecules are also used extensively in a range of commercial processes from drug development and food flavourings to cosmetics and perfumery.

Congqiang Zhang, a Principal Investigator at A*STAR's Singapore Institute of Food and Biotechnology Innovation (SIFBI), said that manufacturing terpenoids requires the use of terpene synthases (TPSes). These elusive enzymes are known to produce terpene scaffolds, which can be further diversified to a catalogue of around 200,000 different terpenoids.

"The products of tens of thousands of TPSes are still unknown, particularly the fungal ones," explained Zhang, adding that this is largely because characterising terpenoids structurally is time-consuming and expensive, a process that requires specialised analytical technologies.

However, overcoming these barriers holds enormous commercial value. "With a deep mechanistic understanding of TPSes, we can eventually predict their main products without extensive experiments, enabling us to engineer next-generation, high-efficiency TPSes for specific terpenoid products," said Zhang.

In collaboration with researchers from CNRS@CREATE and the National

University of Singapore, Zhang's team investigated the crystal structure of a TPS called fungal linalool synthase. This enzyme is known to produce linalool: a natural terpenoid with a lavender fragrance and strong antibacterial properties routinely used in shampoos and soaps.

The team performed a battery of tests to identify key regions and amino acids that influenced fungal linalool synthase's specificity. They zeroed in on a specific amino acid called Tyr299, which dictated whether the enzyme produced linear or ring-

shaped cyclic terpenoids, and discovered that altering Tyr299 resulted in the enzyme shifting its production of linalool to longer, chain-like terpenoid products.

Zhang said that this is the first report of a crystal structure for a fungal monoterpene synthase, which adds to a very limited set of fully characterised TPSes of microbial origin. "Therefore, this study provides an important template to model other uncharacterised microbial terpene synthases in nature," said Zhang.

The study offers fresh insights on how TPS structural features govern product specificity. Its findings open up the prospect of creating customised enzymes with targeted functions for multiple natural product synthesis applications. According to Zhang, the team is optimising other aspects of linalool bioproduction and have filed patents to commercialise the use of their innovative TPS technology. ★



Researchers

Congqiang Zhang and Rehka T.,
SIFBI

IN BRIEF

Alterations in the amino acid sequence of fungal linalool synthase influence the enzyme's terpenoid end-product, offering a strategic blueprint for bioengineering more targeted and efficient terpene synthases for use in a wide range of industrial applications.

1. T. R., Sharma, D., Lin, F., Choong, Y.K., Lim, C., *et al.* Structural understanding of fungal terpene synthases for the formation of linear or cyclic terpene products. *ACS Catalysis* **13** (7), 4949–4959 (2023).

"This study provides an important template to model other uncharacterised microbial terpene synthases in nature."



ARTIFICIAL INTELLIGENCE

Robots gracefully weave through the crowds

A new machine learning framework helps train robots to safely navigate around pedestrians in crowded, real-world settings.

Navigating crowded public spaces at peak hours can sometimes feel like a frustrating maze, where every step forward is met with obstacles of bustling, unyielding people. If this is already challenging enough for humans, imagine its magnitude for robots.

Predicting the future path or movement of objects, or trajectory forecasting, is thus a critical in-built mechanism for robots designed to operate autonomously in dynamic, real-world settings.

“Predicting accurately where pedestrians will move helps robots to navigate in crowded areas without colliding into humans, and to maintain their personal space,” explained Niraj Bhujel, a Research Scientist at A*STAR’s Institute for Infocomm Research (I²R). Additionally, robots equipped with trajectory forecasting can navigate more efficiently by planning a path that side-steps obstacles to minimise delays.

“Predicting accurately where pedestrians will move helps robots to navigate in crowded areas without colliding into humans, and to maintain their personal space.”

Graph Convolutional Networks, or GCNs, have emerged as powerful machine learning (ML) tools for programming trajectory forecasting in complex, highly dynamic environments. GCNs essentially give robots spatial awareness, but they are known to lack accuracy for predicting the future behaviour of moving objects in unfamiliar settings.

Bhujel and I²R colleague, Wei-Yun Yau, hypothesised that breaking crowd interaction data down into spatial and temporal factors can help next-generation ML models achieve more precise forecasting of the trajectory of pedestrians.

