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*Professor Ng Huck Hui of A*Star's Biomedical Research Council outlines the evolution of Singapore's science and technology research and innovation ecosystem over the past 20 years and why the country is now focusing on translational science and building up enterprise.*

Professor Ng, could you start by introducing yourself and A*STAR to our international audience?

Very briefly, I did my Bachelor of Science in cellular and molecular biology at the National University of Singapore and my PhD in molecular genetics at the University of Edinburgh. I then went to Harvard Medical School as a postdoctoral fellow, before returning to Singapore in 2003, where I established my own laboratory at the Genome Institute of Singapore (GIS) to study stem cells. In 2011, I became the executive director of GIS, where I spearheaded Singapore’s effort in human genomics. In 2017, I took on a concurrent appointment as the executive director of the A*STAR Graduate Academy, an A*STAR unit that oversees scholarships and talent development. In January 2020, I was appointed assistant chief executive of the Biomedical Research Council of A*STAR, my current position.

A*STAR’s mission is to advance science and develop innovative technology to further economic growth and improve lives. We aim to translate our scientific discoveries and innovative technologies into economic growth and social impact. Through open innovation, A*STAR and its research institutes collaborate with our partners in both the public and private sectors, and drive scientific discovery and technological innovation that benefits the economy and society.

Having worked in biomedical research in Singapore across various positions over nearly 20 years, how has the science and technology research and innovation ecosystem in the country developed?

Around 2000, Singapore made a commitment to positioning biomedical research as the fourth pillar of the economy, which was when the government started to invest heavily in this space. This led to the creation of Biopolis, the international R&D center for biomedical sciences in Singapore. The strategy was to create something from scratch, so the financial resourcing was the first element. The second element was the infrastructure, including the buildings, facilities and all necessary equipment. The third element was talent. Since we were starting from scratch, while we had researchers and academics in Singapore, we did not have any critical mass then. The idea then was to bring in foreign talent while training and funding local Singaporeans to build the pipeline.

Today, we can see that this strategy has worked very well. We are climbing the global ladder when it comes to excellence in science.

Singapore has an overarching five-year research strategy, which is evaluated and renewed every five years. This planning has been done for a number of cycles now, and each time we do it, we outline a strategy to address existing gaps and to capitalize on new growth areas.

In our current five-year strategy, the Research, Innovation and Enterprise (RIE) 2025 plan, it has been made very clear that we need an ecosystem approach. During the past 20 years, we have built clusters like Biopolis, universities and institutions and so on. The piece that we are doubling down is in translation and building enterprise. We need a new scheme to think about how we channel all our ideas and research into a translational engine and to build end-to-end capabilities in drug discovery and development.

What are the main challenges and opportunities for Singapore in the biomedical innovation space?

Singapore serves as a global Asia node for companies to establish their R&D base in the region. With the growth of Asia as a consumer market, Singapore is geographically well-positioned to act as a base for companies looking to tap into the region and to pursue Asian-centric innovations. Singapore has many strengths for companies looking to set up shop to tap on Singaporean innovations, as well as leverage our geographical location as a base for the region.

The Singapore government has put in stable and long-term investments in R&D, pegged at about 1 percent of our GDP over the years. These investments have allowed us to build up a base of scientific talent and help bolster our status as a technology and innovation hub. Our government recognizes that Singapore's economy rests on human capital and the importance of innovation. It encourages open innovation, and spur research, innovation and enterprise activities by creating a conducive environment at one-north. There is a high concentration of top R&D talent from the public and private sectors work on innovations in state-of-the-art facilities. This physical environment generates opportunities for knowledge- sharing and collaboration, which help to accelerate growth and facilitate success in the marketplace.

With regards to the challenges, Singapore is a small country with limited resources. This means we have to be more focused in where we direct our resources to make an impact. It is always a balance of risk and payoff, and the nature of innovation means there is no 'sure bet'. Despite our size, we have nevertheless been able to punch above our weight in scientific excellence and innovation. This is reflected in recent global innovation reports such as the Bloomberg 2020 Innovation Index, where Singapore leaped three spots and was ranked third in the world.

What role does A*STAR play in this strategy?

Our mission is to advance science and develop innovative technology to further economic growth and improve lives. Looking at all the different players within Singapore, A*STAR's role is to translate research and spearhead innovation, whether basic research from A*STAR or other parts of the ecosystem. We catalyze new programs and new initiatives to bring different partners together. That is our value proposition.

