For information on 23.9.2024

HAB-P352

Hospital Authority

Update on Genetic and Genomic Service Development in Hospital Authority

Advice Sought

Members are invited to note the progress of genetic and genomic **(G/G)** service development in the Hospital Authority **(HA)**, including its participation in the Hong Kong Genome Project **(HKGP)**, and the way forward.

Background

2. Recognising the importance of genomics in contemporary medicine, the Government established a Steering Committee on Genomic Medicine in 2017 to map out the strategies for developing genomic medicine in Hong Kong[1]. Dovetailing with this policy direction, HA formulated the Strategic Service Framework for Genetic and Genomic Services **(GGS SSF)**[2] in October 2019, with an aim to provide structured and coordinated G/G services that are evidence-based and keep pace with advances in G/G development, through professional staff with the relevant skills and expertise, to meet patients' healthcare needs in a timely and equitable manner. It sets out five strategic directions for HA to improve its G/G services, covering service organisation, financial support, governance, talent and expertise, and performance monitoring. To take forward these strategic directions, HA subsequently developed a master implementation plan for GGS SSF that comprises short-term (2020-21 to 2022-23) and medium-term (2023-24 to 2024-25) priorities. With concerted efforts of various stakeholders, the implementation of GGS SSF has been making good progress.

3. In order to further support the government-led initiatives on genomic medicine, HA has collaborated with the Hong Kong Genome Institute **(HKGI)**[3] to implement the HKGP through partnering arrangement. HKGP is the first large-scale genome sequencing project in Hong Kong aiming to sequence 50 000 genomes (or 20 000 cases) by two phases (i.e. the Pilot Phase and the Main Phase[4]) in six years with $1.2 billion earmarked in the

---

[1] For details, please refer to the report "*Strategic Development of Genomic Medicine in Hong Kong*" (accessible at https://www.healthbureau.gov.hk/en/press_and_publications/otherinfo/200300_genomic/index.html).

[2] GGS SSF is an overarching blueprint to guide the planning and development of HA's G/G services, which was approved by the Medical Services Development Committee **(MSDC)** in October 2019 via MSDC Paper No. 582 on "Approval of Hospital Authority Strategic Service Framework for Genetic and Genomic Services".

[3] HKGI was established in 2021 and wholly owned by the Government to launch HKGP.

[4] The Pilot Phase covered patients and their family members with undiagnosed diseases and hereditary cancers, while the Main Phase expanded the scope to cases related to genomics and precision health.

Government's 2019-20 Budget. To achieve such target, HKGI has set up three Partnering Centres **(PCs)** operated by (i) HA at Hong Kong Children's Hospital **(HKCH)**; (ii) The Chinese University of Hong Kong at Prince of Wales Hospital **(PWH)**; and (iii) The University of Hong Kong at Queen Mary Hospital **(QMH)**. In particular, PWH and QMH assisted their respective universities in providing clinical source for participant recruitment. Participation in the project is voluntary. Each PC has established an HKGP team to recruit patients, and, with patients' informed consent, provide genetic counselling, conduct data and bioinformatics analysis, provide clinical reporting support, etc. The results of sequencing analysis will be returned to respective clinical leads and patients once available to aid diagnoses and decision of clinical treatment options.

4. HA has been providing annual updates on the progress of G/G service development and HKGP to MSDC since 2021[5] with the last report made on 5 August 2024. The ensuing paragraphs outline the recent development of G/G services in HA and the improvements achieved to date for the benefits of HA patients.

Recent Achievements of G/G Services in HA

Expedited Provision of New and Additional G/G Services

5. The provision and development of G/G services requires timely financial support. Alongside the prevailing annual plan process for seeking recurrent funding for HA standard services, interim resources are sought as and when necessary to enable the provision of additional G/G clinical services and laboratory tests to address imminent or urgent service needs, such as introduction of breast cancer mutation testing for ovarian cancer patients to dovetail with repositioning of a drug to the safety net of the HA Drug Formulary in 2021-22, advanced recruitment of manpower in HKCH to support transferring the Clinical Genetic Service under the Department of Health **(DH CGS)** to HA in 2022-23 and augmented provision of genetic testing to enhance safe use of allopurinol for HA patients in 2023-24. With the above dual financial arrangement, HA is able to keep pace with the G/G development and expedite the introduction of G/G tests or services to address patients' healthcare needs.

