Ministry of Foreign Affairs

Genomics and Biotechnology R&D in Singapore

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Government of the Netherlands

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Content

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Genomics R&D in Singapore

Singapore wants to be at the forefront of genomic innovation and precision medicine. The vision is to develop a diagnostic manner with the highest accuracy based on the patient's genetic profile, allowing better personalised treatment.

As part of its research and innovation plan, the Singaporean government has mobilised government-backed institutes to drive advances in precision medicine by collaborating with other public and private research entities on developing a comprehensive database of Asian-centric genomes.

1. Current Innovation and R&D Strategy

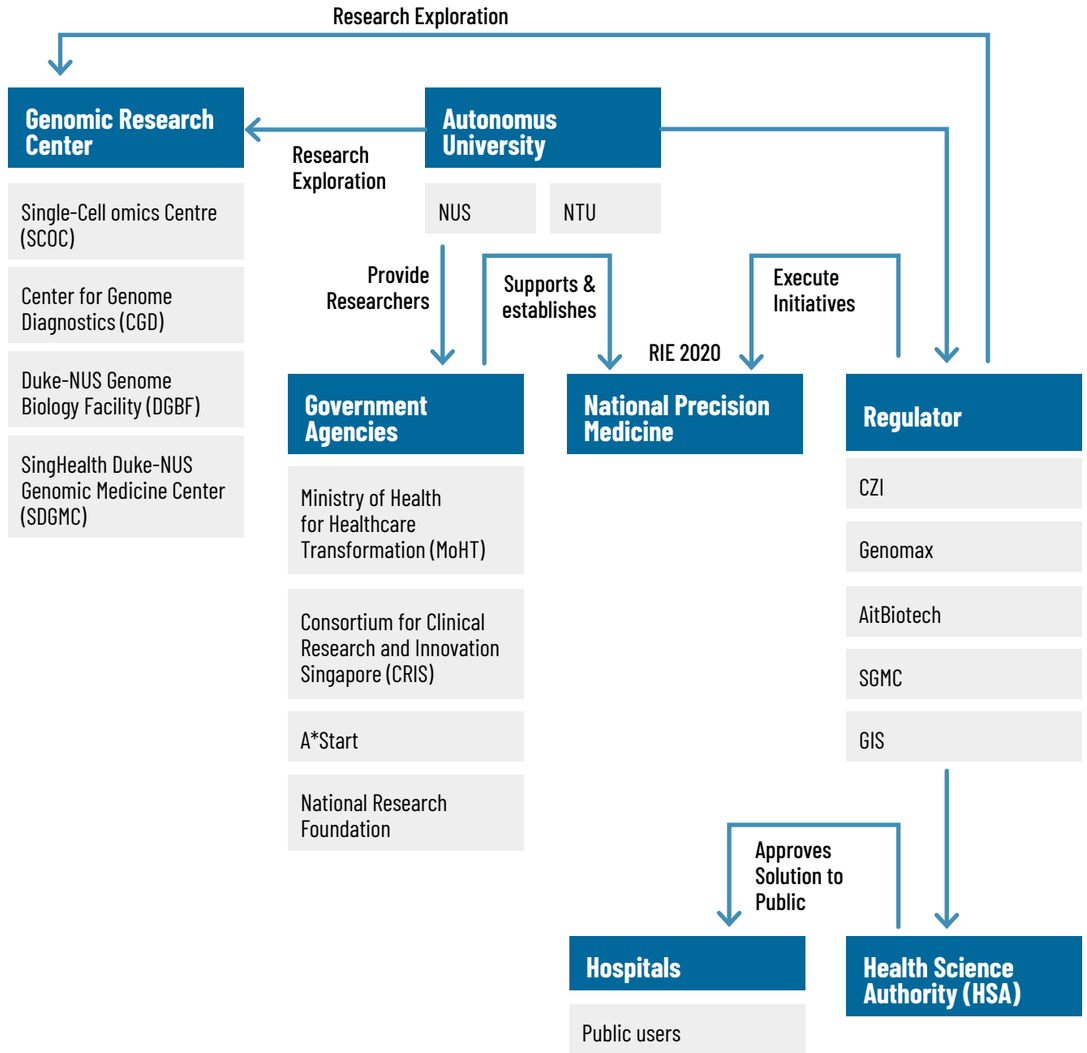
Genomics is one of the top domains of priorities within Singapore's healthcare system. In 2020, the government launched the National Precision Medicine Strategy (NPM) as part of Singapore's RIE 2020 plan to understand better how genomic, phenotypic, lifestyle and clinical factors affect Singaporeans' health[1]. This strategy is assisted by the growing market size of the genomics industry in the Asia Pacific. It is valued at SGD 4.45 billion in 2020 and estimated to reach SGD 7.33 billion by 2025[2].