Their work led to the Disentangled Graph Convolutional Network (DGCN) which features neural message passing, a way to share and process information between different nodes in a network. When a node receives a message from its neighbours, it combines that message with its own data to get a high-resolution picture of the robot’s surroundings.

“Such combinations provide a special lens to the model that shows where humans are and how they change their actions over

time and space,” said Bhujel, adding that the DGCN’s initial prediction is also frequently corrected to improve the reliability of the final prediction.

This innovative approach paid off, with validation data demonstrating that the DGCN showed superior accuracy at a range of prediction horizons compared to conventional GCNs. They also found that the model can effectively account for the influence of pedestrians or vehicles within a radius of up to eight metres without any loss of performance.

Building on a positive momentum, Bhujel and team are currently working to answer unsolved questions on how to computationally capture an individual person’s movement intention in crowded places. Together, these advancements have the potential to enhance the efficiency and safety of autonomous navigation systems as a means of integrating robots into human-centric spaces. ★



Researchers

Niraj Bhujel and Wei-Yun Yau,
I²R

IN BRIEF

The Disentangled Graph Convolutional Network (DGCN) model significantly improves the accuracy of trajectory forecasting in congested environments by effectively encoding and disentangling spatial and temporal interactions between robots and moving objects.

1. Bhujel, N. and Yau, W.-Y. Disentangling crowd interactions for pedestrians trajectory prediction. *IEEE Robotics and Automation Letters* **8** (5), 3078-3085 (2023).

Photo credit: Freepik / Freepik

ELECTRONIC MATERIALS

Smooth operators: high-performance semiconductors for nanoelectronics

Researchers pioneer new pathways towards miniaturised electronics with a scalable, high-efficiency liquid-printing technology for semiconductor manufacturing.

Mobile phones have undergone a remarkable evolution from the bulky bricks of the 1980s to today's sleek, palm-sized powerhouses. Two-dimensional semiconductors have been the backbone behind this miniaturisation. These ultrathin materials can be used to shrink complementary metal-oxide semiconductor circuits, enabling them to power a kaleidoscope of efficient, high-performance nanoelectronics.

However, experts say materials currently being used to fabricate 2D semiconductor materials have reached a tipping point. Without scalable high- κ dielectrics (insulating materials with the ability to hold an electric charge), the full potential of 2D semiconductors remains untapped.

"When such insulators are integrated with 2D semiconductors, they often lead to defective films, resulting in slow devices that waste energy," said Aaron Lau, a Senior Scientist and Emerging Group Leader at A*STAR's Institute of Materials Research and Engineering (IMRE). "Furthermore, traditional methods of combining the two components can cause physical damage, leading to device failure."

Lau and IMRE colleagues collaborated with Michel Bosman from the National University of Singapore and Ang Yee Sin from the Singapore University of Technology and Design to explore ways of packing more electronic performance into tinier gadgets.

To achieve this, they developed a new liquid-metal printing technique for gallium oxide (Ga_2O_3), a semiconductor-compatible high- κ dielectric material ideal for advanced electronic applications.

"The unique advantage of liquid metals is their ability to coat surfaces like paint, creating a dielectric layer that conforms perfectly to the semiconductor beneath it," said Lau, adding that the smoothness of the Ga_2O_3 layer is critical for enhancing the performance and reliability of electronic devices.

"This essentially allows the liquid metal to fill any nanometre-sized gaps and avoid bubbles," Lau added.

Their liquid-metal printing technology achieved incredibly thin and uniform Ga_2O_3 layers, coupled with cutting-edge scalability. "If the film had the thickness of a human hair, we could print it over an area roughly the size of a tennis court, and its

thickness while the thickness would not vary by more than 10 percent," said Lau.

The team's novel semiconductor also achieved low subthreshold swings and gate leakage currents, properties which can translate to compact, super-efficient transistors of the future.