Enhanced Service Efficiency

6. To enhance the governance of G/G services, HA established a Steering Group on G/G Service in HA **(SG GGS)** in January 2019 and revamped the Central Committee on Genetic Services **(CC(GS))** in December 2019, as shown in **Annex 1**. The SG GGS, chaired by HA Chief Executive, steers the overall development of G/G services in HA, while CC(GS) provides a platform for professional exchange among different clinical specialties and experts for a sustainable G/G service development. Under this robust governance structure, essential elements contributing to the development and provision of patient-centred and personalised G/G services have been enhanced through better coordination of service organisation, information technology infrastructure, G/G test introduction and documentation, as well as training and development.

---

[5] Via MSDC Paper No. 624, 673, 698 and 737, all on "Progress Update on Genetic and Genomic Services Development in Hospital Authority" in 2021, 2022, 2023 and 2024 respectively.

7. To ensure systematic G/G service provision and development, informed decision of introducing G/G tests with proven safety and efficacy, and prudent use of public resources, HA has devised a new framework[6] for assessing and prioritising service proposals requiring G/G tests. In addition to making reference to the National Health Service's National Genomic Test Directory, an electronic Genetic and Genomic Test Directory **(GGTD)**[7] was developed in January 2022, accompanied by the Supplement on Test Indications, which enable equitable access to G/G testing service. With the up-to-date Test Directory and the Supplement on Test Indications in place, clinicians now could easily find information for ordering appropriate G/G tests. Furthermore, with detailed testing and referral criteria set out, gatekeeping at the point-of-use is strengthened and G/G services are used more safely and judiciously.

Enhanced Patient Services in Terms of Quality and Quantity

8. Different G/G services in HA are now organised under a tiered approach[8] and programme-based hub-and-spoke service model based on service demand, complexity and expertise requirements as set out in **Annex 2**. Such service organisation has enhanced service accessibility and enabled effective stratification of patients in need of G/G services, as well as facilitated planning and allocation of resources, resulting in remarkable enhancement in service quality and quantity.

9. To cater for patients with different G/G conditions, 19 G/G-related programmes were launched between 2020-21 and 2023-24 (see **Annex 3**), including some programme scale-up. They comprise paediatrics programmes, disease-based programmes on coagulopathy and blood cancer, organ-specific programmes on brain tumour, colorectal cancer, lung cancer and ovarian cancer, as well as G/G testing programmes for pharmacogenetics services and drug prescription. All of them have brought important benefits to our patients. Some examples are cited below to illustrate the improvements achieved.

(a) Cancer-related G/G Testing and Services

10. Since 2021-22, QMH, Queen Elizabeth Hospital **(QEH)** and PWH have increased the availability of the next generation sequencing **(NGS)**[9] panels and the minimal residual disease monitoring assays to provide accurate diagnosis / prognostication of myeloid neoplasms in over 90% of adult patients. This has empowered clinicians to select the most appropriate treatment strategies for patients, and enabled them to closely monitor the patients for any residual cancer after treatment for timely intervention. At the same time,

---

[6] The framework comprises six assessment criteria, namely clinical benefits; clinical demand; technical readiness; service provision; cost impact and deliberation process for three sub-categories of G/G tests (i.e. diagnostic and therapeutic tests, tests on uncommon diseases including prenatal and microbiology / infection diseases tests).

[7] By end 2023, GGTD contains around 1 470 G/G tests and the Supplement on Test Indications covers around 460 G/G tests of eight selected categories.