The National Precision Medicine (NPM) has long been the driver of Singapore's genomics industry. NPM started in 2017 with a 10-year schedule to develop the foundations and infrastructure for precision medicine implementation across the country. The first phase of the project focuses on developing a multi-ethnic Asian genetic database involving 10,000 citizens.

The second phase involves launching The Precision Health Research Singapore (PRECISE) initiative, which will examine the genetic makeup of 100,000 healthy Singaporeans and up to 50,000 people with certain disorders over the next four years. The third phase involves diffusing precision medicine and expanding Singapore's genetic database, involving 1 million citizens. Currently, this phase is still underway, and if it goes according to plan, it will be launched by 2024[3].

The recent growth in market value has resulted in the rise of genomic research entities in Singapore. The advancement of MedTech has provided the country with many untapped potentials in genomics. Therefore, institutions such as The Genome Institute of Singapore (GIS), Genomax, and AITbiotech were established to seize this opportunity. These institutions can utilise the cutting-edge understanding of the human genome to precisely diagnose a patient and quickly detect the presence of certain diseases. With their rise, medical establishments will have more advanced equipment and tools at their disposal to conduct diagnostic activities and administer medicine with greater precision.

2. Genomics R&D Ecosystem Mapping



Universities

Singapore's autonomous universities play an important role in RIE 2025 and the NPM initiative. Both NTU and NUS, two of the largest universities in the country, have strong biology and medicine departments that can support genomic R&D programs in two ways[4]. Firstly, they can supply research institutes with post-graduates, professors, and lab assistants—secondly, the two universities house state-of-the-art laboratories for genomic research.

Top academic institutions in this field are:

1. Nanyang Technological University
2. National University Singapore
3. Genome Institute of Singapore (GIS)

In 2019 Singaporean researchers from among scientists and clinicians from the following public and academic institutions completed the world's largest whole-genome sequencing analysis of multi-ethnic Asian populations[5].

The collaboration included genomics professionals from:

- A* STAR's Genome Institute of Singapore (GIS),
- National University Health System (NUHS),
- Singapore Eye Research Institute (SERI),
- Tan Tock Seng Hospital (TTSH),
- National Neuroscience Institute (NNI),
- Khoo Teck Puat Hospital (KTPH),
- National University Hospital (NUH),
- SingHealth Duke-NUS Institute of Precision Medicine (PRISM),
- National University of Singapore (NUS)
- and Singapore General Hospital (SGH).

This research will help healthcare professionals define an individual's susceptibility to disease and response to treatments, considering the importance of genes in responding to diseases. Nanyang Technological University vigorously conducts R&D in cancer through chromatin studies[6].

Government Agencies

CRIS (Consortium for Clinical Research and Innovation Singapore) and NRF (National Research Foundation Singapore) are government agencies to set research agendas. The former has established PRECISE (Precision Health Singapore), the central entity set up to coordinate the second phase of the National Precision Medicine (NPM) strategy (see below for more information).[7] The latter has been tasked with developing AI technologies that can analyse genomic samples that have been collected by investing as much as SGD 150 million for AI Singapore.[89]

Genomic R&D Institutions

Genomic R&D Institutions, both Singaporean private entities (CZI, Genomax, and AITBiotech) and government-backed (by GIS and SGMC), are tasked with supporting CRIS and NRF in executing NPM. This support can assist in genomic sampling and analysis, data storage and management, and cost reduction. CZI recently awarded a grant to the Genome Institute of Singapore to finance genome mapping of Asian subpopulations. The CZI endowment will help scientists and doctors identify rare diseases and find the causes of chronic illnesses.[10]

Other prominent R&D providers of genomics include Genomax, a private company based in Singapore with internal product development capabilities. It offers, among other things, automated sample processing, which can identify, process, and store genetic samples[11].