Lau's team is eager to explore the synthesis of other oxides using their novel approach and to investigate its potential computing applications such as quantum-information processing. "This could pave the way for 2D semiconductor-based quantum computers, a thrilling prospect that drives our research forward." ★



Researchers

Aaron Lau and Johnson Goh,
IMRE

IN BRIEF

Liquid-metal printed high- κ gallium oxide films achieved atomically smooth interfaces to enhance the efficiency and miniaturisation of two-dimensional semiconductor devices.

1. Zhang, Y., Venkatakrishnan, D., Bosman, M., Fu, W., Das, S., *et al.* Liquid-metal-printed ultrathin oxides for atomically smooth 2D material heterostructures. *ACS Nano*, **17** (8), 7929–7939 (2023).

CLEARING OUT THE DUST

By tracing the molecular pathways affected by a key ingredient in airborne particulates, Rachel Phua is trying to understand how polluted air alters our skin.

Across societies, there's a certain cultural cachet to having the 'ideal' skin. Though what we think of as an appealing tone or texture can depend on where we come from, many beauty-conscious people keep an eye on a common group of factors known to affect the quality of their skin, ranging from sun exposure to dietary choices.

As more of us live in urban environments, however, there's another factor that can take a noticeable toll on skin quality: air pollution. Often consisting of particulate matter (PM)—a blend of microscopic solids like soot, or liquid droplets of various chemicals—air pollutants have been reportedly linked to various skin disorders, including changes in skin pigmentation.

Part of the problem is that PM can be tiny enough to seep under the skin through hair follicles or sweat ducts. PM also often includes polycyclic aromatic hydrocarbons (PAHs), which can trigger our skin cells to produce reactive oxygen species: chemicals that accelerate features of ageing skin, and alter the pattern of pigments it creates.

Many mysteries remain about the precise mechanisms by which PAHs trigger the molecular pathways of pigmentation. Treading through this unexplored realm, A*STAR Graduate Scholar Rachel Phua is among a community of young researchers working to answer some of the basic questions involved.

In this interview with *A*STAR Research*, Phua reviews her 'skin-deep' fascination with the human body's largest organ and its impact on her scientific journey, and provides us with a glimpse into her current work and findings to date.

Q: AS A SELF-DESCRIBED 'BIOLOGY HOME-GIRL', WHAT DRIVES YOUR PASSION FOR THE SUBJECT?

My fascination with science began in adolescence, driven by a curiosity about natural phenomena. Watching science programmes inspired me to delve into questions about the world, and ultimately led me to choose the science stream in school. I thrived in laboratories, relishing in running experiments and finding satisfaction in observable results.

What fuels my passion for biology is the scientist's innate drive to comprehend and solve mysteries. The knowledge of an unknown waiting to be discovered motivates me, instigating a perpetual curiosity that keeps me dedicated to the field.

Q: TELL US ABOUT YOUR JOURNEY AS A YOUNG RESEARCHER.

I earned my bachelor's degree in biomedical science from the National University of Singapore. During that period, I immersed myself in diverse research projects, such as designing a synthetic eukaryotic genome (Sc 2.0) and investigating toxins in the venom of the green mamba snake. These experiences not only ignited a love for research in me, but also taught me the value of perseverance amid challenges and setbacks.

After graduating, I sought to refine my skills in molecular biology and joined Carlos Clavel's team at A*STAR Skin Research Labs (A*SRL), which is a member of the Skin Research Institute of Singapore (SRIS). My work there focused on an industry project that explored the impact of air pollution on skin pigmentation.

Upon its completion, I found myself still grappling with lingering questions about the underlying mechanisms involved in how our skin reacts to pollutants. To answer them, I decided to pursue a PhD at Nanyang Technological University's Lee Kong Chian School of Medicine, with the support of the A*STAR Graduate Scholarship.

“While many acknowledge that air pollution can darken the skin and are willing to invest in skincare products and measures to counter this effect, the precise molecular mechanisms behind this process remain largely elusive; there are significant research gaps in this area.”

— Rachel Phua, A*STAR Graduate Scholar

Q: HOW HAS A*STAR SUPPORTED YOUR SCIENTIFIC JOURNEY?

Applying for the A*STAR Graduate Scholarship felt instinctive; it offered me the opportunity to collaborate with a dynamic and innovative team dedicated to advancing science and pioneering groundbreaking technologies. A*STAR's unique approach in bridging academia and industry resonated with me. It provided me with opportunities to attend conferences, interact with industry professionals and foster meaningful connections in the field.

