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ASIA EDITION

"We foresee more cross-border collaborations leveraging advanced technologies, such as the federated Genome Aggregation Database (gnomAD) platform"

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Singapore is charting the future of precision medicine with a deep dive into the Asian genome. At the heart of this effort is Precision Health Research, Singapore (PRECISE)—the central entity driving Phase II of the National Precision Medicine (NPM) programme. With a mission to revolutionize healthcare through region-specific genomic data and data-driven healthcare solutions, PRECISE is shaping a new era of personalized medicine. Dr Seow Shih Wee, Director of Corporate Services at PRECISE, shares insights on how this initiative is set to transform patient outcomes and redefine precision healthcare in Asia over the next decade.

What are some of the most impactful regional collaborations or initiatives in Asia Pacific that are accelerating the adoption of precision medicine?

Precision medicine has made significant strides in Asia Pacific through collaborative efforts that unite research, clinical expertise, and industry partnerships. Singapore, though a small country, recognises the importance of seizing new opportunities in a rapidly evolving landscape where countries and companies seek to diversify their networks and expand collaborations.

The National Precision Medicine (NPM) programme exemplifies Singapore's commitment to advancing Asian precision medicine insights that will benefit patients worldwide. As the central entity coordinating the current Phase II of the NPM programme, Precision Health Research, Singapore (PRECISE) drives strategic collaborations with ecosystem partners to accelerate precision health adoption through research, innovation, partnerships and data-driven solutions to improve patient outcomes via predictive and preventive care.

Combined efforts of clinicians and health economists to pilot the implementation of precision medicine workflows into public healthcare

PRECISE is collaborating with clinicians and health economists to pilot the implementation of precision medicine workflows into public healthcare institutions. This has been facilitated by PRECISE's Clinical Implementation Pilots (CIPs) rolled out in 2021 in five selected areas – **Breast Cancer, Hereditary & Familial Cancers, Familial Hypercholesterolemia (FH), Primary Glomerular Diseases and Pre-emptive Pharmacogenomics (PPGx).**

The CIPs served as pilots to incorporate genetic/genomic tests into hospital practices and clinical pathways, as well as identify tangible use cases and associated barriers for roll-out of precision medicine approaches. Together, the five CIPs have provided genetic and non-genetic screening to patients and their first-degree relatives, as recommended by their doctors in the public healthcare institutions, to inform them of their disease risks.

Singapore's Ministry of Health announced in October 2024 that FH will be the first genetic condition to be implemented into mainstream clinical pathways from mid-2025. Individuals with FH will be identified early and provided with early intervention such as advice on adopting healthier lifestyles and starting on cholesterol-lowering therapies, if necessary, to reduce their risk of premature heart disease, thereby improving patient health outcomes.

Partnerships with leading companies in genomics that have enhanced the local economy

Additionally, through our partnerships with leading companies in genomics such as Illumina, Oxford Nanopore Technologies (ONT) and PacBio, local companies like NovogeneAIT have benefitted from the flow-through business opportunities stemming from these collaborations and could enhance their business capabilities, creating meaningful jobs and increasing revenue.

A key example is PRECISE and Illumina's collaboration during Phase II of the NPM programme. Seeking a Singapore-based collaborator for Whole Genome Sequencing (WGS), Illumina partnered with NovogeneAIT Genomics. This three-way collaboration between Illumina, NovogeneAIT, and PRECISE created mutual benefits by combining global expertise with local service delivery.

Similarly, LifeStrands Genomics, a Singapore-based laboratory specialising in clinical genomics, partnered with US-based Ambry Genetics to provide clinical genetic testing in Singapore. This collaboration leveraged LifeStrands' regional expertise while allowing Ambry to mitigate risks in a new market, creating a mutually beneficial relationship.

PRECISE is also collaborating with ONT and PacBio on its flagship long-read project. This initiative aims to develop a reference genome for the Asian population, catalogue structural variants in multi-ethnic Singapore, and advance diagnoses for rare diseases and paediatric cancers. ONT and PacBio engaged local service providers, NovogeneAIT and Macrogen Inc. Singapore respectively, to advance capacity building and knowledge transfer, enhancing Singapore's technical capabilities and creating upskilling and employment opportunities for professionals here, in the field of genomics technologies.

Another example is local start-up company, Nalagenetics, which collaborated with the National University Hospital and National University of Singapore to develop an interactive patient-facing Pharmacogenomics (PGx) app as part of the PPGx CIP. In this pilot study, the app allows healthcare providers to access PGx reports of consented CIP patient participants, with the goal of helping them avoid medicine-associated adverse drug reactions. This CIP seeks to implement suitable clinical workflows that will potentially allow for PGx testing to be implemented on a larger scale. The collaboration enables Nalagenetics to scale their solutions to the local healthcare system, supporting future large-scale PGx testing.

