For discussion
on 21 January 2019

Legislative Council Panel on Health Services

Hong Kong Genome Project

Purpose

This paper briefs Members on the details of the Hong Kong Genome Project (HKGP) announced in the 2018 Policy Address.

Background

2. Genomic medicine[1] is an important sphere in contemporary medicine and scientific research, with huge potential in screening, diagnosis and personalised medicine. In particular, with technological advancement in sequencing technology, there is an international trend to introduce large-scale genome sequencing project for clinical and scientific advancement. Genome projects of various scales and focuses are being carried out in the United Kingdom, Singapore, the United States, Iceland, Denmark, Israel, etc., a summary of which is at Annex A.

3. Pursuant to the Chief Executive's 2017 Policy Address, the Steering Committee on Genomic Medicine (the Steering Committee) was established in November 2017 to map out the strategies for developing genomic medicine in Hong Kong.[2] During its deliberation, the Steering Committee put forth a preliminary recommendation to conduct a large-scale genome sequencing project in Hong Kong in order to enhance the clinical application and promote innovative scientific research on genomic medicine. The Chief Executive announced in her 2018 Policy Address

[1] A genome is the complete set of DNA found within a cell. Genomic medicine uses genome data to support clinical treatment.

[2] The Steering Committee is chaired by Professor Raymond Liang Hin-suen and comprises members from academia, professional bodies and experts in genomic medicine. The membership list is at Annex B.

that the Government had accepted the Steering Committee's preliminary recommendation and would provide funding to introduce a large-scale HKGP. In November 2018, the Food and Health Bureau (FHB) set up a Working Group[3] under the Steering Committee comprising experts from the academic, clinical and research sectors to discuss the relevant details of the project.

Policy Objectives

4. The HKGP is a catalyst project to establish genome database of local population, testing infrastructure and talent pool, with the following policy objectives –

(a) enhance clinical application of genomic medicine to benefit patients and their families; and

(b) promote research in genomic medicine and related field to facilitate future medical development in Hong Kong.

Project Design and Scope

5. In essence, under the HKGP, whole genome sequencing[4] would be performed for patients, their families and candidates of research cohorts. The sequencing data would be analysed to aid clinical management (e.g. diagnosis, treatment and prognosis) where appropriate. At the same time, with informed consent of the participants, the anonymised genomic and clinical data would be pooled for access by researchers for approved medical research purposes.

6. Whole genome sequencing has huge potential to benefit a wide spectrum of diseases with genetic components and corresponding medical research areas. Meanwhile, given the pioneering nature of the project and time required to build up relevant expertise and protocol, there is a need to

[3] The Working Group on Hong Kong Genome Project (the Working Group) reports to the Steering Committee on Genomic Medicine. The membership list is at Annex C.

[4] The process to determine all DNA sequence in one's genome, usually engaging next generation sequencing technology currently.

prioritise the areas to be covered and adopt a phased approach to allow more focused efforts in an orderly manner.

7. Taking into account the policy objectives in paragraph 4, we would prioritise the areas to be covered based on the following key considerations –

(a) ***clinical efficacy*** – whether the diagnostic or clinical utility of whole genome sequencing for a particular type of disease is evidence-based and would bring clear clinical benefits, such as earlier and more accurate diagnosis, avoidance of adverse drug reactions, or a change in the treatment option;

(b) ***availability of expertise*** – whether there are sufficient local experts in the sphere who are ready to apply genomic medicine to the relevant diseases to benefit patients; and

(c) ***research edges*** – whether Hong Kong enjoys comparative edges on the research on relevant diseases, which may lead to a higher chance of significant findings and add real value to the global scientific base.

8. As recommended by the Working Group, the HKGP aims to cover 20 000 cases in two phases. Since some cases may involve two or more samples[5] depending on the clinical and research needs, it is estimated that the HKGP would sequence 40 000 to 50 000 genomes in total. The preliminary scope of the two phases is as follows –

(a) ***pilot phase (2 000 cases)*** – undiagnosed disorders and cancers, with clinical clues linked to possible hereditary genetic components.

