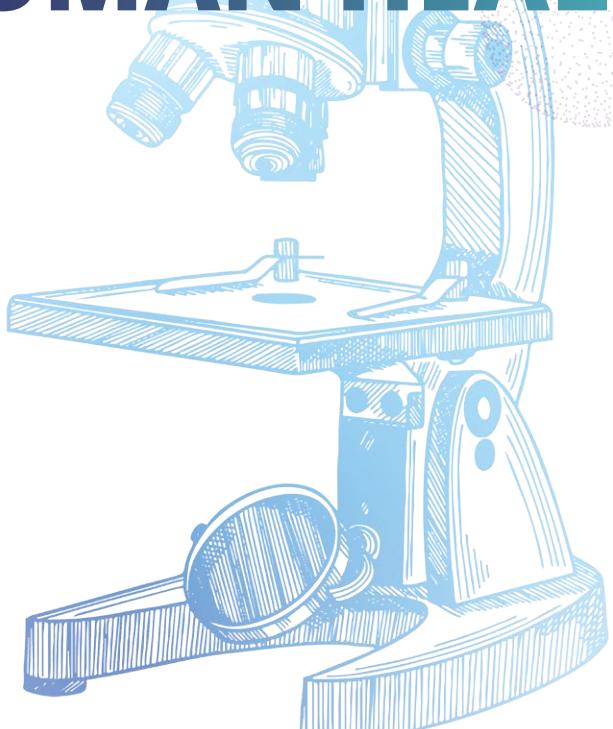
40 A*STAR IMCB ANNIVERSARY

UNLOCKING BIOLOGY TO ADVANCE HUMAN HEALTH



Molecular & Cell Biology the fundamental science fueling innovation understanding cell function the basis of life

Institute of Molecular and Cell Biology
A*STAR IMCB

40 A*STAR IMCB ANNIVERSARY

A*STAR IMCB 40th ANNIVERSARY:

UNLOCKING BIOLOGY TO ADVANCE HUMAN HEALTH

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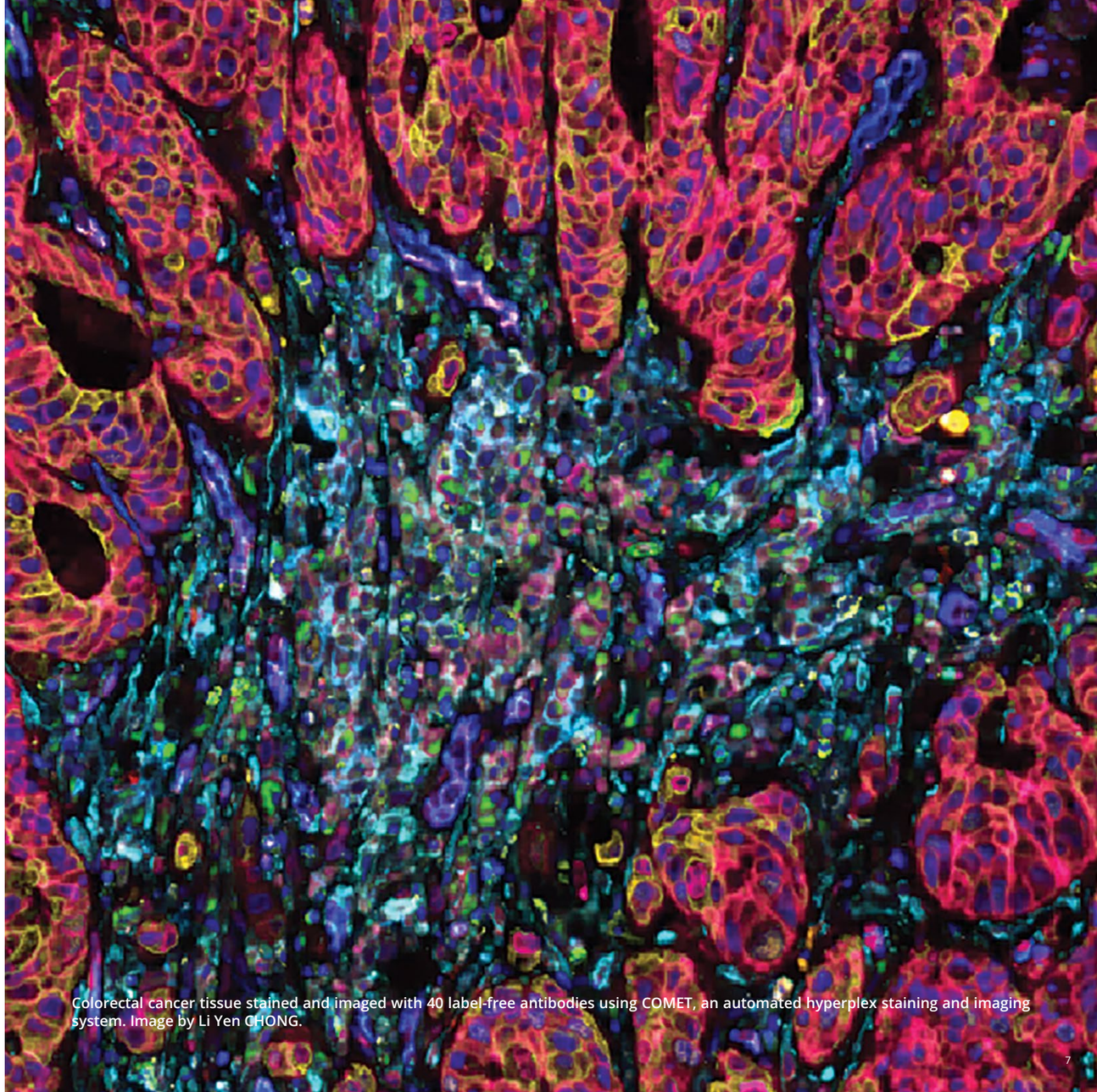


Colorectal cancer tissue stained and imaged with 40 label-free antibodies using COMET, an automated hyperplex staining and imaging system. Image by Li Yen CHONG.

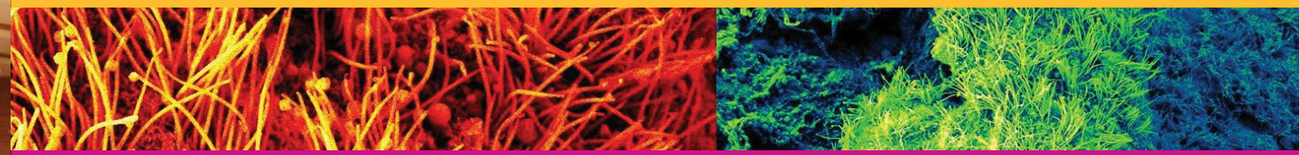
WELCOME NOTES

40 A*STAR IMCB ANNIVERSARY

PIONEERS OF THE PAST

ADVANCING BIOMEDICAL INNOVATIONS

BRIDGING SCIENCE & TECHNOLOGY



OUR PEOPLE, OUR SUCCESS

Professor TAN Chorh Chuan

Chairman,
Agency for Science, Technology and Research (A*STAR)

FOREWORD BY CHAIRMAN

As we commemorate the 40th Anniversary of A*STAR's Institute of Molecular and Cell Biology (A*STAR IMCB), it is a fitting occasion to reflect on IMCB's remarkable journey and many achievements that have shaped Singapore's biomedical sciences ecosystem. Since its establishment in 1985, IMCB has been a trail-blazer, setting the benchmarks for scientific excellence and serving as a major brain-trust and engine for Singapore's ambitious health and biomedical research initiative.

The Singapore Government has long recognised the critical importance of investing in basic research that not only advances scientific knowledge but also has the potential to improve health and contribute to economic value creation. This sustained commitment to basic research has been instrumental in positioning Singapore as a global leader in biomedical sciences research. Strategic investments and initiatives in research, innovation and enterprise have helped foster an environment where cutting-edge discoveries can flourish and be translated into tangible benefits for society.

Looking ahead, IMCB will continue to play a pivotal role in our ongoing biomedical research journey. IMCB's ground-breaking work in elucidating the molecular and cellular mechanisms driving disease biology provides novel insights as well as a strong foundation for discovering novel targets that could result in innovative therapies. In the field of cancer, IMCB's expertise in the study of cancer cell plasticity and resistance can stimulate the development of new strategies to tackle the recurrence of cancer, offering new potential treatment options for patients. In the area of neurobiology, IMCB's research is uncovering the complex interactions between metabolic health and brain health, paving the way for breakthroughs in understanding and treating neurological disorders. The advancements in cell therapy and regenerative medicine, driven by IMCB's pioneering research, offer hope for revolutionary therapeutic approaches that can restore and enhance human health.

As someone who has witnessed the growth and transformation of Singapore's R&D landscape over the past two and a half decades, I am deeply proud of what IMCB has accomplished. IMCB has been fortunate to have had leaders and key supporters of extraordinary vision and ability such as the late Dr Sydney Brenner, Professor Chris Tan and Mr Philip Yeo. The dedication, passion and ingenuity of IMCB's scientists, researchers and staff have been the driving force behind the institute's success. Together, we have built a strong foundation for the future, where IMCB continues to lead the way in

> *"Unlocking Biology to Advance Human Health."*

I would like to express my very heartiest congratulations to the IMCB family, alumni and friends. I am confident that IMCB will continue to thrive and look forward to the many exciting advancements and discoveries that you will make in the years ahead.

MESSAGE FROM CHIEF EXECUTIVE

As we celebrate the 40th anniversary of the A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB), and we reflect on how far we have come — IMCB is not merely an institution, but a symbol of how the nation has embraced the power of science and innovation. IMCB was founded with a bold vision: to position Singapore at the forefront of biomedical research and to nurture homegrown scientific talent. Over the past four decades, it has played a pivotal role as the flagbearer for basic science in transforming Singapore from a nation of technicians to a nation of scientists, laying the foundation for the vibrant biomedical research ecosystem we see today.

Through groundbreaking discoveries — from elucidating the mechanism of protein kinases to pioneering efforts in decoding the fugu genome — it has consistently pushed the boundaries of knowledge. Yet, as we look to the future, our ambition must grow beyond excellence in science. The next phase of our journey calls for us to evolve from a nation of scientists to a nation of scientific entrepreneurs, where deep-tech innovations translate into impactful applications that address global challenges.

IMCB aims to tackle complex scientific challenges of the future — such as healthy ageing, metabolic diseases, neurodegeneration and oncology — through collaborative research which cannot be solved in isolation. These require interdisciplinary, mission-oriented approaches that leverage the collective strengths of our scientific community. IMCB, together with other A*STAR Research Institutes are well placed to tackle these challenges through adopting team science as our modus operandi.

Finally, none of this is possible without the right infrastructure and talent. At BMRC, we look forward to our relocation towards a greater one-north, where we will refresh our research facilities. We do this with one clear purpose: to recruit and retain world-class scientists, engineers, and innovators who will define the next era of biomedical research in Singapore.

IMCB's 40-year journey is a testament to the power of vision, persistence, and collaboration. As we stand on the cusp of the next chapter, let us reaffirm our commitment to excellence in science, translational impact, and an entrepreneurial spirit that will shape the future of Singapore's biomedical ecosystem.

Mr BEH Kian Teik

Chief Executive Officer
Agency for Science, Technology and Research (A*STAR)

Associate Professor SU Xinyi

Executive Director
Institute of Molecular and Cell Biology
(A*STAR IMCB)

MESSAGE FROM EXECUTIVE DIRECTOR

A*STAR IMCB's 40-year journey has been defined by our unwavering commitment to scientific excellence, innovation, and improving human health. This would not be possible without the dedication of our founding members. We are truly fortunate to be standing upon the shoulders of scientific giants such as Professor Sydney Brenner, Professor Chris Tan, Professor Louis Lim, Professor Sir David Lane, and Professor Hong Wanjin. It is through their scientific vision that IMCB was able to transform Singapore into the biomedical research powerhouse that it is today. Hence, it is fitting that IMCB launches our inaugural Alumni Chapter on our 40th anniversary, to recognise and celebrate our alumni.

Looking into the future as IMCB enters the next chapter – it is our vision to continue to push the frontiers of biomedical research, to deepen our engagement with clinicians, and to work closely with our industry partners. At IMCB, we are committed to bridging fundamental research and clinical application, with an eye towards making a lasting impact on human health. This is aptly summarised in our theme for IMCB's 40th Anniversary "Unlocking Biology to Advance Human Health". Building this synergy between bench and bedside is critical, particularly as Singapore faces the challenges of a silver tsunami. Innovative solutions are needed to ensure that Singaporeans not just live a longer life but a more enriching and fulfilling life.

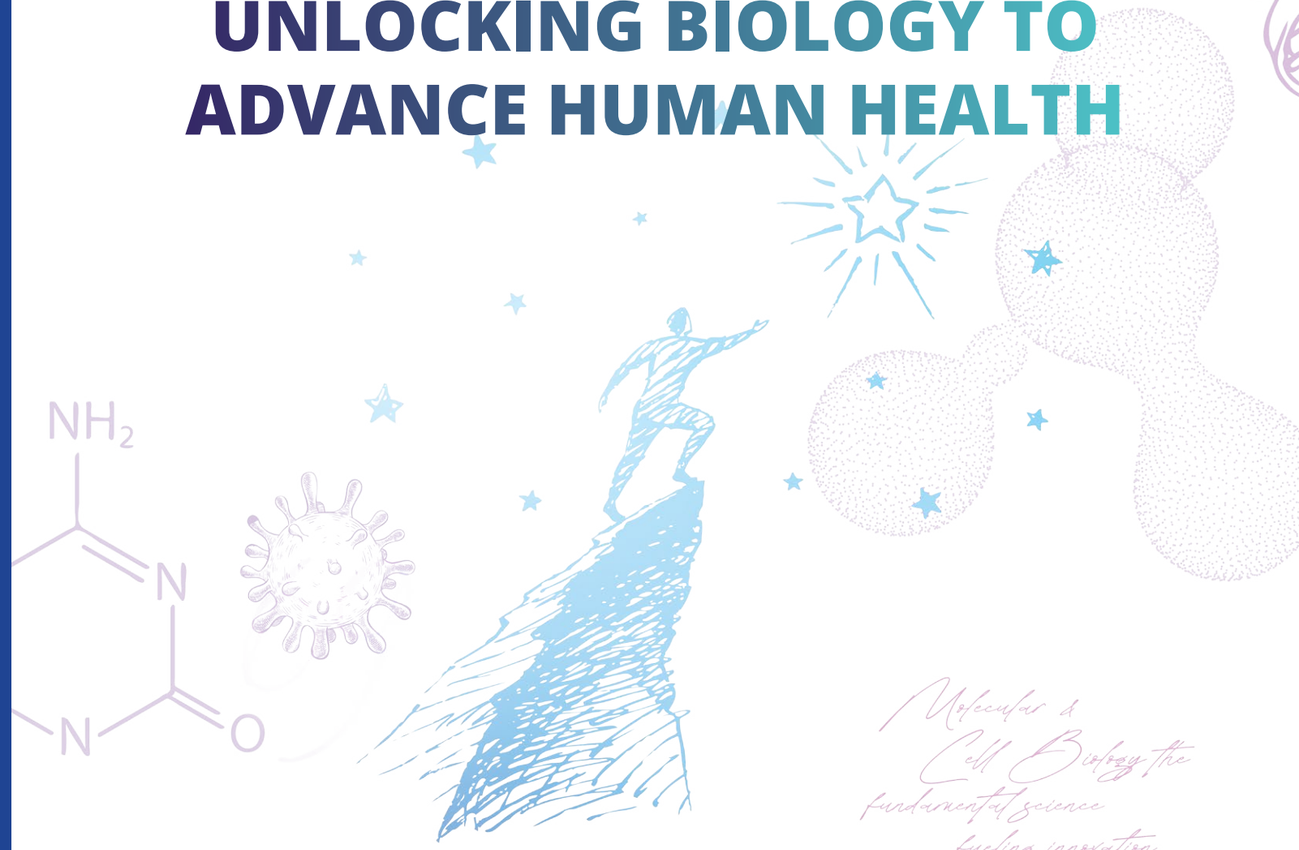
At IMCB, we believe that truly innovative research can only be achieved through inter-disciplinary and collaborative research. This underpins IMCB's approach to create ground-up opportunities for "combine and recombine" to occur between diverse scientific domains and through this, create new frontiers of knowledge. One example of this, is the launch of IMCB Discovery Grants in 2024. IMCB PIs were provided seed funding for exploring completely new, collaborative moon-shot ideas. It is this "can-do" and "risk taking" attitude that we believe is crucial for true scientific breakthroughs. Based on this philosophy, not only will IMCB continue to focus on our current peaks of excellence (i.e. in the areas of regenerative medicine, cancer biology, and neuro-metabolism), we will also build new synergistic programmes in the areas of brain health, neuro-oncology, and immune-cell therapy.

Finally, discoveries cannot change the world if they do not leave the lab. To do this, IMCB is committed to co-create and generate successful biotech spin-offs, in partnership with I&E. These spin-offs will function as receptacles to bring our scientific discoveries into the clinic. This is in line with A*STAR's vision to ensure our research can reach the clinic, impact healthcare, and drive Singapore's economy.

Once again, I would like to extend my deepest gratitude to all who have contributed to IMCB's journey over the 4 decades. May we continue on this journey together - to unlock the secrets of biology, drive medical innovation, and build a healthier future together.

FOLLOW US ON OUR JOURNEY

UNLOCKING BIOLOGY TO ADVANCE HUMAN HEALTH



Molecular & Cell Biology the fundamental science fueling innovation understanding cell function the basis of life

THE IMCB JOURNEY

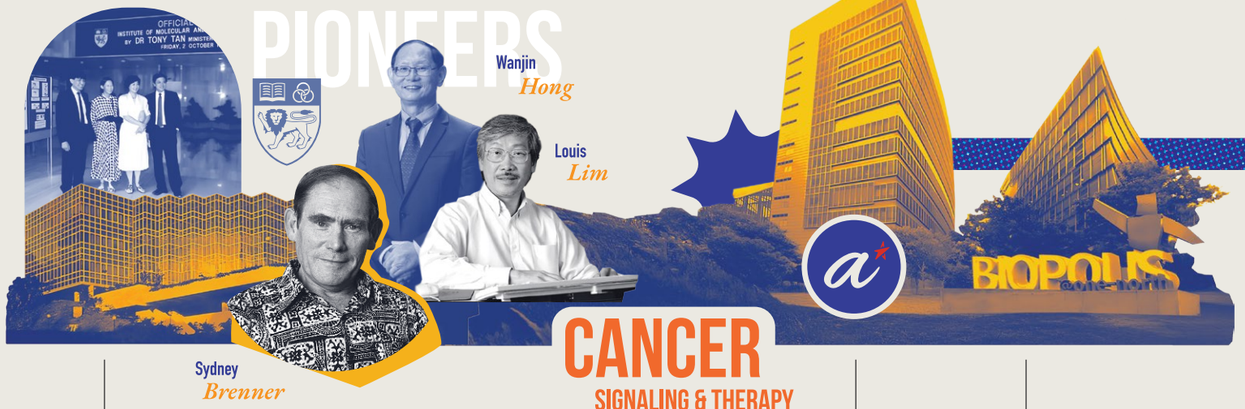
40 YEARS
of Research & Discovery

1985-2000
The Founding of IMCB

2000-2010
Laying the Foundation for Biomedical Research

2010-2020
From Collaboration to Innovation

2020-Present
& Beyond



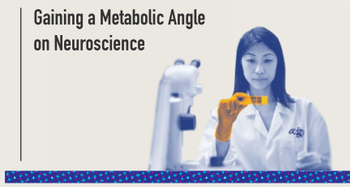
1985
Founding of IMCB
Singapore's first life sciences institute

2002
National Science & Technology Board became Agency for Science, Technology and Research (A*STAR)

2003
IMCB shifted to Biopolis

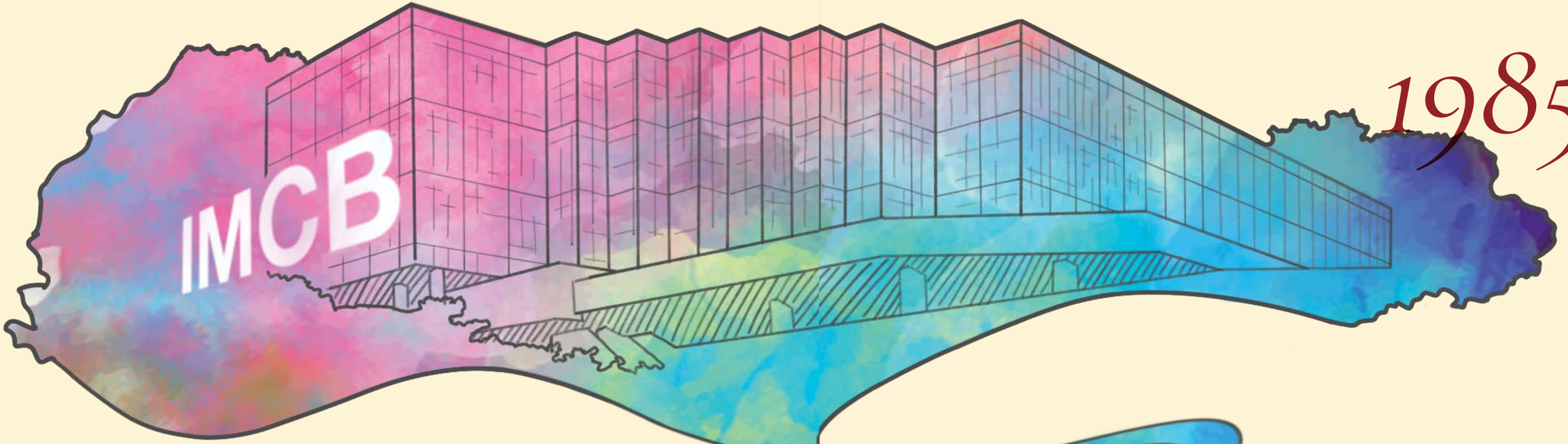
CELL AND MOLECULAR THERAPY

A*STAR/Duke-NUS
Neuroscience Research Partnership



NEUROMETABOLISM

HORIZONTAL TECHNOLOGY PLATFORMS



1985

A CELL-EBRATION OF BEGINNINGS

In 1985, Singapore's **first life sciences institute**, the **Institute of Molecular and Cell Biology**, was founded.

LEGACY TO LEADERSHIP

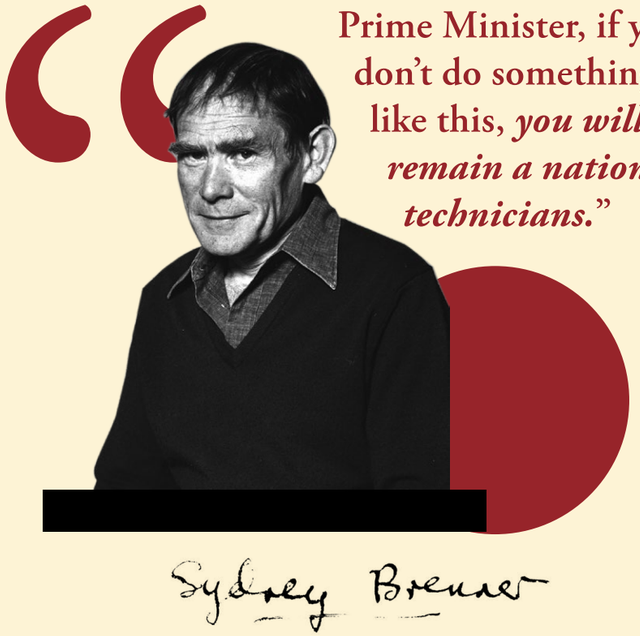
Advancing Singapore's Biomedical Frontier

Approval letter for the establishment of IMCB

In the early 1980s, Singapore sought to level up its economy beyond low-cost manufacturing and establish itself as a knowledge-based and innovation-driven economy. Recognising the potential of biotechnology as a high-value industry, the government saw the need to develop indigenous scientific expertise to support this ambition.

A pivotal moment came in 1984, when the renowned molecular biologist **Sydney BRENNER** was invited to Singapore by then Deputy Prime Minister, **GOH Keng Swee**. During his visit, Brenner met with then Prime Minister **LEE Kuan Yew** and proposed setting up a molecular and cell biology research institute to train Singaporeans at the PhD level, equipping them with the expertise to drive the country's biotechnology sector in addition to placing Singapore onto the global research map in modern biomedical research.

When then Prime Minister LEE remarked that Singapore was a nation of technicians, not scientists, BRENNER famously replied,



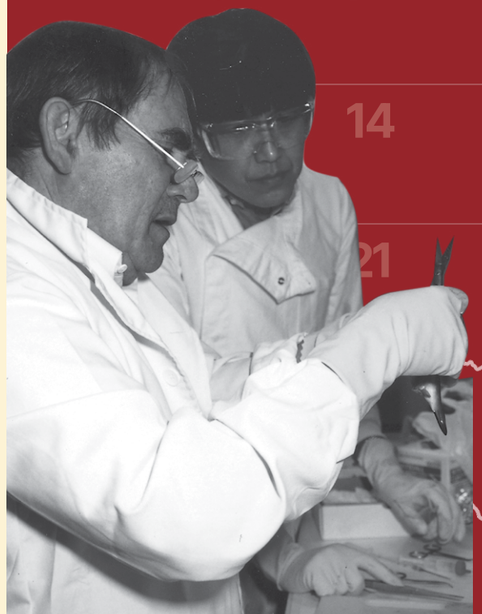
"Prime Minister, if you don't do something like this, *you will remain a nation of technicians.*"

Sydney Brenner

1985 Jan.

the **Institute of Molecular and Cell Biology (IMCB)** was established.

The Institute of Molecular and Cell Biology (IMCB) was established on January 23, 1985, as part of Singapore's nation-building efforts, driven by **GOH Keng Swee** and executed under the visionary leadership of **Philip YEO**. The institute was guided by a distinguished advisory board led by **Sydney BRENNER**, alongside renowned scientists such as **David BALTIMORE, Alice HUANG, Robert GALLO, Louis LIM, CHUA Nam Hai,** and the late **Tony PAWSON**, with **Chris TAN** serving as the founding Director.



For its first 15 years, A*STAR IMCB's success was built on strong governmental and institutional support, particularly **Dr Tony TAN**, then Minister for Education as well as **Prof LIM Pin**, then Vice Chancellor of National University of Singapore (NUS) and its leadership at the time.

The contributions of pioneering scientists such as **Chris TAN, Louis LIM, and Nam-Hai CHUA**, along with the scientific advisory board members, were instrumental in shaping the institute's early research direction and laying the foundation for Singapore's biomedical research ecosystem.

More than just a research institute, **A*STAR IMCB laid the groundwork for Singapore's entire biomedical R&D landscape**, providing the base from which many other research institutions emerged. Its establishment catalysed the growth of a robust scientific ecosystem, enabling the development of world-class research in biomedicine, pharmaceuticals, and translational sciences.

One of A*STAR IMCB's first major industry collaborations came in 1989, when it secured a 15-year research partnership with Glaxo (now GSK) to focus on neurodegenerative diseases. This was a landmark agreement, setting the stage for future collaborations between Singapore's biomedical research sector and multinational pharmaceutical companies.