Genomics Projects in Singapore

With the support of autonomous universities and leading public agencies, several genomic projects are currently in progress. These projects explore different applications of genomic study and on a varying scale of collaboration.

Project	Institutions
Singapore Precision Medicine Program to Analyse Genetics of 150K Citizens[12]	Singapore's Agency for Science, Technology and Research (A*STAR), the Lee Kong Chian School of Medicine, the National Healthcare Group, the National University Health System, the National University of Singapore, and SingHealth Duke-NUS Academic Medical Centre
xPore - Extracts RNA Modifications Software Extracts	Singapore's Agency for Science, Technology and Research (A*STAR) Genome Institute of Singapore (GIS)
The Role of Ezh2-regulated Thymic Dendritic Cells in T cell Development	Nanyang Technological University

Besides the project above, Singapore is now in the next step of its program National Precision Medicine (NPM) conducted by Precision Health Research, Singapore (PRECISE). For the next stage, NPM Phase II aims to transform healthcare in Singapore and improve patient outcomes through new insights into the Asian genome and data-driven healthcare solutions. NPM Phase II will also enhance the breadth and depth of the Precision Medicine-related industry by attracting and anchoring overseas companies in Singapore while yielding new opportunities for home-grown companies.

Regulation

Before advancements in precision medicine can be made accessible to the general public, the technology or procedure must be approved by the HSA. This process is likely to be stringent due to the novelty of precision medicine and HSA's mandate to protect the general public[13]. However, regulatory efforts have been actively made. In 2021, MOH issued updates to the code of practice on the standards for providing clinical genetic/genomic testing services and clinical laboratory genetic/genomic testing services[14], an addendum to MOH directive no. 6/2020 on the use of cell, tissue, and gene therapy products manufactured in-house by healthcare institutions[15], and a guidance document for the provision of non-clinical genetic testing.

MOH likewise intends to launch a consumer education program to increase public awareness on genetic testing, including issues on the use of such tests and the need for proper interpretation of results[16].

3. SWOT Analysis on Genomics R&D for Foreign Research Institutions

The following SWOT analysis is done and summarised to help companies in assessing opportunities to enter Singapore's genomics sector.

STRENGTH

- Strong Government Support
  - The National Precision Medicine (NPM)
- Growth of R&D Institutions
  - Triggered by the growing market value of Genomics landscape in Asia Pacific
- Government's commitment to invest in infrastructure and attract companies
- Multi-ethnic population of Singapore includes 80 % of Asia's genetic diversity,which allows to fill knowledge gaps in Asian-specific precision medicine and complement global efforts in genomics research (which is largely focused on Caucasian populations)

WEAKNESS

- Lack of diversity in genetic databases
  - Currently no large-scale control databases containing Asian-specific genetic variation linked to clinical characteristic
- Research findings are slow to translate into clinical practice

OPPORTUNITY

- Reduced cost
  - Equipment launched by R&D institutions has reduced the price of genetic testing
- The future of AI in genomics
  - The advancement of AI in Singapore make genomic analysis more time-efficient

THREAT

- Data analysis, interpretation and storage
  - Research teams should be completely trained in proper data management procedures
- Security
  - Concern about data misuse and potential harm that a data breach could cause

Strength

Strong Government Support

Long-term contributions from both the government and private sectors are required to make precision medicine in Singapore readily available. NPM also provides the foundation and infrastructure needed to implement precision medicine on a national scale to improve public health, disease prevention, and identify correct treatments[17].There are be three phases to NPM:

Phase I

- Completed in October 2019.
- Contained the complete genetic data of 10,000 healthy Singaporeans.