[8] **Tier 1** comprises routine, high volume and low complexity G/G services, which often require short turnaround time and are delivered in localised or cluster-based provision in HA. **Tier 2** consists of specialised, low volume and high complexity G/G services, which are provided at designated centres to facilitate concentration of caseloads and expertise. **Tier 3** involves innovative clinical and laboratory G/G services, which are mainly provided in the teaching hospitals (i.e. QMH and PWH) by the universities as part of research (e.g. pilots or clinical trials).

[9] NGS refers to a type of high throughput sequencing technology that has the capability to enable millions of deoxyribonucleic acid **(DNA)** strands to be sequenced in parallel, enabling multiple genes up to the whole genome to be studied at the same time.

HA also introduced breast cancer mutation testing for ovarian cancer patients using the NGS panels via four service networks[10], with genetic counselling and clinic follow-up services provided in Tung Wah Hospital **(TWH)** for both patients and their family members.

11. In 2023-24, Clusters altogether had provided about 2 940 tests to lung cancer patients as Tier-1 G/G service, using NGS panels, for clinical decisions on targeted therapy. This represented a paradigm shift in molecular diagnostics for non-small cell lung cancer because G/G testing via NGS panels could cover the existing and those less common mutation targets in one go and thus is more cost-effective, faster and tissue-saving than sequential testing for single gene. Separately, PYNEH, QMH and PWH have ameliorated the therapeutic outcomes of high-grade glioma patients through providing molecular tests for 412 biomarker counts[11] as Tier-2 G/G service, enabling more precise diagnosis and prognosis of patients.

(b) Prenatal Genetic Diagnosis

12. In April 2021, HA introduced the whole exome sequencing **(WES)** and whole genome sequencing **(WGS)** for investigation of fetal structural anomalies in all pregnant women, so as to enhance prenatal genetic diagnosis. With WES / WGS performed, the health conditions and prognosis of the fetus would facilitate patients' informed decision-making in reproductive choice, pregnancy management, postnatal care and future family planning. A multidisciplinary team is involved in the process, including case selection, variant interpretation, genetic counselling and perinatal management, which are essential to reducing parental anxiety. The first-year service has achieved an overall positive clinical impact on 55% of cases, which influenced reproductive decision making, guided perinatal management and helped future family planning. Facing the growing demand, this service will be translated from a Tier-3 to Tier-2 G/G service to benefit threefold increase in service targets (from 20 cases in 2021-22 to 60 cases in 2024-25) with an aim to prevent and reduce perinatal morbidity and mortality.

(c) G/G Testing Services for Pharmacogenetics and Drug Prescription

13. In 2022-23, all Clusters have carried out over 5 794 pharmacogenetic tests for the genotyping of Thiopurine Methyltransferase and Nudix Hydrolase 15 as Tier-1 G/G service for patients to ascertain patients' suitability to receive the mercaptopurine therapy. Meanwhile, HA has built up the laboratory capacity in PWH and QMH to provide over 25 500 HLA-B*58:01 genotyping tests in 2023-24 as Tier-2 G/G service before drug prescription to minimise the risk of allopurinol-induced severe cutaneous adverse reactions for HA patients.

(d) One-stop Clinical Services in HKCH

14. As a Government's initiative, HA has taken up DH CGS from 1 July 2023 to enable the provision of one-stop multi-disciplinary support for patients with genetic diseases

[10] The four service networks are Pamela Youde Nethersole Eastern Hospital **(PYNEH)** for Hong Kong East Cluster and Kowloon West Cluster, QMH for Hong Kong West Cluster and Kowloon East Cluster, QEH for Kowloon Central Cluster, and PWH for New Territories East Cluster and New Territories West Cluster **(NTWC)**.

[11] Biomarker refers to a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.

and their families[12]. After the completion of service transfer by December 2023, referral between DH and HA is no longer required for patients to receive genetic consultation and subsequent management. With all HA's experts under the same roof, patients can now receive one-stop genetic service, including diagnosis, treatment, subsequent management, counselling and prevention. They have also benefitted from the enhanced clinical and laboratory services in HKCH, including new services (e.g. multidisciplinary team meetings, regular inpatient consultations and cross-specialty outpatient clinic sessions), reduced waiting time for new cases of genetic counselling service, higher positive diagnostic yield rate[13] of WES and low recall rate[14] of neonatal screening services.