For instance, A*STAR is supporting Singapore's national platform called the Experimental Drug Development Centre (EDDC), which has the mandate of developing small molecule and biologic drugs. It looks for projects across the ecosystem in Singapore to develop innovative assets that have the goal of ultimately entering the clinic.

How does the Biomedical Research Council choose how to allocate funding?

We take a diversified and balanced portfolio approach in allocating funding, in alignment with the government's new Research, Innovation and Enterprise 2025 (RIE2025) Plan from 2021-2025. Under RIE2025, BMRC will focus on these key areas:

- Pharmbio – Biotech, Drug Development
- Medtech
- Biopharma Manufacturing,
- Food & Nutrition
- Consumer Care
- Precision Medicine and Digital Health
- Epidemic Preparedness
- Human Potential – which focuses on supporting improvements in health, productivity, and learning capacity across an individual's life course.

Research funding is used to build and sustain peaks of excellence and to maintain long term capabilities. The allocation is based on strategic priorities and new opportunities to promote growth areas. Our funding for research is also a proxy for our investment in innovation.

We know that regenerative medicine has been made national priorities in other Asian countries like South Korea and Japan. Does A*STAR focus on any specific therapeutic areas?

Certainly, there are many novel technologies being developed in this sector. Cell and gene therapy are great examples, mRNA technologies are another great example. We are definitely studying cell and gene therapy closely. There are three cell therapy programs in Singapore already. For gene therapy, we are starting to develop a new initiative.

One key area we are building is our capabilities in new therapeutic modalities, particularly cell and gene therapy. There is tremendous potential here in offering cures to many diseases that are currently untreatable. But there are also a lot of challenges yet to be solved, such as efficient, targeted delivery systems and managing immunogenicity.

We must be responsive to new trends. For example, infectious disease research became a key priority when COVID-19 reshaped 2020 and beyond, and reemphasised the importance of pandemic response, from diagnostics to vaccines to therapeutics. It also brought nascent areas like telehealth to the forefront.

With translational science now a strategic priority for A*STAR, how do you work with industry to facilitate this?

Connecting academia with industry has always been one of our key mandates. We are the bridge between academia and industry.

Firstly, there are many multinational pharma companies with R&D presence in Singapore. For instance, MSD's Translational Medicine Research Center (TMRC) is located at the Biopolis, so we benefit from its proximity to the researchers and entrepreneurs at Biopolis. Scientists can mingle with company researchers during lunchtime and exchange ideas.

Secondly, there is an increasing number of biotech and medtech start-ups in Singapore. Many are also at the Biopolis and again, we benefit from the co-location. There are many interactions between us and them, and we also have initiatives to connect start-ups to our research entities to nurture them. For instance, if start-ups need access to a certain type of technology platform, we try to give them access. We also have talent flowing from our institutes to the industry. For instance, through our Technology for Enterprise Capability Upgrading (T-Up) program, our researchers can join small- and medium-sized enterprises for a period of up to two years, to share product development strategy, aid innovation in business processes, and assist companies to develop innovative products.

The Diagnostics Development (DxD) Hub is a national platform hosted by A*STAR to fast track the transformation of IPs into clinically validated diagnostic devices that are ready for market adoption. It plays an instrumental role in facilitating knowledge/technology transfer to the local biotech companies, aiding them from product design, testing to mass production.

How is the homegrown biopharma sector doing? Is there a typical profile for healthcare or biopharma start-up CEOs?

As you would expect, we have a mixture of serial entrepreneurs as well as budding or new entrepreneurs. Successful entrepreneurs in other countries have also been attracted to come to Singapore to establish companies, like Tessa Therapeutics, for instance. It takes time for new entrepreneurs to gain their bearings and also for new ecosystems to develop serial entrepreneurs. We are actively trying to expose our researchers to entrepreneurship, however, because if we do not nurture them today, then we will not have serial entrepreneurs ten or 20 years down the road. We have to start now.

Singapore has a lot of advantages for biomedical research and start-ups but commercially it is a very small market. How should institutions like A*STAR and also companies capitalize on larger markets in the region, especially China, with its rapid growth and development in the biopharma sector?

Singapore has some great advantages. The first is nimbleness. We respond very quickly and every five years we improve our strategy so that gives us an edge. Secondly, we have a skilled workforce. Thirdly, our government is very facilitative and supportive, and therefore we have a great pro-business environment. Due to these factors, among others, we have a very competitive positioning in terms of innovation.