In this way, PRECISE has initiated impactful local partnerships with global companies, providing a conducive ecosystem for accelerating the translation of genomic insights into clinical applications and benefitting the population in terms of improving patient care and public health outcomes.

Given the complex and diverse genetic makeup of the Asia Pacific population, how do you see region-specific genomic data shaping the future of precision medicine in the coming decade?

Asians make up 60% of the global population, making the genetic diversity within this region a critical resource for advancing precision medicine. The SG10K_Health study conducted during Phase I of the NPM programme revealed 98.3 million previously unreported genetic variants across Singapore's multi-ethnic population, offering new insights into disease predispositions and medication responses.

The study also revealed key findings, including a high prevalence of FH and hereditary breast and ovarian cancer-associated variants, at rates of 1 in 140 and 1 in 150, respectively. FH was notably more prevalent among Chinese populations, consistent with studies highlighting higher LDLR mutation burdens in East Asians compared to Europeans.

Researchers also identified genetic variations that can predict adverse drug reactions to widely used drugs such as statins, anti-epileptic medications, chemotherapy, and supportive medications. More than 1 in 4 Singaporeans (26.8%) carries a genetic variant that increases the risk of life-threatening side effects of at least one medication, underscoring the need for tailored pharmacogenomic approaches.

In another study, A Catalogue of Structural Variation across Ancestrally Diverse Asian Genomes published in Nature Communications, scientists found ~65% novel structural variants from 8,392 Singaporeans of East Asian, Southeast Asian and South Asian ancestries, enhancing our knowledge of structural variants across human populations and reducing current ancestry biases in global references affecting equity, diversity and inclusion in genetic research.

Shaping the future of precision medicine through predictive and preventive healthcare by enabling more targeted diagnoses and treatments

These findings provide conclusive evidence of the significant genetic disease burden in Singapore and emphasise the role of genetic variants in determining individual disease risks. These insights have practical clinical applications, which aid in the identification of Asian-specific genetic diseases and contribute to improved design of genetic tests tailored for Asian populations. For example, the findings on FH highlighted the relevance and importance of genetic testing to identify FH. The FH CIP will soon be scaled up nationally, with the goal to pick up as many people in Singapore with the genetic disorder early and reduce the risks of premature heart disease.

Driving insights that will value-add and advance Asian precision medicine

A key pillar of NPM Phase II is the PRECISE-SG100K study, a comprehensive longitudinal study which provides one of the most diverse Asian genomic datasets. As sequencing of the genomes of consented participants from the study is underway and recruitment is almost complete, we anticipate uncovering further insights which will deepen our understanding of Asian-specific health risks and responses.

We also look forward to driving emerging programmes focused on Asian genomics. This is one of several developing precision medicine initiatives, spanning across research and professional development, that PRECISE is committed to enhance precision medicine capabilities for Singapore and beyond.

To further value-add and advance Asian precision medicine, the PRECISE-SG100K study launched a strategic Call for Proposals (CFPs) aimed at accelerating precision health research, which led to the selection of 36 PRECISE-SG100K Driver Projects and Flagship Projects last year.

The Driver and Flagship projects aim to translate genomic insights into actionable healthcare solutions, focusing on key areas and ensuring that research outputs are relevant and beneficial to local and regional populations. This is another example of how the NPM programme endeavours to be a beacon in this region for knowledge exchange to develop Singapore as a hub for precision medicine and innovation in Asia, as well as deliver benefits such as better diagnostics and targeted treatments for Asian populations.

Cross-border collaborations and knowledge exchange

Additionally, we foresee more cross-border collaborations leveraging advanced technologies, such as the federated Genome Aggregation Database (gnomAD) platform, a resource developed by an international coalition of investigators, which brings together large-scale sequencing projects and the wider scientific community to share summary data to enable population genetic studies. Singapore's NPM is a participating member with federated gnomAD, with local researchers in Singapore who are part of this network. This is one way such collaborations enable a Singapore presence on the world stage of genomics research.

Knowledge exchange: Forums like the PRECISE-IHCC Conference, which brought together more than 700 attendees, also act as platforms that connect international audiences, such as leaders and researchers in precision medicine to share best practices and identify future partners in precision health for collaboration opportunities.

Over the mid to long term, we anticipate that region-specific genomic data will yield deeper insights and play a critical role in advancing preventive healthcare, providing insights to shape national health policies, and enabling the development of targeted diagnoses, treatments and therapies that better reflect the genetic diversity of Asia Pacific populations. These efforts promise to deliver improved health outcomes and equity across the region, paving the way for a more transformative era in precision medicine.