Bolstered G/G Expertise and Literacy

15. HA has recently created two new grades[15], namely Bioinformatics Team **(BIT)**[16] and Genetic Counselling Team **(GCT)**[17], under the management of Allied Health **(AH)** Grade with effect from 1 April 2024, to form part of the multidisciplinary team to drive the practice of personalised and precision medicine. G/G data can be as large as 10 Gigabyte **(G)** or even 100G for each patient, and BIT plays a key role between clinicians and pathologists in interpreting and analysing genomic data to identify the disease-causing variants of the patients. GCT also acts as the bridge of communication between doctors and patients about the medical, psychological and familial implications of genetic contributions to disease prior to and after testing. Both of them are G/G professionals needed for deciphering the relationship between genomic variations and diseases, which lays the groundwork for accurate diagnosis and personalised treatment.

16. HA has also taken steps to raise the G/G literacy of healthcare staff for delivering safe and quality service. For example, CC(GS) has organised lunch webinars and central commissioned training programmes on different topics (e.g. neurogenetics, perinatal genetics & genomics, newborn screening) to equip staff with the appropriate expertise and information. To facilitate patients' and healthcare professionals' awareness and understanding of HA's genetic counselling service, two animated videos were produced, which could be accessed via the HA Smart Patient website and other HA social media platforms (e.g. Facebook, YouTube, Instagram), and G/G-related topics were also presented in the HA Convention. Moreover, different grade offices have also coordinated G/G-related training programmes for doctors, nurses and AH professionals to equip them with the latest knowledge and skillsets to take up new and expanded posts.

---

[12] The service transfer divided in two phases. On 1 July 2023, the services of DH's Genetic Counselling Clinic, Genetic Screening Clinic and Neonatal Screening Laboratory were transferred to the then Clinical Genetics Service Unit and Department of Pathology of HKCH. By December 2023, the services of DH's Genetic Laboratory were handed over to HKCH's Department of Pathology. Details were reported to MSDC on 26 April 2024 via MSDC Paper No. 730 on "Transfer of Clinical Genetic Service of Department of Health to Hospital Authority".

[13] Refers to the rate where disease-positive patients are detected by a diagnostic test.

[14] Refers to the rate at which screened babies are recalled for additional assessment.

[15] This new grade creation was supported by MSDC in October 2023 via MSDC Paper No. 706 and HA Board in November 2023 via Administrative and Operational Meeting Paper No. 1911, both on "Development of Expertise to Support Genetic and Genomic Services in Hospital Authority".

[16] BIT comprises experts in computer science, biomedical sciences, bioinformatics, etc. who are familiar with programming and coding for systematic collection, analysis, storage and retrieval of G/G data. They also involve in case discussions with clinicians and genetic counsellors, and share knowledge on guideline updates.

[17] GCT consists of frontline professionals with specialised training or experience in medical genetics and psychosocial counselling who study patient's family backgrounds, provide counselling for risk assessments and carry out tests after obtaining informed consent, and explain the results to patients and their family members.

Promoted Genomic Medicine via HKGP

17. To foster the development of genomic medicine in Hong Kong, HA has partnered with HKGI to recruit eligible participants for HKGP. In the Pilot Phase, each of the three PCs had achieved the target of recruiting 1 700 participants by December 2022. In the Main Phase, as at 1 September 2024, the three PCs had recruited altogether about 20 920 participants, already exceeding the annual total target of recruiting 7 200 participants which is subject to review. Four HA hospitals, namely The Duchess of Kent Children's Hospital at Sandy Bay, Grantham Hospital, TWH, and Alice Ho Miu Ling Nethersole Hospital, have participated in the HKGP as referral network for patient recruitment for QMH PC and PWH PC in 2023. In July 2024, NTWC, including Tuen Mun Hospital, Pok Oi Hospital and Tin Shui Wai Hospital, had also been involved in patient recruitment for HKCH PC.