By 1992, A*STAR IMCB made significant progress in infectious disease research, completing the first sequencing of the Dengue virus genome (Singapore strain S275/90) — a breakthrough that paved the way for further advances in diagnostics and vaccine development.

The 1990s also marked A*STAR IMCB's rise in structural biology and genomics. The institute's expertise culminated in 2002 with the successful sequencing of the fugu (pufferfish) genome, which was published in Science. This research was globally recognised as a milestone in comparative genomics, helping to better understand vertebrate genomes.

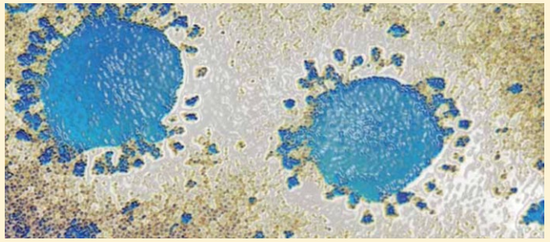

表彰
第5回日経アジア賞
技術開発部門
日本経済新聞社
社長 鶴田卓彦
Nikkei Asian Prize

A National Push for Biomedical Sciences (2000 – 2010)

The turn of the millennium was a defining moment for Singapore's biomedical landscape. In 2000, A*STAR IMCB's contributions were recognised when it was awarded the **5th Nikkei Asia Prize for Technology Innovation**, solidifying its reputation as Asia's first major biological research institute.

That same year, the Singapore government launched the **Biomedical Sciences Initiative (BMSI)** — a bold national strategy to position the country as a global hub for biomedical research. This initiative, masterminded by **Philip YEO**, was developed during an all-night strategy session with three of Singapore's top doctors — **TAN Chorh Chuan, John WONG, and KONG Hwai Loong**. Dubbed the "**biomedical sciences Gang of Four**," this team spearheaded the transformational push that shaped Singapore's leadership in biomedical sciences.

By 2003, A*STAR IMCB took another leap forward by moving to Biopolis, Singapore's premier biomedical research hub. This relocation signified Singapore's commitment to expanding life sciences research into a national priority. That same year, IMCB played a critical role in Singapore's response to the SARS outbreak, rapidly developing two diagnostic kits that were deployed internationally. The ability to translate fundamental research into life-saving solutions demonstrated IMCB's real-world impact, earning the institute a National Day Award for its contributions to infectious disease research.



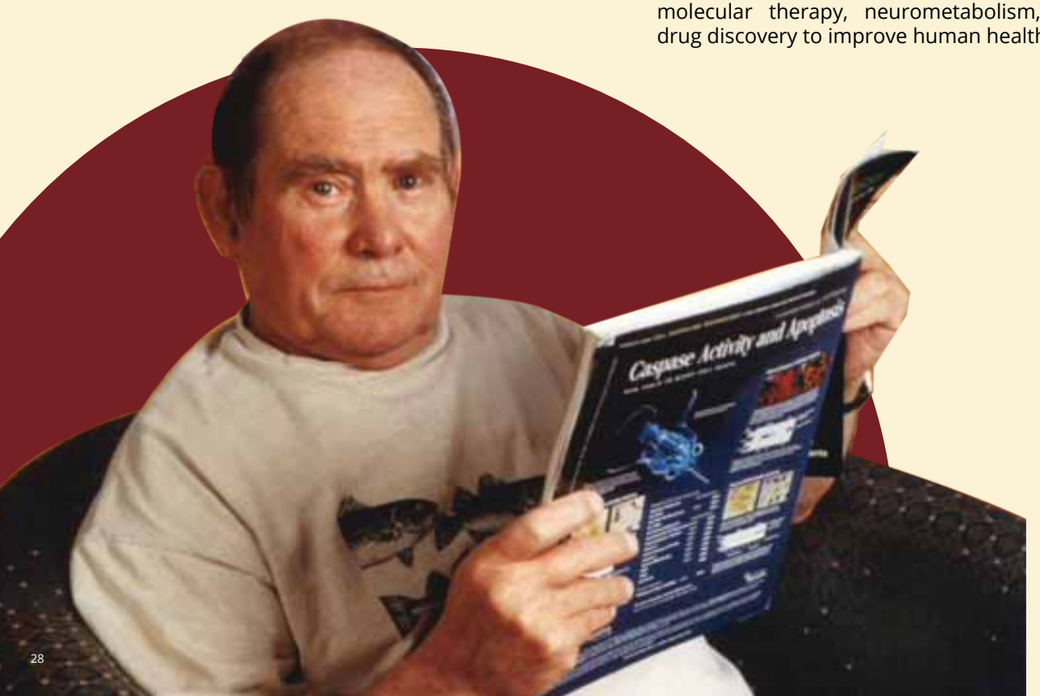
SARS Virus

Under the leadership of **David LANE** from 2004 to 2007, A*STAR IMCB expanded its research focus into cancer biology and translational medicine, leading to groundbreaking discoveries in tumour suppressors and therapeutic development. By 2012, IMCB had strengthened its industry collaborations, working with Johnson & Johnson and Procter & Gamble to advance precision medicine and drug development. That same year, IMCB researchers developed monoclonal antibodies, which were later licensed for commercialisation in diagnostics and therapeutics, further bridging research and industry.

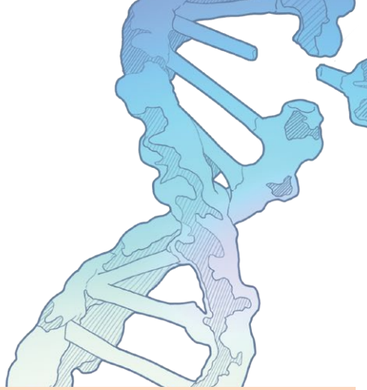
Bridging Science and Industry (2011 – Present)

As A*STAR IMCB's research capabilities grew, so did its impact on Singapore's biotech sector. In 2014, MerLion Pharmaceuticals, an A*STAR IMCB spin-off, became the first Singaporean biotech company to receive FDA approval for an antibacterial drug, Finafloxacin. This milestone validated Singapore's ability to develop homegrown biomedical innovations that could compete on the global stage.

Over the past decade, A*STAR IMCB has continued to build upon its legacy, forging new frontiers and shaping the future of biomedical research from 2014 to 2025. With each milestone, it has expanded its research focus, driving advancements in cancer signaling, cell and molecular therapy, neurometabolism, and AI-driven drug discovery to improve human health worldwide.



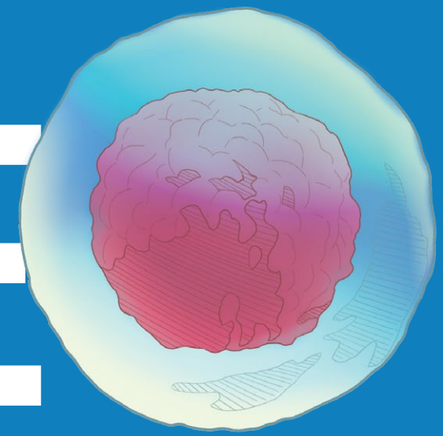
From its bold beginnings in 1985 to its global impact today, A*STAR IMCB remains at the forefront of biomedical innovation, translating fundamental research into real-world applications, including spin-offs that create tangible healthcare impacts. It continues to be a driving force in shaping Singapore's scientific excellence, contributing to breakthrough discoveries, industry collaborations, and the nation's global standing in biomedical research.

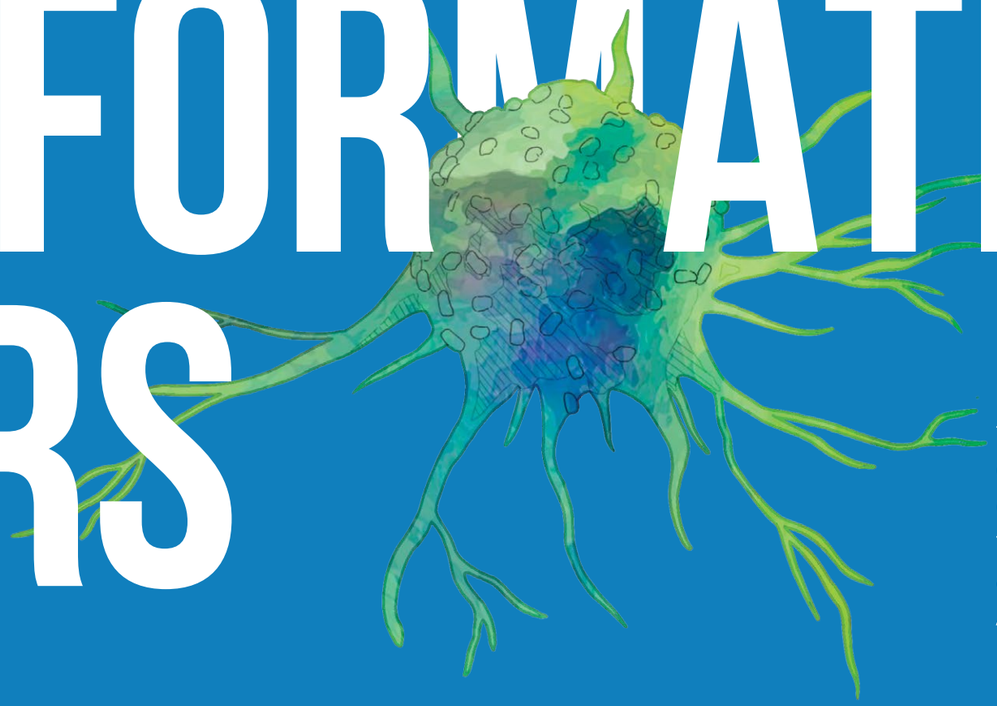


AND HERE IS THE STORY OF OUR JOURNEY OVER THE PAST 40 YEARS.

GENE-ESIS - THE FORMATIVE YEARS

In its formative years, A*STAR IMCB laid the groundwork that shaped Singapore's biomedical research landscape.





Established with the mission of advancing world-class fundamental research, A*STAR IMCB provided an environment where researchers had the freedom to explore groundbreaking scientific questions, as long as they upheld the highest standards of excellence. This approach attracted top minds in the field, establishing A*STAR IMCB as a powerhouse in molecular and cell biology research.

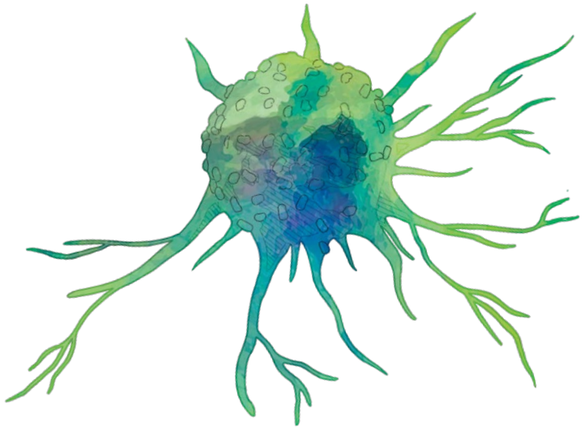
GENE-ESIS : THE FORMATIVE YEARS

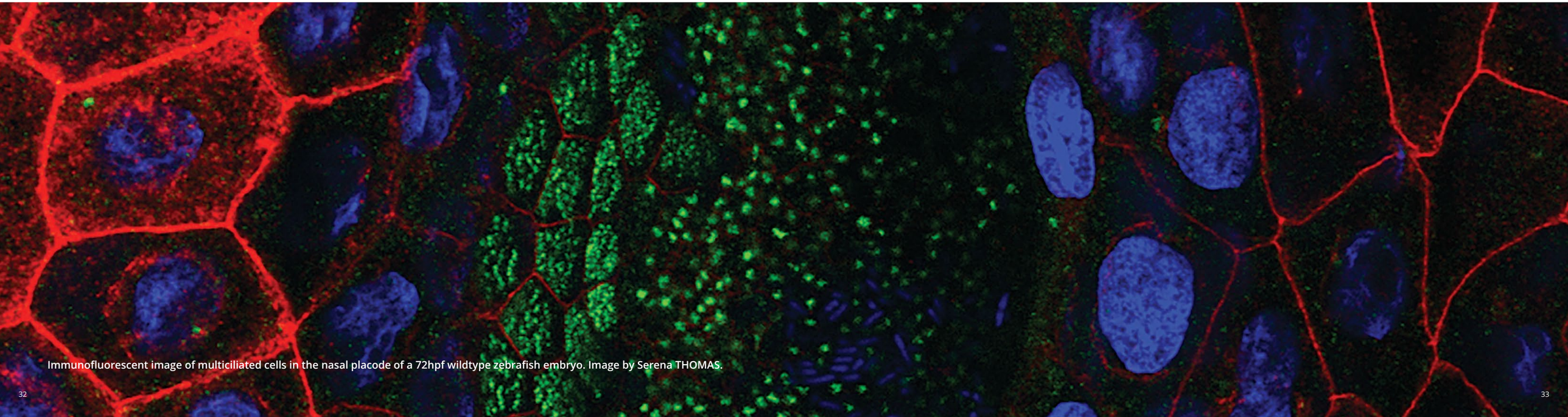
A*STAR IMCB's early focus encompassed several critical research domains, including **cellular signalling, intracellular trafficking, microbiology,** and **genomics**. These research avenues set the foundation for Singapore's biomedical advancements, and paved the way for breakthroughs in disease mechanisms, drug discovery, and therapeutic innovations.

Several early research projects at A*STAR IMCB led to major scientific achievements, such as deciphering the molecular pathways in cancer, understanding microbial infections, and sequencing key genomes that contributed to global genomic research.

The institute's pioneering researchers helped define A*STAR IMCB's reputation as a centre for scientific excellence, whose foundational contributions significantly influenced biomedical science and propelled IMCB's research impact.

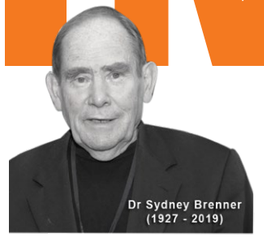
The success of A*STAR IMCB in its first 15 years gave the Singapore government the confidence that the country could compete globally in research, development, and innovation. This led to holistic investments in expanding A*STAR research institutes, transforming National University of Singapore (NUS) and Nanyang Technological University (NTU) into research-intensive universities, and establishing academic medical centres within hospitals. Additionally, significant efforts were made to develop clinician-scientists, strengthening the bridge between medical research and clinical practice.





Immunofluorescent image of multiciliated cells in the nasal placode of a 72hpf wildtype zebrafish embryo. Image by Serena THOMAS.

SPOTLIGHT ON IMCB PIONEERS



Sydney BRENNER

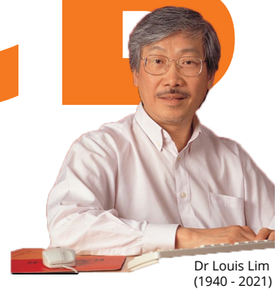
Laying the Foundation for Molecular Biology in Singapore

Sydney BRENNER, a **Nobel Laureate and molecular biology pioneer**, was instrumental in the establishment of **IMCB and Singapore's biomedical research landscape**. Recognising the need to develop **local scientific talent**, he played a key role in shaping **IMCB's research vision**, emphasising fundamental science as the backbone of innovation. His insights into **genetic code and gene regulation** laid the foundation for molecular biology research at IMCB. Beyond IMCB, his contributions have had a lasting impact on **Singapore's transformation into a global biomedical hub**, inspiring generations of scientists. His legacy continues through the countless researchers who benefited from his leadership and mentorship.

Wanjin HONG

Cracking the Code of Cellular Transport

Wanjin HONG is a leader in **intracellular trafficking**, focusing on how protein transport is regulated by **SNARE proteins, GTPases and Sorting nexins**. His work has been instrumental in understanding how disruptions in these processes can lead to diseases such as neurological diseases and cancer. He later expanded his research into **cancer signalling**, particularly the **Hippo pathway (YAP/TAZ-TEAD)**, which regulates cell growth and organ size. His discoveries have influenced the development of **targeted cancer therapies in clinical trials by many biopharma companies**. His contributions have earned him prestigious awards, including the **National Science Award (1999), Public Administration Medal (Silver) (2014), President's Science and Technology Medal (2022)**, **Fellowship of Singapore National Academy of Science (2022)** and a place in the **Asian Scientist 100 (2023).**



Dr Louis Lim
(1940 - 2021)

Louis LIM

Decoding Cell Signalling and Cytoskeletal Regulation

Louis LIM was a trailblazer in **signal transduction research**, establishing **Singapore's first research program on kinase signalling and cytoskeletal dynamics**. His **pioneering work on PAK proteins (p21-activated kinases)** helped define the molecular mechanisms regulating **cell movement and cytoskeletal organisation**, providing key insights into cancer metastasis and neurodegenerative diseases. A pivotal figure in **the discovery of the PAK CRIB motif**, LIM's research was so impactful that it was **featured on Singapore's $10,000 banknote**, a rare honour in scientific recognition. As a **founding scientist of IMCB**, he played a crucial role in establishing Singapore's biomedical research ecosystem, training and mentoring future generations of molecular and cell biologists.

Edward MANSER

Mapping the Cell's Scaffolding for Cancer Clues

Together with Louis LIM, **Edward MANSER** made **pioneering contributions to the study of the PAK kinases (p21-activated kinase)**, which were first described by his group. These findings are depicted in the Singapore $10,000 note that featured two ground-breaking discoveries made by IMCB. The work of the GSK-IMCB group on **Rho (ras homology) proteins** over two decades uncovered many key molecules responsible for cell movement and cancer progression. The Manser lab was **one of the first to apply the BioID (a method invented in Singapore by his colleague Brian BURKE) to characterise signalling complexes within cells**. For example, **PAK1 at focal adhesions** where cells are anchored, and **PAK4 at cell-to-cell junctions**. The application of BioID using mass-spectrometry proteomics is now the method of choice to untangle protein-protein interactions within living cells.

Catherine PALLEN

Unraveling the Role of Protein Phosphatases in Cancer

Catherine PALLEN made significant contributions to the **understanding of protein phosphatases and their role in cancer biology**. Her research focused on **protein tyrosine phosphatases (PTPs)**, which act as key regulators of **cell signalling pathways**, controlling cell growth, differentiation, and survival. By uncovering how **dysregulation of PTPs contributes to cancer progression**, her work has provided **new therapeutic insights into tumour development and potential treatment strategies**. During her time at IMCB, she was at the forefront of **fundamental cancer research**, helping to shape the institute's early focus on **signal transduction and disease mechanisms**. Her legacy continues in cancer biology, influencing approaches to **targeting phosphatases in therapy**.

Alan PORTER

Deciphering Cell Death Pathways

Alan PORTER made significant contributions to the study of **apoptosis (programmed cell death),** which is crucial in understanding cancer progression and treatment resistance. His **landmark work on caspase-deficient MCF-7 cells (1998)** has been highly cited in cancer research, offering fundamental insights into how cell death pathways can be manipulated for cancer therapy. His research continues to influence new therapeutic approaches targeting apoptotic mechanisms.

Byrappa VENKATESH

Uncovering the Evolutionary Secrets of Genomes

Byrappa VENKATESH played a pioneering role in **sequencing the fugu (pufferfish) genome, a major milestone in comparative genomics**. The compact genome of the fugu helped identify conserved genes and regulatory elements in humans, providing valuable insights into the **structure, function and evolution of the human genome**. His research also extended into rare genetic diseases, helping in precise diagnosis and effective management of such diseases. His work remains integral to understanding genetic conservation across species and its biomedical implications.

Yue WANG

Illuminating Fungal Pathogenicity

Yue WANG pioneered IMCB's research into **fungal pathogens**, specifically focusing on the **Candida** species and its interactions with the human microbiome. His studies have provided critical insights into how fungal infections develop and persist, leading to a better understanding of drug resistance and new treatment strategies. His work has been widely recognised, earning him the **2012 President's Science Award**. His contributions to **infectious disease research** continue to shape approaches to antifungal therapeutics.

FUN FACT:

2 of the pioneers are still in A*STAR today - 36 years and counting!

Wanjin HONG joined IMCB in 1989 and is still running his research lab at IMCB today, on top of his other hat as Chief Business Development Officer at BMRC.

Yue WANG joined IMCB in 1989 and is now at Infectious Disease Labs.

BREAKING BAD (CELLS):

THE SCIENCE OF CANCER THERAPY

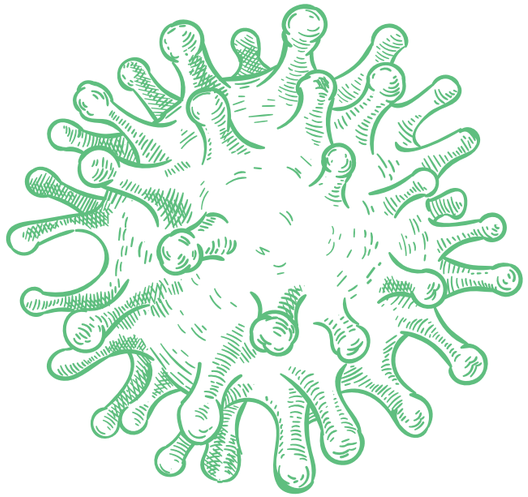
Following its foundational years concentrating on broad-based basic biology research, A*STAR IMCB evolved to focus on cancer research in the early 2000s.

Recognising the urgent need to understand cancer mechanisms and develop targeted interventions, A*STAR IMCB built on its strong scientific expertise to drive cutting-edge research and translational impact in the field that had quickly gained prominence due to its global and clinical significance.

LAYING A STRONG SCIENTIFIC FOUNDATION FOR TRANSLATION & SPIN-OFFS

A*STAR IMCB drew on its established research in cell biology to unravel **cell cycle regulation and signalling pathways**, aiming to uncover the molecular mechanisms that drive tumour growth and progression. By delving deeper into these processes, A*STAR IMCB scientists made significant contributions to the fundamental understanding of how cancers develop, proliferate, and evade treatments.

This strong foundation in fundamental science laid the groundwork for translational applications, leading to innovative projects and spin-offs.



DECODING INTRACELLULAR TRAFFICKING AND CANCER SIGNALLING

Few cellular processes are as precisely orchestrated as intracellular trafficking, the movement of proteins and lipids between cellular compartments. **Wanjin HONG** has dedicated his first two decades to unravelling this system, identifying half of all mammalian SNARE proteins and defining key SNARE complexes that regulate vesicle docking and fusion. His lab was among the first to discover that VAMP8/endobrevin is essential for regulated secretion in the exocrine system. He also pioneered the identification of the PX domain as a motif for PI3P interaction, demonstrating its role in synaptic transmission through SNX27-mediated neurotransmitter recycling. His original discoveries extended to small GTPases, uncovering how Arl1 regulates Golgi recycling and Rab34 controls lysosomal positioning.

Similarly, his research into intracellular trafficking has revealed that disruptions in Golgi-mediated protein transport contribute to cancer cell survival and resistance to treatment.

Beyond trafficking, his work identified TAZ as an oncogenic driver, interacting with TEAD transcription factors to promote tumour progression. His team also solved the crystal structure of YAP/TAZ/Vgll1-TEAD4, identifying a druggable pocket in TEAD and discovering Flufenamic acid as its first binder, laying the groundwork for global cancer drug development.

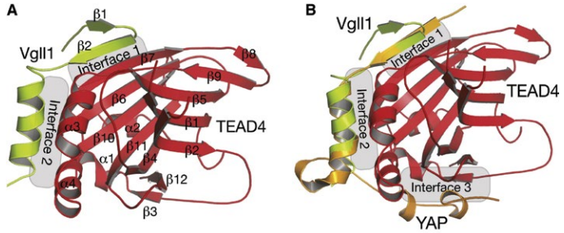
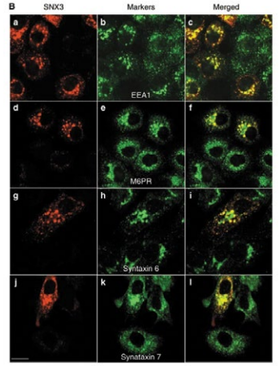


Figure panel adapted from Pobbati et al. Structure, 2012.



Left: Figure panel adapted from Xu et al. Nat Cell Biol, 2001; Right: Wanjin HONG

HONG has also played a pivotal role in shaping Singapore's biomedical ecosystem. As Executive Director of A*STAR IMCB (2011-2023), he fostered scientific collaborations, industry partnerships, and biotech spin-offs, including MerLion Pharmaceuticals. His research group continues to explore novel cancer signaling mechanisms to identify new therapeutic targets. In recognition of his research contributions, HONG has received the National Science Award (1999), Singapore National Academy of Science Fellowship (2022), and the President's Science and Technology Medal (2022).

FROM INTRACELLULAR TRAFFICKING TO TARGETED CANCER THERAPEUTICS

Following Wanjin HONG's pioneering work on intracellular trafficking and oncogenic signaling, **Haiwei SONG**'s research builds on this foundation by targeting key oncogenic proteins in the Hippo pathway and other cancer-driving proteins using small molecule inhibitors, PROTAC molecules, and circular RNAs. His lab was the first to solve the structures of YAP-TEAD and TAZ-TEAD complexes (together with Wanjin HONG), paving the way for the development of cancer therapies targeting the YAP/TAZ-TEAD complex.

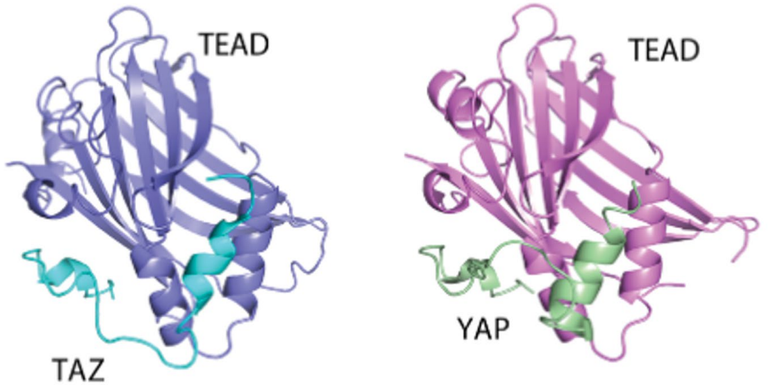


Figure panel adapted from CHEN et al. Genes & Development, 2010

Expanding on the role of Hippo signaling in cancer, SONG's research explores strategies to inhibit tumour growth and promote tissue regeneration, addressing both cancer therapy and tissue repair. His current research focuses on long non-coding RNAs (lncRNAs), including developing small molecules that disrupt oncogenic lncRNAs, offering a novel therapeutic approach to overcoming drug resistance.

Left: Haiwei SONG

BioCheetah
SPEED PRECISION HEALTH

HARNESSING BIOMARKER MAPPING FOR NON-INVASIVE CANCER DIAGNOSTICS

Advancements in spatial biology have enabled the discovery of highly specific biomarkers with clinical applications. Research at A*STAR IMCB has led to the identification of key bladder cancer biomarkers, forming the foundation for precision diagnostics. **BioCheetah**, an A*STAR IMCB spin-off, was established to translate these discoveries into clinical practice. Co-founded by **Jean Paul THIERY** and **Kian Chung LEE**, BioCheetah leverages a multiplex urine-based biomarker panel to develop high-sensitivity diagnostic assays. These provide a non-invasive alternative to traditional cystoscopy, significantly improving early detection and patient monitoring. Through ongoing clinical validation with Singapore General Hospital and hospitals in China, BioCheetah is positioning itself at the forefront of next-generation cancer diagnostics.

