

FROM  
RESEARCH  
TO REAL LIFE:  
SINGAPORE  
AS A HUB FOR  
**HEALTHCARE**  
**INNOVATION**



Agency for  
Science, Technology  
and Research

# THE HEALTHCARE INNOVATION VALUE CHAIN

The Agency for Science, Technology and Research (A\*STAR) is home to numerous capabilities and partnerships in pharmaceuticals, biologics and medical technology. These span the entire value chain from discovery to manufacturing, laying the foundation for healthcare innovation and personalised medicine.

## DISCOVERY

Understanding disease mechanisms for the creation of future therapies

## DEVELOPMENT

Accelerating lab-to-market through integrated translational engines

## TRANSLATION

Taking discoveries into the clinic to impact lives

## MANUFACTURING

Process innovation to transform industry capabilities

Dr Danny Soon  
Senior Director,  
Biomedical Research Council



Dear colleagues,

*As life expectancies across Asia increase and countries grow more affluent, the region's biomedical sciences and healthcare sectors are expected to flourish. Frost & Sullivan expects the Asia Pacific healthcare industry to grow at a rate of 11.1 percent in 2018—more than double the average annual growth rate of the global healthcare economy—and to reach US\$517 billion the same year.*

This robust growth heralds many exciting opportunities and challenges for healthcare innovation and entrepreneurship. For one, practices in the research, pharmaceutical and healthcare sectors are constantly evolving, with stakeholders increasingly seeking external sources of innovation through in-licencing or partnerships with public or private institutions.

Another trend centres on the rise of healthcare consumerism, where increasingly affluent and knowledgeable consumers expect greater transparency and a certain degree of empowerment when it comes to taking charge of their own healthcare and health-related data.

Finally, next-generation advances in technology are paving the way for better patient outcomes—cheaper, faster DNA sequencing methods have made clinical genomics and precision medicine much more feasible; high-end surgical robots are drastically reducing patient recovery time; and powerful artificial intelligence algorithms are helping clinicians make better diagnostic and treatment decisions.

With these developments in mind, we in Singapore and at A\*STAR are committed to advancing sustainable healthcare solutions for patients in Asia and throughout the world. Our efforts are already bearing fruit, and the biomedical sciences are increasingly a key pillar of Singapore's manufacturing sector.

Our efforts have not escaped international attention. Singapore was ranked third on the

2018 Bloomberg Innovation Index of the world's most innovative economies; first among newcomer markets on the 2017 Pugatch Consilium survey of biopharmaceutical innovation; and second on the 2016 Scientific American Worldview scorecard for innovation potential in biotechnology. In 2017, A\*STAR itself was ranked among the top ten biotech innovators in cancer research in Asia by Clarivate Analytics.

On the back of this success, A\*STAR remains dedicated to nurturing a vibrant and comprehensive biomedical sciences ecosystem to facilitate the translation of research innovations into real-life applications.

The focal point of this ecosystem is one-north, an innovation hotspot that is home to world-class science, comprehensive research facilities, and a diverse mix of public and private sector enterprises. One-north also hosts some 4,200 A\*STAR scientists and engineers, who offer expert talent and deep capabilities that span the biomedical sciences, physical sciences and information technology.

Co-locating these players on the same campus opens up numerous opportunities for productive and creative partnerships to form. The future of medicine is collaborative, and we at A\*STAR look forward to co-creating innovations that will lead to more effective and patient-centric care.

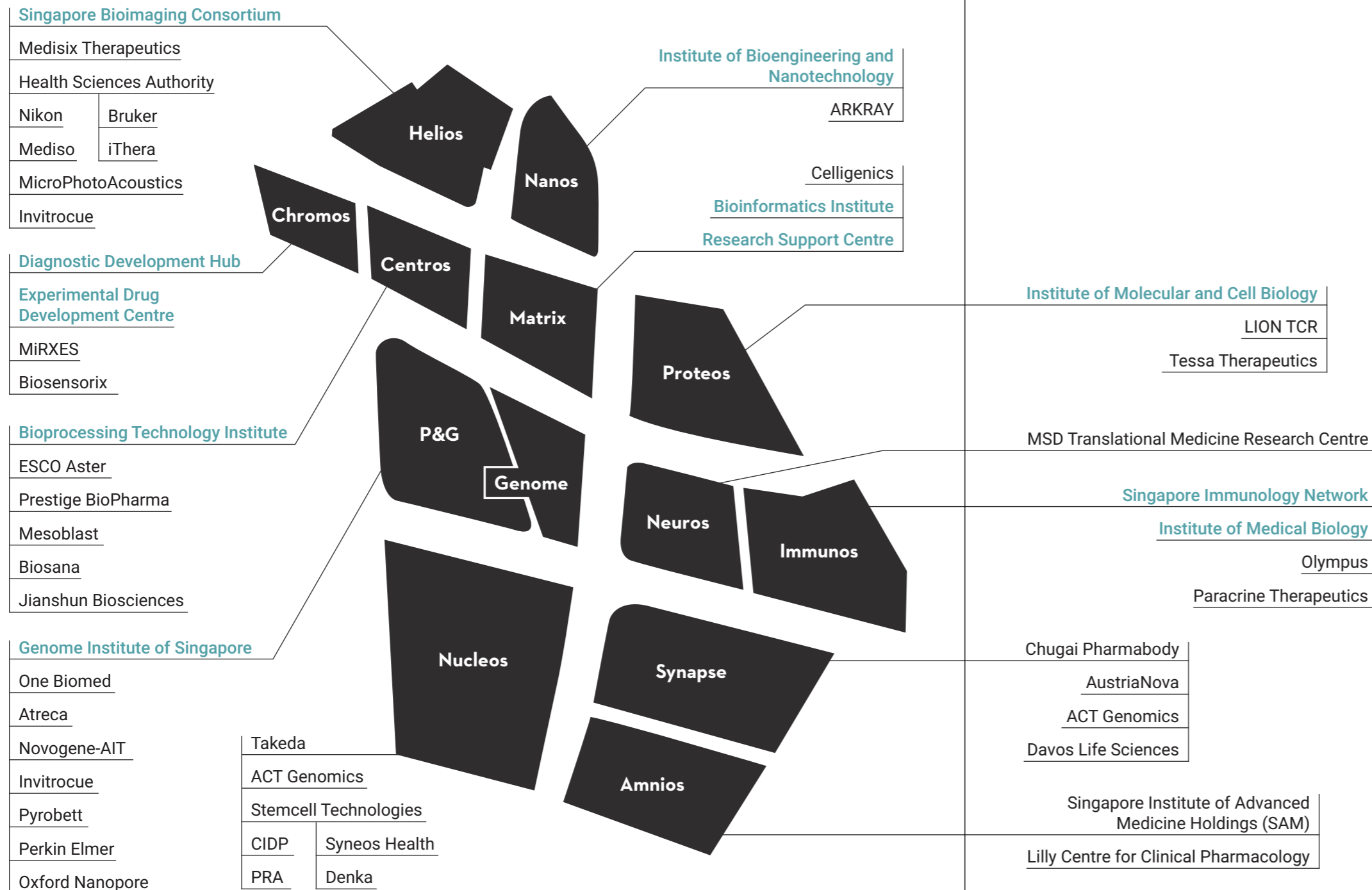
Dr Danny Soon  
Senior Director, Biomedical Research Council  
A\*STAR