18. HKGP participants with disease-causing genetic variants identified through WGS analysis will be referred to HA for clinical investigations if deemed necessary. HA would accordingly take care of / provide these patients with clinical validation of WGS results, post-test genetic counselling, subsequent surveillance and clinical care. Multi-disciplinary meetings conducted periodically between HKGI and each of the three PCs also yielded fruitful results regarding the refinement of diagnosis and clinical treatment plans for individual participants. So far, HKGP has helped identify the disease cause for some HA patients after years of diagnostic odyssey, allowed professional medical teams to formulate clinical measures for respective patients to improve their health conditions, and benefitted other patients with similar disorders by effective and early identification of their diseases.

<u>Way Forward</u>

19. HA is committed to supporting the Government's directions in accelerating local development of genomic medicine so as to deliver more personalised and patient-centred care, amid the rapid advancements in the field. Following the completion of the Master Implementation Plan of HA GGS SSF in 2024-25, the Subject Team will work with relevant stakeholders to formulate the work plan for the next three to five years for ongoing development of G/G services in HA, which would be submitted to MSDC for consideration in due course. To carry on the progress achieved, the next stage of G/G service development in HA would focus on enhancing the service scope and efficiency, strengthening research and collaboration, nurturing more talents and expertise, adopting new technologies and infrastructure, and developing other measurement tools, for the long-term benefit of the community. Internal and external communication would also be bolstered to further promote staff and public awareness of G/G service development in HA. Continuous efforts would also be made to provide more precise diagnosis, enable more tailored clinical management of uncommon genetic disorders, and allow more targeted treatment for cancer patients. To assist more patients and their families in finding out the potential disease-causing genetic variations through WGS analysis, HA will liaise with HKGI about other Cluster hospitals' involvement in achieving the HKGP target.

20. In close collaboration with HKGI and with the experience gained from HKGP, HA would continue to integrate genomic medicine into clinical application and further widen

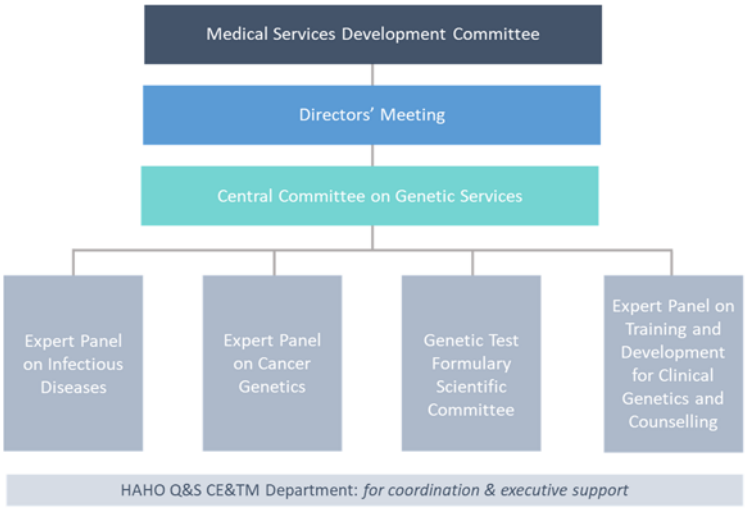
the application of G/G with a view to guiding more advanced clinical treatments such as gene therapy and Chimeric Antigen Receptor T Cell Therapy in shaping the future service direction of HA.