Q: WHY EXAMINE THE LINKS BETWEEN SKIN AND AIR POLLUTION?

You could say my initial interest in this field was thanks to a 'skin-deep' fascination. Our skin often holds immense societal significance as it's closely tied to the concept of beauty, particularly as it relates to women. It's also the largest organ of the human body and the first line of defence against environmental insults—like chemical and physical pollutants in the air around us.

While many acknowledge that air pollution can darken the skin and are willing to invest in skincare products and measures to counter this effect, the precise molecular mechanisms behind this process remain largely elusive; there are significant research gaps in this area. In my view, it's crucial to obtain a fundamental understanding of how air pollutants affect pigment production and transfer cycles before we can identify the optimal compounds to block or reverse this effect.

My ultimate goal is to better understand these molecular mechanisms and potentially identify their related optimal compounds, which will hopefully add valuable insights to the field of skincare research.



Rachel Phua

A*STAR Graduate Scholar



**Q: CAN YOU TELL US
ABOUT YOUR CURRENT
WORK AT A*STAR?**

As part of my PhD studies, I am exploring how polycyclic aromatic hydrocarbons (PAH), a major component of PM, affect our skin's pigmentation. Employing a combination of 2D, 3D *in vitro* and *in vivo* methods, as well as downstream assays, I am rigorously testing my hypothesis, which is that PAH causes an increase in pigmentation.

Our preliminary data not only indicates a direct correlation between PAH and pigmentation, but also hints at a novel molecular mechanism that hasn't been previously studied. Our work is progressively unveiling more details about it, which is a development I find very exciting.

Earlier this year, my colleagues and I also achieved a significant milestone by publishing a manuscript in *STAR Protocols*, where we discussed our work on the *in vitro* quantification of pigment production and transfer in 2D co-cultures and 3D skin organotypic models. This project was a long-standing endeavour fuelled by our determination to find an unbiased method for quantifying pigment production and transfer.

**Q: WHAT ADVICE WOULD YOU
SHARE WITH YOUNG STEM
RESEARCHERS?**

When applying for my PhD degree, a senior student in the lab emphasised the importance of inherent passion and dedication to your subject. This passion has been my driving force during challenging times. I credit much of my progress to the supervision and support of my mentor, who not only encouraged my active participation in talks, seminars, and conferences but also facilitated engaging discussions with fellow professionals.

I firmly believe that aspiring young talents in STEM fields should seek a supportive and nurturing lab environment. The invaluable assistance from my seniors has been pivotal throughout my journey; they continue to support me every day. I am profoundly grateful to them for contributing to my research journey. I hope that everyone pursuing an academic degree finds mentors and peers like them. ★

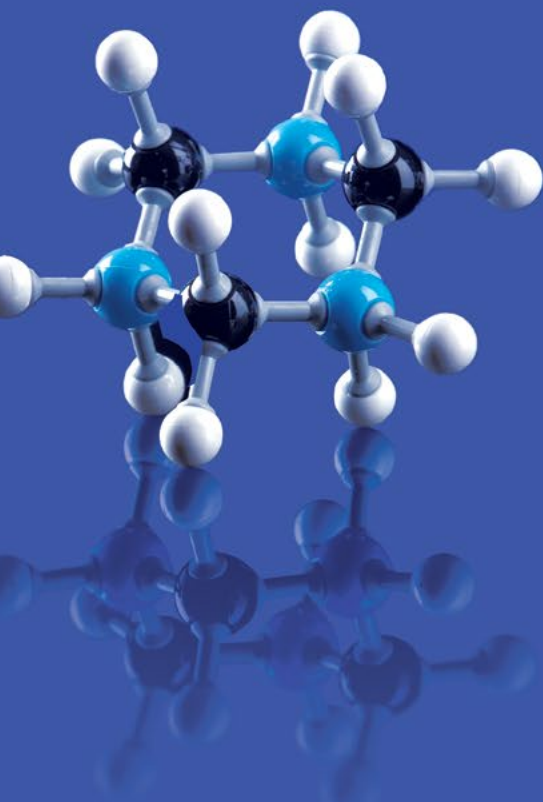
CHEMICAL ENGINEERING

Picking the perfect mirror image

In a medicinal chemistry breakthrough, researchers develop a precise and efficient method of creating chiral sulfones for safe and effective medicines.