Jean Paul THIERY

Kian Chung LEE

ADVANCING CANCER THERAPEUTICS FROM MOLECULAR TARGETS TO IMMUNOTHERAPY

Building on A*STAR IMCB's expertise in cancer signaling and targeted therapies, **Qi ZENG** pioneered PRL3 cancer research, identifying PRL3 phosphatase in 1998 and demonstrating its role in cancer migration, invasion, and metastasis. Her work revealed that PRL3 is overexpressed in 80.6% of cancers but absent in healthy tissues, establishing it as a pan-cancer druggable target.

While PRL3 is an intracellular oncoprotein, ZENG took an unconventional approach by developing **PRL3-zumab**, the first-in-class humanised antibody designed to target PRL3-expressing tumours. Her research uncovered how PRL3 externalises on the cancer cell surface, allowing antibody-based targeting to trigger an immune response while reducing off-target effects.

Left: Journal cover of EGF-stimulated human cancer cells stained for PRL-3 from Al-aidaroos et al. JCI, 2013.

JCI insight

RESEARCH ARTICLE

PRL3-zumab, a first-in-class humanized antibody for cancer therapy

Min Thura,[1] Abdul Qader Omer Al-Aidaroos,[1] Wei Peng Yong,[2,3] Koji Kono,[3,4] Abhishek Gupta,[1] You Bin Lin,[1] Kousaku Mimura,[3] Jean Paul Thiery,[1,3] Boon Cher Goh,[2,3] Patrick Tan,[5] Ross Soo,[2,3] Cheng William Hong,[6] Lingzhi Wang,[3] Suling Joyce Lin,[5] Elya Chen,[4] Sun Young Rha,[7] Hyun Cheol Chung,[7] Jie Li,[1] Sayantani Nandi,[1] Hiu Fung Yuen,[1] Shu-Dong Zhang,[8] Yeoh Khay Guan,[9] Jimmy So,[9,10] and Qi Zeng[1]

ARTICLE

https://doi.org/10.1038/s41467-019-10127-x OPEN

PRL3-zumab as an immunotherapy to inhibit tumors expressing PRL3 oncoprotein

Min Thura[1,12], Abdul Qader Al-Aidaroos[1,12], Abhishek Gupta[1], Cheng Ean Chee[2], Soo Chin Lee[2], Kam Man Hui[3], Jie Li[1], Yeoh Khay Guan[4], Wei Peng Yong[2], Jimmy So[5], Wee Joo Chng[2], Chin Hin Ng[2], Jianbiao Zhou[2], Ling Zhi Wang[6], John Shyi Peng Yuen[7], Henry Sun Sien Ho[7], Sim Mei Yi[7], Edmund Chiong[5], Su Pin Choo[8], Joanne Ngeow[1,8,9], Matthew Chau Hsien Ng[8], Clarinda Chua[8], Eugene Shen Ann Yeo[10], Iain Bee Huat Tan[8], Joel Xuan En Sng[1], Nicholas Yan Zhi Tan[1], Jean Paul Thiery[1], Boon Cher Goh[2] & Qi Zeng[1,11]

IISG

The translation of PRL3 research from basic science to clinical application led to the formation of **Intra-ImmuSG**, an A*STAR spin-off driving PRL3-zumab's development. Phase I trials at NUHS (2018) confirmed its safety, and ongoing multi-national Phase II trials in the US, Singapore, China, and Malaysia have demonstrated promising clinical benefits, significantly extending Progression-Free Survival (PFS) in cancer patients. PRL3-zumab represents a breakthrough in cancer immunotherapy, offering new hope for patients with aggressive, treatment-resistant cancers.

The IMCB scientists behind Intra-ImmunSG's technology
From left to right: Kelvin KUAN Kam Yew, Jie LI, Qi ZENG, Pei Ling CHIA, David Koon Hwee ANG, Thura MIN.

MAPPING ECM REMODELING IN CANCER PROGRESSION

The ability to visualise and analyse the tumour microenvironment at high resolution has not only advanced our understanding of cancer biology but also paved the way for therapeutic innovations. Research at A*STAR IMCB has uncovered key regulators of the extracellular matrix (ECM), which plays a fundamental role in tumour progression, metastasis, and tissue remodeling. **Albatroz, an A*STAR IMCB spin-off**, was founded to translate these discoveries into novel cancer therapeutics.

Building upon research by **Frederic BARD**, Albatroz is developing therapeutic antibodies against Calnexin, a protein involved in ECM degradation, which is crucial for both tumour metastasis and cartilage breakdown in arthritic disorders.

As the first company in the world to target Calnexin, Albatroz is pioneering a new therapeutic approach bridging cancer biology and targeted therapy.

Co-founder, Frederic BARD posing next to an Albatross, the inspiration behind the company's name.

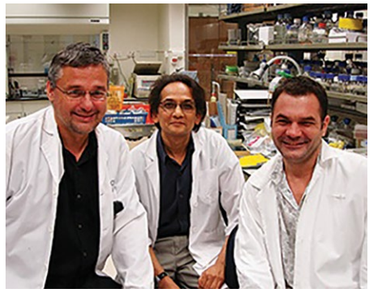
The scientists behind Albatroz's technology
A*STAR IMCB scientists involved are Anh Tuan NGUYEN (2nd from left), Felicia Pei Ling TAY (3rd from left), Frederic BARD (centre), Jasmine THAM Keit Min (3rd from right), Xavier LE GUEZENNEC (2nd from right), Joanne Zhi Hui CHIA (far right).

SAFEGUARDING GENOME INTEGRITY

Understanding genome stability is key to preventing uncontrolled cell division and cancer. **Uttam SURANA** has pioneered studies on cell cycle checkpoints, which regulate DNA replication and division. Using yeast as a model, his team was the first to identify the mitotic spindle as a critical checkpoint target, preventing premature chromosome movements and maintaining genomic integrity. His work has revealed how checkpoint defects drive cancer, laying the groundwork for new therapeutic strategies.

To translate these discoveries, SURANA co-founded **SiNOPSEE Therapeutics** with A*STAR scientists, establishing a biopharmaceutical company focused on small-molecule drug discovery. Leveraging proprietary screening technology of A*STAR IMCB & Bioprocessing Technology Institute (A*STAR BTI), SiNOPSEE is developing highly selective inhibitors for wet-AMD and cancer, with optimised topical eye drop formulations for targeted delivery.

For his groundbreaking contributions to cell cycle regulation and cancer biology, **SURANA** received the National Science Award in 2007. His work continues to bridge fundamental research with therapeutic innovation.



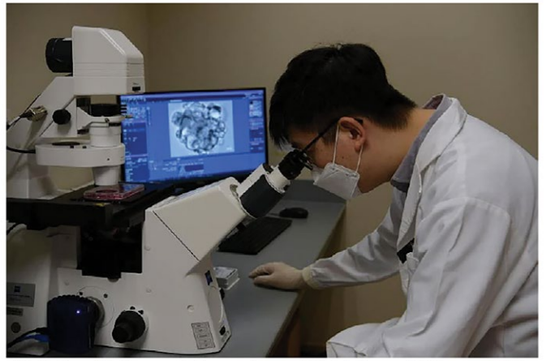
Uttam SURANA (centre) and colleagues

Uttam SURANA and Wanjin HONG

WORKING WITH CLINICIAN-SCIENTISTS ON LARGE COLLABORATIVE PROJECTS

Building on the foundational work at A*STAR IMCB, our PIs work closely with clinicians across the Singapore ecosystem. One of the first collaborations that was competitively funded by the NMRC Translational and Clinical Research Grant was the **Precision Medicine in Liver Cancer across an Asia-Pacific Network (PLANET)** study. Thereafter, **PLANet 2.0** led by **Pierce CHOW**, A*STAR IMCB Joint Investigator from NCCS, secured follow-on funding from the **NMRC Open Fund – Large Collaborative Grant (OF-LCG)** in 2022 with **Han Chong TOH**, IMCB Joint Investigator from NCCS, and **Vinay TERGAONKAR**. PLANet 2.0 focuses on using biomarker-driven clinical trials to pave the way for more effective tailored treatments for liver cancer.

S'pore dedicates $25m to liver cancer research to find targeted treatments



Dr Timothy Shuen analysing immune aspects of liver cancer. Liver cancer is tricky to tackle compared with other cancers. ST PHOTO: NG SOR LUAN

Researchers involved in PLANet 2.0 LCG including IMCB PI Wanjin HONG (far left) and Joint Investigators Han Chong TOH (3rd from left), Pierce CHOW (4th from left). Missing from photo: Vinay TERGAONKAR

The **VICTORY (Virus-Induced Cancer: Translational Oncology Research & Immunology)** program led by A*STAR IMCB Joint Investigator, **Han Chong TOH**, alongside **John CONNOLLY and Weiping HAN,** was funded in 2018 under the NMRC OF-LCG. The host-viral interaction was studied across three major types of virally-driven cancers (VDCs), each associated with distinct viruses: (1) Epstein-Barr virus (EBV)-driven cancers, including nasopharyngeal cancer, lymphoepithelioma-like carcinoma (LELC), EBV+ gastric cancer, and NKT lymphoma; (2) Human papillomavirus (HPV)-driven cancers, such as oropharyngeal and cervical cancer; and (3) Hepatitis B virus (HBV)-driven hepatocellular carcinoma. In particular, the immunosuppression induced in VDCs was of focus with an eye towards target discovery and validation for potential generation of therapeutics targets.

Researchers involved in VICTORY LCG including IMCB PI John CONNOLLY (far left) and Joint Investigator Han Chong TOH (fifth from left). Missing from photo: Weiping HAN.

Researchers involved in Symphony 2.0 LCG including IMCB PI Valerie YANG on the far right

In 2024, two OF-LCG grants were awarded - **Singapore lYMPHoma translatiONal studY 2.0 (SYMPHONY 2.0)** and **Colo-SCRIPT: Colorectal cancer subtype-specific research informs phenotypes, diagnostics & treatment**.

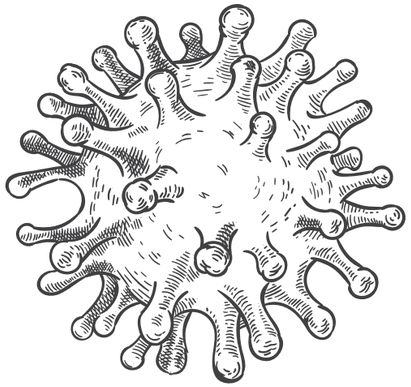
SYMPHONY 2.0, led by **Soon Thye LIM** at NCCS, is a continuation of 10 years of work by this group, under the **Translational and Clinical Research (TCR) Flagship Programme** and **SYMPHONY 1.0**, which has laid the groundwork to establish Singapore as a hub of translational and clinical expertise in lymphomas. **Valerie YANG**, a clinician-scientist from A*STAR IMCB and NCCS is part of the team looking at transforming lymphoma care with artificial intelligence through the integration of clinical, molecular and socioenvironmental data.

Colo-SCRIPT, led by **Iain TAN** from NCCS and **Wai Leong TAM** from GIS seeks to harness insights on the distinct biology of different molecular subtypes in CRC to guide subtype-specific prevention, diagnosis, and treatment of disease. **Ashok VENKITARAMAN** leads a team focusing on decoding early events influencing the transition of pre-invasive to invasive cancer while **Vinay TERGAONKAR** focuses on the role of environmental, metabolic and microbial risk factors in the progression of colorectal cancer.

Researchers involved in Colo-SCRIPT LCG including IMCB PIs Ashok VENKITARAMAN (5th from right), Vinay TERGAONKAR (2nd from right) and Qi-Jing LI (far right)

To date, A*STAR IMCB continues to work closely with the **Singapore Translational Cancer Consortium (STCC)** to drive transformative cancer research and translation. We are fortunate to have 13 clinician scientists from various oncology departments across **SingHealth, National Healthcare Group (NHG)** and **National University Hospital System (NUHS) hold joint appointments at IMCB**. This includes two STCC platform leads – **Anand JEYASEKHARAN (NUHS) and Ern Yu TAN (TTSH)**.

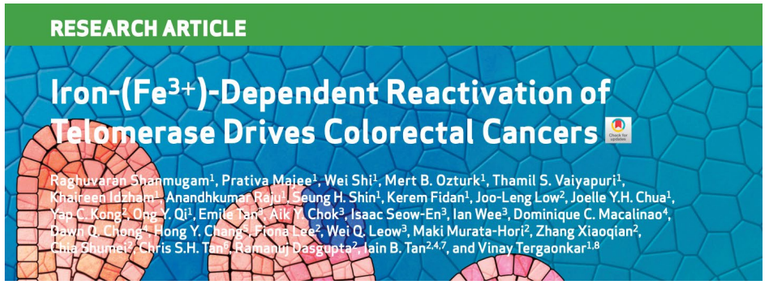
TACKLING KEY CHALLENGE IN CANCER BIOLOGY - UNDERSTANDING CANCER PLASTICITY AND RESISTANCE



Building on its strong foundation in basic research, A*STAR IMCB has now expanded its focus towards tackling one of the biggest challenges in oncology - cancer plasticity and resistance - collectively as one-IMCB. Tumours frequently adapt to treatment, developing resistance that leads to disease progression and recurrence. A*STAR IMCB researchers are now working to unravel the molecular drivers of resistance and develop strategies to enhance treatment efficacy. Through large-scale collaborative grants, A*STAR IMCB is bridging fundamental discoveries with translational applications to improve patient outcomes.

INFLAMMATION AND CANCER RESISTANCE

Chronic inflammation is a key driver of cancer progression, promoting tumour survival, therapy resistance, and immune evasion. **Vinay TERGAONKAR**'s research has uncovered how NF-κB signaling fuels cancer adaptation by enhancing cell survival and resistance to treatment. His work provides a mechanistic framework for understanding how inflammation-driven pathways shape tumour plasticity, opening avenues for targeted therapeutic interventions.

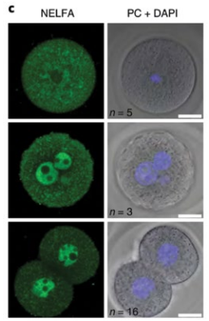


From left to right: Vinay TERGAONKAR; SHANMUGAN et al. Cancer Discov, 2024.

Building on this expertise, **TERGAONKAR** leads the Inflammation and Cancer Signalling Competitive Research Programmes (CRPs), which explore key regulators of inflammation-driven tumour adaptation and identify potential therapeutic interventions to disrupt these pro-tumour signaling networks. He also co-leads **Liver Cancer Research ('PLANet 2.0' LCG)**, applying genomic and molecular profiling to develop precision medicine approaches that overcome resistance mechanisms in liver cancer. By integrating advanced multi-omics technologies, these initiatives aim to develop personalised therapies to target liver cancer resistance mechanisms. His research achievements have received international recognition, including the British Council Development Award (2014), the Premiers' Fellowship from the Government of South Australia (2015), and the University of Macau Distinguished Professorship (2019).

EPIGENETIC PLASTICITY AND THERAPY RESISTANCE

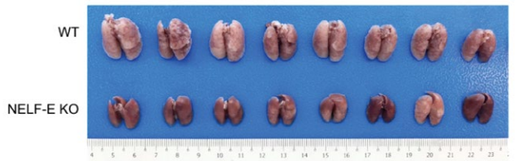
Cancer cells exploit epigenetic plasticity to adapt, survive, and resist treatment. **Wee-Wei TEE** focuses on chromatin dynamics and disease epigenetics, studying how epigenetic modifications regulate gene expression in cancer. His research investigates how chromatin architecture influences tumour progression and therapy resistance, drawing insights from early development. By understanding how developmental cell fate plasticity is hijacked during tumorigenesis, his lab aims to discover new cancer therapies that reprogram cancer cell states and improve the effectiveness of existing treatments. Importantly, TEE's work has been recognised with the National Research Foundation Fellowship in 2016 and the European Molecular Biology Organization Global Investigatorship in 2022.



nature cell biology
ARTICLES
https://doi.org/10.1038/s41556-019-0453-8

Maternal factor NELFA drives a 2C-like state in mouse embryonic stem cells

Zhenhua Hu[1,8], Dennis Eng Kiat Tan[1,8], Gloryn Chia[2,8], Haihan Tan[1], Hwei Fen Leong[1], Benjamin Jieming Chen[1], Mei Sheng Lau[1], Kelly Yu Sing Tan[3], Xuezhi Bi[3,4], Dongxiao Yang[3], Ying Swan Ho[3], Baojiang Wu[5], Siqin Bao[5], Esther Sook Miin Wong[6] and Wee-Wei Tee[1,7*]



nature communications
Article
https://doi.org/10.1038/s41467-023-38132-1

Dependency of NELF-E-SLUG-KAT2B epigenetic axis in breast cancer carcinogenesis

Top: Figure panel from HU et al. Nature Cell Biology, 2020;
Bottom: Figure panel from ZHANG et al. Nature Communications, 2023

DECIPHERING THERAPY RESISTANCE IN LUNG CANCER

Lung cancer remains a major cause of cancer-related deaths due to therapy resistance. **Wee-Wei TEE** is tackling this challenge through the **Lung Cancer Plasticity and Resistance Research ('DEBUT' CRP)** as the lead PI, and the **Lung Cancer Large Collaborative Grant (LCG)** as a Theme PI. His research explores the epigenetic mechanisms driving lung cancer adaptation, uncovering key molecular regulators that allow tumours to evade treatment. By targeting these pathways, his team aims to reprogram resistant cancer cells, improving patient responses to therapy.

Researchers involved in DEBUT CRP including IMCB PIs Wee-Wei TEE (2nd from left), Jayantha GUNARATNE (3rd from left) and Manikandan LAKSHMANAN (4th from left).

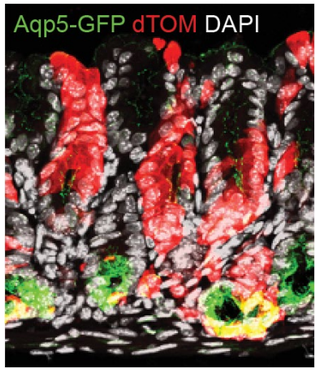
Researchers involved in the lung cancer resistance CRP including IMCB PIs Qingfeng CHEN (1st from left) and Wanjin HONG (2nd from left).

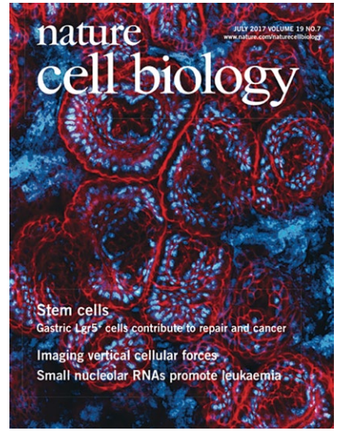
Similarly, **Wanjin HONG** leads another Lung Cancer Resistance CRP, investigating how lung tumours adapt under therapy pressure. His team is identifying resistance-enabling pathways and developing novel drug strategies to overcome lung cancer plasticity. These efforts are advancing the understanding of lung cancer therapy resistance, laying the foundation for innovative treatment approaches.

TARGETING CANCER STEM CELLS TO PREVENT RECURRENCE

Tumours are sustained by a population of highly plastic cancer stem cells (CSCs), which drive metastasis, therapy resistance, and tumour relapse. **Nick BARKER**'s pioneering work on Lgr5+ cancer stem cells has reshaped the understanding of tumour maintenance and recurrence. His research has demonstrated that targeting Lgr5+ and Aqp5+ CSCs can significantly improve treatment efficacy, preventing tumours from regenerating after therapy. BARKER's work provides a critical foundation for future strategies aimed at eliminating CSC-driven cancers, reducing the likelihood of disease relapse. Notably, BARKER's work has earned him recognition internationally, through the National Research Foundation Investigatorship (2017), Japanese Cancer Association International Award (2022), and the European Molecular Biology Organization Associate Membership (2022). In addition to his scientific excellence, Nick BARKER has mentored many young talents over the years, including **Grace LIM**, a 2024 Laureate of the L'Oreal-UNESCO For Women in Science Singapore Fellowship.

Grace LIM receiving L'Oreal-UNESCO For Women in Science Singapore Fellowship 2024





From left to right: Figure panel of Aqp5+ gastric stem cells adapted from TAN et al. Nature, 2020; Nick BARKER; Journal cover of Lgr5+ gastric stem cells from LEUSHACKE et al. Nature Cell Biology, 2017

OVERCOMING THERAPY RESISTANCE IN LIVER CANCER

Liver cancer, particularly in Asia, is strongly linked to chronic hepatitis B infection, which accelerates tumour progression. As a Theme PI, **Wanjin HONG** is part of the Hepatitis B Liver Cancer LCG, investigating how persistent viral infection contributes to therapy resistance. His team is working to uncover key vulnerabilities in hepatitis-associated liver cancer, laying the groundwork for more effective targeted therapies to address one of the most pressing oncology challenges in Asia.

UNDERSTANDING AND PERSONALISING LYMPHOMA TREATMENT

Hematological malignancies such as lymphoma also exhibit high plasticity and treatment resistance, making them particularly challenging to treat. **Valerie YANG**, a clinician-scientist and A*STAR IMCB investigator, co-leads the **Lymphoma Research ('Symphony 2.0' LCG)**, which aims to decode the molecular and genetic landscape of lymphoma.


$50m grant for research to find better ways of treating lymphoma, colorectal cancer in S'pore

Left: Dr. Valerie YANG, pictured on the left; Right: Press release in The Straits Times on Symphony 2.0.

With participation from **Wanjin HONG**, this initiative focuses on identifying therapeutic vulnerabilities in lymphoma and designing personalised treatments that better account for the complexity of different lymphoma subtypes. By integrating genomic profiling and functional studies, **YANG**'s work is paving the way for more effective, patient-specific treatment strategies.

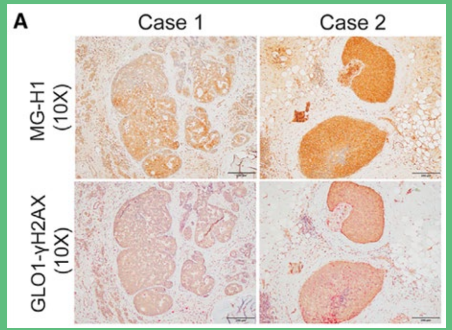
COLORECTAL CANCER: TACKLING DRUG RESISTANCE

Colorectal cancer, one of the most common malignancies worldwide, is a major focus in precision oncology. Through **'Colo-SCRIPT' LCG (Systems-based Colorectal Cancer Research & Innovation Programme for Therapeutics)**, Theme PIs, **Vinay TERGAONKAR** and **Ashok VENKITARAMAN** are investigating tumour progression and drug resistance mechanisms. Their research seeks to develop novel combination therapies that can counteract treatment resistance, enhancing patient survival and improving long-term treatment efficacy.

TARGETING GENOME INTEGRITY TO OVERCOME CANCER RESISTANCE

Genome integrity plays a crucial role in preventing cancer progression and resistance to therapy. **Ashok VENKITARAMAN**, who joined A*STAR IMCB in 2021, is recognised for uncovering tumour suppressive mechanisms that maintain genome integrity through his pivotal studies on the breast cancer gene, BRCA2. His work has illuminated the role of a class of genes frequently inactivated in human cancers. He has developed innovative technologies to accelerate drug discovery that have successfully led to multiple spinoff companies, extending the reach of next-generation therapeutics. In recognition of his remarkable research achievements, VENKITARAMAN has been awarded the Academy of Medical Sciences Fellowship (2001), European Molecular Biology Organization Membership (2004), Basser Global Prize (2017) and the American Association for Cancer Research Fellowship (2025).


Cell
Article
A glycolytic metabolite bypasses "two-hit" tumor suppression by BRCA2



From left to right: Ashok VENKITARAMAN; Figure panel adapted from KONG et al. Cell, 2021

UNRAVELING THERAPY RESISTANCE IN SOLID TUMOURS

Chuan YAN focuses on therapy resistance mechanisms in hepatocellular carcinoma, soft-tissue sarcoma, and ovarian carcinoma. His team employs next-generation bulk and single-cell sequencing, along with xenograft-based animal modeling using immunodeficient zebrafish and mice, to uncover new combination therapies and diagnostics for clinical applications. By identifying key resistance pathways and vulnerabilities in these cancers, his research aims to guide the development of more effective therapeutic strategies. YAN's work has been recognised via the National Research Foundation Fellowship (2023).

Chuan YAN

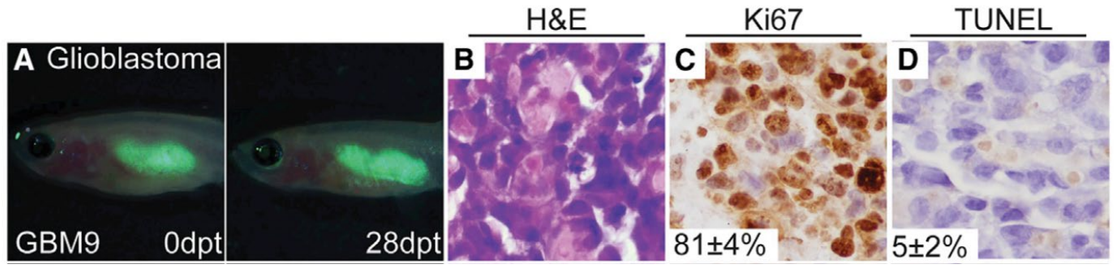


Figure panel adapted from Yan et al. Cell, 2019

A*STAR IMCB's work in cancer plasticity and resistance marks a critical transition from understanding tumour biology to actively disrupting mechanisms of therapy resistance. Through large-scale collaborative grants, A*STAR IMCB has built a research ecosystem that integrates fundamental cancer biology with translational applications. With breakthroughs in inflammation-driven tumour progression, cancer stem cell targeting, and resistance mechanisms in lung, liver, lymphoma, and colorectal cancers, A*STAR IMCB is laying the foundation for the next generation of cancer therapies.

LOOKING AHEAD

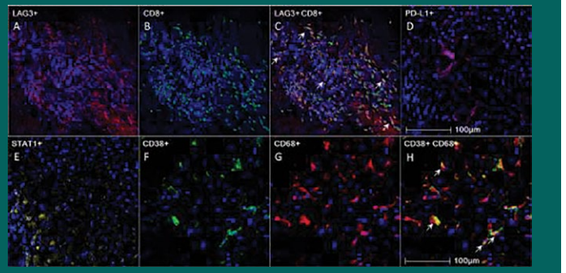
To stay ahead of cancer's evolving complexities, A*STAR IMCB is accelerating its efforts to develop next-generation treatments. Recognising the need for more precise and targeted interventions, researchers are charting new territories—harnessing spatial biology to map the tumour microenvironment with unprecedented precision and pioneering novel therapeutic strategies to tackle previously undruggable cancer targets.