Hospital Authority
HAB\PAPER\352
16 September 2024

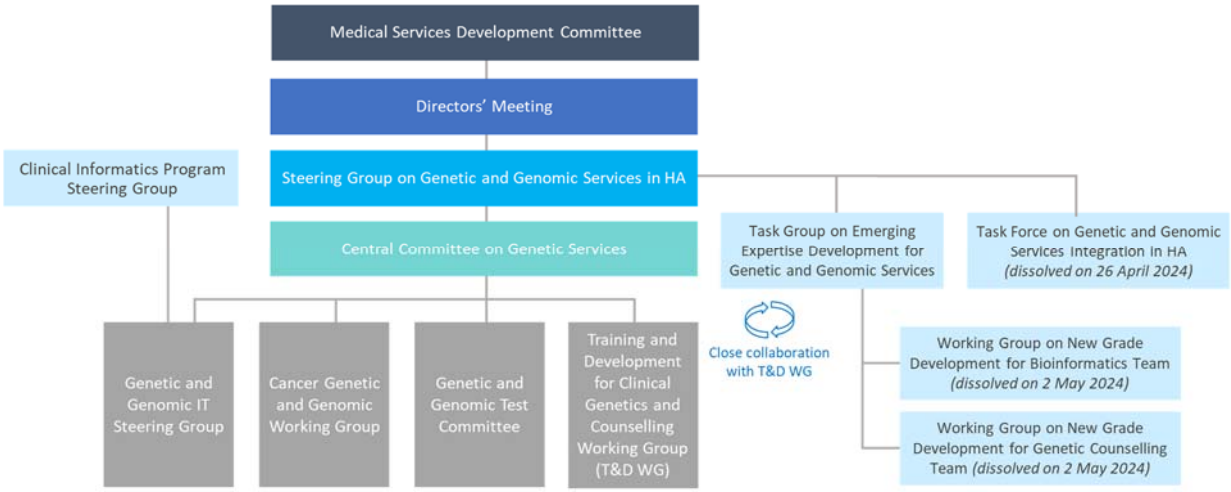
Annex 1 to HAB-P352

Governance Structure of Genetic and Genomic Services
(as at September 2024)

Before revamped in December 2019



After revamped in December 2019



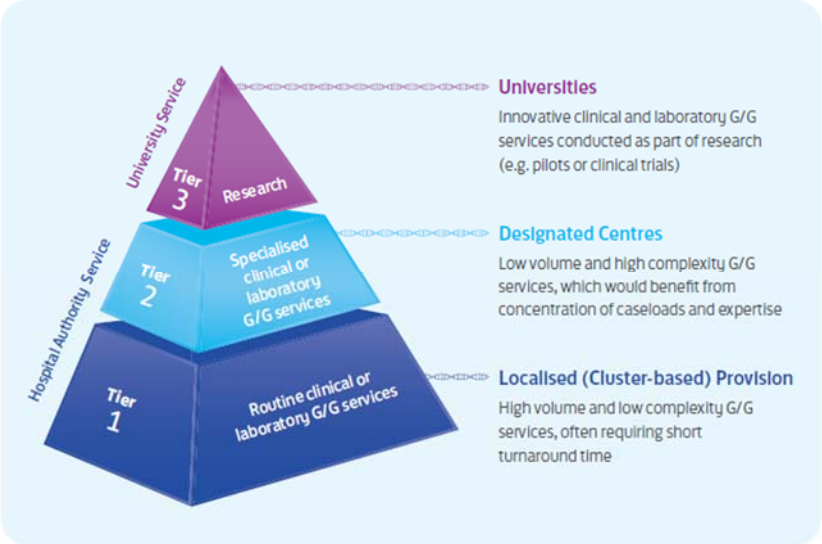
Notes:

1. With the completion of service transfer from the Department of Health to the Hospital Authority (HA) in December 2023, the Task Force on Genetic and Genomic Services Integration in HA was dissolved on 26 April 2024.

2. Upon the creation of Bioinformatics Team and Genetic Counselling Team (effective from 1 April 2024), the Working Group on New Grade Development for Bioinformatics Team and the Working Group on New Grade Development for Genetic Counselling Team were dissolved on 2 May 2024.