(b) ***main phase (18 000 cases)*** – diseases covered in pilot phase, plus other diseases and research cohorts which would benefit from whole genome sequencing.

[5] For instance, two samples (tumor and non-tumor) from one cancer patient, a trio of patient and parents for undiagnosed genetic disorders, etc.

9. Participants may be referred by the Hospital Authority (HA), the Department of Health (DH) and local universities with the exact protocols and resource implications to be agreed. After sequencing, clinical care and genetic counselling of the participants would continue to be followed up by HA, DH or universities as appropriate. Details of the project design and scope would be further defined by the Working Group and approved by the Steering Committee.

10. A key feature of similar overseas projects is the establishment of a large-scale database of anonymised genomic and clinical data for access by approved researchers, in order to facilitate the discovery of new medical findings. The same would be established under the HKGP where researchers, with approval by the specific advisory committee and under an ethically approved research protocol, could access the anonymised data to carry out various studies including cancer genomics, pharmacogenomics, other phenotype-genotype association and epigenomics, etc. Given the time required to build up the relevant infrastructure platform, system to protect patient privacy and data access guidelines and protocols, the database would be implemented in phases. Informed consent would be sought from participants and a stringent set of protocol on ethics and privacy would be followed.

Benefits of HKGP for Patients

11. As mentioned in paragraph 4 above, one of the objectives of HKGP is to enhance clinical application of genomic medicine to benefit patients and their families, particularly for diagnosing uncommon disorders and enabling more personalised treatment for cancer patients.

Higher diagnostic yield and earlier diagnosis for uncommon disorders

12. As some uncommon genetic disorders do not have distinctive clinical features and are highly variable in presentation, it is often difficult for clinicians to diagnose these cases using traditional approaches and routine testing. This "diagnostic odyssey" may take years with numerous tests, hospital visits and false leads, which create huge burden to the patients, their families as well as the healthcare system. Based on

international experience, the introduction of the HKGP would enhance the diagnostic rate of uncommon genetic disorders[6], enabling more targeted clinical management which ranges from targeted diagnostic testing, medication, surgical procedures, surveillance to lifestyle changes. It also provides psychological relief to the patients and their families, and informs parents of hereditary risks that may help in reproductive decisions. The new services will unavoidably lead to an increase in clinical service load. Enhancement of such service capacity is essential to sustain the HKGP project.

More personalised treatment for cancer patients

13. In addition to improving diagnosis in uncommon disorders, the HKGP would also give insight into the genomic changes that cause an individual's cancer. This information can improve diagnosis and help clinicians to select the treatments most likely to be effective in each individual case. It allows more personalised treatment strategy according to the molecular profiles of patients.

14. Genomic medicine evolves rapidly in global healthcare community. Some areas of patient benefit (such as those for uncommon disorders in paragraph 12) are clearer and more mature with reference to international experience, while some (such as those for cancer in paragraph 13) present huge potential awaiting the proof of sufficient evidence and genomic data. There is wide international consensus that the earlier the introduction of genome sequencing technology to clinical service, the earlier patients could benefit from the scientific breakthrough once available. In this regard, the HKGP serves as a catalyst to equip the healthcare services and professionals with the knowledge and experience of applying genomic medicine, which would significantly improve our healthcare services in the long run.

[6] According to international and local experience, the diagnostic yield of uncommon diseases could be raised from around 10% up to around 30-40% by using whole genome sequencing.

Benefits of HKGP for Medical Research and Healthcare Policies

15. The majority of existing genome profiles used in global medical research is based on Caucasian population, and there is a lack of quality genome data of Chinese population. The data generated by the HKGP would fill in this critical gap, presenting huge opportunities for investigation to diseases specific to our population. By better characterisation of the genomic profile associated with different disease conditions in our population, and identification of driver genes in diseases such as cancers, more precise therapeutic targets could be found which might greatly enhance future treatment, and better preventive strategies can be formulated.