# BIOPOLIS @ ONE-NORTH:

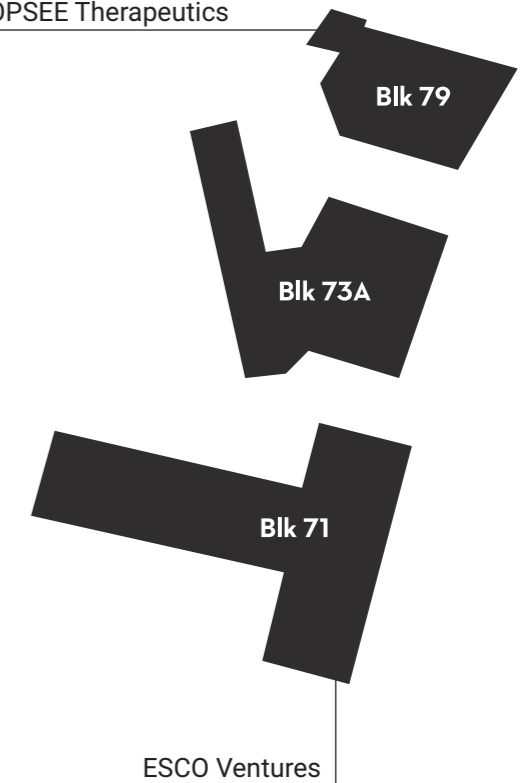
Public-private partnerships flourish at the Biopolis research hub in Singapore, where companies and A\*STAR researchers work together to shape the future of the medicine and healthcare industry. This innovation ecosystem facilitates the translation of laboratory findings into novel treatments with commercial value.

# ASIA'S BIOMEDICAL SCIENCES R&D HUB

## Anchoring the Entire Value Chain for Biomedical Sciences



- [A\\*STARTCentral](#)
- [The Biofactory](#)
- [Engine Biosciences](#)
- [Nalagenetics](#)
- [Astraltec Group](#)
- [SiNOPSEE Therapeutics](#)



## JTC LAUNCHPAD @ ONE-NORTH

**Fostering a Conducive Environment and Nurturing Ecosystem for Startups**

DISCOVERY

# UNDERSTANDING DISEASE MECHANISMS FOR THE CREATION OF FUTURE THERAPIES

A\*STAR leads a variety of initiatives and partnerships aimed at understanding disease mechanisms, uncovering novel targets and biomarkers, and engineering new drug modalities, with a strong focus on the unique characteristics of Asian populations.

## NOVEL BIOLOGY AND TARGET DISCOVERY

Our research seeks to understand the complex biology underlying various diseases, thus providing the insights necessary for the development of novel and effective therapies.

### Genetic Orphan Diseases

Working with hospitals in Singapore and around the world, researchers have used techniques such as genome and methylome sequencing to identify germline (epi)-mutations that cause orphan and unique conditions in humans, with the aim of finding new diagnostic biomarkers and therapeutic targets for common disorders. To date, the GODAFIT programme has successfully resolved close to 100 orphan genetic diseases. For example, in a 2016 publication in *Cell*, the researchers reported that mutations in the *NLRP1* gene result in a familial skin cancer syndrome with unique self-healing properties, and in 2018, the team published an article in *Nature* on the role of *RSPO2* mutations in tetra-amelia syndrome, a recessive congenital disorder characterized by the absence of lungs and all four limbs.

“Through elaborate mechanistic studies, we’ve made important discoveries that have furthered the understanding of a large number of conditions affecting embryonic, metabolic, ageing, immune and neurodegenerative diseases, as well as familial cancers. These have led to collaborations with a multitude of industry partners such as GSK, Merck, Takeda, Galderma, EReal, AmorePacific, Novartis, Teva Pharmaceuticals, STEMCELL Technologies and Ferring Pharmaceuticals,” said Professor Bruno Reversade, Programme Lead of GODAFIT and Research Director at the A\*STAR Institute of Medical Biology and Institute of Molecular and Cell Biology.

#### Platforms/capabilities:

- Clinical genome/methylome sequencing and interpretation
- Animal modeling in *C. elegans*, zebrafish, *Xenopus* and mice
- CRISPR/Cas9 genome-wide screens
- Assay development and target validation using patient-derived iPSCs and organoids

## NOVEL BIOLOGY AND TARGET DISCOVERY

## Rare, Undiagnosed Diseases in Children

A partnership between A\*STAR researchers and clinicians at the National University Hospital and KK Women's and Children's Hospital uses whole genome and exome sequencing to detect rare disease-causing mutations in babies. The SUREkids programme has boosted diagnosis rates by a further 30 percent, and in some cases has allowed doctors to recommend life-saving treatments.

"By establishing a standardized clinical genomics pathway at KKH and NUH, we have now improved access to best-practice genomic analysis services and reduced the time and cost required to reach a diagnosis. This pipeline is now translated across all hospitals in Singapore, making the Diagnostic Clinical Exome test available to patients in Singapore and the region," said Professor Roger Foo, SUREkids Co-lead and Group Leader at the A\*STAR Genome Institute of Singapore.

### Platforms/capabilities

- Exome sequencing
- Whole genome sequencing
- Bioinformatics

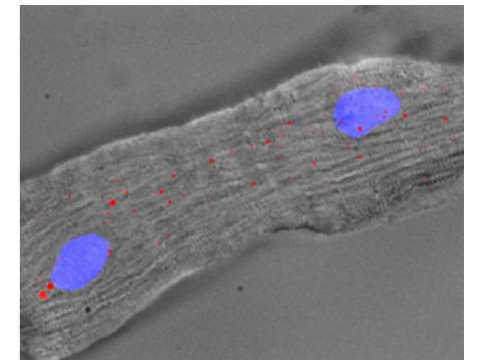


## Asian Heart Failure Study

Led by A\*STAR, a multi-agency effort aimed at increasing our understanding of heart disease in the Asian context will leverage Singapore's expertise in cardiac imaging, genetics, proteomics and molecular biology to build a one-stop platform that supports translational cardiovascular research from target discovery to preclinical and clinical studies.

To date, researchers in the ATTRaCT programme have described a unique "lean diabetic phenotype" of heart failure with preserved ejection fraction which is unique to Asia, and discovered several attractive therapeutic targets in heart failure including *Singheart* — an RNA molecule that prevents heart muscles from repairing themselves and which, if blocked, may allow the heart to heal itself.

"One in three of us is going to die of heart disease. If we are able to detect heart disease early, it is treatable and death preventable. ATTRaCT is the first integrated platform for translational cardiovascular research that leverages Singapore's competitive advantages to identify and validate novel targets in heart disease progression. By understanding the mechanisms underlying heart disease progression, we can win the fight against heart disease," said Professor Carolyn Lam, ATTRaCT programme lead, Senior Consultant Cardiologist at the National Heart Centre Singapore and Professor at Duke-NUS Graduate Medical School.



A mouse heart cell with 2 nuclei (blue) and *Singheart* RNA labelled by red fluorescent dyes.

## NEW MEDICINES

Drawing on expertise in protein engineering, nucleic acid engineering and bioinformatics, A\*STAR researchers are developing new drug modalities aimed at targets previously considered undruggable.