Annex 2 to HAB-P352

Tiered Approach in Hospital Authority Strategic Service Framework for Genetic and Genomic Services (HA GGS SSF)

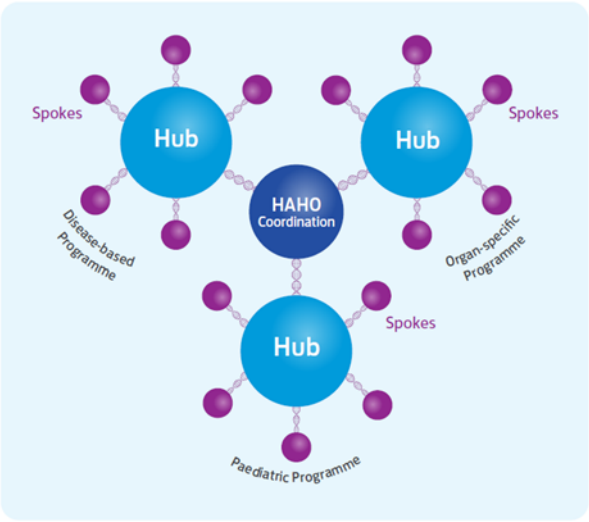


Tier 1 comprises routine, high volume and low complexity genetic and genomic (G/G) services, which often require short turnaround time and are delivered in localised or cluster-based provision in the Hospital Authority.

Tier 2 consists of specialised, low volume and high complexity G/G services, which are provided at designated centres to facilitate concentration of caseloads and expertise.

Tier 3 involves innovative clinical and laboratory G/G services, which are mainly provided in the teaching hospitals (i.e. Queen Mary Hospital and Prince of Wales Hospital) by the universities as part of research (e.g. pilots or clinical trials).

Illustration of the Programme-based Hub-and-Spoke Service Model in HA GGS SSF



Programme-based hub-and-spoke service model is to organise the different tiers of G/G services, particularly Tiers 1 and 2 services, into coordinated networks (e.g. paediatric, disease-based and organ-specific programmes). In the model, the "hubs" are Tier 2 designated centres providing specialised services, while the "spokes" are Tier 1 routine services provided locally. The Hospital Authority Head Office will act as the central coordinator and sponsor for the programmes, with each programme working out its own hub-and-spoke service arrangement.

Annex 3 to HAB-P352

Approved Genetic and Genomic Services-related Annual Plan Programmes

2020-21	
20-387HKW	Enhance Genetics Services and Colonoscopy Screening for Hereditary Colorectal Cancer Patients & Families
20-388HKW-17-168	Provision of NGS Genomics Services for Blood Cancers
2021-22	
21-123GEN	Enhancement of Prenatal Diagnosis for Special Cases with the Introduction of WES or WGS *(3-year time-limited)*
21-127GEN	A Territory-wide Network Service in Advanced Adult Myeloid Blood Cancer Genomics
21-128GEN	Tier-One Genetic and Genomic Testing Service in HA: Pharmacogenetic Services
21-239KCC	Clinical Genetics Service and Support of Uncommon Disorders in HKCH
21-497GEN	Introduction of BRCA Mutation Testing for Ovarian Cancer Patients in HA *(unbudgeted item)*
2022-23	
22-010GEN	Service Enhancement in Coagulopathy Genetics Network Service
22-035GEN	Introduction of BRCA Mutation Testing for Ovarian Cancer Patients in HA
22-335NTE	Enhance Clinical and Laboratory Services for G/G Medicine
22-429KCC-17-221	HKCH Service Development in 22/23
22-455QSD	Transfer of DH CGS to HA *(unbudgeted item)*
2023-24	
23-103GEN	Adoption of NGS Platform Testing for Non-small Cell Lung Cancer
23-106GEN	Enhancing the Therapeutic Outcomes of High-grade Glioma Patients
23-107QSD	Transfer of DH CGS to HA
23-116QSD	Provision of Clinical Care to Support HA's Participation in HKGP for Pilot Phase
23-118GEN-21-127	Scale Up Bid for a Territory-wide Network Service in Advanced Adult Myeloid Blood Cancer Genomics
23-400GEN	Provision of Genetic Testing in Prescribing Allopurinol for HA Patients *(unbudgeted item)*
24-084GEN-21-123	Scale-up for the Enhancement of Prenatal Diagnosis for Special Cases with the Introduction of WES or WGS