16. The HKGP also enables big data analysis for biomedical research and innovation, and would create synergies with the biomedical technology and the information and communications technology clusters accommodated in the Hong Kong Science Park. Local universities have indicated strong support for the HKGP and keen interest in participation.

Implementation Agent and Funding

17. Genomic medicine and the relevant technology (e.g. data analytics) are developing rapidly. There is a need to implement the HKGP through a flexible and efficient agent to bring the most benefits to patients and healthcare research in an effective and innovative way. With reference to overseas practices, we propose to set up a limited by guarantee company wholly owned by the Government, tentatively named the Hong Kong Genome Institute (HKGI), to coordinate the implementation of the HKGP in partnership with FHB, DH, HA, universities, private hospitals, and the research and development sector. The HKGI will drive the collaboration of existing infrastructure and expertise for maximum synergy and innovation to achieve the policy objectives of the HKGP. The HKGI would also assist FHB in other initiatives to facilitate the development of genomic medicine as part of the public healthcare policies. The operation of HKGI would be governed by its board of directors, which would comprise representatives from the Government, HA, universities, private hospitals, patient groups and lay members. A system of advisory

committees would be set up to advise on the scientific, data and ethics issues.

18. Given the benefits brought by HKGP to patient management and research development, the project cost of HKGP and the recurrent operating expenses of the HKGI would be borne by the Government. For planning purpose, the Government has earmarked a non-recurrent provision of $682 million to meet the project cost of HKGP, and a subvention of about $87 million per year on average for six years starting from 2019-20 to support the operation of the HKGI to implement the HKGP, including patient recruitment, procurement of sample handling, sequencing and interpretation, bioinformatics analytics services, genetic counselling, etc.. We will review the outcomes of the HKGP after implementing the project for about four to five years.

19. FHB will reserve sufficient funding in the Estimate of the Health Branch to cover the above expenditure. In addition, five time-limited civil service posts and a few non-civil service positions will be created in FHB in 2019-20 to support the setting up of HKGI and the relevant publicity work. As the project will lead to an increase in service load for FHB, HA or DH, etc., FHB will seek extra resources in accordance with the established mechanism.

20. To ensure the proper use and disbursement of Government funds, we will subject HKGI to financial control measures applicable to subvented bodies and designed to meet HKGI needs. The Permanent Secretary for Food and Health (Health) will act as the controlling officer of the funds allocated to HKGI. We plan to sign a Memorandum of Administrative Arrangement with the HKGI, incorporating important checks and balances to ensure transparency and public accountability of HKGI on the use of the funds. Furthermore, HKGI would be subject to examination by the Director of Audit of its accounts and the economy and efficiency with which HKGI has expended its resources in performing its functions and exercising its powers.

Advice sought

21. We welcome any views which Members may have on the HKGP.

Food and Health Bureau
January 2019

Annex A

Summary on Overseas Genome Projects

A. United Kingdom (UK): The 100 000 genome project[1]

Background

In December 2012, the UK Prime Minister announced a programme of whole genome sequencing (WGS), i.e. the 100 000 Genomes Project, as part of the Government's Life Sciences Strategy. The principal objective of the 100 000 Genomes Project was to sequence **100 000 genomes** from patients with cancer, and rare disorders, etc., and to link the sequence data to a standardised, extensible medical information of diagnosis, treatment, and outcomes. The Project was designed to produce new capability and capacity for genomic medicine that would transform the National Health Service (NHS). It also aimed to produce new capability for clinical genomics research. As part of the proposal, a secure infrastructure was established for the protection and analysis of clinical and genomic data. This was made available for approved academic and industrial research purposes, including those of the contributing clinical organisations from the NHS.