Phase II

- Launched in 2020 alongside PRECISE.
- Aims to accumulate the genomes of 100,000 healthy Singaporeans and 50,000 others with certain diseases.
- Will also test the practical application of precision medicine and build a data infrastructure to combine genomic data with electronic health records.

Phase III

- Will run from 2024 to 2027.
- Sequencing up to 1 million people's genomes.
- The genetic data will be combined with clinical and lifestyle information to develop a larger Singaporean database.

Growth of R&D Institutions

The growing market value of genomics and the expanding MedTech landscape in the Asia Pacific has brought new R&D institutions to provide novel solutions using the study of genomes. Valued at SGD 4.35 billion in 2020, the industry is estimated to grow at a CAGR of 10.5%, reaching SGD 7.18 billion by 2025. The market's growth is attributed to the increase of awareness and adaptation of genomic applications in Asian Pacific countries. The industry also grew rapidly due to improvements in health infrastructure, numerous urgently needed advances, increased patient disposable income, and rising medical expenditures[18] .

The growth of genomics in Singapore has further improved research institutions' understanding of the human genome. For instance, Singapore's Genome Institute has recently built the world's most extensive genetic data bank of Asian populations. Furthermore, The SingHealth Duke-NUS Genomic Medicine Centre (SGMC) also launched a new hub for genomic medicine in Singapore that provides doctors with the ability to offer advanced genetics services to patients and families with genetic disorders and promote genomics research and education.

Government's commitment to invest in infrastructure and attract companies

In addition to improving the detection of diseases, applying precision medicine to clinical practice, the goal is to create new economic opportunities for Singapore's healthcare and biomedical technology industry. With this aim was created a central actor to steer NPM - Precision Health Research, Singapore (PRECISE),

Professor Patrick Tan, executive director of GIS explains: "Pharmaceutical, biotechnology, and data science companies are a key component of Singapore's NPM strategy. They bring our research from bench to bedside by developing and manufacturing new drugs and therapies for patients. PRECISE will be looking to develop meaningful public-private partnership models to facilitate growth and drive innovation across the healthcare and biotechnology industry - creating higher-value jobs, nurturing the next generation of scientists and clinicians, and strengthening Singapore's status as the region's leading medical hub to deliver precision medicine based treatments."[19]

Weakness

Lack of diversity in genetic databases

DeDespite best efforts in Singapore, large-scale control databases containing Asian-specific genetic variation linked to clinical characteristics are still lacking compared to European initiatives. This is a major obstacle to the practice of precision medicine in the region, as extensive databases are required to minimise misdiagnosis and overtreatment due to incorrectly identified pathogenic mutations[20]. In response to this problem, Singapore has released a program called SG10K_Health as part of NPM to analyse 10,000 Chinese, Indian, and Malay volunteers for genomic sequencing analysis.

SG10K_Health is a multi-institutional research cooperation that has allowed Singapore to further create the infrastructure to store and analyse genetic data. It has also provided a near-complete assessment of common genetic variations in Singapore's three major ethnic groups. Doctors can better manage Asian patients with a genetic disease and as a control data set for clinical research[21].

Research findings are slow to translate into clinical practice

Because the genomics industry is still nascent, the cost and complexity of genetic data analysis and other factors, it takes time to translate the findings into standard clinical practice. However, as Professor Tai E Shyong assures – "In NPM Phase II, we will be working with doctors, healthcare institutions and the Ministry of Health to find ways to apply precision medicine to improve the health of Singaporeans in a way that is affordable and maximizes the benefit to the patient.[22]"

Opportunities

Reduced Cost

Genome sequencing is becoming more cost-effective, with new equipment launched by R&D institutions drastically reducing the price of genetic testing. According to data from NHGRI (National Human Genome Research Institute), the cost of producing a high-quality entire human genome sequence in mid-2015 was a little over SGD 5,306. However, by late 2015, it had dropped below SGD1,989. The cost of producing a whole-exome sequence was often less than SGD 1,326 in other regions such as North America or the Asia Pacific[23]. This massive cost cut occurred due to Illumina's new NovaSeq technology, which has generated more than 90% of the world's sequencing data. Illumina is recognised for providing the first genomic sequencing under USD 1,000, and the business aspires to cut prices even further.