SPATIAL BIOLOGY: MAPPING THE TUMOUR MICROENVIRONMENT

Understanding the tumour microenvironment is crucial for developing more effective, targeted cancer therapies. A*STAR IMCB has been a pioneer in spatial biology, enabling high-resolution visualisation of tumour-immune interactions and identifying new biomarkers that predict patient responses to immunotherapy.

TRANSFORMING TUMOUR PROFILING WITH MULTIPLEX IMMUNOHISTOCHEMISTRY

Research led by **Joe YEONG** has played a transformative role in this field, particularly through the development of automated multiplex immunohistochemistry. His work has enabled comprehensive mapping of immune cell populations within tumours, allowing researchers to analyse spatial relationships between tumour and immune cells with unprecedented precision. These spatial analyses have identified new biomarkers that predict patient responses to immunotherapy, laying the groundwork for more personalised cancer treatments.

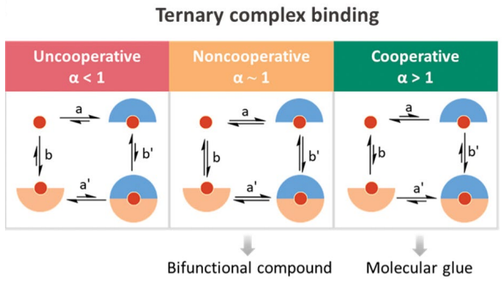


Left: Joe YEONG; Bottom: Figure panel adapted from CHEUNG et al. Frontiers in Immunology, 2023.

DRUGGING THE UNDRUGGABLE: UNLOCKING NEW THERAPEUTIC STRATEGIES

Many of the most critical cancer-driving proteins remain inaccessible to traditional drug discovery methods due to their structural complexity and lack of drug-binding pockets. Researchers at A*STAR IMCB are tackling this challenge through innovative approaches in chemical biology, expanding the druggable proteome to target previously undruggable cancer proteins.

ENGINEERING TARGETED PROTEIN DEGRADATION WITH MOLECULAR GLUES



From left to right: Figure panel adapted from LIU et al. Journal of the American Chemical Society, 2023; Shuang LIU

Shuang LIU has been at the forefront of developing molecular glues, small molecules that induce interactions between previously unlinked proteins, triggering targeted degradation of cancer-associated proteins. This approach expands the landscape of druggable targets, offering a promising strategy for modulating oncogenic pathways. Her research has the potential to revolutionise cancer therapeutics by enabling the selective degradation of proteins that were previously considered undruggable.

Through its pioneering research in cancer cell plasticity, spatial biology, and drug discovery, A*STAR IMCB continues to bridge the gap between fundamental discoveries and translational applications. By integrating multidisciplinary expertise and leveraging state-of-the-art technologies, the institute remains at the forefront of innovation, shaping the future of oncology and improving patient outcomes worldwide. For her research achievements, LIU has been awarded the National Research Foundation Fellowship (2025).

PIONEERING THE FUTURE:

IMCB THROUGH THE LENS

1985 Singapore's first life sciences institute, IMCB, was founded. Its founding director was Chris Tan

1987 IMCB moved into its own building at NUS

1988 The National Biotechnology Programme was established by the Singapore Economic Development Board (EDB) to spearhead the development of biotechnology

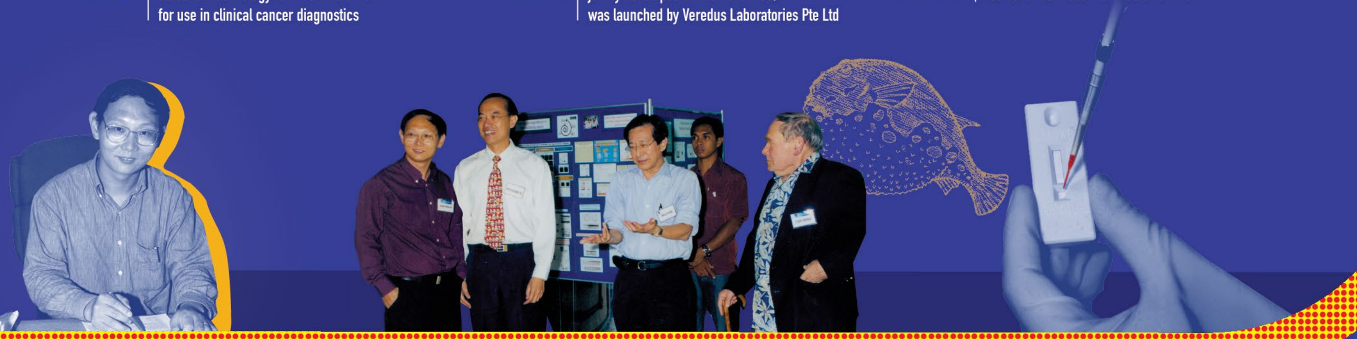
1989 IMCB entered into a 15-year partnership with Glaxo, for research on degenerative brain diseases. The team, led by Louis Lim, included Thomas Leung and Edward Manser

1992 A research team at IMCB, led by Chris Tan, completed and published the first sequence of dengue virus type 1

1993 IMCB undertook a $60-million joint venture with Glaxo and EDB to discover bioactive compounds via the Center for Natural Products Research (CNPR)

1999 IMCB held the first Gordon Research Conference in Singapore

2000 IMCB was conferred the 5th Nikkei Asia Prize in the category of Technology Innovation for its contributionsas the first major centre of biological research in Asia



2001 IMCB founding director Chris Tan stepped down, and Wanjin Hong took over as Acting Director

2002

- CNPR was spun off as MerLion Pharmaceuticals
- An international consortium, led by IMCB and the Joint Genome Institute of the US Department of Energy, published the draft sequence of the fugu genome in Science

2003 IMCB co-developed two rapid and accurate diagnostic kits during the SARS outbreak, which was recognised by a National Day Award later that year

2004 IMCB moved to Biopolis. David Lane took over as Executive Director of IMCB

2005 A PCR-based malaria diagnostic kit, jointly developed at IMCB and NUS, was launched by Veredus Laboratories Pte Ltd

2006 IMCB licensed DNA methylation detection technology to Hitachi Asia Ltd. for use in clinical cancer diagnostics

2007 Neal Copeland took over the helm of IMCB as Executive Director

2009 IMCB and Genome Institute of Singapore (GIS) researchers developed an assay to detect H1N1 swine flu strains during the 2009 pandemic

2010 Stephen Cohen became the Acting Director of IMCB

10

J&J

P&G

MERLIONPHARMA

abcam

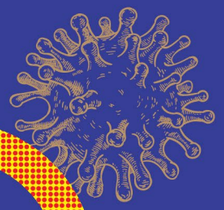
IISG

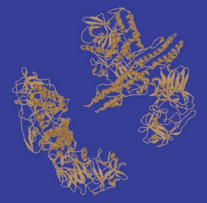
2011

- Wanjin Hong appointed Executive Director of IMCB
- A*STAR and Duke-NUS established the Neuroscience Research Partnership (NRP) to seed collaborations in neuroscience

2014

IMCB developed close industry links including partnerships with Procter & Gamble on skin biology and Johnson & Johnson on humanised mouse models





TESSA THERAPEUTICS

2015

- IMCB launched a collaboration with Abcam to develop a range of rabbit monoclonal antibodies for diagnostic use
- MerLion Pharmaceutical's lead antibacterial candidate, finafloxacin, was approved by the US Food and Drug Administration (FDA) for clinical use
- Intra-ImmuSG spun off to develop antibodies targeting PRL-3, clinical stage biotech

2017

Tessa Therapeutics Joint Lab

Indivumed Therapeutics

LION TCR WE HUNT VIRUSES

2018

- Indivumed Announces an International Partnership with IMCB to Establish an Asian-Centric Multiomics Cancer Database for Personalized Oncology
- LionTCR Joint Lab

2019

Singapore Cell Therapy Advanced Manufacturing Programme (STAMP 1.0) brought together 11 research institutions to address bottlenecks in cell therapy manufacturing

20

Beyond

2020-2021

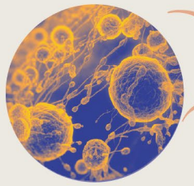
Contribute in running of Stronghold Diagnostic Lab, which aims to rapidly boost Singapore's COVID-19 screening capacity through A*STAR's research capabilities, processing thousands of tests annually

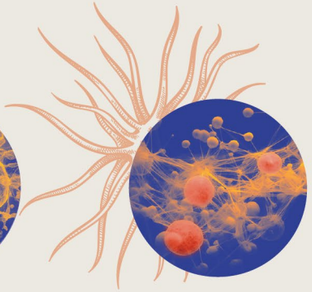
2023

IMCB spin-off Albatroz spun off to develop antibodies against Calnexin

2024

- Tikva announces setting up of joint laboratory with IMCB to progress its pipeline of promising cell therapies against solid tumors
- Su Xinyi appointed Executive Director of IMCB
- IMCB Leads Collaborative Efforts at the SIMM-IMCB-ZIDD Joint Research Symposium: Advancing Biomedical Research Between China and Singapore
- SCG Joint Lab with BTI and IMCB

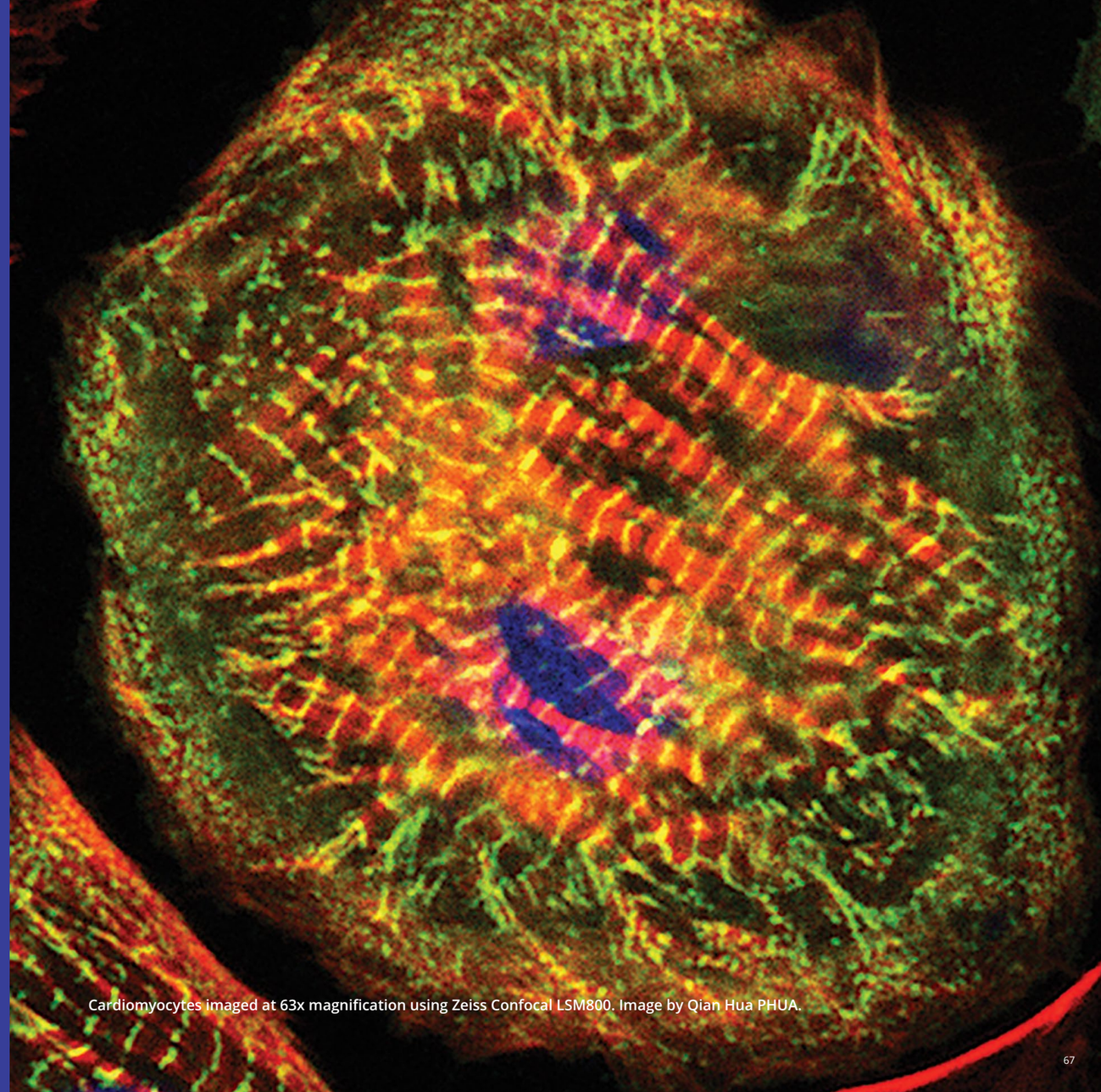




Cancer Signalling & Therapy

Cellular & Molecular Therapy

Neurometabolism in Health & Disease



Cardiomyocytes imaged at 63x magnification using Zeiss Confocal LSM800. Image by Qian Hua PHUA.

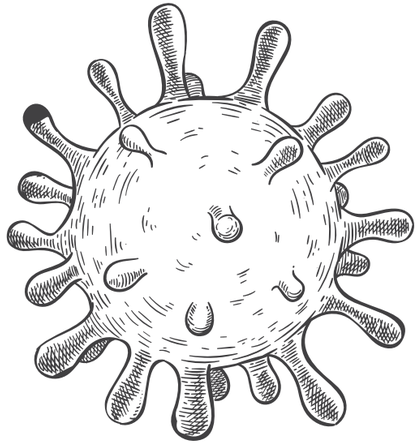
CRACKING THE MOLECULAR CODE OF LIFE

The beginning of 2010 saw Singapore transitioning towards an innovation-driven, knowledge-based economy, with national priorities shifting toward translating scientific discoveries into real-world health solutions.

A*STAR IMCB, with our strong foundation in cellular biology, evolved along these priorities and expanded our capabilities into cell and nucleic acid therapies. With the approval of the first CAR-T cell therapy, tisagenlecleucel, in 2017, the potential of cell-based medicines is gradually realised.

The **Cell and Molecular Therapy Division** was established to deep dive into regenerative medicine, cell and gene therapies - with the goal of unlocking biology for the treatment of otherwise intractable diseases.

CELL & MOLECULAR THERAPY



A*STAR IMCB's pioneering efforts in cell therapy leveraging on expertise in stem cell biology and developmental biology marked our first therapeutic frontier to focus on a specific therapeutic modality in the early 2000s. The power of stem cell therapy can be unlocked in three critical ways. Firstly, stem cells can be used as regenerative medicines in the form of cell therapy, offering novel solutions for repairing or replacing damaged tissues or organs. Secondly, stem cells serve as powerful in vitro models of diseases, enabling researchers to study human disease biology in a controlled manner allowing accelerated development of new therapeutics. Thirdly, stem cells can be harnessed for their potential in cell therapy for cancer immunotherapy, offering innovative approaches to enhance immune responses against cancer.

By harnessing these applications, A*STAR IMCB has been at the forefront of advancing regenerative medicine and precision therapies, laying the foundation for future innovations in cell-based treatments. Indeed, A*STAR IMCB is beginning to bear the fruits in the field of regenerative medicine, as we launch multi-disciplinary programs in the areas of improved manufacturing for cell therapy and advancing allogeneic cell therapy for immuno-oncology.

HARNESSING STEM CELL TECHNOLOGY FOR REGENERATIVE MEDICINE THERAPY AND IN VITRO DISEASE MODELS

Jonathan LOH

Singapore initiated the **Singapore Cell Therapy Advanced Manufacturing Programme (STAMP 1.0)** in 2019 that brought together 11 public research institutions, including **A*STAR BTI, NUS, NTU, Duke-NUS, SUTD, SingHealth Singapore-MIT Alliance for Research and Technology (SMART), NUHS and Health Science Authority (HSA)**. STAMP 1.0 addresses bottlenecks in cell therapy manufacturing by expanding product portfolios and supporting clinical development of biotech assets.

The **Allogenic Stem Cell Manufacturing (ASTEM)** was one of the programmes under **STAMP1.0**. ASTEM, led by **Simon COOL**, aims to revolutionise cell therapy by enabling the large-scale manufacturing of highly potent mesenchymal stem cells (MSCs) with proven therapeutic efficacy. To overcome critical challenges in scalability, quality control, and outdated manufacturing technologies, ASTEM focused on three key strategies: (1) identifying and selecting the most potent MSCs, (2) optimising scalable GMP-compatible bioprocessing solutions, and (3) demonstrating clinical efficacy in cartilage repair using large animal models. This comprehensive approach streamlined the entire MSC production pipeline, integrating expertise across donor selection, cell isolation, regulatory science, and bioprocessing.

ASTEM's success in optimising media formulation for MSC growth, led to the spin-off of **InnoCellular**, a start-up founded by **Jonathan LOH**, focused on commercialising next-generation cell culture media.

By translating cutting-edge research into industry-ready solutions, ASTEM has not only accelerated the clinical translation of MSC therapies but also positioned Singapore as a key player in regenerative medicine and biomanufacturing innovation.

Beyond developing practical solutions of MSC manufacturing, LOH's lab made important discoveries dissecting the mechanism regulating cell fate changes. These discoveries have the potential to uncover factors that could be incorporated into different media formulations to promote specific cell differentiation. The strong understanding of cell fate also allowed the team to reprogram fibroblasts into hematopoietic progenitors capable of becoming blood cells.

(Left) Jonathan LOH at InnoCellular's feature alongside Applitech partner during the Chinese Society for Stem Cell Research Conference 2024 in Harbin, China. (Right) InnoCellular cell media products featured at the Cell and Gene Therapy Conference 2024 in Tianjin, China.

By understanding the intrinsic developmental program of cells, LOH's team was able to generate blastoids that closely resembled blastocysts. This allowed the creation of more clinically relevant models to better study disease biology. His lab also developed high throughput screening tools for uncovering determinants of viral silencing in mouse embryonic stem cells, which remain powerful tools for target discovery.

Nuclear receptor-SINE B1 network modulates expanded pluripotency in blastoids and blastocysts

Received: 8 October 2023
Accepted: 4 November 2024
Published online: 19 November 2024

Ka Wai Wong[1,3,6], Yingying Zeng[1,2,3,6], Edison Tay[1], Jia Hao Jackie Teo[1], Nadia Omega Cipta[1], Kiyofumi Hamashima[1], Yao Yi[1], Haijun Liu[3], Tushar Warrier[1], Minh T. N. Le[4,5,7], Soon Chye Ng[3,7,8], Qi-Jing Li[4,7], Hu Li[9] & Yuin-Han Loh[1,3,10,11,12]

Systematic Identification of Factors for Provirus Silencing in Embryonic Stem Cells

Bin Xia Yang,[1,22] Chadi A. EL Farran,[1,2,22] Hong Chao Guo,[3,22] Tao Yu,[1,2,22] Hai Tong Fang,[1] Hao Fei Wang,[1,2] Sharon Schlesinger,[4,5] Yu Fen Samantha Seah,[1] Germaine Yen Lin Goh,[6] Suat Peng Neo,[7] Yinghui Li,[8] Matthew C. Lorincz,[10] Vinay Tergaonkar,[9,21] Tit-Meng Lim,[2] Lingyi Chen,[3] Jayantha Gunaratne,[7,8] James J. Collins,[11,12,13,14] Stephen P. Goff,[4,5,15] George Q. Daley,[14,16,17,18,19] Hu Li,[20] Frederic A. Bard,[6,21] and Yuin-Han Loh[1,2,*]

(Left) WONG et al, Nature Communications (2024) (Right) YANG et al, Cell (2015)

Ernesto GUCCIONE

Ernesto GUCCIONE also made important discoveries behind retaining the pluripotency of cells by controlling the transcriptional network of transcription factors. These PR-domain-containing proteins (PRDMs) have essential roles in embryonic development and cell fate decisions. By modifying the activity of PRDM15, the naive pluripotency of mouse stem cells was preserved.

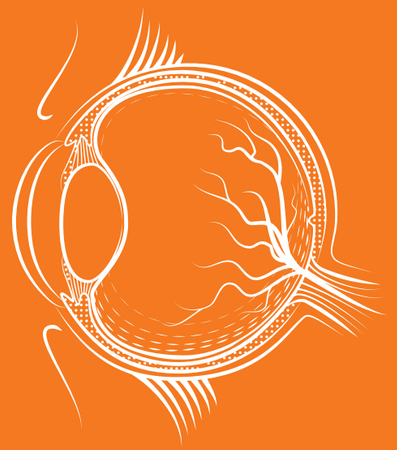
Article | Published: 24 July 2017

PRDM15 safeguards naive pluripotency by transcriptionally regulating WNT and MAPK–ERK signaling

Slim Mzoughi, Jingxian Zhang, Delphine Hequet, Shun Xie Teo, Haitong Fang, Qiao Rui Xing, Marco Bezzi, Michelle Kay Yi Seah, Sheena L M Ong, Eun Myoung Shin, Heike Wollmann, Esther S M Wong, Muthafar Al-Haddawi, Colin L Stewart, Vinay Tergaonkar, Yuin-Han Loh, N Ray Dunn, Daniel M Messerschmidt & Ernesto Guccione

Nature Genetics **49**, 1354–1363 (2017) | Cite this article

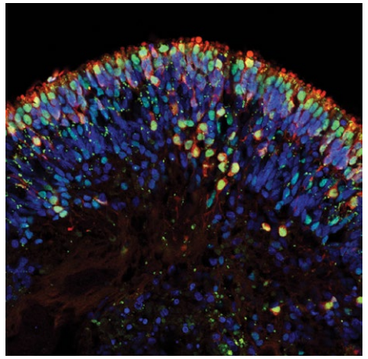
MZOUGHI et al, Nature Genetics (2017)

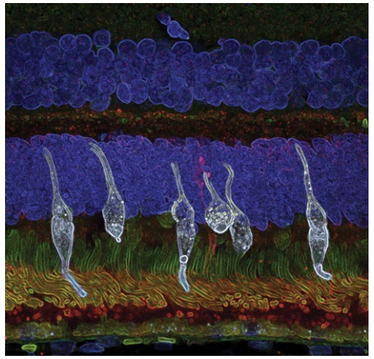


Beyond understanding the fundamental mechanisms of stem cell differentiation, stem cell technology can also be used as a transformative approach for treating ophthalmological conditions. The eye is an ideal target for this therapy due to its accessibility for transplantation and imaging, as well as the relatively small volume of cells required for effective treatment. Cellular therapy offers renewed hope for patients with late-stage degenerative retinal diseases, where conventional treatments remain limited.

The **Translational Retinal Research Laboratory**, led by **Xinyi SU**, is actively addressing key scientific and translational challenges in retinal cell therapy. The team leverages on large animal models and high-resolution capabilities of single-cell transcriptomics to profile cell fate and integration of transplanted retinal cells, providing critical insights into transplantation biology.

In collaboration with **Cell Research Corporation**, a Singapore-based biotechnology company, the lab is also developing hypo-immunogenic RPE cell lines derived from human umbilical cord lining cells for transplantation. If successful, this approach could enable off-the-shelf, universal cell resources for RPE transplantation, significantly lowering costs and improving accessibility to cell-based therapies for retinal diseases.





(Left) Xinyi SU and her team enjoying a barbecue party. (Middle) A fully matured and lab grown retinal organoids derived from human pluripotent stem cells. (Right) Transplanted human stem cell derived retinal cells (white) completely integrated into a non-human primate retina (Below) PARIKH et al, PNAS (2023)

PNAS RESEARCH ARTICLE | APPLIED BIOLOGICAL SCIENCES OPEN ACCESS

Single-cell transcriptomics reveals maturation of transplanted stem cell–derived retinal pigment epithelial cells toward native state

Bhav Harshad Parikh[a,1], Paul Blakeley[a,b,1], Kakkad Regha[a,b], Zengping Liu[a,b,c], Binxia Yang[a], Mayuri Bhargava[a,b,d], Daniel Soo Lin Wong[b], Queenie Shu Woon Tan[a], Claudine See Wei Wong[a], Hao Fei Wang[a], Abdurrahmaan Al-Mubaarak[a,b], Chai Chou[a], Chui Ming Gemmy Cheung[e], Kah Leong Lim[a], Veluchamy Amutha Barathi[a,e,f], Walter Hunziker[a,g], Gopal Lingam[b,c,e], Tim Xiaoming Hu[a,2], and Xinyi Su[a,b,c,d,h,2]

USING STEM CELL TECHNOLOGY FOR DISEASE MODELLING

Diabetes is a major metabolic disease affecting more than 500 million individuals worldwide. The demise of insulin-secreting pancreatic beta cells ultimately results in an inability to maintain glucose homeostasis. Therefore, **Adrian TEO**'s lab has been elucidating the role of genetic factors that determine pancreatic beta cell health and their insulin secretion function.

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-021-22843-4 OPEN

Decreased GLUT2 and glucose uptake contribute to insulin secretion defects in MODY3/HNF1A hiPSC-derived mutant β cells

Blaise Su Jun Low[1,2], Chang Siang Lim[1,3,9], Shirley Suet Lee Ding[1,9], Yaw Sing Tan[4,9], Natasha Hui Jin Ng[1], Vidhya Gomathi Krishnan[5], Su Fen Ang[6], Claire Wen Ying Neo[1,2], Chandra S. Verma[4,7,8], Shawn Hoon[5], Su Chi Lim[3,6], E. Shyong Tai[2] & Adrian Kee Keong Teo[1,2]✉

nature communications

Article https://doi.org/10.1038/s41467-023-41860-z

PAX4 loss of function increases diabetes risk by altering human pancreatic endocrine cell development

Received: 26 June 2022
Accepted: 20 September 2023
Published online: 30 September 2023
Check for updates

Hwee Hui Lau[1,2,10], Nicole A. J. Krentz[3,4,15,16], Fernando Abaitua[4], Marta Perez-Alcantara[4], Jun-Wei Chan[1,2], Jila Ajeian[5], Soumita Ghosh[6], Yunkyeong Lee[3], Jing Yang[3], Swaraj Thaman[3], Benoite Champon[4], Han Sun[3], Alokkumar Jha[3], Shawn Hoon[7], Nguan Soon Tan[2,8], Daphne Su-Lyn Gardner[9], Shih Ling Kao[10,11], E. Shyong Tai[10,11,12], Anna L. Gloyn[3,4,6,13,17]✉ & Adrian Kee Keong Teo[1,11,14,17]✉

(Left) LOW et al, Nature Communications (2021). (Right) LAU et al, Nature Communications (2023).

nature communications

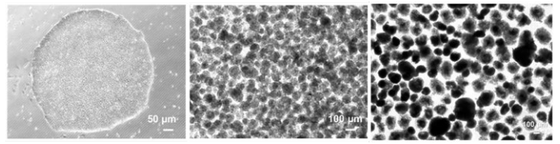
Article https://doi.org/10.1038/s41467-024-48647-w

HNF4A and HNF1A exhibit tissue specific target gene regulation in pancreatic beta cells and hepatocytes

Received: 3 February 2023
Accepted: 8 April 2024
Published online: 22 June 2024

Natasha Hui Jin Ng[1], Soumita Ghosh[2], Chek Mei Bok[1], Carmen Ching[1], Blaise Su Jun Low[1], Juin Ting Chen[1,2,3], Euodia Lim[1,3], Maria Clara Miserendino[4,5], Yaw Sing Tan[4], Shawn Hoon[6] & Adrian Kee Keong Teo[1,2,3,7]✉

(Left) NG et al, Nature Communications (2024), (Right) TEO's lab group dinner celebrating a successful PhD defence of their PhD student.