Implementation

2. The UK Department of Health established Genomics England as a wholly owned, limited company to deliver the project. Genomics England worked with NHS England (NHSE), Health Education England (HEE), NHS Trusts, the Northern Ireland Department of Health (DoH NI), and a number of other stakeholders. This was to ensure that the project was fully aligned with NHS transformation and sat within a programme of related initiatives in clinical and laboratory genetics, molecular pathology, service innovation, disease registration, clinical audit, training, and technology advancement. The project created NHS Genomic Medicine Centres (GMCs) to identify and enrol participants, which harnessed the existing capability and capacity of the NHS across England to contribute to the Project.

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[1] Reference: https://www.genomicsengland.co.uk/

3. Genomics England also worked with research groups, to ensure that the new research capability would be fit for purpose and that the data was acquired and managed to appropriate standards. In addition, Genomics England and its partners ensured that the tools provided within the secure infrastructure would both accelerate scientific progress and support the focused, interdisciplinary collaboration needed for clinical interpretation and patient benefit. To maximise the value of the programme, Genomics England created the Genomics England Clinical Interpretation Partnership (GeCIP) which brought researchers, NHS teams, trainees and potentially industrial partners together to enhance the value of this dataset for healthcare benefit.

Aims of project

4. The aims of the 100 000 Genomes Project were:

(a) **Patient benefit**: providing clinical diagnosis and in time, new or more effective treatments for NHS patients;

(b) **Scientific insights and discovery**: with the consent of patients, creating a database of 100 000 whole genome sequences linked to continually updated long-term patient health and personal information for analysis by researchers;

(c) **Accelerating the uptake of genomic medicine in the NHS**: working with NHS and other partners to deliver a scaleable WGS and informatics platform to enable these services to be made widely available for NHS patients, and creating through the GeCIP a mechanism to both continually improve the accuracy and reliability of information fed back to patients and add to knowledge of the genetic basis of disease;

(d) **Stimulating and enhancing UK industry and investment**: by providing access to this unique data resource by industry for the purpose of developing new knowledge, methods of analysis, medicines, diagnostics and devices; and

(e) **Increasing public knowledge and support for genomic medicine**: delivering a transparent programme which has public trust and confidence and working with a range of partners to increase knowledge of genomics.

Scope covered by the project

5. Rare diseases and cancer were selected as the focus for the 100 000 Genomes Project as they present high potential for significant health gain from this Project. Focus on these diseases offered the strongest prospect of patient and scientific benefits and the ability to drive the transformation of the NHS in terms of application of genomic medicine. Furthermore, given the current state of knowledge regarding the genetic architecture of these diseases, the application of WGS might enable major new biological insights that would enable new diagnostics and therapeutic innovation.

Outcomes of the project and way forward

6. 100 000 Genomes Project was announced in 2012 with a cost of about **GBP 300 million**. There were 13 GMCs, 85 NHS Trusts and 1 500 NHS staff (doctors, nurses, laboratory staff, pathologists, genetic counsellors) involved. 100 000 genomes were completely sequenced in **December 2018, taking a total of around six years**. NHS is now equipped with enhanced genomic medicine service. With the established infrastructure, UK Department of Health has set out another vision for genomic medicine in the NHS, and **plans to sequence 5 million genomes over the next five years**.

B. Singapore: National Precision Medicine Strategy[2,3]

Background

7. The Singapore Ministry of Health is coordinating a multi-agency effort to develop an integrated national strategy for precision medicine (NPMS) and its subsequent implementation. An overarching Precision Medicine Steering Committee was established to lead the NPMS, with six working groups

[2] Reference: http://dx.doi.org/10.1101/390070
[3] Reference: https://www.moh.gov.sg/news-highlights/details/speech-by-dr-lam-pin-min-senior-minister-of-state-for-health-at-the-moh-committee-of-supply-debate-2018

overseeing different issues including regulation and ethics, public and community trust, enabling platforms, clinical adoption, industry development and workforce development.

Implementation

8. The Genomic Institute of Singapore (GIS) was set up under the Ministry of Trade and Industry in 2000 to develop genomic sciences in Singapore with a focus on driving economic development ultimately. **The Singapore 10K Genome Project (SG10K)** led by the GIS **was introduced in 2016** and included as one of the initiatives under the NPMS. The primary purpose was to establish an at-scale infrastructure and to map out the genomic profile of Singaporeans according to their three main ethnicities (namely, Chinese, Malay and Indian), in view of the constraint that current genomic profiles for clinical and research purposes are predominantly from Western countries.