### Peptide Engineering

A\*STAR's Peptide Engineering Programme, led by Dr Charles Johannes and Dr Chris Brown, supports peptide based research and harnesses computational design and novel synthesis technologies to develop new and improved peptide therapeutics. Key areas of focus include understanding cellular uptake of peptides, as well as the development of synthesis technologies that generate unique peptide diversity and development of macrocyclic pre-clinical compounds. The PEP has slowly become the centre of peptide based research, supporting the **Cancer Immuno Therapy Imaging Programme (CITI)** and other national research efforts.

"Investment in peptide science will continue through broad initiatives and collaboration with the growing Singapore scientific ecosystem in peptide-based research. The aim is to catalyse the development of leading edge technology or a new industry sector in Singapore. The expected outcomes include the creation of novel products and services in the pharmaceutical, biopharmaceutical and the care chemicals spaces, thereby providing an attractive environment for continued investment by companies in R&D," said Dr Charles Johannes, PI of the A\*STAR p53lab and President of the P2S2 society.

#### PARTNERSHIPS

#### A\*STAR and MSD collaborate on macrocyclic peptide therapeutics

A\*STAR and American pharmaceutical company MSD set up a two-year collaboration to improve the delivery of macrocyclic peptides into cells. Macrocyclic peptides are attractive drug candidates because they can disrupt intracellular protein-protein interactions. These interactions were previously considered undruggable due to their lack of obvious binding sites for small molecules and inaccessibility to antibody-based therapies.

"We believe that by combining expertise with A\*STAR, we will make significant advances in our ability to apply peptide therapeutics to highly validated intracellular targets that have historically been out of reach," said Dr Rich Tillyer, Senior Vice President, Chemistry, MSD.

### Molecular Therapeutics

A\*STAR's Molecular Therapeutics Programme is Singapore's first and only initiative aimed at developing novel medicines that focus on gene therapy using genome-editing technologies. The Programme advances methods such as adeno-associated viruses to deliver CRISPR/Cas9-related technologies to patients. This groundbreaking DNA-editing system holds promise to cure genetic diseases and revitalize immunotherapies.

The programme consists of a cross-disciplinary, multi-institutional team of investigators and is inspired by breakthroughs such as the first demonstration of disease gene correction with CRISPR/Cas9 in live animals and illustrations of CRISPR/Cas9 to correct RNA-mediated diseases.

"New Crispr/Cas systems will be identified to serve as a menu of options for future therapeutics, said Dr Shawn Hoon, Co-lead of the Molecular Therapeutics Programme and Senior Research Fellow at the A\*STAR Molecular Engineering Lab.

## NEW SCREENING PLATFORMS

Our innovative screening platforms allow researchers to identify clinically relevant biomarkers and therapeutic targets in a high-throughput fashion.

### Combating Non-Alcoholic Fatty Liver Disease (NAFLD)

A\*STAR researchers, clinicians and engineers are working to combat Non-alcoholic Fatty liver disease (NAFLD), an imminent worldwide epidemic due to growing affluence and sedentary lifestyles. The EMULSION programme allows researchers to model NAFLD using a variety of cutting-edge technologies—including an organoid screening platform, a 'human-on-a-chip' platform utilising human primary tissue samples, and humanised mouse models—with the goal of developing novel diagnostics and therapeutics for this complex disease.

"A national initiative towards battling an imminent healthcare crisis, EMULSION aims to be the unifying platform for clinician, scientist and bioengineers working on Non-alcoholic Fatty liver disease (NAFLD). The program aims to create a comprehensive Clinical and Omics database and Bio-resource from a unique Asian patient cohort to enable Biomarker discovery and validation. These foundational resources will also fuel research platforms that utilizes advance technologies such as Organoid culture system, Microfluidic platform and Humanized mouse model to advance NAFLD Therapeutics discovery," said Prof Ng Huck Hui, Programme Co-Lead of EMULSION and Executive Director of the A\*STAR Genome Institute of Singapore

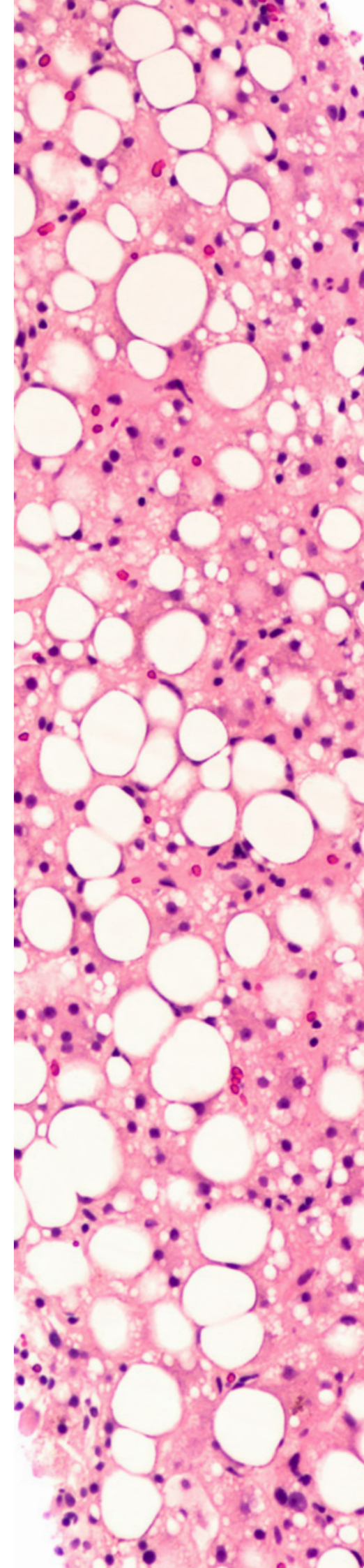
### High-throughput Screening for Precision Oncology

#### PARTNERSHIPS

#### A\*STAR and PerkinElmer launch joint laboratory for precision oncology

A\*STAR's Genome Institute of Singapore (GIS) and PerkinElmer launched the PerkinElmer-GIS Centre for Precision Oncology to develop a state-of-the-art, high-throughput screening platform to test drug efficacy in next-generation tumour models. The ability to perform screens in patient-derived tumour models such as organoids and micro-spheroids enables researchers to discover novel therapeutic targets and identify biomarkers for patient stratification, with the ultimate goal of taking precision oncology research into the clinic.

"PerkinElmer's integrated solutions empower researchers to reach greater insights for greater outcomes. Combined with GIS's knowledge and experience, this partnership has the potential to unlock new doors in the future of applying precision medicine to cancer treatment," said Mr Brian Kim, President, Life Sciences & Technology, PerkinElmer.



**DEVELOPMENT**

# ACCELERATING LAB-TO-MARKET THROUGH INTEGRATED TRANSLATIONAL ENGINES



A\*STAR's integrated translational engines accelerate the development of commercially viable, clinically validated therapeutics and diagnostics.

## Experimental Drug Development Centre (EDDC)

Formed in 2019, EDDC is a national platform for drug discovery and development formed from the integration of the Experimental Therapeutics Centre (ETC), Drug, Discovery and Development (D3), and Experimental Biotherapeutics Centre (EBC).

EDDC possesses a full range of capabilities including assay development, high throughput screening, antibody cloning, medicinal chemistry and ADME/toxicology; these capabilities allow the unit to identify drug hits and leads, and develop them to preclinical candidate stage in-house. It also has internal expertise to support candidates through First-in-Human/Patient Phase, and is able to conduct Proof-of-Mechanism and Proof-of-Concept Studies.