Like modern-day alchemists, medicinal chemists use the ‘magical’ chemical properties of compounds to transform them into safe and effective treatments. Sometimes, a molecule’s mirror image (or its chiral counterpart) can hold the secret to unlocking its full therapeutic potential.

For instance, the two different forms, or enantiomers, of chiral sulfones can exert very different effects in biological systems. Used as building blocks for bioactive compounds, chiral sulfones hold the potential to treat an extensive array of diseases, from breast cancer to tuberculosis.



Unsurprisingly, chiral sulfone synthesis has garnered extensive research attention, especially around innovations that can enhance the efficiency and selectivity of producing specific enantiomers.

“We wanted to develop a new method that overcomes the limitations of current strategies, particularly the challenge of precisely functionalising complex sulfone-based molecules,” said Xinglong Zhang, a Scientist at A*STAR’s Institute of High Performance Computing (IHPC). “The method also broadens the range of substrates we can use, providing chemists with a new tool for synthesising these compounds.”

Together with researchers from Guizhou University, China and Nanyang Technological University, Singapore, Zhang employed a catalyst called N-heterocyclic carbene (NHC) in the hopes of developing a novel, efficient and selective method for attaching sulfone groups to organic molecules located at a distance from the catalyst’s substrate reaction site.

“For long-range spatial control, we need a carbene catalyst that can extend beyond its immediate reactive centre, which requires thought on the desired features of carbene catalysts,” said Zhang.

The team explored NHC-catalysed reactions between two groups of molecules (enone aryl aldehydes and sulfonyl chlorides), identifying the conditions and substrates required for optimal chiral sulfone synthesis.

The team leveraged advanced modelling techniques such as density functional theory (DFT) simulations to pinpoint the reaction’s critical transition states and deduce the most probable mechanistic pathways.

“Our computational tools helped identify the unusual key intermediate from the catalytic cycle, which was eventually captured experimentally by high-resolution mass spectroscopy (HRMS),” said Zhang. “The computational insights we gained were instrumental in determining the rate-limiting steps and unravelling the key molecular underpinnings governing the reaction’s enantioselective outcome.”

Ultimately, this approach led to the successful development of a new highly enantioselective method for chiral sulfone synthesis which produced high yields of a single, specific mirror-image form of the desired chemical. Moving forward, the team aims to delve deeper into the applications of this novel mode of carbene activation.

“From a computational point of view, we want to further investigate and understand the detailed mechanisms behind such sulfonylation reactions, such as how bases affect reaction rate and yield,” said Zhang. “From an experimental angle, plans are in place to capitalise on the dual reactivity nature of sulfonyl chlorides and explore the additional usage of such reagents in chemical synthesis and catalysis.” ★

Researcher

Xinglong Zhang,
IHPC



IN BRIEF

Using an N-heterocyclic carbene catalyst, researchers achieved an efficient and highly selective synthesis of chiral sulfones with high enantiomeric purity, pioneering new pathways for pharmaceutical development.

1. Deng, R., Wu, S., Mou, C., Liu, J., Zheng, P., *et al.* Carbene-catalyzed enantioselective sulfonylation of enone aryl aldehydes: a new mode of Breslow intermediate oxidation. *Journal of the American Chemical Society* **144** (12), 5441–5449 (2022).

GREEN ENERGY

Crystals catalyse a clean future

New insights on multi-metal alloy catalysts show how their structural order boosts chemical reaction efficiency in renewable energy systems.