Scope covered

9. By design, the SG10K was a pilot research project **utilising existing cohort data, including healthy cohorts free of major diseases and patient cohorts**.

Outcomes of the project and way forward

10. The goal was to sequence 10 000 genome for further analysis. The initial findings of about 4 800 genomes showed that the genomic profiles of Asians are different from those of Caucasians and there are differences between Chinese, Malays and Indians too. Some common deleterious mutations (with Minor Allele Frequency > 0.01) which were absent in the existing public databases were found, highlighting the importance of local population reference for genetic diagnosis. The current reliance only on Caucasian data might reduce the clinical effectiveness of genomic medicine. The data could be used to improve genotype imputation not only for Singapore populations, but also for population across Asia and Oceania.

C. United States: All of Us[4]

Background

11. The All of Us Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers aim to uncover paths towards delivering precision medicine. The mission of the All of Us Research Program is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for the whole population.

Implementation

12. The All of Us Research Program is a key element of the Precision Medicine Initiative (PMI). Through advances in research, technology, and policies that empower patients, the PMI will enable a new era of medicine in which researchers, health care providers, and patients work together to develop individualised care. PMI was launched in fiscal year 2016 when **USD 130 million** was allocated to National Institute of Health (NIH) to build a cohort with national, large-scale research participant group, and **USD 70 million** was allocated to the National Cancer Institute to lead efforts in cancer genomics as part of PMI for Oncology. The All of Us Research Program seeks to extend precision medicine to all diseases by building a national research cohort of **one million or more participants.** Enrollment of participants started in mid-2018.

13. If one decides to join All of Us, he will be asked to share different kinds of information over time. The programme will also ask questions about one's health, family, home, and work. The programme may also ask for access to his electronic health record. Physical examination will be conducted at clinics and the participants will be asked to give samples, such as blood or urine at the appointment.

Scope covered

14. This large-scale cohort does not focus on a specific disease, and instead will be a broad resource for researchers working on a variety of important health

[4] Reference: https://allofus.nih.gov/

questions including precision medicine approaches in treating cancers and other diseases. The Program will also look into ways to increase an individual's chances of remaining healthy throughout their life.

Outcomes and way forward

15. Precision medicine is an approach to disease prevention and treatment that takes into account individual variability in genes, environment and lifestyle to aid in the development of personalised care. It can take many years to understand the contribution of a single unique variable on a given disease or treatment. It will take even more time to develop new treatments and methods of disease prevention. By launching a study of the size and scope of the All of Us Research Program, the NIH hopes to accelerate the understanding of disease onset and progression, treatment response, and health outcomes.

D. Iceland: deCODE genetics[5]

Background

16. Genome sequencing of Iceland population is led by deCODE, a genome sequencing and analysis company based in Iceland. Using Iceland's uniquely comprehensive genealogical records, deCODE has also put together a genealogy database covering the entire present day population and stretching back to the founding of the country. The database has been very useful in research purpose including to detect *de novo* mutations (new mutations which are not known before).

Implementation

17. Since the establishment of the company in 1996, deCODE has gathered genotypic and medical data from more than **160 000 volunteer** participants, comprising well over half of the adult population. DeCODE has been identifying disease-related variants since it started, by correlating their genetic database with medical data from Iceland. The company has also discovered significant number of people with a special kind of genetic mutation that completely disables a gene (knocked-out genes). Finding individuals with

[5] Reference: (a) https://www.decode.com/ (b) https://www.nature.com/articles/sdata2017115

knocked-out genes is made possible by the low background noise in Iceland.

Outcome and way forward

18. Some results has already been published in renowned journals including *Nature Genetics*, including the identification of a new Alzheimer's-associated gene. The findings will help to guide medical research and the understanding of human evolution, through understanding of sequence diversity.