Alongside the full suite of capabilities, EDDC aims to foster strong collaborations with both public institutions and industry partners. Taken together, EDDC is well-poised to enable Singapore's translational drug discovery and development activities.

**CASE STUDY**

### First made-in-Singapore publicly-funded cancer drug enters clinical trials

Researchers at A\*STAR's ETC/D3 partnered Duke-NUS GMS to discover and develop ETC-159 which targets a number of cancers including pancreatic and colorectal cancer. In 2015, ETC-159 became the first Singapore publicly-funded cancer drug to enter Phase 1 clinical trials.

"The development of ETC-159 illustrates A\*STAR's approach to an integrated drug discovery and development ecosystem that incorporates the infrastructure, resources and human capital from the wider community. ETC-159 is a testament to the centre's capability to conduct global-standard drug discovery and development activities, and the centre's commitment to building strong partnerships," said Damian O'Connell, CEO of EDDC.

## Diagnostics Development Hub (DxD Hub)

Led by A\*STAR's commercialisation arm A\*ccelerate, DxD Hub accelerates the transformation of research findings into clinically validated diagnostic devices that are ready for market adoption. The initiative works with clinicians, researchers and companies on areas such as regulatory navigation, dossier preparation and product design.

**CASE STUDY**

### Fast-tracking a blood test for gastric cancer

DxD Hub worked with cancer diagnostics company and A\*STAR spinoff MiRXES to develop GASTROClear, a liquid biopsy test for early detection of gastric cancer. DxD Hub's productisation and regulatory expertise accelerated the CE-Marking of GASTROClear for the European market (amounting to 32 countries), as well as the regulatory submission to the Health Science Authority of Singapore in late 2018.

"Early detection of cancer before clinical symptoms significantly improves patient prognosis while reducing treatment cost. By developing non-invasive cancer early detection solutions that are accurate and affordable, we are one-step closer to the vision of a world without late stage cancer. Our partnership with A\*STAR through DxD Hub has been instrumental in laying a firm foundation for us to develop new technologies and clinical diagnostic tests," said Dr Zhou Lihan, co-founder and CEO of MiRXES.

**PARTNERSHIPS**

## Fighting Dengue with Therapeutic Antibodies

A\*STAR's Singapore Immunology Network (SIgN) is partnering with Chugai Pharmabody Research to develop a new therapeutic antibody against dengue virus. The antibody, which neutralises all four dengue virus serotypes, was discovered by SIgN researchers and optimised using Chugai's proprietary antibody engineering technologies. Aided by a grant from the Global Health Innovative Technology Fund, SIgN and Chugai are continuing to develop and evaluate the antibody for use in humans.

"A\*STAR's collaboration with Chugai will advance treatment for dengue and create impactful healthcare outcomes. This public-private partnership is an endorsement of the strength of this research team to combat one of the world's major infectious diseases," said Dr Wang Cheng-I, PI at the A\*STAR Singapore Immunology Network (SIgN)

"This project is the result of the collaboration of Chugai's proprietary antibody engineering technologies and SIgN's expertise in the biology of the dengue virus. It is our hope that this novel anti-dengue virus antibody will provide a new treatment option to minimize disease and economic burden in endemic countries globally," said Dr. Tomoyuki Igawa, CEO, Chugai Pharmabody Research Pte Ltd.

TRANSLATION

# TAKING DISCOVERIES INTO THE CLINIC TO IMPACT LIVES

A\*STAR researchers are leveraging the latest advances in next-generation sequencing, data analytics and artificial intelligence to improve disease detection and monitoring, reduce overtreatment and unnecessary testing, and recommend the best treatment options.

*“We are united by a common passion, which is to improve patient outcomes and healthcare.”*

– Professor Patrick Tan,  
Programme Director, POLARIS

## BRINGING COST-EFFECTIVE PRECISION INTO THE CLINIC

Our precision medicine initiatives bring the detection of genetic and biochemical signatures of disease and drug response into the clinic in an affordable manner.

### Clinical Genomics to Treat and Diagnose Diseases

Researchers are piloting the application of clinical genomics in the treatment and diagnosis of diseases. One of the first labs in Asia to obtain accreditation from the College of American Pathologists (CAP) specifically for next-generation sequencing services, the POLARIS network offers a wide range of diagnostic tests, including genetic testing for eye diseases and cancer, clinical exome sequencing and pathogen whole genome sequencing.

#### CASE STUDY

#### Preventing corneal blindness with a genetic test

POLARIS researchers have developed a genetic test for corneal stromal dystrophy (CD), an eye disease that can lead to blurring and loss of vision. The test detects mutations in the *TGFBI* gene, enabling clinicians to identify asymptomatic patients and their family members with CD, who are at risk for complications during eye surgery procedures such as LASIK. Based on research from the Singapore National Eye Centre and Singapore Eye Research Institute (SERI), the test was developed by the Genome Institute of Singapore and Singapore General Hospital, and validated by the National University Hospital.

“It has been our privilege, as POLARIS, to work with the best and brightest clinicians and scientists across Singapore, to bring research findings back to Singapore patients. We are united by a common passion, which is to improve patient outcomes and healthcare,” said Professor Patrick Tan, Programme Director, POLARIS.



## BRINGING COST-EFFECTIVE PRECISION INTO THE CLINIC

## A Precision-Oncology Platform for Liver Cancer

Researchers are developing the world's first patient-specific precision oncology platform for liver cancer that can predict which drugs may work for individual liver cancer patients. The PuRPOSE programme is a collaboration between the National Cancer Centre Singapore, A\*STAR's Institute of Molecular and Cell Biology and Genome Institute of Singapore, the National University of Singapore, and South Korea's Samsung Medical Centre. The platform is capable of delivering high-throughput drug response data from patient-derived liver cancer cell cultures within a clinically relevant timeframe of three to four weeks. This pharmaco-genomic information will help the patient and his doctors select the drug that is able to deliver the best response in that individual patient.

"While Singapore has achieved much excellence in upstream and translational research in HCC, this initiative brings together the strengths of our institutions, combining the efforts of the existing flagship programme in liver cancer with other programmes," said Professor Pierce Chow, Lead Principal Investigator of PuRPOSE and Senior Consultant at the National Cancer Centre Singapore.

### Platforms/capabilities

- Generation of patient-derived cell cultures and models
- Functional screening of drugs
- Multi-omics data integration by leveraging on the Translational and Clinical Research (TCR) Flagship Programme for Liver Cancer in Singapore



The PuRPOSE Team

## Immune Profiling for Targeted Immunotherapy

A\*STAR researchers are developing immune profiling methods to map immune responses and identify biomarkers that predict how patients will respond to immunotherapies for cancer and other diseases.

### SPINOFF COMPANY

#### Immunoscape: high-dimensional immune profiling

A spinoff company from the lab of A\*STAR researcher Dr Evan Newell, Immunoscape's high-dimensional immune profiling platform uses mass cytometry and a combinatorial multiplexing method to map multiple immune cell specificities simultaneously. Immune cell profiles obtained from this platform can help predict treatment responses for a wide range of diseases spanning cancer, infectious diseases and autoimmunity.

Immunoscape aims to help industry partners optimise their early R&D pipeline and help doctors design new combinations of treatments, bringing down the cost of immunotherapy in the long run.