(Left) A human pluripotent stem cell colony on a feeder free monolayer culture. (Middle) Human pluripotent stem cells cultured as 3D spheroids before initiation of differentiation. (Right) hPSC-derived islet clusters after completion of 35 days of directed differentiation.

These discovery efforts thereby led to an A*STAR IMCB spin-off, **BetaLife**, driving scalable stem-cell-based solutions for tissue engineering and cell replacement therapies. This IMCB spin-off from TEO's lab focuses on developing pancreatic islet cells from clinical-grade human iPSCs, offering a potential breakthrough in cell therapy for diabetes. By providing a sustainable cell replacement solution, BetaLife aims to restore insulin production in diabetic patients, addressing the growing need for curative treatments beyond insulin injections.

BetaLife Co-founders Adrian TEO (back row, right) and Natasha NG (front row, right) with the leadership team of BetaLife. NG was a postdoctoral fellow in TEO's lab from 2017 to 2025, and is currently the CEO and CSO at BetaLife.

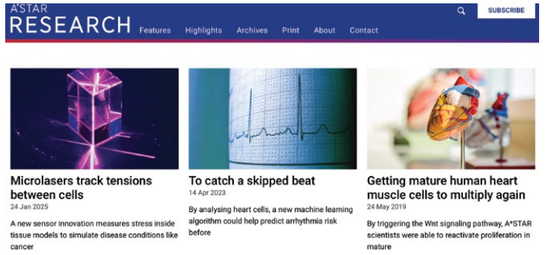
Together, **Jonathan LOH, Adrian TEO and Xinyi SU** are leading the **Reliable Cell Production for Stem Cell-based Therapy (ReCePro)** programme. In this programme, they want to realise the immense promise of human induced pluripotent stem cells (hiPSCs) for cell replacement therapies, offering the ability to differentiate into any cell type for regenerative medicine. Translation of hiPSCs into clinical applications has been hindered by manufacturing bottlenecks, including clonal variability, batch inconsistency, low efficiency, and a lack of standardised quality control assays. To address these critical challenges, the ReCePro programme is pioneering innovative solutions to enhance iPSC production efficiency, scalability, and clinical readiness.

ReCePro is focused on developing cutting-edge technologies that will accelerate iPSC manufacturing while ensuring consistent, high-quality outputs. The programme is advancing methods to boost differentiation efficiency, create robust, scalable production pipelines, and implement rapid quality control assays to validate iPSC-derived products for clinical use. By resolving key barriers in manufacturing, quality assessment, and regulatory compliance, ReCePro will provide reliable and scalable solutions that support iPSC-based therapies.

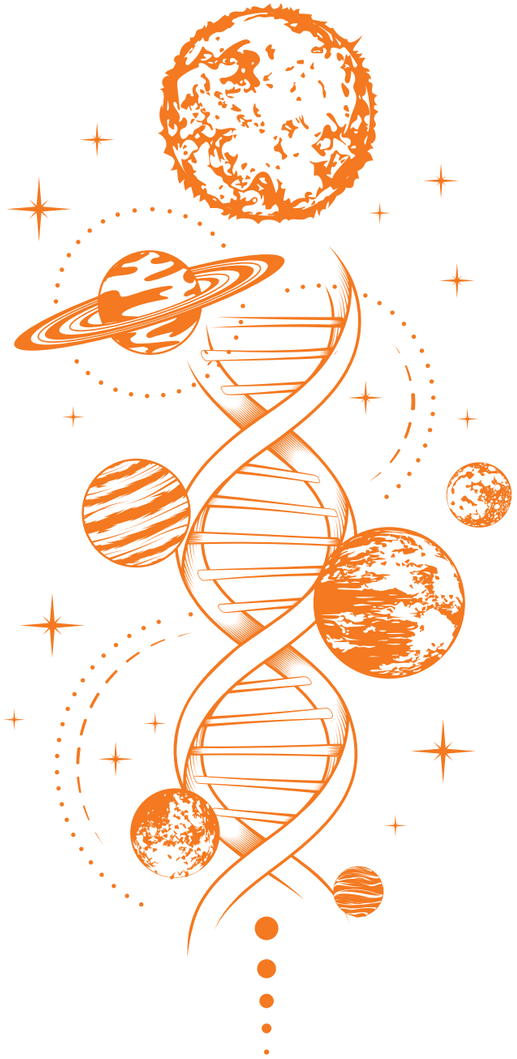
Beyond therapeutic applications, stem cell technologies can enable the development of relevant disease models to study the mechanism and drivers of diseases. These models also provide a platform for testing new therapeutics.

Heart failure remains a leading cause of mortality worldwide, with limited treatment options and a growing need for innovative therapeutic strategies. **Boon Seng SOH** is pioneering a collaborative, multi-institutional effort to create a comprehensive, one-stop platform that integrates expertise from NHCS (National Heart Centre Singapore), A*STAR IMCB, and NUS Medicine. This cross-disciplinary initiative brings together stem cell technology, chambered cardiac organoid models, and multi-omics profiling to accelerate target identification and validation for industry partners seeking to develop novel heart failure treatments. By merging advanced stem cell models with high-resolution molecular analyses, this platform provides an unparalleled preclinical testing ground for evaluating potential drug targets.

Beyond target validation, this integrated cardiac research ecosystem is designed to de-risk and fast-track drug development. Leveraging human stem cell-derived cardiomyocytes and chambered cardiac organoids, researchers can assess new drug candidates for their effects on arrhythmogenesis, contractile function, and metabolism, ensuring cardiac safety early in development. The platform also allows pharmaceutical and biotech companies to test proprietary tool compounds, providing industry-ready solutions for evaluating therapeutic efficacy and cardiotoxicity. By offering a robust, scalable, and clinically relevant model, this initiative is poised to drive breakthroughs in cardiovascular medicine, fostering strong industry collaborations and positioning Singapore as a global leader in heart failure research and precision cardiology.



(Top) Featuring research highlights from Boon Seng SOH's lab.
(Middle) Boon Seng SOH and his team enjoying lunch. (Bottom) Boon Seng SOH and his team celebrating Christmas.



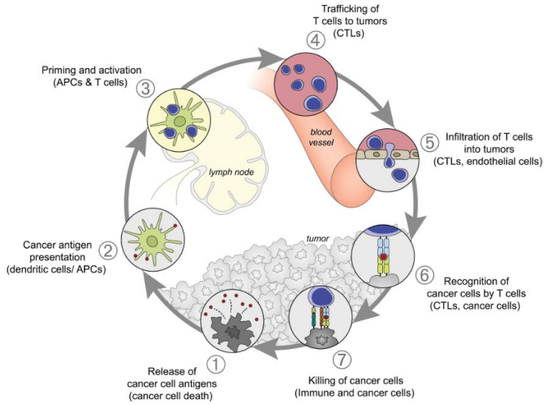
TRAILBLAZING IN IMMUNOTHERAPY

Immunotherapy has revolutionised cancer treatment, offering new hope for patients by harnessing the body's immune system to target tumours. However, a deeper mechanistic understanding of primary and acquired resistance to current treatments remains lacking — an essential gap that must be addressed to improve efficacy and durability, particularly for solid tumours. Meanwhile, the high cost and complex manufacturing processes of these therapies, especially cell therapy, continue to pose significant barriers to widespread clinical adoption. To address this challenge, A*STAR IMCB has spearheaded efforts to develop scalable, cost-effective immunotherapy solutions, leading to the birth of key initiatives such as **SPECTRA, Panakeia, IMPACT, and ASPHALT** – ASPHALT being a continuation of STAMP 1.0. These projects aim to refine and accelerate immunotherapy production, with the goal of making these cutting-edge treatments more accessible and impactful for patients worldwide.

I. PANAKEIA: DEVELOPING COST-EFFECTIVE, OFF-THE-SHELF IMMUNE CELL THERAPIES

A leader in immunotherapy research, **Qi-Jing LI** is dedicated to understanding the lifecycle and function of T cells and Natural Killer (NK) cells in solid tumours to advance next-generation cancer immunotherapies. Awarded the NRF Investigatorship 2024, his research focuses on the intricate mechanisms by which tumours manipulate T cell immunity at both local and systemic levels. His work also aims to develop innovative strategies to empower T cells for effective metastasis protection, paving the way for more durable and targeted immunotherapeutic solutions.

As the Lead Investigator of iPSCs-differentiated Natural Killer cells for cancer immunotherapies **(Panakeia)**, LI is spearheading efforts to engineer iPSC-derived Natural Killer (NK) cells, offering an off-the-shelf solution that eliminates the need for complex and costly patient-specific cell therapies. The Panakeia initiative aims to establish a robust NK cell production platform that differentiates mature CAR-NK cells from iPSC master cell banks, ensuring consistency and unlimited scalability. With the unprecedented feasibility of iPSCs in editing and reprogramming, these iPSC-NKs will be armoured with novel functionalities, enhancing their therapeutic potential in the battle against solid tumours. This initiative is co-led by **Jonathan LOH**, who specialises in stem cell reprogramming and differentiation, and other leading researchers contributing to immune engineering and cellular therapy innovations.



(Top) Proposed mechanism of action of NK cells in targeting and eliminating cancer cells. (Below) Qi-Jing LI and team at the Sky Bridge in A*STAR IMCB, Proteos.

II. ASPHALT: DRIVING INNOVATION IN CAR-T AND T-CELL THERAPIES

(Top) John CONNOLLY in centre and the IMCB team behind ASPHALT.
(Bottom) CONNOLLY group lab lunch.

To further improve the accessibility and potency of engineered T-cell therapies, **John CONNOLLY** is leading the charge as Team PI of **Assembling Screening, Productions, High-throughput Analytics, and Lentiviral Targeting for T cells (ASPHALT)**, an initiative focused on revolutionising CAR-T cell production. ASPHALT will further develop technologies from IMPACT (a part of STAMP 1.0) to bring it closer to commercialisation.

CONNOLLY is tackling one of immunotherapy's biggest challenges: the high cost and complexity of CAR-T cell manufacturing. While CAR-T therapies have transformed treatments for certain blood cancers, they remain expensive and difficult to adapt for solid tumours. ASPHALT is designed to scale up production efficiency and reduce costs, with a focus on achieving 24-hour CAR-T cell manufacturing. By tightly integrating clinical translation with high-throughput analytics, the project is benchmarking two CAR-T cell therapies: one targeting B7-H3 for relapsed/refractory paediatric neuroblastoma, and another targeting CD-19 for severe autoimmune diseases such as idiopathic inflammatory myopathy (IIM) with rapidly progressive interstitial lung disease (RP-ILD) and refractory systemic sclerosis (SSc).

Leveraging on the insights on immunotherapy, CONNOLLY is the scientific co-founder of **Twain Therapeutics**, a company developing antibody-based IL-2 receptor agonists designed to selectively expand CD8 effector and memory T cells and NK cells while avoiding the activation of regulatory T cells (Tregs), which can dampen immune responses. This approach enhances immune activation and has shown complete and durable regression of metastatic disease in a subset of renal cell carcinoma (RCC) and melanoma patients. ASPHALT continues to explore novel immunomodulatory strategies, refining how the immune system can be precisely manipulated for superior therapeutic outcomes.

III. SPATIAL MULTIOME CARTOGRAPHY IN HUMAN THYMUS TO GUIDE NEXTGEN CELL-BASED THERAPIES (SPECTRA)

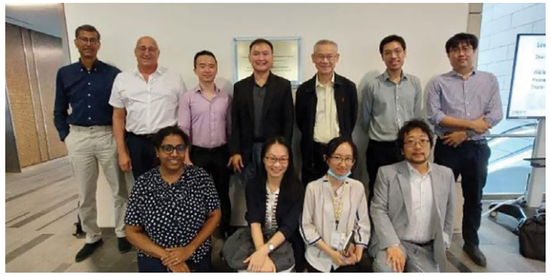
Funded by the NRF Competitive Research Fund Programme (CRP) grant and led by **Jonathan LOH**, **Spatial Multiome Cartography in Human Thymus to Guide NextGen Cell-based Therapies (SPECTRA)**, is a collaborative effort between A*STAR IMCB, Genome Institute of Singapore (GIS), Singapore Immunology Network (SIgN), National University of Singapore (NUS), National University Health System (NUHS) and Shanghai Jiao Tong University.

Its co-investigators include **Qi-Jing LI** (IMCB & SIgN), **Nicholas RJ GASCOIGNE** (NUS), **Qingfeng CHEN** (IMCB), **Ching Kit CHEN** (NUHS), **Shyam PRAHBAHAKAR** (GIS), and **John Kit Chung TAM** (NUHS).

SPECTRA aims to develop a more comprehensive understanding of both thymic ageing as well as the underlying mechanisms behind autoimmune conditions.

The thymus is a major site for T-cell development. Hematopoietic progenitors migrate from the bone marrow into the thymus, where massive engagements between migrating thymocytes and spatially ordered stromal cells, mainly thymic epithelial components, occur to promote T-cell differentiation and maturation. During ageing, thymus shrinks in size, with the key epithelial components being gradually replaced by adipocytes. The reduced output from thymus could contribute to declining immunity in ageing populations. However, the mechanistic details governing both the development and ageing processes of the thymus remain unclear.

The insights gained in SPECTRA can enable better engineering for autologous cell manufacturing, which could benefit patients who are suffering from either old age or autoimmune diseases.



The 'SPECTRA' team. Standing (left to right): Shyam PRABHAKAR (Team PI, GIS), Nicholas RJ GASCOIGNE (Team PI, NUS), Ching Kit CHEN (Team PI, NUHS), Jonathan Yuin-Han LOH (Lead PI, IMCB), Andy HOR (Deputy Chief Executive (Research), A*STAR), Leslie BEH (Collaborator, IMCB), Lai Guan NG (Collaborator, Shanghai Jiao Tong University). Front row (left to right): Uma Sangumathi KAMARAJ (Principal Scientist working for the project, IMCB), Jinmiao CHEN (Collaborator, SIgN), Ying CHEN (Principal Scientist working for the project, IMCB), Qi-Jing LI (Team PI, IMCB & SIgN)

IV. HUMANISED MOUSE MODELS FOR IMMUNO-CELL THERAPY

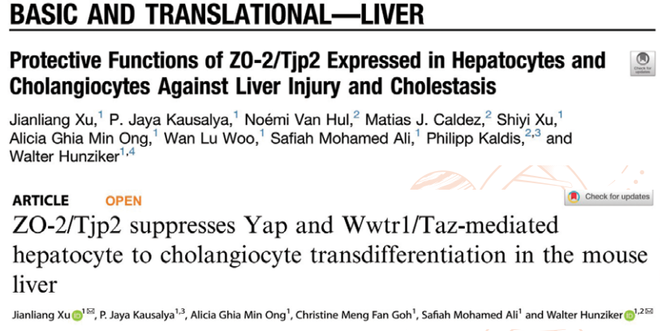
Qingfeng CHEN, a 2017 NRF Fellow, has played a crucial role in developing humanised mouse models that have been crucial as a platform to validate novel cell therapies. His work had enabled close industry partnerships including a joint lab with Tikva Allocell. Further, the expertise developed in drug testing led to the co-founding of **Invivocue**, a start-up that accelerates drug discovery through preclinical immunotherapy screening. Such models better recapitulate human biology and are an important tool to validate novel immunotherapies and cell therapies, ensuring that promising treatments can be efficiently tested and scaled for clinical use.

Qingfeng CHEN

By bridging the gap between basic research, clinical translation, and industry partnerships, A*STAR IMCB remains at the forefront of immunotherapy innovation. Through strategic initiatives such as SPECTRA, Panakeia and ASPHALT, A*STAR IMCB is not only advancing immunotherapy science but also making these life-saving treatments more affordable and accessible, ensuring that the next generation of cancer therapies reaches those who need them most.

UNDERSTANDING FUNDAMENTAL BIOLOGY TO DRIVE NEXT GENERATION SIRNA THERAPY: RIPE FOR SPIN OFF

With deep expertise in epithelial cell polarity, membrane trafficking, and cytoskeleton organisation, **Walter HUNZIKER** has been instrumental in developing in vivo preclinical mouse models for kidney and liver diseases, eenabling target identification and validation for therapeutic development. These models also allow siRNA screening leading to the identification of two validated therapeutic modalities that provide liver protection against injury and cholestasis. This has potential applications in treating cholestatic liver disease and reverse liver fibrosis. Currently, the team is completing preclinical work to enable future spin-off of the technologies.



BASIC AND TRANSLATIONAL—LIVER

Protective Functions of ZO-2/Tjp2 Expressed in Hepatocytes and Cholangiocytes Against Liver Injury and Cholestasis

Jianliang Xu,[1] P. Jaya Kausalya,[1] Noémi Van Hul,[2] Matias J. Caldez,[2] Shiyi Xu,[1] Alicia Ghia Min Ong,[1] Wan Lu Woo,[1] Safiah Mohamed Ali,[1] Philipp Kaldis,[2,3] and Walter Hunziker[1,4]

ARTICLE OPEN

Check for updates

ZO-2/Tjp2 suppresses Yap and Wwtr1/Taz-mediated hepatocyte to cholangiocyte transdifferentiation in the mouse liver

Jianliang Xu[1✉], P. Jaya Kausalya[1,3], Alicia Ghia Min Ong[1], Christine Meng Fan Goh[1], Safiah Mohamed Ali[1] and Walter Hunziker[1,2✉]

(Left) Walter HUNZIKER and his team out for lab lunch. (Top right) Xu et al, Gastroenterology (2021). (Below right) Xu et al, npj Regenerative Medicine (2022)

RECOMBINATION - INTEGRATING MOLECULAR ENGINEERING WITH CELL THERAPY TO DEVELOP NEXT GENERATION THERAPIES

With growing understanding of the human genome and underlying genetic factors driving diseases, new therapeutic modalities such as viral-based gene therapy, RNAi-based medicines and nucleic acid therapeutics have emerged as game changing genomic medicines.

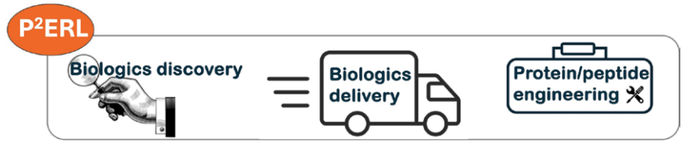
A. ENGINEERING PEPTIDES AND PROTEINS

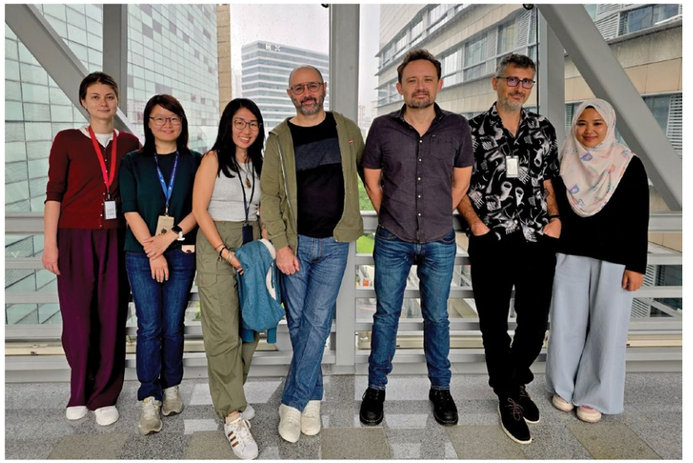
Founded in 2009 by the late **Sydney BRENNER**, the Molecular Engineering Laboratory (MEL) at A*STAR embodies his vision of fostering left-field research and interdisciplinary innovation. As a pioneer in Singapore's biomedical research ecosystem, BRENNER established MEL as a platform where young scientists could push the boundaries of molecular science, driving transformative discoveries. The lab's research spans molecular biotechnology, microbial engineering, bioinformatics, device fabrication, and therapeutics, with applications in health, sustainability, and bioengineering.

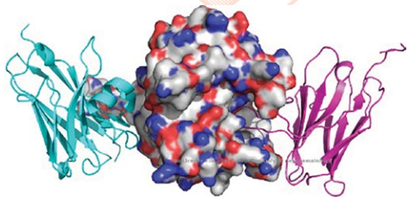
Today, under the leadership of **Fong Tian WONG** and **Yiqi SEOW**, MEL continues to push the frontiers of molecular engineering, integrating expertise from biochemistry, bioinformatics, enzyme engineering, and biotechnology to address economically valuable use cases. The work at MEL led to the founding **of Einprot**, a startup co-founded by **Fong Tian WONG, Yiqi SEOW** and **Winston KOH** (MEL Alumni). Leveraging AI-driven protein design, Einprot pioneers custom-engineered proteins with enhanced functionality, revolutionising medicine, enzyme production, and sustainable bioprocessing. Their proprietary protein language model (LLM) generates optimised digital twins, unlocking new possibilities in therapeutic development and biomanufacturing.

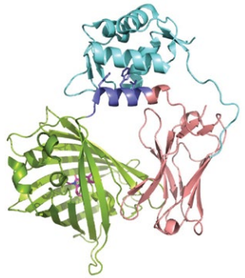
(Left) Lab photo with Sydney BRENNER in 2016. (Middle) Darren LUI, CEO of Einprot, at the 2024 Edition of Singapore Week of Innovation and Technology (SWITCH). Einprot was selected as one of the Top 10 grand finalists of SLINGSHOT 2024, a deep tech startup competition held as part of SWITCH, providing a platform for promising startups to showcase their technology and business ideas. (Right) 2024 Chinese New Year celebration

Established in 2024, the **Protein and Peptide Engineering and Research Laboratory (P²ERL)** led by **Farid GHADESSY** and **Christopher BROWN** primarily focuses on discovery and delivery of biologic therapeutics. Protein and peptide assets have been developed against eIF4E and MDM2, key drivers of certain cancers. Novel delivery technologies including phase-separating cell-penetrating peptides are being developed for targeted delivery of assets in vivo. Other research focuses on development of novel protein/peptide engineering methods, AI-guided protein engineering, and development of improved enzymes for molecular diagnostics.









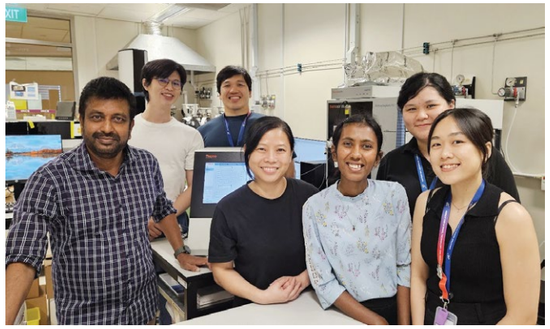
(Left) Members of P²ERL. Structures of engineered biologics targeting eIF4E (top right) (Frosi et al Nat. Commun. 2022) and MDM2 (bottom right) (Chee et al Sci. Rep. 2021).

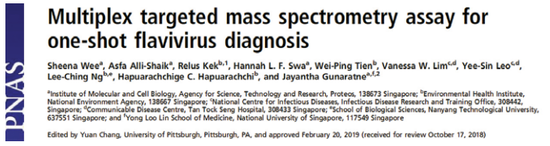
ADVANCING TRANSLATIONAL PROTEOMIC-CENTRIC DISCOVERIES

Cutting-edge mass spectrometry-based technologies, primarily quantitative proteomics, form the backbone of **Jayantha GUNARATNE**'s work at IMCB. His research deciphers the disease ectoproteome, investigating sheddome, surfaceome, matrisome, and biofluid proteomes to identify molecular targets for precision diagnostics and therapeutic intervention.

Beyond developing diagnostic mass spectrometry assays, GUNARATNE's proteomics-centric research has led to the discovery of novel therapeutic targets for ocular neovascularisation and highly aggressive breast cancer subtypes. His strong collaborations with research institutions, hospitals, and government agencies ensure that his discoveries transition seamlessly from the lab to clinical applications, driving advancements in translational medicine.

GUNARATNE, who joined IMCB in 2007, was also instrumental in establishing proteomics capabilities in A*STAR, working alongside **Walter BLACKSTOCK** to build a state-of-the-art proteomics facility. Their combined efforts laid the groundwork for cutting-edge protein research infrastructure, enabling large-scale proteomic analyses that have since driven numerous biomedical discoveries. This foundation continues to support IMCB's mission in developing next-generation biomarker discovery and precision medicine solutions.





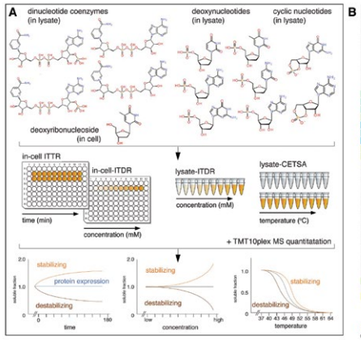
(Upper Left) GUNARATNE group photo 2025, (Upper Right) ALLI-SHAIK et al. Theranostics paper inside front cover article (2022). (Below Left) WEE et al, PNAS (2019), (Upper Right) A*STAR Research highlight on Theranostics paper (2022) (9 Oct 2023).

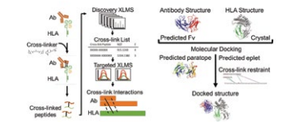
Mass spectrometry proteomics is a powerful technique for identifying biomarkers, profiling clinical samples and drug target deconvolution. **Radoslaw SOBOTA** leads a mass spectrometry lab with cutting-edge equipment, enabling collaborations with the Singapore ecosystem and beyond. He applied the use of mass spectrometry cellular thermal shift assay (CETSA) pipeline that was developed for cancer by Par NORDLUND. This opened up multiple new application avenues in infectious diseases, proteome wide drug discovery and contributing to new endogenous metabolite targets.

His long-term research interest is focused on the integration of cell biology and immunology with quantitative mass spectrometry-based proteomics. His lab pursues research in clinical proteomics and body fluid biomarker discovery with the capability for multiple sample analysis of more than 300 samples, which will contribute to new clinical predictive biomarkers. His lab also developed a method for hybrid structural modelling of the antibody to human leukocyte antigen interaction in the context of clinical transplantation.

Beyond quantitative proteomics, his lab is currently developing multi-omics approach utilising spatial multi-omics and single cell proteomics for efficient detection and validation of cancer neoantigens for cancer diagnostics and T-cell based personalised therapies supported by patient specific drug treatment selection.

SOBOTA has developed and extended mass spectrometry proteomics to different biomedical applications. His lab, together with NUS, was awarded the NRF-SIS grant to establish the National Laboratory for Mass Spectrometry "SingMass". His research group continues to push the boundaries of mass spectrometry proteomics for integrated precision medicine.





(Left) Developed MS-CETSA workflow (Lim et al. PLOS ONE 2018.) (Top right)) Radoslaw SOBOTA and his team enjoying Christmas eve (2024). (Below right) Developed antibody-HLA modelling workflow (Ser et al. Cell Rep Methods 2023).