Having said that, we know that Singapore is not the market for many, if not most, of the companies we support and nurture. The important question is: how do we move from value creation to value capture? We want the foundation to be built and based in Singapore but the companies would have to scale globally – it could be the Chinese market or North American markets. It ultimately depends on the therapeutic area, the technology, the opportunities and so on. That is the reason that we encourage open innovation and we work with both start-ups and multinational companies.

How closely does A*STAR work with Singapore's regulator, the Health Sciences Authority (HSA), especially when it comes to supporting the regulatory evaluations and approvals of novel therapies, which can be challenging for regulators?

Regulators play a critical role in approving novel therapies and other products, and they make decisions based on data and are independent from the industries.

There are circumstances that regulator needs to understand some novel technology or product, and they will approach institutions like A*STAR to leverage our experience and expertise.

A hot topic in the industry today is AI and the use of AI in biomedical research. What is your perspective on this?

In terms of AI, data and analytics, there are diverse applications in healthcare and life sciences:

- AI can be used to automate and augment clinical workflows – e.g. analysis of medical images (e.g. CT, MRI, pathology), triaging of patients and speech/text recognition and analysis
- AI can also be used to analyse correlations and patterns across large and varied datasets - this in turn can be applied to predict risk and progression of disease, as well as to personalize diagnoses and treatments for conditions such as cancer
- Bioinformatics also has important applications in infectious diseases - for example, Dr Sebastian Maurer-Stroh and his team from A*STAR's BioinformaticsInstitute (BII) has been playing a pivotal role in studying the genetic sequence of SARS-CoV-2 virus strains, in order to monitor virus evolution and develop effective diagnostics
- Healthcare and life sciences also have synergies with areas such as photonics (e.g. Prof Malini Olivo and team's work in developing new non-invasive imaging devices), as well as with materials (e.g. Dr Su Xinyi and team's work on Vitreogel – a smart polymer for retinal repair)

These synergies have the potential to transform healthcare by improving the quality and efficiency of care, reducing costs, and enabling value-based, personalized and preventive care, as well as to accelerate innovation in the life sciences by enhancing and speeding up data analysis.

On a personal note, as mentioned, I used to helm GIS. You can imagine the amount of sequencing data generated at GIS. Without AI and data analytics, there would have been no way of processing that amount of data. Data and AI are truly the future. I would even go as far as to say that they are already the present. Without data capabilities, it is very difficult to play in this competitive area of biomedical research.

A*STAR has already built up AI capabilities. But we are still actively growing our talent base in this area, and it is not easy because there is huge competition for these types of talent from the tech and financial sectors but we have to keep pushing so we can build critical mass.

We also have an advantage because we are well-positioned in terms of advanced manufacturing and the related engineering capabilities. A*STAR has both a Biomedical Research Council and the

Science and Engineering Research Council, which complement each other. We also have the Bioprocessing Technology Institute (BTI). Aspects like robotics, cell manufacturing and so on are very important for us and we can leverage on our capabilities here to advance our efforts.

Precision medicine and genomic medicine are other hot topics, and quite specifically, for instance, researchers globally have talked about the lack of genomic mapping for non-Caucasian populations. With your background in genomic medicine, what do you think about this concern?

This is a very critical point. In genomic research, there is very little Asian representation. That is why we have established the SG10K project where we sequenced the genomes of 10,000 people of different ethnicities in Singapore. This research was published in *Cell* in 2019, and was a very important achievement for the study of Asian genomics.

Singapore also has our National Precision Medicine program, which aims to sequence our genomes and connect them with our health record data. We hope to be able to link genetic variants to phenotypes, and answer other important questions. It is a huge advantage for us that Singapore's healthcare records are fully digitalized, and there is a lot of research we can do through this initiative.

On a more personal note, what is something in science that excites you today?

I am driven by my passion for discovery and its pull-through to translation and commercialization. From my perspective, having had the opportunity to look at all the different research capabilities within A*STAR and more generally in Singapore, I think one of the biggest opportunities I see is the ability to unlock the potential of biomedical science through multidisciplinary research. That is number one. The model of doing science has changed a lot in the past few decades. I trained as a traditional molecular biologist where the conventional approach was to work on one question over a lifetime. Previously, you could publish major papers alone if you were brilliant. Today, however, the kinds of innovation being discovered and developed come from the collaboration between many brilliant minds working to implement very sophisticated and complex ideas. That is very exciting and a game-changer. Multidisciplinary research is the future. Convergence – in ideas, in operations, in goals – is key. Specifically, for A*STAR, that will also be a key differentiation factor. The more we are able to embrace multidisciplinary research, the more innovation we can create.

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