## Diabetes Clinic Of the Future (DCOF)

DCOF is a joint effort between A\*STAR, SingHealth and the National University of Singapore's Centre for Behavioural Economics to address the significant healthcare and economic burden of type 2 diabetes mellitus (T2DM) in Singapore. Uniting multidisciplinary capabilities in digital technology, advanced data analytics and behavioural economics, DCOF aims to develop smart solutions for customising T2DM care for each patient, improving disease management and minimising T2DM complications.

## BRINGING COST-EFFECTIVE PRECISION INTO THE CLINIC

## Surveillance and Pharmacogenomics for Adverse Drug Reactions

Researchers are working to improve drug safety by reducing adverse drug reactions (ADRs). Initiatives within the SAPHIRE programme include a surveillance network to monitor ADRs via electronic medical records, a discovery platform to identify novel molecular signatures of ADRs in Asian populations, and the development of molecular diagnostic tests to predict ADRs. SAPHIRE's pharmacogenomics test for predicting ADRs to carbamazepine is now considered the standard of care in Singapore prior to initiation of treatment.

## SPINOFF COMPANY

### Nalagenetics: reducing ADRs through genetic testing

A spinoff from SAPHIRE, Nalagenetics offers a commercial genetic testing platform for the screening of ADRs. The company's first test kit detects a genetic marker for hypersensitivity to dapsone, a drug used to treat leprosy, and has been validated in patients in Papua, Indonesia.

"Adverse drug reactions are responsible for 8 percent of hospital admissions today, wasting about US\$30 billion of healthcare resources in the US and a similarly significant amount in Asia. Knowing a person's genetic makeup can therefore save patients from unwanted – sometimes deadly – adverse side effects," said Dr Liu Jianjun, Co-Founder of Nalagenetics and PI at the A\*STAR Genome Institute of Singapore



***“Knowing a person’s genetic makeup can therefore save patients from unwanted — sometimes deadly — adverse side effects.”***

— Dr Liu Jianjun, Co-Founder of Nalagenetics and PI at the A\*STAR Genome Institute of Singapore

## ENHANCING HEALTHCARE WITH ARTIFICIAL INTELLIGENCE

Our researchers are developing powerful computer vision and artificial intelligence-based solutions for research and clinical applications.

## CASE STUDY

### Computer vision and pattern discovery for medical imaging

A\*STAR researcher Dr Lee Hwee Kuan combines computer vision, machine learning and mathematical models to develop improved image analysis methods for research and healthcare purposes. Projects include machine learning approaches to assess prostate cancer risk from clinical data, as well as intelligent software for the detection of prominent nucleoli, irregularly shaped nuclei and other features of cancerous cells in histology images.

"We aim to address the increasing healthcare demands by developing automated, artificial intelligence based systems to analyse histopathological images, assess tumour risk and dissect tumour heterogeneity. Our research would support pathologists and medical professionals in diagnosis, treatment plans, medication management and precision medicine of cancer," said Dr Lee Hwee Kuan, Senior PI of the Imaging Informatics division at the A\*STAR Bioinformatics Institute.

## CASE STUDY

### Video analytics for disease surveillance

In addition to image analytics, A\*STAR researcher Dr Cheng Li is also developing machine learning and computer vision algorithms that can analyse video. One of his projects focuses on detecting flu-like symptoms such as sneezing and coughing in video footage, with the aim of carrying out disease surveillance in public areas such as airports.

## CASE STUDY

### High-throughput toxicity prediction

A\*STAR researcher Dr Loo Lit Hsin develops next-generation *in vitro* and computational methods to predict the toxicity and efficacy of chemical compounds. Combining high-throughput cell imaging, quantitative phenotypic profiling and machine learning models, Dr Loo's methods accurately classify compounds according to their modes of action without prior knowledge of chemical structure. The approach is suitable for screening large numbers of chemicals with diverse modes of action, and serves as a high-throughput alternative to animal testing.

"Phenotypic profiling is automated digital pathology for cells. It can automatically quantify changes in cellular morphology and organelle structures in response to a chemical, and accurately predict whether the chemical is safe to a specific cell type or not. It can even be used to derive points of departure for broad bioactivity when no other safety data or information is available," said Dr Loo Lit Hsin, Senior PI at the A\*STAR Bioinformatics Institute

## CASE STUDY

### Machine learning approaches for magnetic resonance image analysis

Researchers at A\*STAR's Singapore Bioimaging Consortium are applying machine and deep learning approaches to magnetic resonance imaging (MRI) data processing applications, such as increasing image resolution, improving image reconstruction and generating quantitative maps. These improvements are aimed at reducing imaging-related costs and patient discomfort, developing new diagnostic biomarkers and increasing imaging throughput efficiency.

## CAPABILITIES

# IMAGING AT A\*STAR

A\*STAR's research entities host a comprehensive array of imaging platforms that support diverse biomedical research needs from discovery to translation.

## Light and Electron Microscopy

The A\*STAR Microscopy Platform (AMP) brings together a broad range of light and electron microscopy techniques to meet the needs of the Singapore biomedical research community, from fine ultrastructural electron microscopy, through high spatiotemporal imaging of dynamic cellular processes, to 3D intra-vital imaging deep within living tissues. This includes the critical complementary techniques of sample preparation and quantitative image analysis. AMP's team of dedicated expert staff have the experience to consult, train, support and offer high-quality service to scientists.

## Bioimaging

The Singapore Bioimaging Consortium (SBIC) has an extensive suite of advanced preclinical and clinical bioimaging systems. These include systems for magnetic resonance imaging (MRI) and spectroscopy (MRS), single-photon emission computed tomography (SPECT), positron emission tomography (PET), X-ray computed tomography (CT), as well as hybrid systems such as PET-MRI. Advanced developments and training are conducted at SBIC in collaboration with its industry partners, Nikon, Mediso, Bruker and Siemens.

SBIC is a pioneer in bio-optical imaging, including new imaging devices and optical biosensors. SBIC is a leader in photoacoustic imaging, and has developed a host of photoacoustic modalities ranging from tomography to microscopy in partnership with iThera Medical and MicroPhotoAcoustics Inc. Applications include skin imaging and detection of breast cancer tumours.

SBIC has extensive expertise in the development and generation of novel imaging probes and tracers. In addition, deep learning and artificial intelligence-based techniques are routinely developed and deployed at SBIC for processing preclinical and clinical images acquired on the multimodal imaging platforms.

## Artificial Intelligence in Imaging

Aside from the capabilities at SBIC, researchers at the Bioinformatics Institute (BII), the Institute for Infocomm Research (I<sup>2</sup>R) and the Institute of High Performance Computing (IHPC) are also developing powerful artificial intelligence (AI)-based image analysis solutions that could improve the accuracy and speed of disease diagnosis, enhance clinical workflows, as well as reduce healthcare costs.

## GE Healthcare and A\*STAR team up on diagnostic imaging

GE Healthcare and A\*STAR are collaborating to develop innovative medical technologies in imaging diagnostics and patient monitoring. These technologies have been built into GE Healthcare's products across a range of different patient care equipment and applications, with others in the process of being implemented into GE Healthcare's solutions globally.