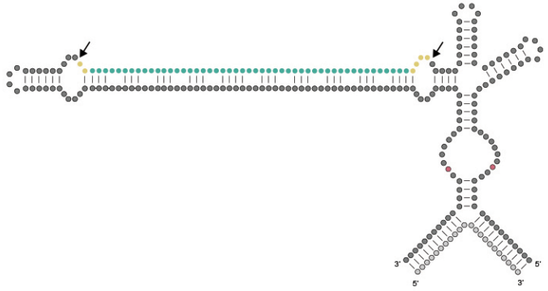
B. ENGINEERING RNA

At the forefront of RNA-based therapeutics, A*STAR IMCB researchers have developed a platform for the modular design of therapeutic antisense oligonucleotides (ASOs) to regulate RNA expression through splice switching and nonsense-mediated decay. RNAi-based medicines have emerged as a powerful modality for treating genetic diseases, with major biotech companies like Ionis and Alnylam leading the charge in this space. One of the key bottlenecks in designing efficacious oligonucleotide therapeutics is the reliance on empirical screening. To solve this, **Dave WEE** was able to design algorithms based on first principle mathematical models that takes into consideration biophysics, biochemistry, thermodynamics and other factors.

With this technology, he co-founded **ImmuNOA**, aiming to harness ASOs to enhance immunotherapy efficacy in treating multiple pathologies. To further enable others to leverage on the deep know-how of the lab, **TechNOA** was founded and it designs and tests custom ASOs tailored to user applications. TechNOA is the first company to sell pre-designed ASOs (>2 million in our libraries) for target discovery and functional genomics since 2019. These initiatives contribute to the broader goal of developing next-generation therapies that can boost immune responses and improve treatment outcomes, positioning A*STAR IMCB as a leader in precision medicine and immunotherapy.

(Left) Official launch of TechNOA at the 24th Annual RNA Society Meeting, Krakow, Poland, 2019. (Right) Dave Keng Boon WEE

The intersection of RNA biology and disease is a rapidly growing field. **Sherry AW**'s lab explores how microRNA and RNA pathways regulate neurodegeneration and movement disorders, and develops RNA technologies to enable novel insight into, and manipulation of, RNA. A major focus is on engineered ribozymes, catalytic RNA molecules modified to modulate gene expression, as well as investigation into mechanisms of and methods for RNA delivery. Her lab holds multiple patents for first-in-class RNA technologies, which they are currently advancing for both therapeutic and diagnostic applications.

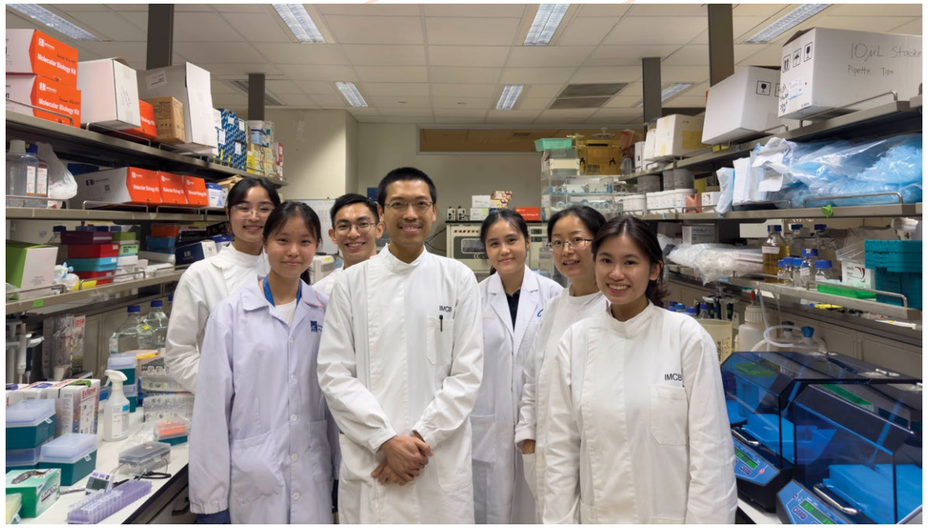


(Left & Top) RNA sensors being developed in Sherry AW's lab. (Bottom Right) Lab celebrating X-Mas party at AW's home.

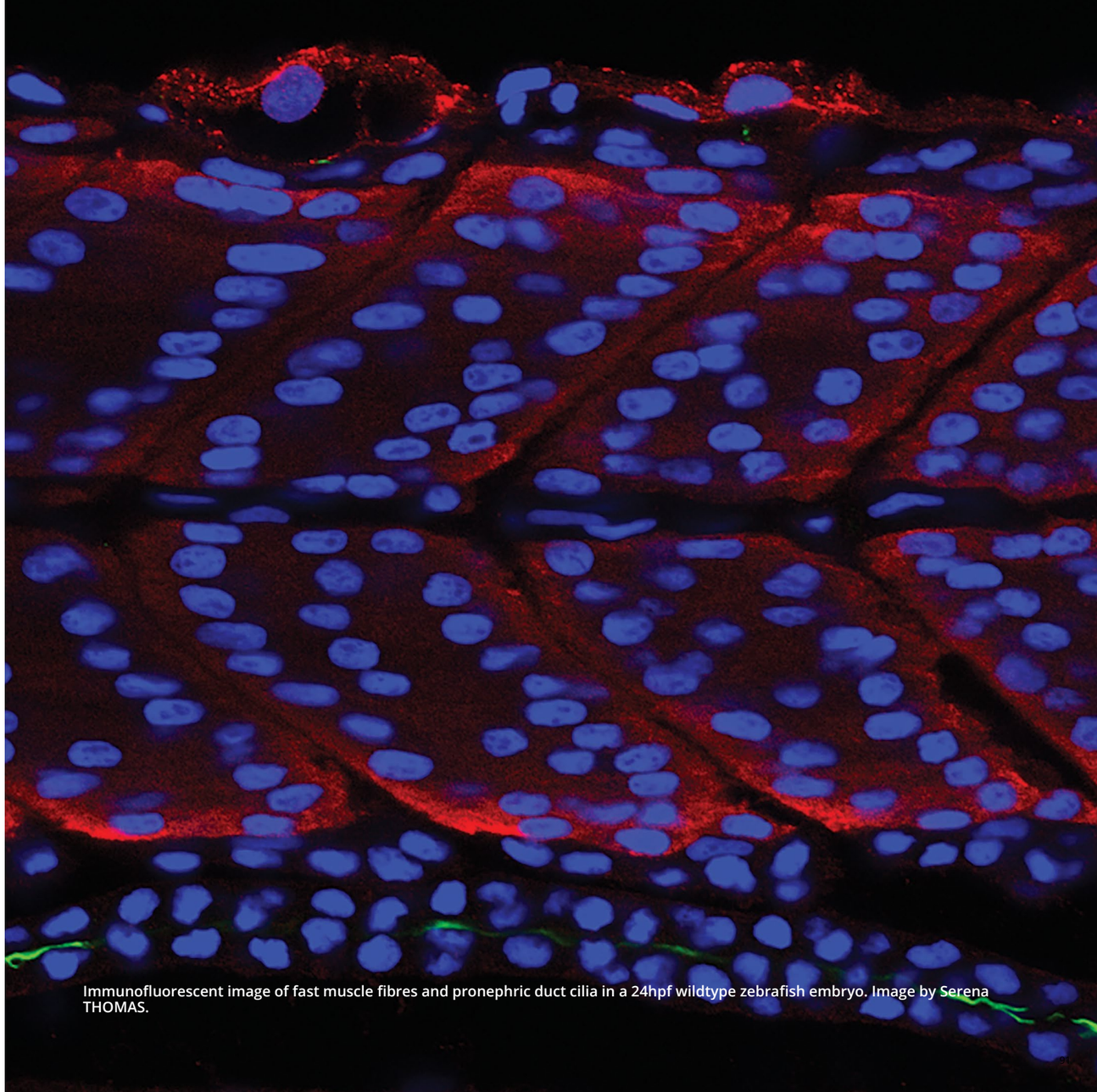
C. ENGINEERING DNA

Expanding A*STAR IMCB's expertise in genome and RNA engineering, **Leslie BEH**, a 2024 NRF Fellow, has joined the team after a career in industry, with a focus on developing precise gene-editing tools and understanding RNA modifications that regulate gene expression. His research enhances the potential of genetic medicines by targeting both DNA and RNA levels, opening new avenues for treating complex genetic disorders.

Through a diverse spectrum of proteomics, enzyme engineering, and RNA-based therapeutic innovations, A*STAR IMCB remains at the forefront of next-generation genetic medicines, addressing urgent medical needs and paving the way for groundbreaking therapies.



BEH's lab group photo 2024



Immunofluorescent image of fast muscle fibres and pronephric duct cilia in a 24hpf wildtype zebrafish embryo. Image by Serena THOMAS.

BRAIN BODY INTERTWINED

Forging a New Frontier in Brain-Body Interactions for Metabolic and Brain Health

A*STAR IMCB has had a long-standing legacy of neuroscience research, delving into the molecular mechanisms underlying neurodevelopment, brain function, and neurological diseases. Over the years, our focus has expanded beyond fundamental discoveries in neurobiology to pioneering translational research programmes aimed at tackling mental health disorders and neurodegeneration. By bridging fundamental research with clinical applications, we are shaping new frontiers in neuroscience to develop innovative diagnostic tools and therapeutic solutions.

PERSPECTIVE FROM AN IMCB ALUMNI KAH LEONG LIM

Pioneering work in neuroscience research began in **Louis LIM**'s Neurobiology laboratory in 1985 when IMCB was inaugurated. The late Louis LIM had longstanding interest in characterising brain-specific mRNAs, especially those related to metabolism. Together with **Edward MANSER, Thomas LEUNG** and team, they also nailed an early industry collaboration with Glaxo, which culminated into the signing of the 'Glaxo-IMCB research venture' aimed at identifying molecular targets involved with neurodegeneration.

Other than Louis LIM's lab, few (if any) A*STAR IMCB laboratories at that time worked directly on neuroscience-related topics. Taking the path less trodden, PhD student **Tuck Wah SOONG** became the first IMCB Alumni to pursue a research career in Neuroscience after graduation. SOONG did his postdoctoral training at UBC with **Terry SNUTCH** and published his seminal discovery of a novel member of the low voltage-activated calcium channel family in 1993 in Science before returning home to be one of our pioneers in neuroscience research. A few others, myself included, followed his footsteps.

Neuroscience research at A*STAR IMCB remained rather nascent until 2011, when A*STAR and Duke-NUS established the Neuroscience Research Partnership (NRP) at A*STAR IMCB's premise that capitalised on the complementary research strengths and resources between the two institutions. NRP was physically located at level 4 of Proteos and was led by the late **Colin BLAKEMORE** as Chair and **Dale PURVES** as its Executive Director. It housed several neuroscience research groups from Duke-NUS and A*STAR IMCB including the laboratories of **George AUGUSTINE, Edward MANSER, Suresh JESUTHASAN, Thomas LEUNG, Adam CLARIDGE-CHANG** and my lab. Despite its short history, several significant breakthrough discoveries were made by NRP investigators, including the discovery that the fear factor (Schreckstoff), a danger cue that fish release when they encounter predators is a mixture, and can modulate the activity of the habenula in the brain. Notably, the lead author of the discovery, **Ajay MATHURU**, is now an independent faculty at NUS and a joint PI with A*STAR IMCB.

Fast forward to today, neuroscience has become one of the major strategic programs at A*STAR IMCB, with a focus on Neurometabolism in Health and Disease. The division has been led by **Weiping HAN** together with a team of talented PIs that collectively seeks to unravel the crosstalk between neural and metabolic systems relevant to brain and body health. This bidirectional relationship between the brain and the body has now emerged to be a hot topic for research globally. Key discoveries from A*STAR IMCB include the elucidation of a novel mechanism of feeding regulation that operates through orexigenic somatostatin neurons that was published in Science (2018) by **Yu FU**'s lab, with first author **Sarah LUO** (now a PI in the division), which provided a new perspective for understanding appetite changes.

At the national level, the Neurological and Sense Disorders Taskforce panel on ageing-related diseases and complications that I chaired has identified neurodegenerative diseases as the singular priority theme, with a focus on vascular dementia & Parkinson's disease. Notably, the gut-brain axis is now considered relevant and important for the development of these devastating neurological disorders. A*STAR IMCB neuroscientists are contributing to solving the significant socio-economic and healthcare problems associated with age-related neurodegenerative diseases. NRF Fellows **Caroline WEE** and **Sarah LUO** are leading the research program REPLENISH, looking at how the gut-brain nutritional axis may be exploited to augment brain health and prevent cognitive decline in at-risk individuals.

It is important to highlight that although neuroscience research at A*STAR IMCB is differentiated from others in the ecosystem, it complements the efforts of the wider Singapore Neuroscience community in tackling diseases of national priority and at the same time helps to position Singapore as a global hub for translational neuroscience research. Towards achieving these, I am pleased to note that A*STAR IMCB neuroscientists are working collaboratively with various partners across the whole Singapore neuroscience ecosystem, including clinical institutions, in an integrated manner. Through a comprehensive understanding of Brain-Body interactions, I envision that neuroscience research at A*STAR IMCB will not only result in fundamental advancements in knowledge but also lead to the development of more holistic treatment for neurological disorders that affects both the central and (oft-underappreciated) peripheral nervous systems.

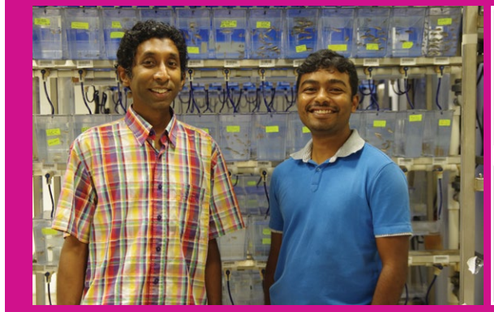
"Through a comprehensive understanding of Brain-Body interactions, I envision that neuroscience research at A*STAR IMCB will not only result in fundamental advancements in knowledge but also lead to the development of more holistic treatment for neurological disorders that affects both the central and (oft-underappreciated) peripheral nervous systems"

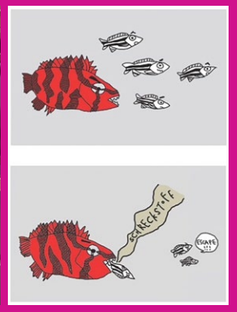
KAH LEONG LIM

A NEW ERA OF MULTIDISCIPLINARY NEUROSCIENCE RESEARCH

A pivotal milestone in this journey was the establishment of the **Neuroscience Research Partnership (NRP)** between A*STAR and Duke-NUS in October 2007. This multidisciplinary initiative sought to integrate molecular neuroscience with clinical research, fostering a collaborative ecosystem for studying brain disorders, neuropsychiatric conditions, and neurodegenerative diseases. By bringing together A*STAR IMCB researchers, clinicians, and behavioural scientists, the NRP ensured that fundamental discoveries were seamlessly translated into medical applications.

Several key A*STAR IMCB scientists have been instrumental in shaping the research landscape under NRP, contributing to breakthroughs with potential clinical and industry applications:





(Left) Suresh JESUTHASAN and (Right) Ajay MATHURU in 2012.

Cartoon depicts the alarm response in fish which both scientists dissected in Lee et al, Current Biology, 2010 and Mathuru et al, Current Biology, 2012 (Credit: Joanne Shu Ming CHIA)

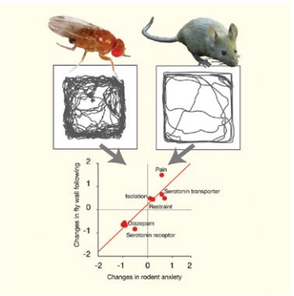
Suresh JESUTHASAN and **Ajay MATHURU**'s research utilises zebrafish as a model organism to study stress, anxiety, and fear responses. This work has uncovered the neural circuits and molecular pathways that regulate fear and emotional memory, paving the way for novel interventions for anxiety-related disorders and PTSD.

Scan to watch video feature of JESUTHASAN and MATHURU's research

Leveraging the Drosophila model, **Adam CLARIDGE-CHANG**'s Lab at A*STAR IMCB and A*STAR's NRP established itself as a leader in neurobehavioural research using Drosophila. The lab made meaningful contributions to understanding circuits controlling anxiety, memory, and feeding behaviour. Notable achievements include developing anion channelrhodopsins for optogenetic inhibition (Mohammad et al., Nature Methods 2017), discovering ancient anxiety pathways in flies (Mohammad et al., Current Biology 2016), and pioneering estimation statistics for biological data analysis (Ho et al., Nature Methods 2019). The lab revealed how flies learn efficient foraging paths (Navawongse et al., 2016) and conducted the first systematic reviews in behavioural genetics (Yildizoglu et al, 2015, Tumkaya et al., 2018). The lab maintained productive collaborations with other A*STAR IMCB researchers, working with **Suresh JESUTHASAN**'s lab on zebrafish neurobehaviour and optogenetics (Mohamed et al., BMC Biology 2017; Krishnan et al., Current Biology 2014) and with **Sherry AW**'s lab on automated tracking of Drosophila neurodegeneration models (Wu et al., PLOS Biology 2019).

Adam Claridge-Chang and his team at Biopolis.

Adam CLARIDGE-CHANG's work on anxiety pathways was published in Mohammad et al, Current Biology, 2016.



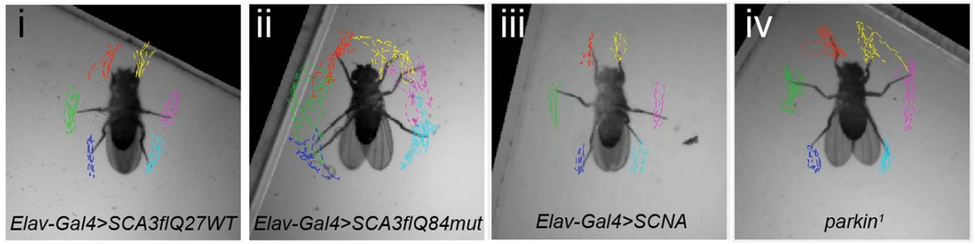
PLOS BIOLOGY

METHODS AND RESOURCES

Fully automated leg tracking of *Drosophila* neurodegeneration models reveals distinct conserved movement signatures

Shuang Wu[1], Kah Junn Tan[2☯], Lakshmi Narasimhan Govindarajan[1☯], James Charles Stewart[2,3], Lin Gu[1], Joses Wei Hao Ho[2,3], Malvika Katarya[2], Boon Hui Wong[4], Eng-King Tan[5], Daiqin Li[4], Adam Claridge-Chang[2,3], Camilo Libedinsky[2,6,7], Li Cheng[1,8+], Sherry Shiying Aw[2+]

Focusing on the role of RNA in neurodegenerative diseases, **Sherry AW**'s research employs Drosophila fruit fly models to study the molecular and cellular mechanisms that drive neurodegeneration and movement disorders. With computer scientist collaborators from the Bioinformatics Institute (BII, A*STAR), she co-developed a machine-learning method for automated measurement of movement disorders like tremor. Through this line of work, new therapeutic targets and cell types have been discovered that have potential applications in drug development for conditions such as Parkinson's disease and Spinocerebellar ataxias. Her innovative approach has also led to the invention of first-in-class RNA biosensors and therapeutic technologies with promising commercial and clinical applications in many disease areas, including neurological diseases. She was awarded the L'Oréal For Women in Science Singapore Fellowship (2017) and the International Fellowship (2019), and was recognised as one of the Asian Scientist 100 (2020).



Sherry AW developed a fully-automated machine-learning algorithm to study tremors in fruitfly neurodegeneration models. Figure panel adapted from WU et al., PLoS Biol, 2019.

GAINING A METABOLIC ANGLE: REGULATION OF METABOLISM THROUGH A NEUROSCIENCE PERSPECTIVE

One of the most transformative developments in A*STAR IMCB's neuroscience research is the emergence of **neurometabolism**—a field that investigates how metabolic pathways regulate brain function and contribute to neurological disorders. This shift has provided a metabolic perspective to neuroscience, revealing how the brain interacts with systemic metabolism to influence functions such as feeding regulation, energy balance, and cognitive health.

A key neuroscience program was established in the Singapore Bioimaging Consortium (A*STAR SBIC) with **Tom SÜDHOF**, Nobel Laureate, as part of the A*STAR Joint Council Office (JCO) Visiting Investigatorship Programme (VIP) program. The program was directed by **Weiping HAN**, with involvement of key scientific minds across the island, including **Wanjin HONG** and **Eng King TAN**. This provided a synergy with the existing strength in metabolism, and would in time form the foundation of the A*STAR IMCB **Neurometabolism in Health and Disease** division where research teams from A*STAR SBIC (**Weiping HAN, Yu FU, Sarah LUO**) were right-sited into A*STAR IMCB in 2021. **Weiping HAN** served as the founding director and led the team (**Yu FU, Sarah LUO** and **Caroline WEE**) to form the major driver for the Brain-Body Initiative (BBI), an A*STAR Strategic Research Program. The boost of expertise transformed the field of neurometabolism, where the understanding of metabolic states through brain-body coordination would impact neuron and brain health, and enhancing such interactions would build resilience and improve overall metabolic health. Significant efforts were also made to gain international recognition for the program, with annual symposiums held since 2007 and a re-branding to Singapore Symposium on Brain-Body Interactions in 2024 to reflect the significant expansion of the contents and the themes of the conference. A*STAR IMCB researchers are pioneering new strategies to understand how metabolic disruptions contribute to neurological diseases, paving the way for novel therapeutic interventions.

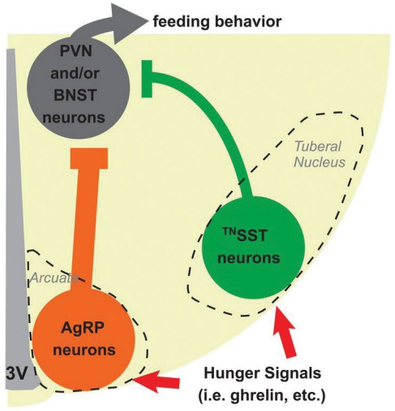
(Left) Tom SÜDHOF receiving the Britton Chance Memorial Award and (right) group photo of the speakers at the Singapore Symposium on Brain-Body Interactions (SSBBI) & Neuroscience Singapore 2024.

UNRAVELING THE NEURAL MECHANISMS OF FEEDING REGULATION

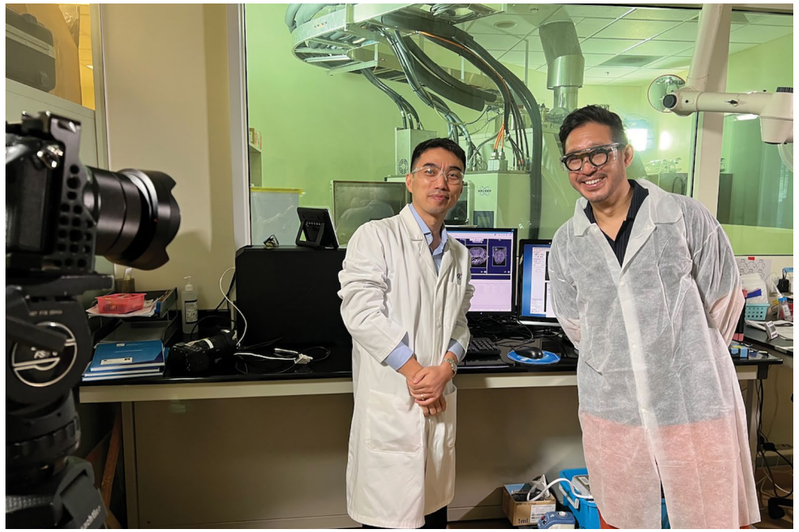
The regulation of food intake involves a complex interplay between neuroendocrine signals, brain circuits, and external metabolic cues. **Yu FU**'s research focuses on identifying the molecular and neuronal pathways that control feeding behaviour and metabolic homeostasis. His studies have led to a better understanding of how neural populations in the hypothalamus and other brain regions integrate metabolic signals to modulate hunger and satiety.

His lab discovered the first physiological function of the tuberal nucleus in hypothalamus and opened a new field of feeding regulation research. His lab also revealed how palatable food makes us over consume food in specific environmental contexts. By pinpointing key regulatory molecules and pathways, his work has the potential to inform the development of targeted therapies for obesity, diabetes, and metabolic diseases.

His research excellence has been acknowledged with the National Research Foundation Investigatorship (NRFI) in 2022. He has been featured in Channel News Asia's "Food to Change the World" and "Nudge - Nudges To Eat Healthier". He also started an international series of symposia on neurometabolism by collaborating with Cell Press, and held the first one in A*STAR.



(Top) Schematic showing the discovery of a novel neural circuit regulating hunger in LUO et al., Science, 361, 76-81, (2018). (Bottom) A follow-up study implicated these neurons in context-induced over-eating, as reported in MOHAMMED et al., Nature Neuroscience, 24(8), 1132-1141 (2021)



Top to bottom: The inaugural Cell Symposium on Neurometabolism in 2023; Yu FU being interviewed by ChannelNewsAsia in 2023

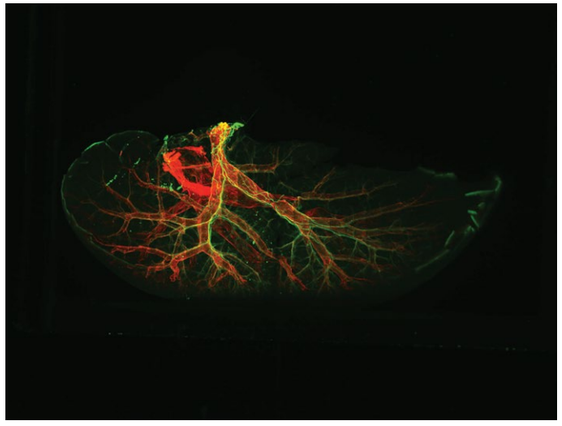
Scan to watch the CNA Feature "Nudge - Nudges to Eat Healthier" showcasing the research of Yu FU.

DECIPHERING BRAIN-ORGAN INTERACTIONS IN FEEDING REGULATION

The intricate communication between the brain and metabolic organs plays a crucial role in maintaining energy balance and regulating feeding behaviour. Research has shown that peripheral metabolic signals — such as hormones from the gut and adipose tissue — can influence neural circuits that control appetite and satiety.

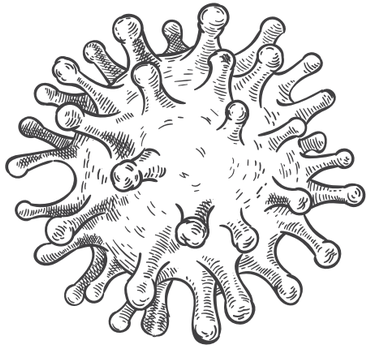
Sarah LUO's work delves into these brain-organ interactions, examining how neuronal pathways linking the brain and organs process cues from the body to regulate food intake and energy balance. Her research is shedding light on how disruptions in these pathways are dysregulated and contribute to conditions such as obesity and metabolic syndrome, opening new avenues for therapeutic interventions. Her work has been featured in a 2024 Nature Index publication "Four change-makers seek impact in medical research", highlighting how her research is pushing the boundaries in the field of neurometabolism.