With NovaSeq, the company hopes to demonstrate that a genome can be sequenced for less than USD 100[24]. Other companies such as Navogene and Medgenome have also established their presence in Asia to cut the cost of genome sequencing. Medgenome has collaborated with NTU Singapore to implement South-East Asia's first Illumina Hiseq X technology to reduce the cost per sample of genomic sequencing by 80%[25].

The Future of AI in Genomics

The advancement of AI will make genomic analysis more time-efficient. Artificial Intelligence can help clinicians organise the thousands of genes and mutations in the human genome, making it easier to associate particular genes with specific diseases. AI can also assist clinicians in mining medical findings and extracting valuable information. This includes applying machine learning to map rare mutations against relevant screening tests or recommending well-supported treatment regimens. AI could also merge other data sets with genetic data, such as family history and environmental data[26] .

An example of AI usage is A*STAR's Genome Institute of Singapore (GIS), which developed new machine learning computer models to spot cancer mutations reliably. These models were developed to scan the whole genomes of 212 stomach cancer tumors in just a few months[27].

Threats

Data Analysis, Interpretation and Storage

As genome data gathering becomes cheaper and more straightforward, subsequent challenges arise. There is currently a lack of capacity to translate the gathered data into reliable theoretical and practical knowledge, which is much more expensive than data gathering[28].

Extensive files of extremely sensitive genomic sequencing data must be appropriately managed. Genomic laboratories must now analyse thousands of genetic samples from the expanding genetic databases. Unfortunately, research teams are frequently untrained in proper data management procedures[29]. Singapore created the Centre for Big data and Integrative Genomics (c-BIG), a collaboration between four A*STAR research institutes to mitigate the threat of data mismanagement. They constructed an IT infrastructure to store, analyse, and exchange genomics data at scale and safely. Cloud-based, big-data infrastructure was also constructed to assist Singapore's biomedical research community. c-BIG's data sharing services will allow for secure resource sharing[30]. Nevertheless, databases will continue to grow, and the rising data storage and protection costs will be inevitable.

Security

Concerns about the privacy and security of a patient's medical information are surfacing as biological data accumulates. DNA information is especially sensitive because of its very personal and also cultural component[31].

Although many businesses have deployed cloud solutions, personal medical and scientific data security and privacy are still at risk. According to a study by BioMed Central, Singaporeans are largely comfortable collecting and exchanging personal information. However, there is still concern about data misuse and the potential harm that a data breach could cause. The study also shows that Singaporeans are less likely to share health data with private companies than government entities. In response, the Genome Institute of Singapore (GIS) has launched a digital platform capable of supporting genomics research and analysis on a bigger scale with enhanced security measures[32].

Nevertheless, it is not the ultimate solution, even if perfectly implemented. Even if personal data is aggregated and depersonalised among thousands of other individuals, there is still a risk/possibility to re-identify it. The public release of DNA information is irrevocable: once it is released, there is no means to know whether it has been used or to recall, withdraw, or control its use. At present, re-identification risks are considered low. However, they are expected to grow. Overall, it is estimated that MOH and more general SG is working on trust technologies that enable data sharing in a privacy perserving manner, one of the key technologies in the smart nation pillar of the Research Innovation Enterprise Plan 2025.

Endnotes

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Singapore and the Netherlands have strong economic ties and collaborate closely in the fields of life sciences and health, digitalisation, water, circular economy and agriculture & food. This article/report will give insight in the strategy, developments and opportunities for collaboration in life sciences and health, focusing on medtech and digital health/ biotech. The report is commissioned by the Netherlands Innovation Network (NIN). NIN is part of the Netherlands Embassy in Singapore and supports R&D partnerships. By working closely together with government, leading research institutes and companies, including start-ups and scaleups, their aim is to build and expand collaborations. TTo connect with the Netherlands Innovation Network at the Netherlands Embassy in Singapore please reach out via e-mail sin-ia@minbuza.nl.

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Prinses Beatrixlaan 2
PO Box 93144 | 2509 AC The Hague
T +31 (0) 88 042 42 42
Contact us
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