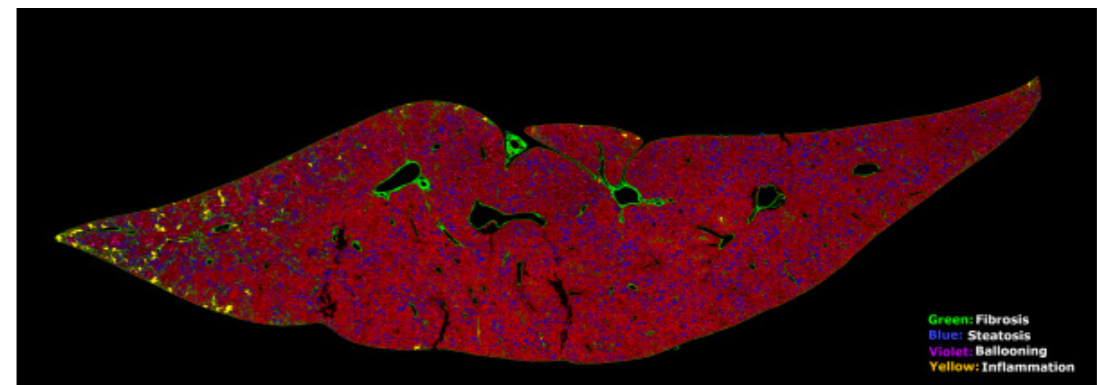
## ENHANCING HEALTHCARE WITH ARTIFICIAL INTELLIGENCE

## Digital pathology

### HistoIndex: Fully Automated AI-based Digital Pathology and Analysis for liver diseases

HistoIndex, a spinoff from A\*STAR's Institute of Bioengineering and Nanotechnology, offers an AI-based digital pathology platform based on its proprietary Second Harmonic Generation & Two-Photon Excitation (SHG/TPE) technology. With a focus on non-alcoholic steatohepatitis (NASH), this state-of-the-art technology provides an accurate and objective assessment of NASH characteristics for stain-free tissue assessment as well as to track treatment efficacy.

HistoIndex's SHG/TPE platform is currently being used in Phase II/III NASH clinical trials, as biopsy-based endpoints are required for U.S. Food and Drug Administration (FDA) approval. A chronic liver disease, NASH is expected to become the leading cause of liver transplants by 2020 and is still waiting for its first FDA-approved drug.



Preclinical NASH Animal Model

### Invitrocue: Cell- and image-based bioanalytics solutions

Invitrocue, A\*STAR's first publicly listed spinoff, is a leading bioanalytic solutions company built on technology developed by Dr Hanry Yu. The company offers in vitro testing platforms, including a liver organoid model for the testing of drugs and vaccines, as well as a digital pathology workflow going from sample preparation to computer-aided diagnosis and automated reporting.

"By enabling assessments of the best ways for drugs to be developed, we impart to the industry valuable knowledge in creating better, faster and more affordable disease treatments. We have also developed a clinical service called Onco-PDO, leveraging Invitrocue's extensive expertise and know-how in 3D cell culture to grow patient-derived cancer cells in its proprietary scaffolds and other platforms to test them against a range of cancer therapies. These technologies are a key advance in the personalised treatment of a range of cancers, and we are working with a number of the world's leading pharmaceutical companies and clinical centres in Singapore, China (including Hong Kong SAR), Germany, and Spain," said Dr Hanry Yu, Founder of Invitrocue and Group Leader at the A\*STAR Institute of Bioengineering and Nanotechnology.

BIOMANUFACTURING

PROCESS  
INNOVATION

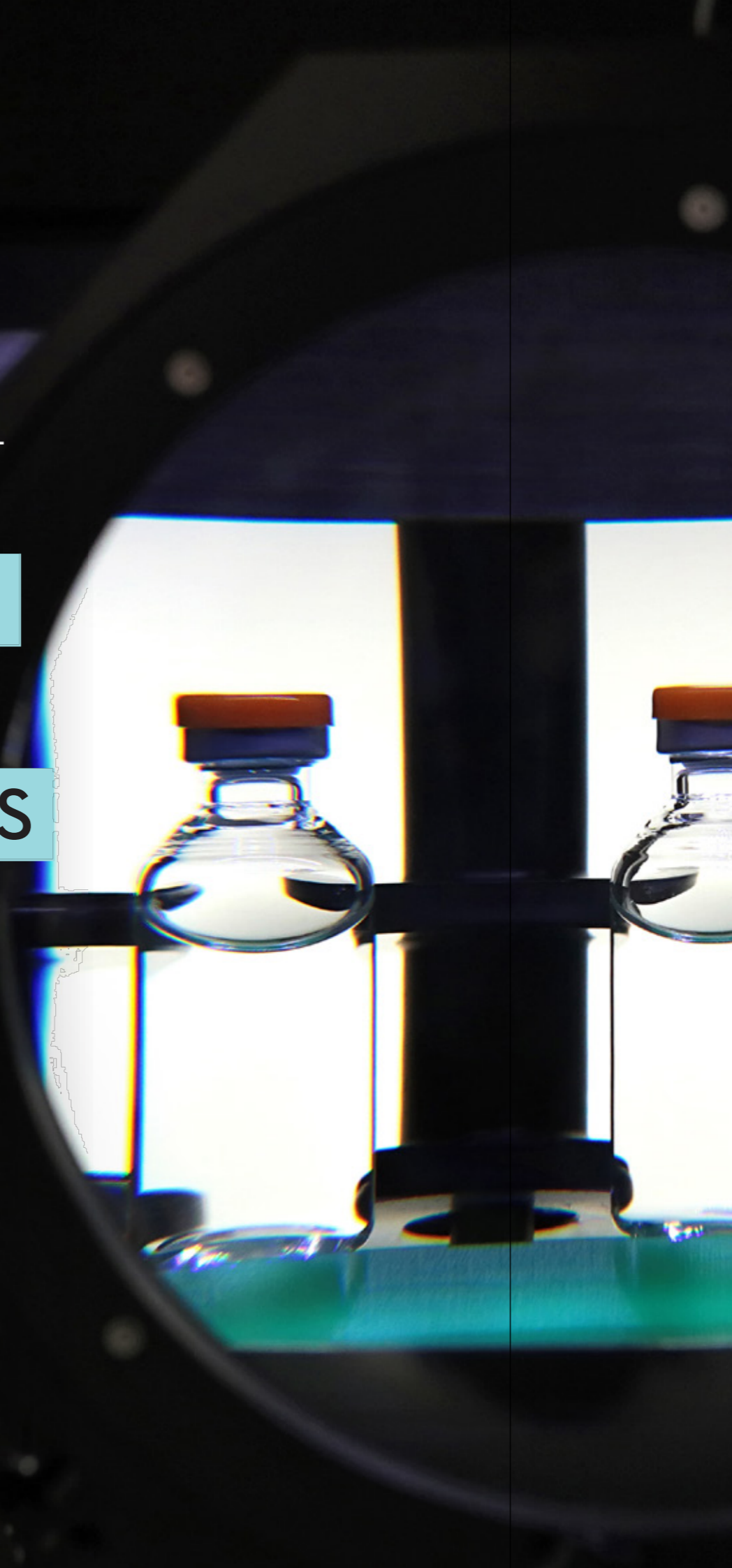
TO

TRANSFORM

INDUSTRY

CAPABILITIES

A\*STAR's biomanufacturing R&D programmes leverage on our bioprocessing expertise to optimise expression systems, improve and monitor quality, as well as enhance productivity yield.