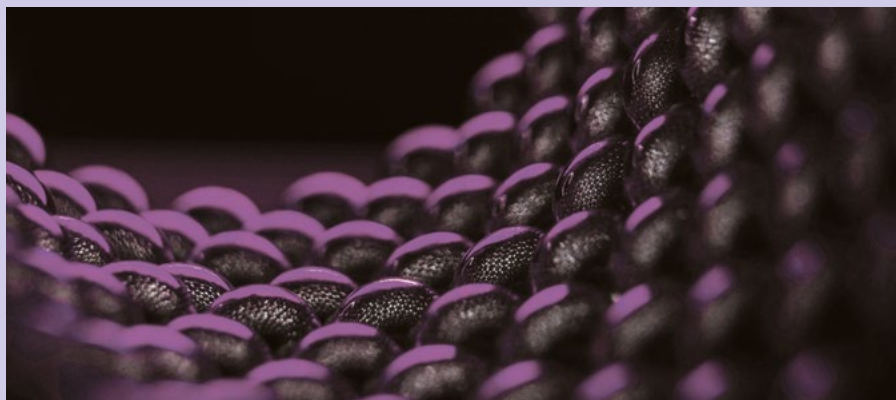
Chemical catalysts are quietly working behind the scenes to speed up essential reactions that drive innovation and production across a wide range of industries. Of these catalysts, multicomponent intermetallics are particularly valued for their capacity to power green technologies like clean-energy systems.

Multicomponent intermetallics are high-entropy alloys (HEAs)—mixtures of metallic elements specifically combined to form distinct crystalline structures—often used as catalysts in fuel cells and electrolyzers that generate electricity from clean sources such as water.

However, scientists have not yet deciphered the optimal arrangement of the metallic elements to maximise their catalytic activity for industrial use. “As a result, the durability of some HEAs, such as those involving platinum, has been a long-standing challenge, affecting their large-scale application,” said Na Gong, a Scientist at A*STAR’s Institute of Materials Research and Engineering (IMRE).

Gong’s team, in partnership with Yong Wang from Nanyang Technological University, Singapore, proposed that having more organised and specific arrangements of the metals within multicomponent intermetallics can ultimately bolster their stability.

The researchers tested their theory using multicomponent intermetallic nanoparticles containing platinum, iron,



“By carefully controlling the temperature and the duration of heating, we were able to fine-tune the degree of orderliness in the alloy.”

cobalt, copper and nickel with varying degrees of ordering.

“The ordering process is driven by atomic diffusion, a phenomenon where atoms move and rearrange themselves,” Gong explained. “By carefully controlling the temperature and the duration of heating, we were able to fine-tune the degree of orderliness in the alloy.”

They analysed their nanoparticle structures and electrocatalytic efficiencies to discover that their approach paid off—the team identified a highly ordered HEA structure that significantly outperformed commercial catalysts in enhancing the oxygen reduction and hydrogen evolution reactions.

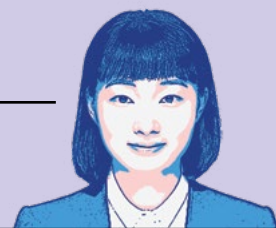
Critically, the study revealed a clear link between the structure (highly

ordered stacking of the individual metal layers) and the resulting electrocatalytic efficiency, providing fresh insights for future catalyst design.

Gong and colleagues hope that these findings will pave new inroads into the development of sustainable energy systems through cost-effective and durable catalysts for fuel cells and electrolyzers.

“To further our research, we are now investigating the application of machine learning in expediting the exploration of alternative high-entropy intermetallics,” said Gong. ★

Researcher
Na Gong,
IMRE



IN BRIEF

Multicomponent intermetallic high-entropy alloys with highly ordered structures outperformed industry standards in catalysing the hydrogen production and oxygen reduction reactions, marking a significant step forward in clean energy catalysis.

1. Wang, Y., Gong, N., Liu, H., Ma, W., Hippalgaonkar, K., et al. Ordering-dependent hydrogen evolution and oxygen reduction electrocatalysis of high-entropy intermetallic Pt₄FeCoCuNi. *Advanced Materials* **35** (28), 2302067 (2023).

INDUSTRIAL AND MANUFACTURING ENGINEERING

Tiny tweaks propel major manufacturing leaps

A breakthrough in 3D-printed manufacturing technologies creates alloys with superior mechanical properties, offering exciting new possibilities for diverse industrial applications.