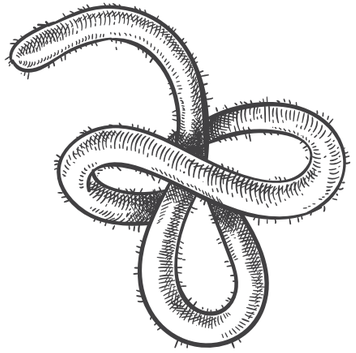
Her contributions to the field have been recognised with the National Research Foundation Fellowship (NRFF) in 2021 and the Young Scientist Award (YSA) in 2021.



A fluorescent lightsheet image of a whole liver lobe with sympathetic nerves (green) encircling vasculature outlined by alpha smooth muscle actin (red).

Link to 2024 Nature Index Publication





Young Scientist Award recipients break new ground

(From left) Dr Zhang Hanwang, Dr Yvonne Gao and Dr Sarah Luo at the 2021 President's Science and Technology Awards ceremony in the Istana on Dec 10, 2021. ST PHOTO: KEVIN LIM

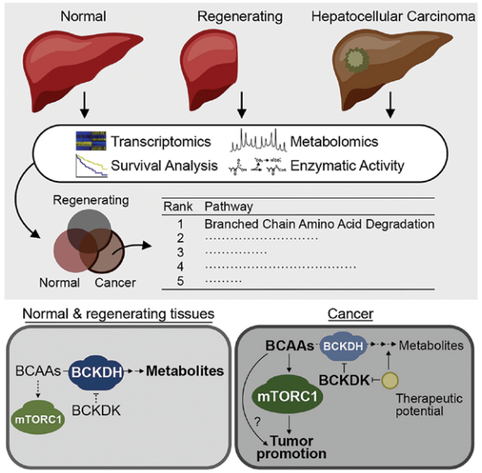
Sarah LUO receiving the 2021 Young Scientist Award in Biological and Biomedical Sciences from the Singapore National Academy of Science.

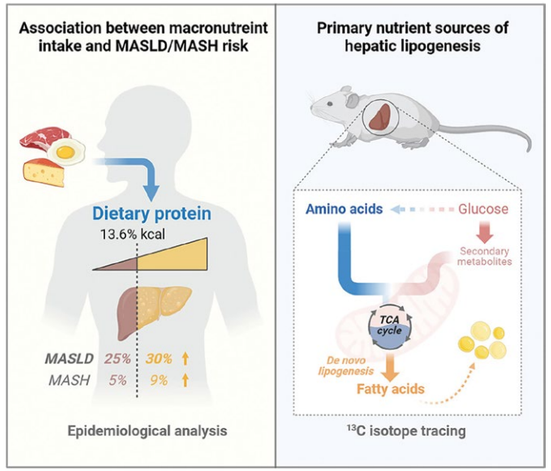
EXPLORING METABOLISM AND ITS IMPACT ON BRAIN FUNCTION

Metabolic disorders such as diabetes, obesity, and metabolic syndrome have been increasingly linked to cognitive dysfunction and neurological diseases, and research in this area has highlighted how metabolic imbalances can affect brain and body function. **Weiping HAN**'s research investigates the critical role of metabolic states in maintaining cell survival and function, with a specific focus on the dysregulation and reprogramming of metabolic activities in the development of metabolic diseases and associated complications, especially liver cancer. His team has identified branched-chain amino acid, proline, and purine metabolism as key dysregulated pathways in human hepatocellular carcinoma and are actively pursuing pharmacological approaches to target these metabolic nodes for therapeutic intervention.

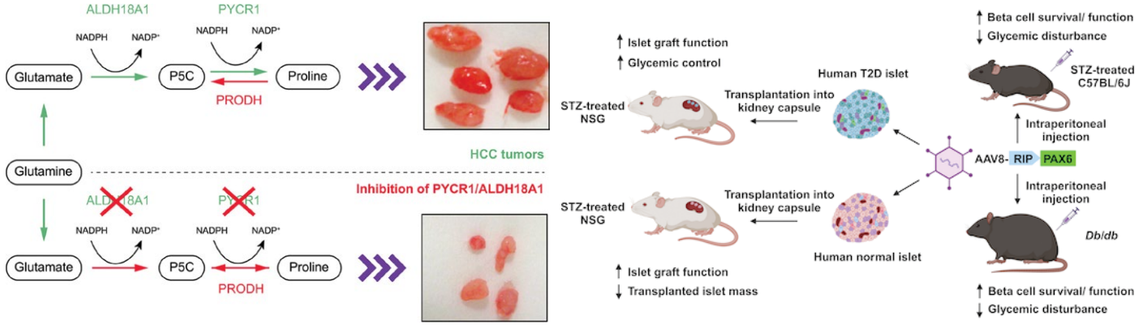
His research has provided critical insights into how cancer cells reprogram their metabolism to adapt to metabolic disturbances, and holds significant promise for developing novel treatments for this devastating disease, which currently has limited effective options.

Left to right: Chiea Chuen KHOR, Leonard YEO, Suchun ZHANG and Weiping HAN as part of the BRAINSTORM (Investigating the Basis foR AsiaN Intracranial STenosis - a pRecision Medicine approach) team.



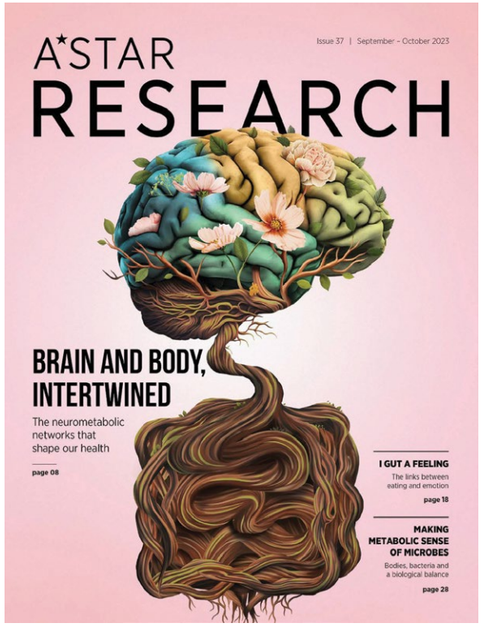


(Left) Figure panel adapted from ERIKSON et al., Cell Metab, 2019; (Right) LIAO et al., Cell Metab, 2024



(Left) Figure panel adapted from SO et al., EMBO Mol Med, 2023; (Right) DING et al., J Hepatol, 2020

Besides his research efforts in cancer metabolism, he is also leading research programs and industry collaborations to develop next generation anti-obesity medications, and has been featured in A*STAR Research and Nature Portfolio. One such program is A*STAR Strategic Research Program (SRP) Brain-Body Initiative (BBI), of which the Neurometabolism division was an integral part. BBI integrated expertise in neuroscience, metabolism, computer science, bioinformatics, and biotechnology across A*STAR to target scientific and economic impact. As Program Director of Neurometabolism, he developed a comprehensive strategic roadmap supporting thematic research projects enhancing integrated activity across A*STAR, building new capabilities and seeding projects aimed at securing competitive fundings, such as the programmatic grant **REPLENISH** (REsearch on Post-biotic, LifestylE and Nutritional Interventions to Support brain Healthspan).



The Brain-Body Initiative was featured on the cover of A*STAR Research Magazine, Oct 2023

DEVELOPING MODEL SYSTEMS FOR NEUROMETABOLIC RESEARCH

To better understand the biological mechanisms underpinning brain and metabolic disorders, researchers are leveraging diverse experimental models, including larval zebrafish, human-derived neuron models, and brain organoids. These models enable scientists to study real-time interactions between metabolic and neural pathways in a controlled and high-throughput setting.

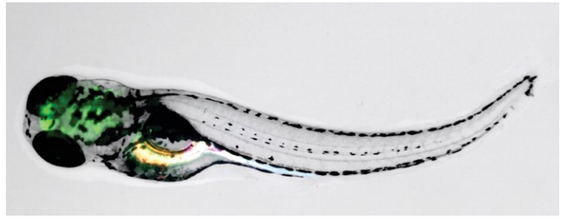


Image of a larval zebrafish showing neurons and enteroendocrine cells (green), food (red) and a commensal microbial species (cyan) in the gut, allowing a holistic understanding of diet-microbiome and brain-body interactions, Image by Wen LIE from Caroline WEE's team.

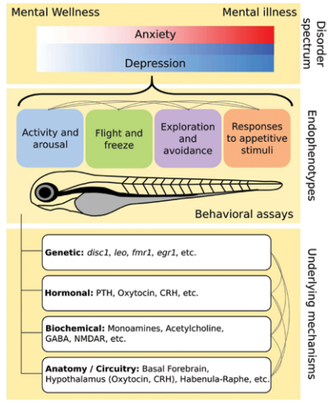
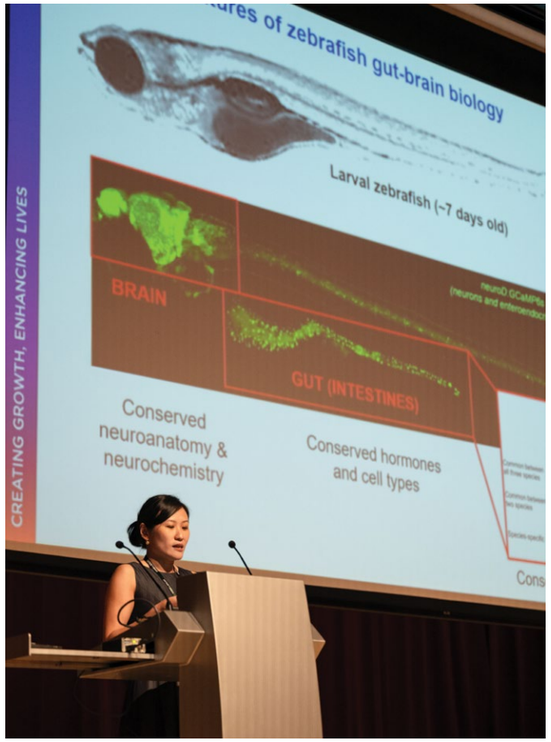


Figure panel adapted from TAN, ANG, WEE, Front. Mol. Neurosci (2022), a review article on how zebrafish are effective models of mental health endophenotypes

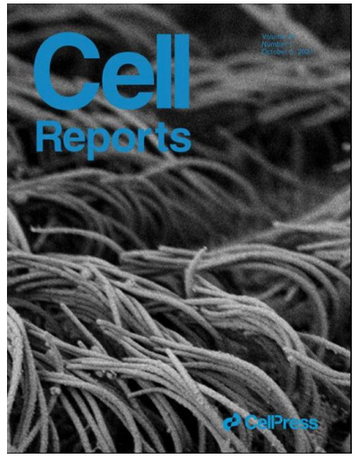
Using larval zebrafish models, **Caroline WEE**'s work is shedding light on gut-brain signalling, especially how the food we eat influences the genes, microbes, molecules, and neural circuits that ultimately shape our brains and behaviours.

Her research has advanced knowledge on how nutrient-metabolic interactions influence appetite, sleep, and anxiety-related behaviours, creating a foundation for potential therapeutic interventions for metabolic disorders and associated neurological conditions. She was awarded the National Research Foundation Fellowship (NRFF) in 2021 to pursue this research direction, and was featured in Channel News Asia's "Food to Change the World" episode on food and its impact on mental health, including how zebrafish can contribute to such research. She is also the elected president (2024-2027) of the Society for Neuroscience, Singapore Chapter (SfN.SG) which helps promote neuroscience research, collaboration, and education by connecting neuroscientists and neuroscience interest groups across Singapore.

Scan to watch CNA Feature "Food to Change the World" showcasing the research of Caroline WEE and Yu FU.



(Left) Caroline WEE presenting at the inaugural Singapore Symposium on Brain-Body Interactions, an international symposium jointly organised with the Society for Neuroscience, Singapore Chapter. Photo credit: Lynette LIM. (Right) Caroline and her lab won the costume contest at the 2024 A*STAR IMCB retreat, dressed as zebrafish!



nature genetics

Foxj1 transcription factors are master regulators of the motile ciliogenic program

Xianwen Yu[1], Chee Peng Ng[1], Hermann Habacher[1] & Sudipto Roy[1,2]

Motile cilia induce fluid movement through their rhythmic beating activity. In mammals, the transcription factor Foxj1 has been implicated in motile cilia formation. Here we show that a zebrafish *Foxj1* homolog, *foxj1a,* is a target of Hedgehog signaling in the floor plate. Loss of Foxj1a compromises the assembly of motile cilia that decorate floor plate cells. Besides the floor plate, *foxj1a* is expressed in Kupffer's vesicle and pronephric ducts, where it also promotes ciliary differentiation. We show that Foxj1a activates a constellation of genes essential for motile cilia formation and function, and that its activity is sufficient for ectopic development of cilia that resemble motile cilia. We also document that a paralogous gene, *foxj1b,* is expressed in the otic vesicle and seems to regulate motile cilia formation in this tissue. Our findings identify a dedicated master regulatory role for Foxj1 in the transcriptional program that controls the production of motile cilia.

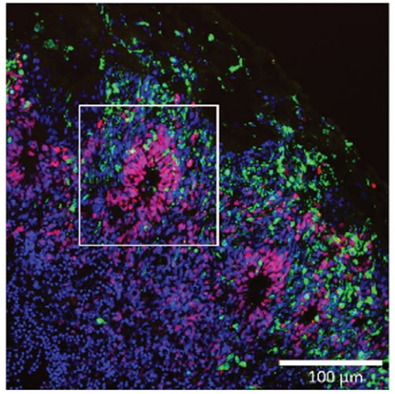
Figure caption: (Left) Cover of Cell Reports featuring work on zebrafish brain ependymal motile cilia from the ROY lab. (Rihgt) Pioneering work from the ROY lab on the discovery of the Foxj1 transcription factor in programing motile cilia formation was published in Nature Genetics, and has been cited more than 500 times.

Sudipto ROY joined A*STAR IMCB in 2002. Research in his laboratory focuses on differentiation of cilia and the investigation of their manifold functions in animal development and physiology. His group uses genetic and cell biological analysis of cilia with animal models, like the zebrafish and mouse, as well as human embryonic stem cell-derived ciliated tissues.

His research has been instrumental in understanding how genetic mutations in ciliary genes lead to congenital disorders in humans, with widespread impact on the etiology of respiratory and kidney disease, fertility and reproduction as well as development and function of the nervous system and sense organs.

He is very keen to examine the role of cilia in the ageing process as a future area of research. In the span of 23 years he has been associated with A*STAR IMCB, he has trained more than a hundred graduate students, post-docs and undergraduates, some of whom are now independent investigators, or are active with translational research in industry. He is widely recognised as a leading authority on cilia biology across the world, receiving several awards for his research accomplishments, and is the current chair of the Gordon Research Conference on cilia and mucociliary interactions.

Sudipto ROY (right) receiving the BMRC mentor award from ACE BMRC Sze Wee TAN



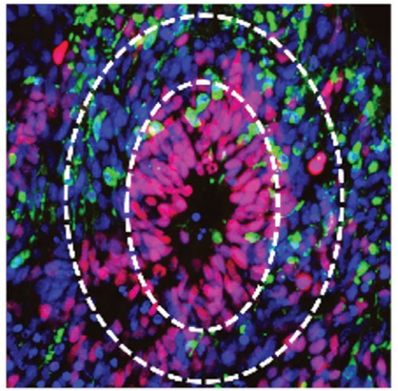


Image of a human neural organoid , showing self-organising features such as neural rosettes, a ring of neural stem cells, marked by magenta stain. A magnified image of the boxed area is shown on the right

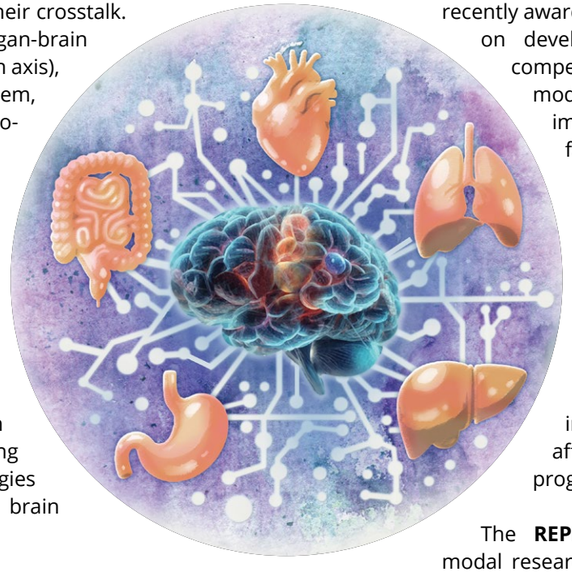
Shi Yan NG receiving the 11th L'Oreal-UNESCO For Women in Science Award in 2019 from then Jury President, Christina CHAI.

Since 2015, NRF Fellow **Shi Yan NG** has been investigating altered metabolic pathways in neurodegeneration using novel cellular andorganoid models. By integrating multi-omics approaches and high-throughput screening, NG's research bridges the gap between basic neuroscience and translational applications, paving the way for precision medicine approaches in neurodegenerative disease treatment. For her work, she won the 2019 L'oreal Women in Science Fellowship and the SCSS Dr Susan Lim Award for Outstanding Young Investigator in 2021.

NG has a longstanding interest in studying the molecular pathophysiology of the fatal motor neuron disease Amyotrophic Lateral Sclerosis (ALS). Although this is a rare disease affecting approximately half a million people worldwide and about 200 in Singapore, the team believes that their findings in ALS can be applied to more common neurodegenerative diseases including dementia. NG's lab is one of the pioneers in developing a human spinal cord-like organoid model that allows accurate disease modelling of motor neuron diseases.

TOWARDS THE FUTURE OF BRAIN HEALTH AND THERAPEUTICS: CROSS-SYSTEMS NEUROSCIENCE

Looking ahead, A*STAR IMCB is advancing cross-systems neuroscience, a multi-disciplinary approach that integrates neurobiology, immunology, and metabolism to gain a holistic understanding of metabolic and brain health as well as their crosstalk. These include studying organ-brain communication (e.g, gut-brain axis), the peripheral nervous system, neuro-immune and neuro-cancer interactions.



The neuroscience teams at A*STAR IMCB, together with collaborators, are developing novel strategies for understanding the mechanisms of vagus nerve stimulation on modulating brain and body health, de-coding gut-brain communication and developing precision intervention strategies for effectively improving brain health for healthy longevity.

Building upon her expertise in neurodegenerative disease modelling, **Shi Yan NG**'s research has expanded to investigate how immune and metabolic systems influence neurodegeneration. Her team is developing a human immuno-competent spinal organoid model to study neuro-immune-metabolic interactions, a pioneering approach that enables researchers to explore how immune system dysregulation contributes to neurodegenerative disorders. This work is crucial for identifying novel therapeutic strategies that target immune-mediated neurodegeneration, with potential implications for a range of conditions, including ALS, Parkinson's disease, and multiple sclerosis. For example, NG's recently awarded CRP grant, which focuses on developing a human immuno-competent spinal organoid model, aims to uncover novel immunomodulatory targets for the fatal motor neuron disease, Amyotrophic Lateral Sclerosis (ALS). This platform will allow researchers to study neuro-immune-metabolic interactions in both health and neurodegeneration, providing crucial insights into how immune system dynamics affect neurodegenerative progression.

The **REPLENISH** study is a multi-modal research initiative led by **Caroline WEE and Sarah LUO**. This programme aims to harness the gut-brain axis to prevent cognitive decline over ageing, by combining advanced multi-omics in middle-aged Singaporeans with preclinical gut-brain models. By examining interactions between nutrients, the gut microbiome, and brain-body physiology, they hope to develop novel preventative diagnostics therapeutics for brain health and longevity.

The focus of the division moving forward will be on brain-body crosstalk. Image credit: Ace Khong.

Beyond academic research, A*STAR IMCB is strengthening its ties with industry through key collaborations. A strategic partnership with **Cerecin** has been formed to collaborate on research in neurometabolism, and neurodegeneration. This combines A*STAR IMCB's preclinical modelling tools and multi-omics approaches with Cerecin's clinical cohort to uncover the metabolic origins of neurological diseases, identify new therapeutic targets, and develop innovative treatments. An ongoing project focuses on migraine genetics, which will be expanded to dementia in the near future.

An MOU was signed in 2024 with the Shanghai Institute of Materia Medica (SIMM) and Zhongshan Institute of Drug Discovery (ZIDD) to establish the Greater Bay Area Innovation Research Center for New Drug Discovery. Co-directed by **Weiping HAN, Jia LI** (Director of SIMM) and **Kan DING** (Director of ZIDD), the centre will focus on metabolic targets and regulators in metabolic diseases and associated complications, such as cancer and dementia.

(Left) Cerecin and A*STAR IMCB signed an MOU for collaboration in neurometabolism. (Right) SIMM, ZIDD and A*STAR IMCB signed an MOU to establish the Greater Bay Area Innovation Research Center for New Drug Discovery.

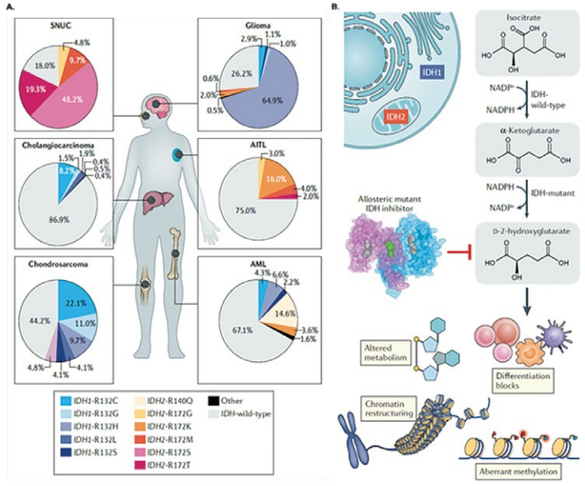
REVOLUTIONISING TRANSLATIONAL NEURO-ONCOLOGY

One example of cross-systems neuroscience is neuro-oncology, especially understanding the interactions between nerves and tumours, including gliomas. **Hai YAN** was strategically hired to strengthen our capability in neuro-oncology and translational research.

YAN and his team are revolutionising neuro-oncology by transforming cutting-edge research into practical, real-world medical solutions. YAN and his colleagues have pinpointed key brain cancer markers, including IDH1/2, TERT promoter, ATRX, CIC, and FUBP1 mutations. These pivotal discoveries have reshaped the WHO's CNS Tumour Classifications and revolutionised global treatment protocols. A major milestone from YAN's research is the development of vorasidenib, an FDA-approved targeted therapy for gliomas in 2024, which is now benefiting patients globally.

Currently, YAN's lab at A*STAR IMCB utilises advanced technology to perform detailed analyses of the genetics, epigenetics, and metabolism of brain tumours with unmatched precision. Capitalising on these insights, YAN's lab has developed a pioneering platform to create precision therapies tailored for solid tumours, specifically designed for the genetic profiles of Asian populations. By employing advanced computational methods for protein design and utilising high-throughput screening techniques, the lab leads efforts to significantly reduce both the time and cost of drug development. This seamless integration of genetic discovery with drug development showcases the dynamic cycle of innovation at A*STAR IMCB.

Hai YAN



PIRROZI and YAN, Nature Reviews Clinical Oncology

Inaugural 2024 IMCB Discovery Catalyst Award

Collaborations between A*STAR IMCB divisions have been seeded by the award of the inaugural 2024 IMCB Discovery Catalyst Award to a team comprising of **Sarah LUO**, **Caroline WEE** and **Shawn TAN** from the Neurometabolism division, and **Chuan YAN** from the Cancer division.

This award aims to incubate innovative 'moonshot' ideas while building a culture of team science and fostering collaborations among A*STAR IMCB investigators. The multidisciplinary team is leveraging their diverse expertise to tackle neuro-cancer interactions in obesity-associated heptatocelullar carcinoma and aims to shed new light on how nerve innervation in the liver may influence cancer development and pathogenesis. Understanding the interactions between cancers and the nervous system, and targeting the crosstalk between neurons and tumours will bring fresh insights and novel opportunities for diagnostic and therapeutic development.

Looking to the future, together with collaborations among local clinical partners, the team aims to bridge this pioneering research to the clinic.

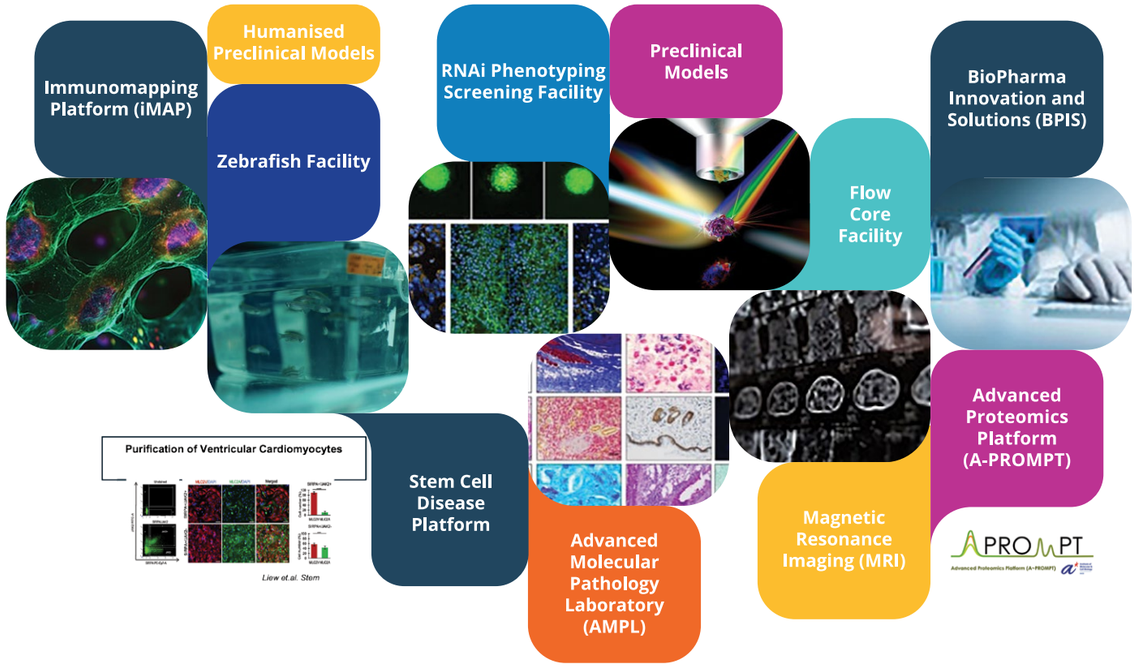
The neurometabolism division is also actively engaging in discussions with pharmaceutical companies to advance the discovery of novel secreted factors influencing metabolic pathways. This collaboration aims to leverage the pharma partners' extensive experience in metabolic disease therapeutics and A*STAR IMCB's cutting-edge research capabilities. By combining their strengths, these IMCB-pharma partnerships aspire to identify and develop innovative treatments targeting metabolic disorders, potentially offering new hope to patients worldwide. This partnership underscores a shared commitment to accelerating translational research and bringing forth effective therapeutic solutions in the realm of neuro-metabolism.