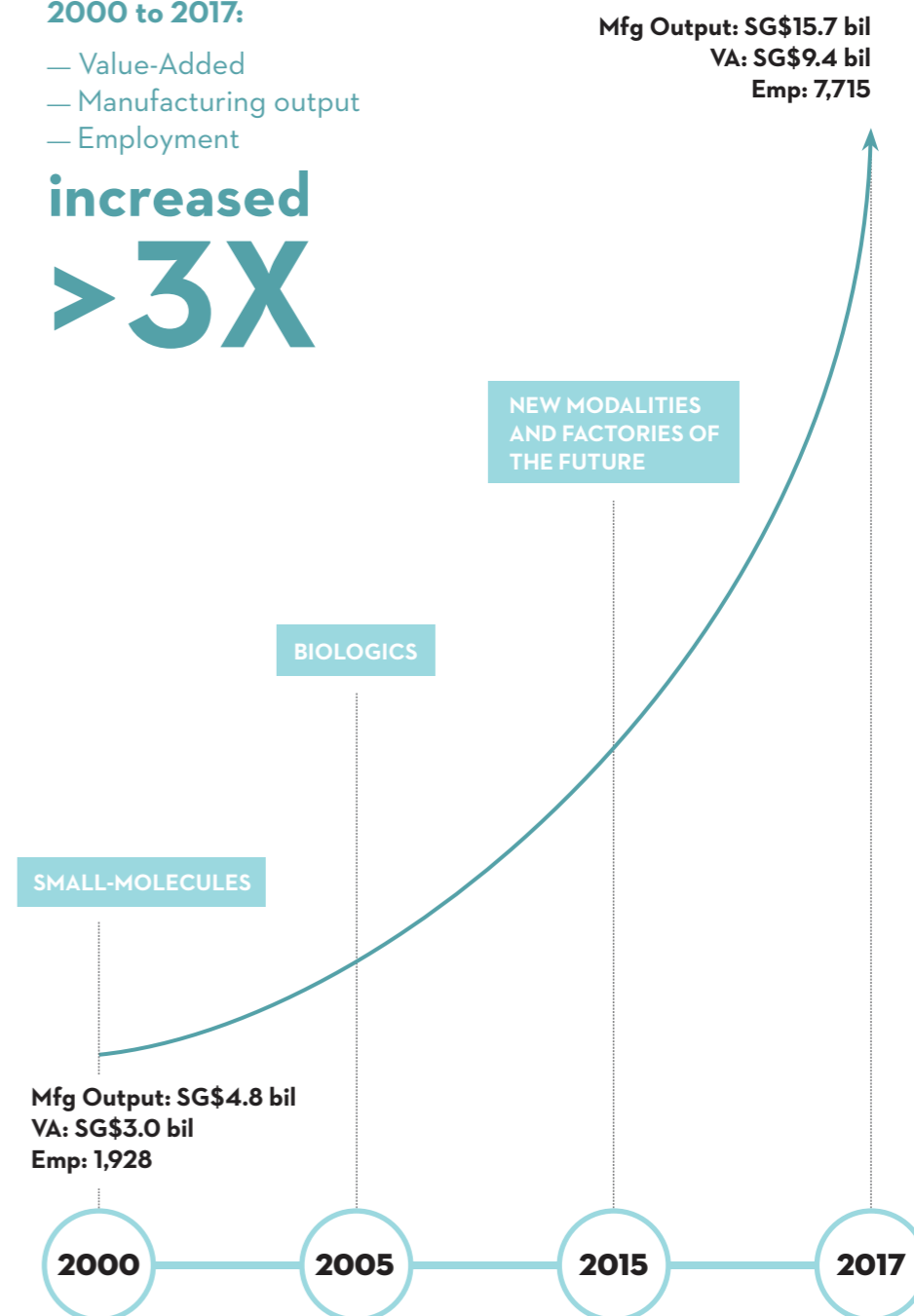


## The Journey of Singapore's Biopharmaceutical Manufacturing Sector

Between  
2000 to 2017:

- Value-Added
- Manufacturing output
- Employment

increased  
>3X



## BIOLOGICS

A\*STAR's biologics R&D programmes leverage on our bioprocessing expertise to optimise expression systems, improve and monitor quality and enhance productivity.

### PARTNERSHIPS

#### A\*STAR and pharma giants partner on biomanufacturing innovation

Led by A\*STAR in partnership with the National University of Singapore, the Pharma Innovation Programme Singapore (PIPS) brings together pharmaceutical giants GlaxoSmithKline, MSD International and Pfizer Asia Pacific to enhance productivity in biomanufacturing. PIPS will develop continuous manufacturing processes to improve efficiency; explore the use of biocatalysis technologies to make high-value, complex chemicals more sustainably; and employ data analytics and automated supply chains to raise productivity.

### PARTNERSHIPS

#### A\*STAR's Bioprocessing Technology Institute teams up with industry leaders to develop new biologics capabilities

A\*STAR's Bioprocessing Technology Institute (BTI) partners with numerous industry leaders to co-develop new capabilities. BTI's collaboration with analytical technology company SCIEX develops accurate, high-throughput methods of contaminant analysis during biologics production, with the aim of facilitating validation of therapeutic candidates and ensuring the safety and efficacy of biologic drugs.

BTI is also partnering with analytical laboratory instrument company Waters to develop a glycoconjugate database and spectral library that will facilitate the identification of glycans as potential clinical biomarkers. This effort unites BTI's expertise in glycomics with Waters' ion mobility mass spectrometry technology.

BTI is also a participant in BioPhorum, a consortium of academic, regulatory and industrial partners seeking to accelerate innovation in biologics manufacturing, with an emphasis on speed, flexibility, quality, and cost.



## CELL THERAPY MANUFACTURING

A\*STAR's research programmes address key challenges in the large-scale manufacturing of cell therapy products. They aim to equip industry partners with manufacturing solutions to deepen our understanding of cell quality attributes relating to safety and efficacy, and to develop improved analytical technologies to assess the quality of manufactured cells.