Industry leaders are abuzz with what the manufacturing future holds thanks to additive manufacturing (AM), an innovative group of technologies that fabricates products with 3D printing processes. “The increasing intrigue surrounding AM technologies stems from their multifaceted potential to revolutionise industries,” said Mojtaba Salehi, a Scientist from A*STAR’s

Singapore Institute of Manufacturing Technology (SIMTech).

In binder jet AM, a liquid binding agent is selectively deposited to join powder particles together, layer by layer, to form a solid object. Salehi explained that compared to other AM techniques, binder jet AM offers unmatched design flexibility; faster, greener and more cost-

effective alloy fabrication processes for high-volume production; as well as the prospective use of novel materials.

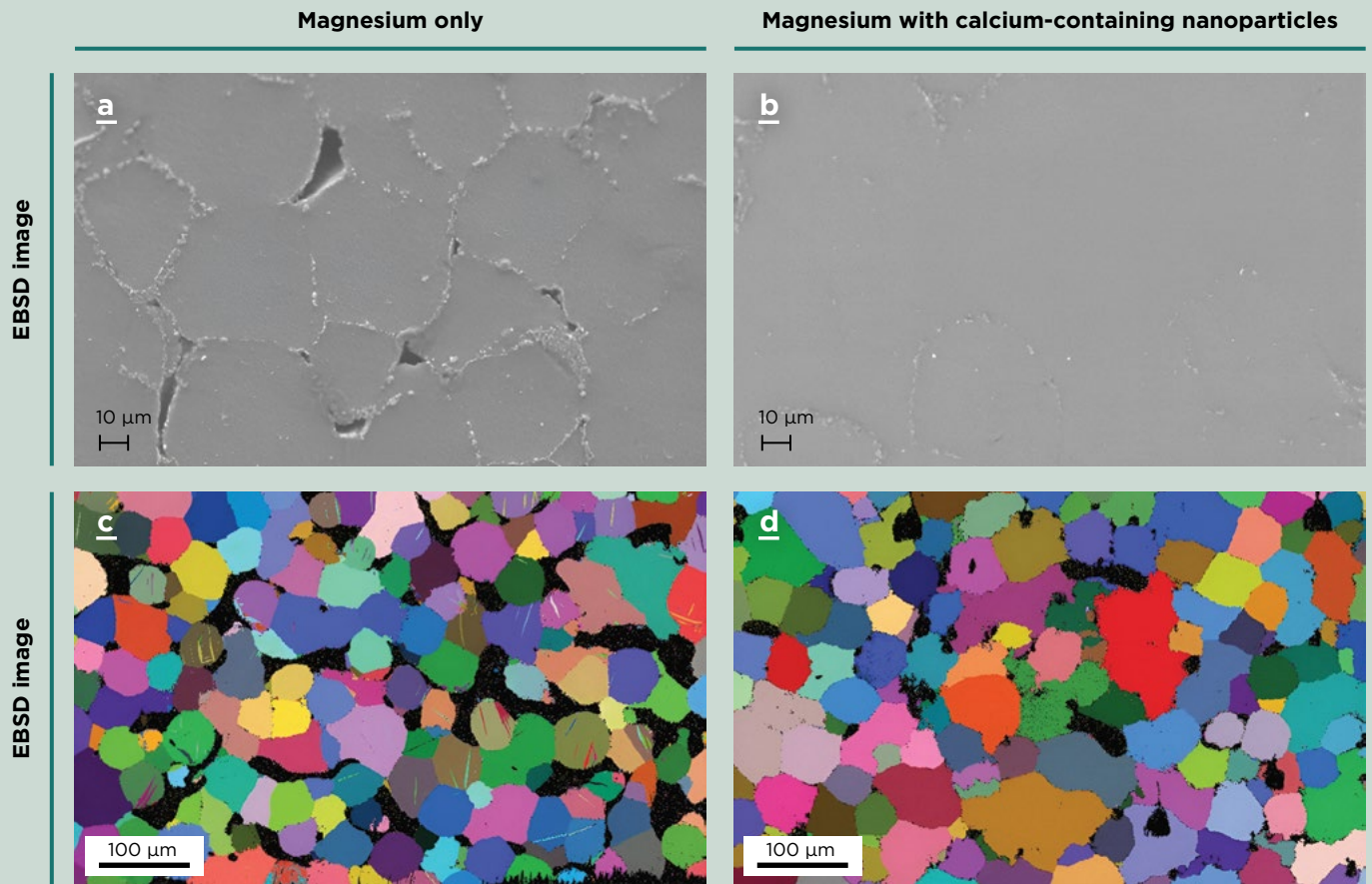
Salehi and team have been investigating the challenges of deploying AM for magnesium metal alloys, used in aerospace and biomedical engineering thanks to their light and biodegradable features. “Each magnesium powder particle used in AM is inherently covered with a magnesium oxide film,” said Salehi, adding that this naturally forming layer acts as a barrier that prevents powder particles from effectively sticking together, thereby weakening the end product.