By **integrating molecular neuroscience, clinical research, and cross-systems approaches**, A*STAR IMCB remains at the forefront of **advancing neuroscience for improved brain-body health and therapeutics**. These collaborative efforts, combining fundamental research, translational science, and industry engagement, will drive the next generation of **innovative treatments for neurological and metabolic disorders**.

BRIDGING SCIENCE & TECHNOLOGY: A*STAR IMCB'S INNOVATION PLATFORMS

A*STAR IMCB offers a diverse portfolio of technology platforms that provide capabilities and support at all stages of the **preclinical drug discovery and development journey**, from target and lead discovery, efficacy studies in different animal models, to PKPD, toxicology and histopathology. Several of the capabilities are unique to Singapore or South-East Asia.

Managed by the A*STAR IMCB Horizontal Innovative Tech Division, these platforms are offered through A*STAR Research Support Centre (RSC). Investigators from A*STAR, universities, hospitals, and industry, leverage these capabilities to propel their research. Besides providing high quality, reliable and timely routine services, the platforms can be engaged to explore the (co)development of bespoke protocols and assays. The Division also aims, based on interest or demand, to develop or deploy novel next-generation technologies.



PLATFORM LEADS

Qingfeng CHEN
Humanised Preclinical Models
Division Director

Daniel Anand SILVA
Flow Cytometry platform
Deputy Division Director

Xavier LE GUEZENNEC
RNAi Screening Facility

Manikandan LASHMANAN
Tan Soo Yong
Biopharma Innovations and Solutions (BPIS)

Siok Ghee LER
Radoslaw SOBOTA
Advanced Proteomics Platform (A-PROMPT)

Ravisankar RAJARETHINAM
Tan Soo Yong
Advanced Molecular Pathology Lab (AMPL)

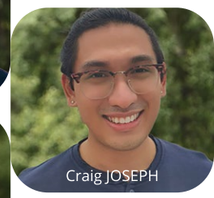
Qunxiang ONG
Paul CASSIDY
Magnetic Resonance Imaging (MRI)

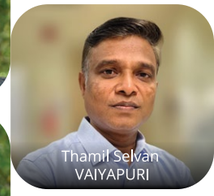
Michael Raj BOSE
Sudipto ROY
Zebra Fish Facility

Craig JOSEPH
Immunomapping platform (iMAP)

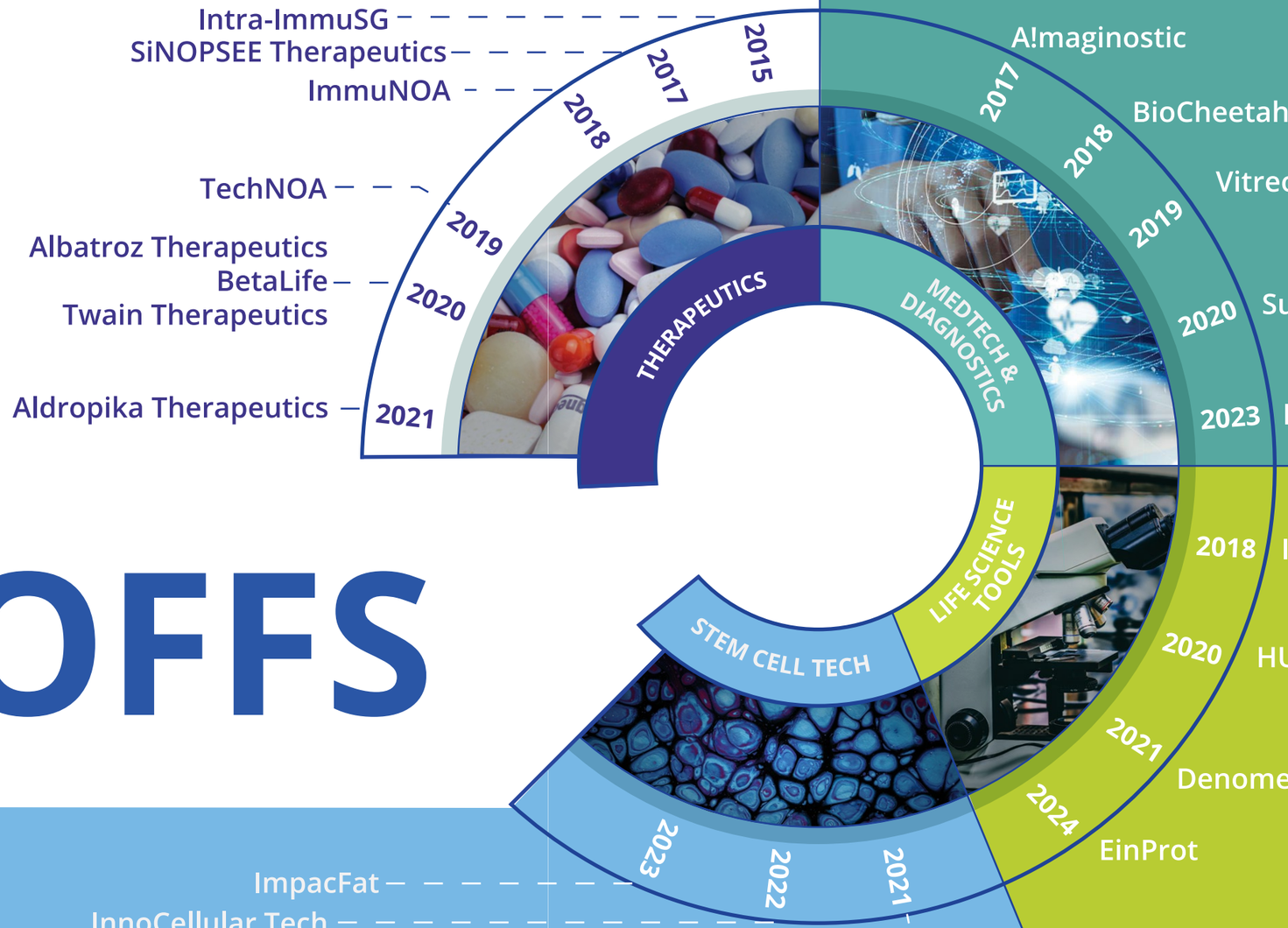
Andrea PAVESI
Advanced Microfluidic Platform

Vinay TERGAONKAR
Thamil Selvan VAIYAPURI
Preclinical Models of Human Disease





SPINOFFS


THERAPEUTICS
MEDTECH & DIAGNOSTICS
LIFE SCIENCE TOOLS
STEM CELL TECH
2015
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Intra-ImmuSG
SiNOPSEE Therapeutics
ImmuNOA
TechNOA
Albatroz Therapeutics
BetaLife
Twain Therapeutics
Aldropika Therapeutics
A!maginostic
BioCheetah
Vitreogel Innovations
Sunbird Bio
ImmunoQs
Invivocue
HUMLAB GLOBAL
Denome Technologies
EinProt
ImpacFat
InnoCellular Tech
Meatiply

A*STAR IMCB CULTURE: CREATING THE A TEAM

A*STAR IMCB Staff Retreat 2024 - Raffles Marina

A*STAR IMCB Principal Investigators Retreat - October 2024

Bringing People Together

Junior RSE Mentorship Program (JuMP)

Elevate Your Research Career - Group mentoring initiative connecting early-career researchers with seasoned mentors and like-minded peers

Fireside Chat Cozy Session

A*STAR IMCB staff get up close and personal with Jennifer Grandis on June 4, 2024, in a collaborative event with DWG, focusing on the vital discussion of Gender Equity in Science and Medicine.

IMCB Fellowship Program

Launchpad for Future Scientific Leaders - Salary support, overseas training opportunities, and career mentorship to help early-career scientists supercharge their expertise and expand their networks

IMCB Fellowship 2024 Awardees: Grace LIM, Lele WU, Beverly MOK.

TechWorks@ROCK

Sharpening skills, mastering techniques—tech training in action

Network@ROCK

Good vibes, great company, and career-boosting connections

LRTT! (Let's ROCK the Table!)

Science isn't the only thing we're advancing—let's talk career moves

PhD Society

The PhD Society at IMCB fosters research exposure, mentoring, networking and career development through a range of engaging initiatives for IMCB's PhD student community.

PhD Seminar Series

Big ideas, brilliant minds, and breakthrough discussions!

The Candid Couch

The Candid Couch brought together inspiring scientists to share their unfiltered journeys, challenges, and passion for academia, offering valuable insights and solidarity for those navigating the world of research.

Student Organised Workshops

PhD Society x A*STAR Microscopy Platform (AMP) Workshop: A dynamic session offering expert-led microscopy training, hands-on experience, and insights to elevate imaging skills for researchers at all levels.

ROCK - Research Officers Career Kinetics

Launched on 22 March 2022, ROCK (Research Officers Career Kinetics) was created by IMCB to bring RTS staff together, and has been adopted across A*STAR. From career development discussions, technical workshops, to mentorship guidance and social events, ROCK is all about connecting, learning, and thriving.

IMCB-ROCK RTS Mentorship Workshops

IMPACT - IMCB Post-docs Achieving Collaborations Together

Launched in 2024, the IMPACT Society is a postdoc-driven community fostering collaboration, networking, and career growth at IMCB. This year, IMPACT aims to build stronger ties among postdocs, scientific experts, and the wider research community both within and beyond IMCB.

STAR Mentor Award & Recognition of Mentorship Excellence

Shining bright—the mentors who help us reach for the stars

Leslie BEH
Qingfeng CHEN
Qunxiang ONG
Adrian TEO
Caroline WEE
Kylie YONG
Weimiao YU

ACHIEVING COLLABORATIONS THROUGH JOINT APPOINTMENTS

CANCER SIGNALLING & THERAPY

Dedrick CHAN
Colorectal cancer, clonal evolution, tumour initiation
Consultant, Surgery
NUHS

Chit Fang CHEOK
Molecular therapeutics in cancer and aging
Assistant Professor, Department of Pathology
NUS

Pierce CHOW
PuRPOSE programme
Senior Consultant, Surgery and Surgical Oncology
NCCS

Anand JEYASEKHARAN
Tumour microenvironment and chemotherapy
Senior Consultant, Haematology Oncology, Assistant Professor
NUS

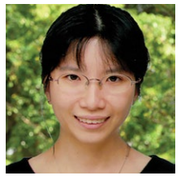
Darren LIM
IMCB NCC MPI Singapore oncogenome program
Senior Consultant, Medical Oncology
NCCS

Chwee Ming LIM
Cell-based immunotherapy, cancer immunology and immunotherapy
Senior Consultant, Otorhinolaryngology/ENT, Surgery & Surgical Oncology
SGH

Johnny ONG
Advanced cancer translational therapeutics
Senior Consultant, Surgery and Surgical Oncology
NCCS

Andrea PAVESI
3D tumour microenvironment for disease modelling
Assistant Professor, Lee Kong Chian School of Medicine
NTU

Kanaga SABAPATHY
Molecular carcinogenesis
President's Chair Professor and Chair, School of Biological Sciences
NTU



Ern Yu TAN
Breast diseases, biomarker discovery, artificial intelligence imaging and data analytics.
Head of Service (Breast & Endocrine Surgery), Senior Consultant
TTSH

CELL & MOLECULAR THERAPY

Bin Tean TEH
Chromatin therapeutics
Deputy Chief Executive Officer (Research)
NCCS

HUYNH The Hung
Patient-derived xenograft (PDX) models for immunotherapy and targeted therapies
Principal Investigator, Division of Cellular & Molecular Research
NCCS

Shawn CHEN Xiaoyuan
Molecular imaging and nanomedicine
Director of Research (CIRC) and Professor, Yong Loo Lin School of Medicine
NUS

Christine CHEUNG
Molecular and vascular medicine
Associate Professor, Lee Kong Chian School of Medicine
NTU

Justin CHU
Collaborative translation unit for hand, foot and mouth disease
Associate Professor, Department of Microbiology and Immunology
NUS

Roger FOO
Cardiovascular metabolic disease, genomics, cell states, heart regeneration
Vice-Dean (Research) and Professor, Yong Loo Lin School of Medicine
NUS

Yiqi SEOW
Genetic control and specific delivery of genes for therapy and health
Senior Research Scientist
GIS

Yee Joo TAN
Hepatitis and influenza virology, protein chemistry
Associate Professor, Department of Microbiology and Immunology
NUS

Xiaomeng WANG
Vascular biology
Associate Professor, Centre for Vision Research
Duke-NUS

NEUROMETABOLISM IN HEALTH & DISEASES

Christopher ANG
Precision medicine in glioblastoma
Senior Consultant, Neurosurgery, Surgery & Surgical Oncology
NNI

John CHUA
Interactomics and intracellular trafficking
Assistant Professor, Department of Physiology
NUS

Camilo LIBEDINSKY
Neurotechnology
Assistant Professor, Department of Psychology
NUS

Sriram Ajay MATHURU
Mechanisms underlying behaviour *Associate Professor, Department of Physiology*
NUS

Derrick ONG
Mechanisms of proliferation/ self-renewal of cancerous and normal brain stem cells
Assistant Professor, Department of Physiology
NUS

Benjamin TAN
Translational stroke research
Consultant, Division of Neurology
NUHS

Wan Yee TEO
Lab unit of paediatric brain tumour research office
Clinician Scientist, Division of Medicine
KKH

Kah Leong LIM
Neurodegenerative diseases - mechanisms and therapeutics
Professor, AVP for Research, Biomedical and Life Sciences
NTU

Yibin WANG
Mechanisms and therapeutic development of cardiometabolic diseases
Professor and Programme Director, Signature Research Programme in Cardiovascular & Metabolic Disorders
Duke-NUS

Crystal YEO Jing Jing
Neurological and neuromuscular diseases
Consultant, Division of Neurology
NNI

Leonard YEO
Acute stroke, neurointervention, intracranial stenosis
Senior Consultant, Division of Neurology
NUHS

HORIZONTAL INNOVATIVE TECHNOLOGY PLATFORMS

Tim HU
Interdisciplinary research of artificial intelligence and genomics
Senior Scientist
*A*STAR BII*

Weimiao YU
Cell morphology and migration in pathology for drug response
Principal Scientist II
*A*STAR BII*

Edward MANSER

Retired

Peng LI

President

Zhengzhou University (China)

Zeng LI

Associate Professor, Signature Research Programme in Neuroscience & Behavioural Disorders

Duke-NUS Medical School

Kanaga SABAPATHY

President's Chair Professor and Chair, School of Biological Sciences

Nanyang Technological University

Venkatesh BYRAPPA

Retired

Daniel Martin MESSERSCHMIDT

Associate Professor, Department of Cellular and Molecular Medicine, SUND, University of Copenhagen

SUND, University of Copenhagen

Kah Leong LIM

Professor, Associate Vice President (Biomedical & Life Sciences), Lee Kong Chian School of Medicine

Nanyang Technological University

Su Ling YEO

Director, Venture Creation and Growth, I&E

A*STAR

Huck Hui NG

Assistant Chief Executive for Research and Talent Development

A*STAR

Kong Peng LAM

Executive Director

A*STAR Singapore Immunology Network (SIgN)

Ruifen WENG

CEO

Diagnostics Develop-ment (DxD) Hub

Masafumi INOUE

Senior Principal Scientist

Diagnostics Develop-ment (DxD) Hub

Huilin SHAO

Founder

Sunbird Bio

Anwesha DEY

Distinguished Scientist and Executive Director, AI-Oncology, Cancer Biology

Genentech

Lewis HONG

VP (Discovery Research) and Site Head (Singapore)

Paratus Sciences(US)

Ying Xim TAN

Director of Discovery Operations

MediSix Therapeutics

Shawn HOON

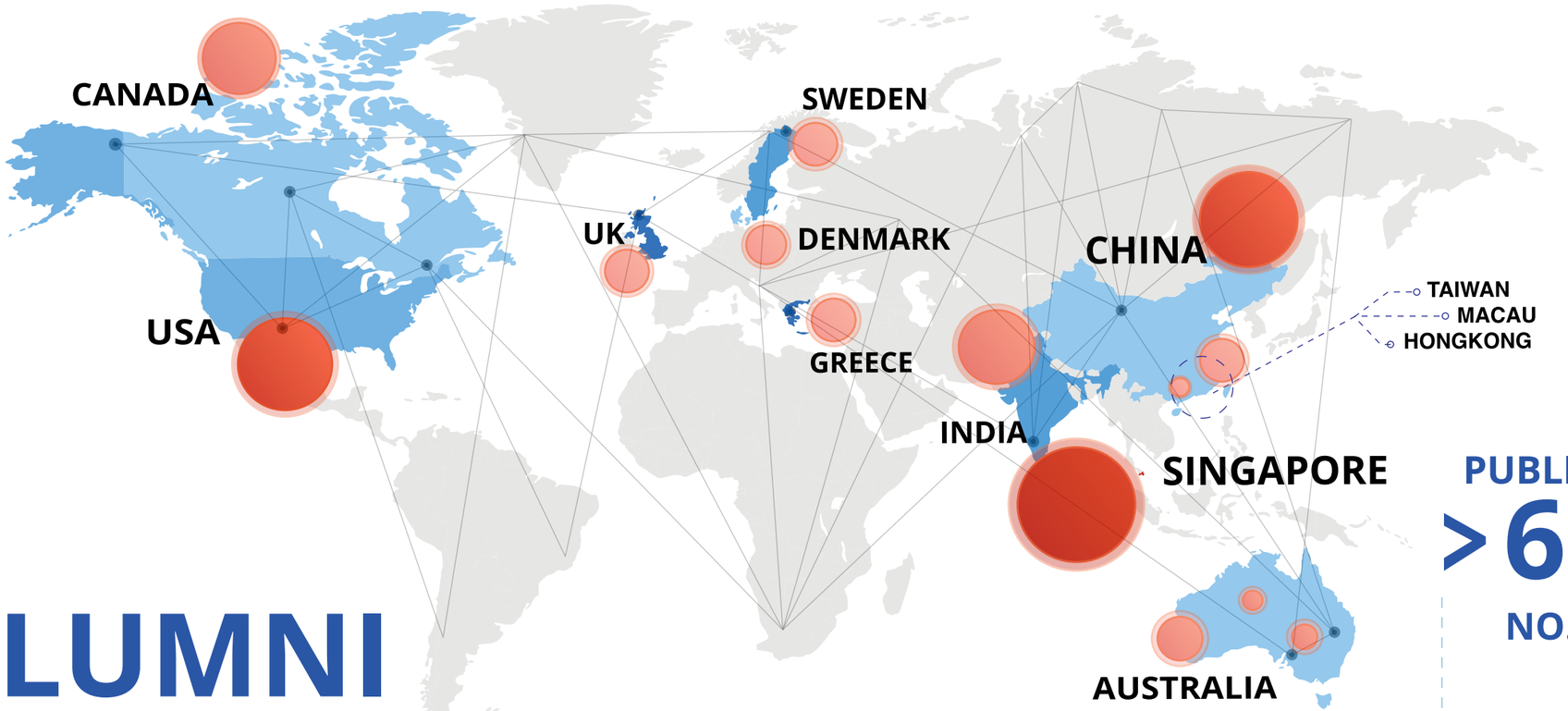
Chief Scientific Officer

Automera

Rosemary TAN

CEO

Leyden Labs Asia



IMCB ALUMNI
SCIENTIFIC TRAILBLAZERS

NO. OF PUBLICATIONS

> 6000

NO. OF SPINOFFS

Since 1985

20

AWARDS

Asia Pacific Eye 100 Award
Xinyi SU *2025*

Asian Scientist 100
Wanjin HONG *2023*
Sherry AW *2020*

A*STAR Fellow
Yu FU *2024*
Qingfeng CHEN *2024*

Basser Global Prize
Ashok VENKITARAMAN *2017*

EMBO Associate Membership
Nick BARKER *2022*

EMBO Global Investigator
Wee-Wei TEE *2021*
Yu FU *2021*

EMBO Membership
Ashok VENKITARAMAN *2004*

Fellow, Academy of the American Association for Cancer Research
Ashok VENKITARAMAN *2025*

Fellow, UK Academy of Medical Sciences
Ashok VENKITARAMAN *2001*

International Society for Stem Cell Research (ISSCR) Public Service Award
Jonathan LOH *2025*

Japanese Cancer Association (JCA) International Award
Nick BARKER *2022*

JCI Ten Outstanding Young People Award (Gold)
Xinyi SU *2021*
Adrian TEO *2019*

L'Oreal For Women in Science International Fellowship
Sherry AW *2019*

L'Oreal For Women in Science Singapore Fellowship
Grace LIM *2024*
Shi Yan NG *2019*
Sherry AW *2017*

Macula Society Membership
Xinyi SU *2021*

National Research Foundation (NRF) Fellowship
Shuang LIU *2025*
Leslie BEH *2023*
Chuan YAN *2023*
Caroline WEE *2021*
Sarah LUO *2021*
Shi Yan NG *2018*
Qingfeng CHEN *2017*
Wee-Wei TEE *2016*

National Research Foundation (NRF) Investigatorship
Qi-Jing LI *2023*
Yu FU *2022*
Jonathan LOH *2018*
Nick BARKER *2017*

National Science Award
Uttam SURANA *2007*
Wanjin HONG *1999*

NMRC Clinician Scientist Investigator Award (CSA)
Xinyi SU *2022*

President's Science Award (PSA)
Yue WANG *2012*

President's Science and Technology Medal (PSTM)
Wanjin HONG *2022*

Public Administration Medal (Silver)
Wanjin HONG *2014*

Singapore National Academy of Science Fellow
Wanjin HONG *2022*

Singapore Stem Cell Society Susan Lim Award
Xinyi SU *2022*
Shi Yan NG *2021*
Adrian TEO *2018*
Jonathan LOH *2017*

World Immunotherapy Council Asian Chapter Research Contribution Award
Joe YEONG *2024*

Young Scientist Award (YSA)
Sarah LUO *2021*
Huilin SHAO *2019*
Shifeng XUE *2018*
Huili GUO *2016*
Melissa FULLWOOD *2014*

ACKNOWLEDGEMENTS

The A*STAR IMCB 40th Anniversary Book is the result of the dedication and collaborative efforts of many individuals. We extend our sincere gratitude to all who contributed to its creation.

We would like to express our appreciation to the A*STAR IMCB 40th Anniversary Book Committee, whose commitment, writing, and editorial efforts have shaped this publication:

IMCB 40th Anniversary Book Committee & Editorial Team

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Farid John GHADESSY
Grace LIM
Sarah LUO
Beverly MOK
Andrea PAVESI
Phyllis PHUAH
Xinyi SU
Jialin SUN
Tommaso TABAGLIO
Wee Wei TEE
Caroline WEE
Han Teng WONG
Veon LEE

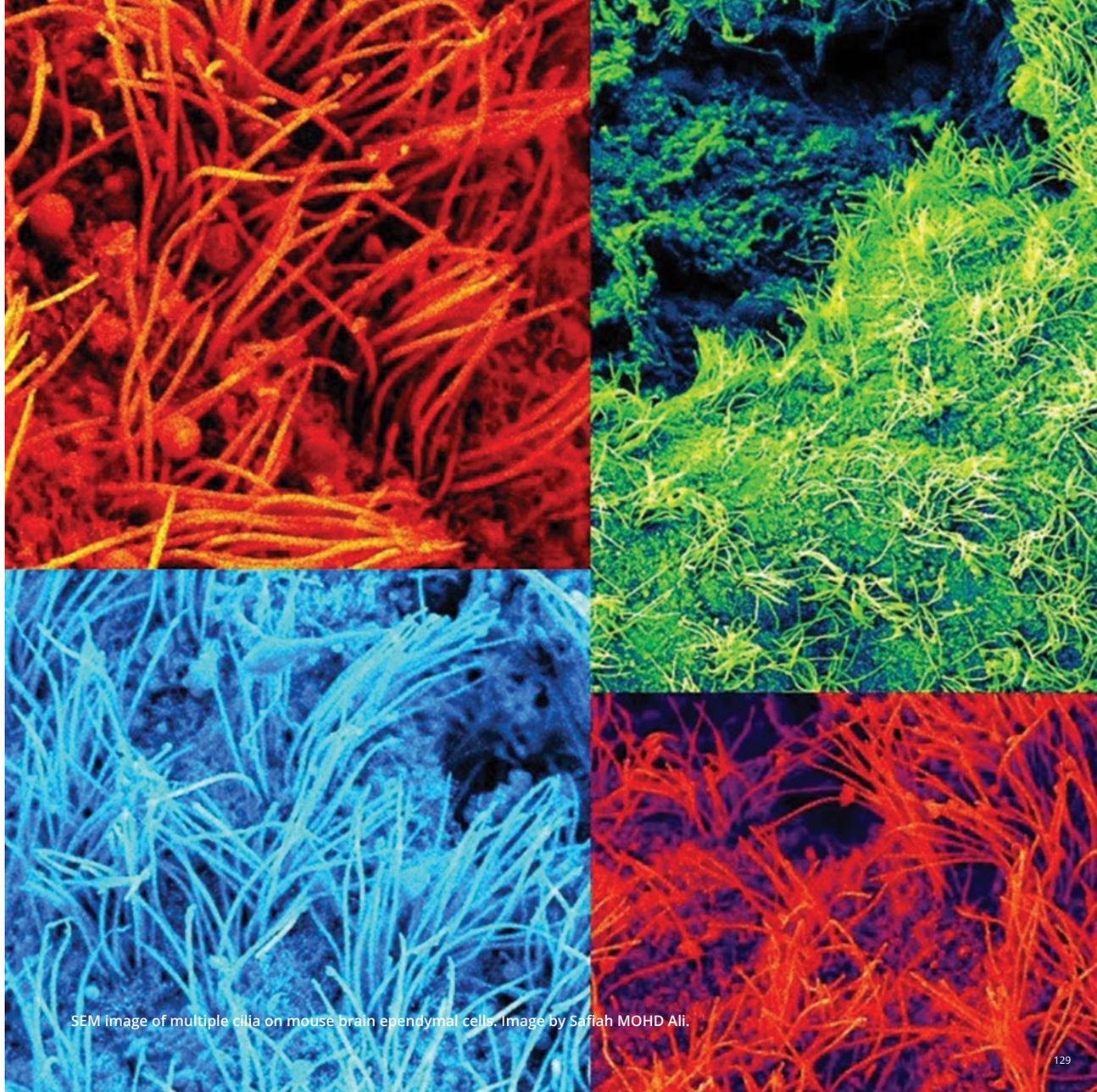
We are deeply grateful to all A*STAR IMCB members, alumni, and colleagues for your contributions—whether through research, guidance, support, or sharing your stories and materials. Each of you has played a vital role in shaping IMCB's journey and legacy.

Finally, we extend our appreciation to Digital Blowfish, whose creativity and expertise in design and production have brought this book to completion.

This book is a tribute to the people who have shaped A*STAR IMCB's story, and we look forward to the next chapter of discovery and innovation together.

Scan this QR Code for the soft copy of A*STAR IMCB's 40th Anniversary Publication

Scan to view the full list of citations.



SEM image of multiple cilia on mouse brain ependymal cells. Image by Safiah MOHD Ali.

40 A*STAR IMCB
ANNIVERSARY