### CASE STUDY

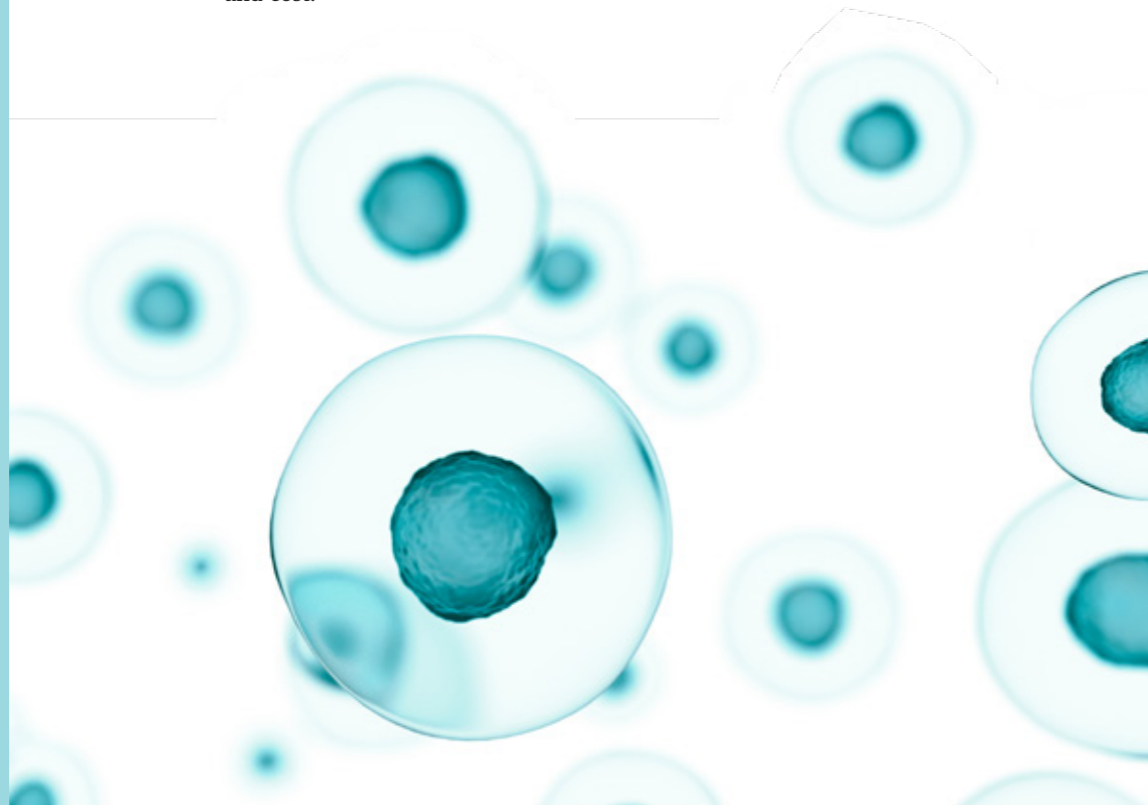
#### Autologous clinical cell therapy manufacturing programme

A joint effort between A\*STAR, National University Hospital, SingHealth and HSA, the Autologous programme aims to develop a commercially scalable and integrated platform for autologous cell therapy addressing bottlenecks in the entire autologous cell therapy manufacturing process. This will include a scalable system design and GMP compliant manufacturing processes, development of rational genetic modification of primary human lymphocytes, and downstream assessment of their cellular potency, and development of clinical scaling and evaluation.

### CASE STUDY

#### Potent Mesenchymal Stem Cells programme

This programme addresses donor selection, critical quality attributes and optimal culture conditions with the aim of transforming allogeneic cellular therapy and establishing therapeutically-potent adult human mesenchymal stem cells for clinical translation. This includes identifying biomarkers of stem cells with significant growth and therapeutic potency and generating optimal culture conditions that favour the growth of highly potent stem cells with enhanced therapeutic potential.





# CREATING A VIBRANT BIOTECH & MEDTECH INNOVATION ECOSYSTEM

Singapore's biotech and medtech ecosystems have reached an inflexion point, with the biomedical sciences fast becoming a vital pillar of the country's manufacturing sector. About 300 biotech and medtech companies have incorporated in Singapore as of 2018. Our efforts to move discoveries from lab to market have played a key role in nurturing the ecosystem—A\*STAR spin-offs now comprise 30 percent of local biotech companies, and A\*STAR has had touchpoints with half of all Singapore-incorporated biotechs.

## A\*StartCentral

Managed by A\*ccelerate, A\*StartCentral incubates startups, trains and supports technopreneurs, and promotes the use of A\*STAR-developed technologies in business ventures.

### CASE STUDY

#### A great start for A\*StartCentral alumni

A\*StartCentral has incubated a diverse range of spinoff companies that address key unmet medical needs with innovative technologies.

- Medisix Therapeutics: novel CAR-T based therapies for T-cell leukaemias and lymphomas
- Lion TCR: T-cell based therapies for hepatocellular carcinoma and other virus-induced cancers
- Engine Biosciences: machine learning- and genomics-based drug discovery platforms
- Privi Medical: medtech innovations for haemorrhoids pain relief
- Advent Access: medtech innovations to reduce dialysis costs and improve quality of life for kidney failure patients

## Research Support Centre (RSC)

The RSC is a unit of A\*STAR that hosts one of Singapore's largest e-commerce portal offering life science research products and scientific services. RSC partners with over 60 qualified suppliers and more than 26 scientific service providers to offer over 5,000 research consumable items and access to the latest technologies in genomics, immunology, bioimaging, proteomics and more.

The RSC e-commerce portal is an open platform where public institutions and private companies connect, search and order on a single website for any lab product or service.

### CASE STUDY

#### AWAK uses RSC's Partner Services to advance its innovative wearable peritoneal dialysis system into the clinics

AWAK Technologies Pte. Ltd. was connected to Pharma Research Services (PRS) team at IMCB through RSC. Dr Manikanadan and Dr Venkataramanan, lead scientists at PRS generated high quality reproducible safety data on inflammatory biomarkers. This crucial data in combination with AWAK's clinical data helped to demonstrate the safety of the AWAK Peritoneal Dialysis System, which is an ultra-portable/wearable peritoneal dialysis system that allows dialysis to be performed on-the-go.

"Dr Mani and Dr Venkat provided strategic technological support to resolve the analytical challenges that we faced. I would also like to express my gratitude to RSC for facilitating this collaboration. I look forward to more collaborations." Mr Suresha Venkataraya, CEO, AWAK Technologies Pte Ltd

## Partnerships with Local Biotechs

### PARTNERSHIPS

#### Teaming up for T-cell therapies

In 2017, A\*STAR's Institute of Molecular and Cell Biology (IMCB) established a joint immune-oncology laboratory with Tessa Therapeutics, an immunotherapy company focused on developing novel CAR-T-based therapies for cancer. Combining IMCB's cancer immunology expertise with Tessa's T-cell platforms and clinical trial experience, the joint laboratory will conduct research on advanced T-cell and CAR-T technologies, with the aim of developing next-generation immunotherapies for solid tumours.

"The combination of Tessa's R&D, clinical, and commercial expertise with A\*STAR's world-class facilities and research capabilities holds great promise for us to accelerate life-saving research and to further strengthen Tessa's clinical trial pipeline," said Mr Andrew Khoo, co-founder and CEO of Tessa Therapeutics.

### PARTNERSHIPS

#### Developing a novel antibody immunotherapy

ASLAN Pharmaceuticals and A\*STAR's p53 Laboratory are collaborating to develop and commercialise an antibody against RON, a receptor tyrosine kinase, as a novel immunotherapy against a range of cancers. The p53 Laboratory, which discovered the antibody, will lead preclinical studies, while ASLAN will be responsible for clinical development and commercialisation.

"We are pleased to accelerate the development of this novel agent with ASLAN and to leverage the team's expertise in advancing clinical programmes. This will pave the way for better treatment of cancers that are common in Asia, which will eventually improve lives in Singapore and beyond," said Professor Sir David Lane, Chief Scientist of A\*STAR and Director of the p53 Laboratory.

### PARTNERSHIPS

#### Leveraging bioanalytics and genomics for precision medicine

A joint laboratory established by A\*STAR's Genome Institute of Singapore (GIS) and bioanalytics company Invitrocue will develop tumour models to help clinicians tailor treatment plans to individual patients. The laboratory will combine patient-derived tumour models, functional genomics and machine learning to identify biomarkers of drug resistance and response, with the aim of providing clinicians with real-time treatment guidance.

"The new lab will bring our work another step closer to commercialisation, [resulting in] life-saving technologies that essentially take the guesswork out of cancer treatment and improve quality of life for the patient," said Dr Steven Fang, co-founder and Executive Director of Invitrocue.



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