In their study, the researchers discovered a nano-sized solution to these big engineering obstacles. They found that adding calcium-containing nanoparticles during the binder jet AM process helps to break down the oxide layer on the magnesium powder, allowing particles to fuse strongly and enhance the sintering process.

Samples printed with the addition of these nanoparticles were subjected to

Photo credit: Nordoden / Shutterstock





Micrographs of binder jet-printed and sintered samples of (a, c) a magnesium (Mg) powder feedstock, and (b, d) a blend of Mg and calcium (Ca) nanoparticles. Images were captured via scanning electron microscopy (SEM) and analysed with Electron Backscatter Diffraction (EBSD). Each EBSD colour represents individual Mg grains while black areas represent pores. Circular grains originated from the primary Mg powder, while the irregular grains resulted from Mg particles coalescing together during the sintering process.

a battery of tests including microscopy, chemical analyses and mechanical testing through collaborations with Daniel John Blackwood's laboratory at the National University of Singapore. The team found that calcium-containing nanoparticles boosted densification rates by 25 percent, which translated to impressive gains in strength and flexibility for the magnesium samples produced.

"The resulting physical and mechanical properties can potentially match or exceed those of cast magnesium components," said Salehi, adding that over 95 percent of magnesium components are currently made using traditional casting techniques.

These results highlight how a targeted nano-alloying approach can catalyse innovation across diverse industries.

Salehi and colleagues are currently working on developing denser, stronger and easy-to-manufacture magnesium alloys using AM to support the trend towards customised, on-demand manufacturing in various sectors. ★

"The resulting physical and mechanical properties can potentially match or exceed those of cast magnesium components."



Researchers

Mojtaba Salehi and Sharon Nai,
SIMTech

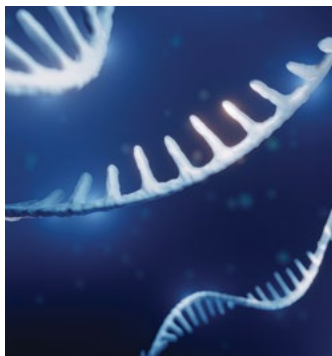
IN BRIEF

Introducing calcium nanoparticles to magnesium powder for binder jet additive manufacturing significantly enhances the physical and mechanical properties of magnesium alloys.

1. Salehi, M., Kuah, K.X., Huang, Z., Blackwood, D.J., Zhang, S.X., *et al.* Enhancing densification in binder jet additive manufacturing of magnesium via nanoparticles as sintering aids. *Journal of Manufacturing Processes* **99** (4), 705-717 (2023).

NEXT ISSUE

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



INFECTIOUS DISEASES **CUTTING IT SHORT FOR RNA VIRUSES**

Gene-editing tools that slice up viral RNA genomes present powerful therapeutic options for untreatable viral infections.



GREEN ENERGY **A CATALYTIC BOOST TO FUEL CELLS**

A novel nanoscale approach to creating palladium catalysts could clear a longstanding roadblock in formic acid fuel cell development.



ARTIFICIAL INTELLIGENCE **AN AI EYE FOR MACHINES PAST PRIME**

Researchers develop an adaptive neural network that predicts the remaining useful life of industrial machine systems.



ORGANIC CHEMISTRY **EXPANDING VIEWS OF NATURE'S CHEMICALS**

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*a**



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Yang Le

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& Music Enthusiast



“

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”

Sean Chia

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