E. Denmark: Danish Reference Genome Project[6]

Background

19. GenomeDenmark is a national platform for sequencing and bioinformatics, which includes universities, hospitals and private firms. The main objective of GenomeDenmark is to establish a platform with research infrastructure to develop know-how, advance national coordination and create synergy within the field of genomics through broad cooperation across research fields and sectors. Genomic references are important and fundamental tools because they facilitate analyses of individual patients and their genes, including how hereditary disorders arise.

Implementation

20. One of the key projects by GenomeDemark is to establish a high quality Danish reference genome, in order to generate knowledge that can support the development of personalised treatment, based on genomic information, in the healthcare system. The project also generates knowledge that can be applied to the Danish pharmaceutical and food industries.

21. The project maps the genomes of 150 healthy Danes selected to represent the normal citizens in order to examine which variations can be observed in the Danish genetic material. The joint genomic information from all donors constitutes a Danish reference genome of high quality. The reference helps determine the structure and development history of the Danish genome and serve as a tool for research and development of genomics and public health.

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[6] Reference: http://www.genomedenmark.dk/english/about/referencegenome/

Outcome and way forward

22. In the future, it is expected that it will be possible to exploit genomic information generally in the healthcare system via large genomic data collected from many individuals. Establishing a Danish reference genome is an important step in the development of a far more individualised diagnosing and treatment process.

F. Israel: National Genomic and Personalised Medicine Initiative[7]

Background

23. Israel Government started in 2018 a national initiative to develop a genomic and clinical data research platform aiming to improve digital health technology and infrastructure to benefit the Israeli population.

Implementation

24. The Government plans to spend about **NIS 1 billion** (about **HKD 2.1 billion**) to support the National Genomic and Personalised Medicine Initiative, which aims to sequence **over 100 000 patients' genomes by 2023** in order to improve targeted patient healthcare services. The multi-disciplinary program also aims to begin collaborating with Israeli health medical organisations (HMOs) and collecting patient samples in early 2019. The project team will establish a national database for health researchers working in genetics and medical information, which will show long-term disease and illness trends of Israeli citizens. Researchers wishing to inquire about the participants' genomic data can apply for access to the database.

Outcome and way forward

25. The project team will begin signing agreements with Israeli HMOs in 2019 and commence sample collection by the middle of the year. The team envisions **collecting samples from over 100 000 participants by 2023**.

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[7] Reference: https://www.genomeweb.com/sequencing/israel-sequence-100k-people-create-genomic-database-support-digital-health#.XC7LZFwzY2w

Annex B

Steering Committee on Genomic Medicine

Membership

Chairman

Professor Raymond Liang Hin-suen

Expert Members

Dr Derrick Au Kit-sing
Dr Joseph Au Siu-kie
Professor Stephen Lam Tak-sum
Professor Lam Tak-wah
Professor Lau Yu-lung
Professor Leung Tak-yeung
Professor Dennis Lo Yuk-ming
Professor Sham Pak-chung
Dr Mary Tang Hoi-yin
Dr Wong Kit-fai

Institutional Members

Representative from the Hospital Authority
Representative from the Hong Kong Academy of Medicine
Representative from The Chinese University of Hong Kong
Representative from The Hong Kong University of Science and Technology
Representative from The University of Hong Kong

Ex-officio Members

Under Secretary for Food and Health or representative
Commissioner for Innovation and Technology or representative
Director of Health or representative

Annex C

Steering Committee on Genomic Medicine
Working Group on Hong Kong Genome Project

Membership

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Prof Raymond Liang Hin-suen

Deputy Convenor

Under Secretary for Food and Health

Members

Dr Chong Shuk-ching
Dr Brian Chung Hon-yin
Professor Nancy Ip
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Prof Lam Tak-wah
Professor Leung Suet-yi
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Deputy Secretary for Food and Health (Health) 3, Food and Health Bureau
Consultant Clinical Geneticist, Department of Health
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Representative from the Innovation and Technology Commission