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The Hong Kong Genome Project is helping patients and their families by identifying the causes of their diseases and formulating personalised treatment plans

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Dr Brian CHUNG Hon-Yin, Chief Scientific Officer at the Hong Kong Genome Institute (HKGI) and Clinical Associate Professor at the University of Hong Kong (HKU) discusses the creation of the HKGI and the launch of its monumental undertaking, the Hong Kong Genome Project, the first of its kind in the region. Aimed at integrating genomic medicine into clinical care while advaning genomic science, the genome project has completed its pilot phase covering undiagnosed diseases and hereditary cancer and is already giving results back to patients.

Could you introduce yourself and your role within the Hong Kong Genome Institute?

I completed my medical training at the University of Hong Kong (HKU) in 1999 with a specialisation in paediatrics, but then really found my calling in clinical genetics. At that time there was no local Hong Kong training to become a clinical geneticist, therefore, I moved to Canada and studied at the University of Toronto and the Hospital for Sick Children. I was there for three years and qualified under the Canadian College of Medical Geneticists before returning to Hong Kong in 2010. I now teach at HKU, do my own research, and see patients, mostly those with genetic disorders.

Over the course of my career, I have been able to witness big changes in the field as it moved from genetics to genomics. Genetics is the study of genes, and before you could write an entire scientific paper on one gene. But with the introduction of new technologies, such as next generation sequencing, we can study all the genes within one human genome, which has really shifted how we approach this field of medicine.

The Hong Kong Special Administrative Regionâ??s (HKSAR) Government has been very insightful in this also, and in 2017 the Chief Executive at the time put forth a policy directive to catalyse the use of new technologies to improve clinical outcomes for patients and direct health policies. As a result, a very important decision was to set up a steering committee to map out strategies for developing genomic medicine in Hong Kong. Subsequently, with the full support from the government and the Health Bureau, the Hong Kong Genome Institute (HKGI) was established to launch the Hong Kong Genome Project, the first in the region with the aim to serve as a catalyst in the development of genomic medicine.

Regarding my role within HKGI as the Chief Scientific Officer, I oversee all scientific activities including the clinical applications, ethics and research protocols of the Hong Kong Genome Project. I also supervise the operation of the genomic laboratory and lead the scientific team to work closely with local and international partners and collaborators towards achieving HKGIâ??s vision of â??availing genomic medicine to all for better health and well-being.*â?•*

With your experience in the field, how relevant is it for the HKSAR to have its own human genome project?

You hit the nail on the head. Hong Kong has many researchers and universities that are doing a lot of excellent research in genetics and genomics, but the question should be about how to create a more concentrated effort to translate these important findings into clinical application. We have put in place some key steps to move in that direction.

Firstly, a system with the correct infrastructure was put in place that shows what needs to be done to reach our targets, and so we set up an end-to-end servicing model within this Hong Kong Genome Project. End-to-end means assessing patients to see if they would benefit from gene sequencing, getting informed consent to store their DNA, analysing the data, and then giving feedback to these patients.

This is not a small-scale operation and requires collaboration between many players. To this end, we are working closely with patients, local authorities such as the Department of Health and Hospital Authority, medical schools and research teams of top-notch universities and hospitals, such as the Queen Mary Hospital, Prince of Wales Hospital, and Hong Kong Childrenâ??s Hospital, as well as the Chinese University of Hong Kong and the University of Hong Kong. Furthermore, we are building the system by identifying personnel with an interest in genetic medicine, such as healthcare professionals, researchers, genetic counsellors and genome analysts, and including them in the project. Each of these members has a role to play.

For example, clinicians would contribute by identifying the correct patients that would benefit from gene sequencing. Genetic counsellors would then explain to the patient the project to make sure that they understand exactly what they are undertaking. The scientist would then contribute by doing the genome sequencing in the laboratory and the genetic analyst would analyse the data obtained. The genome data of a patient contains around 3 million genetic variations, but a genetic mutation that creates a medical condition normally only represents one or two changes from this huge data set, meaning that finding these mutations can be very time-consuming work.

Once we have all the results, we give them back to the physicians who would relay this information back to the patient with the genetic counsellors. The aim of this approach is to create a personalised treatment and management of a condition for each patient, which falls squarely within the new trend of precision medicine. If we can identify what genetic changes are causing a problem in a patient, we can then know better how to treat it or find a cure. That is precision medicine in action.

Have you had results thus far?

Yes. We are already giving results back to patients, and there are successful cases showing how the Hong Kong Genome Project is helping patients and their families by identifying the causes of their diseases and formulating personalised treatment plans.

When the Project was first launched, it was strategically split into two phases, the Pilot Phase and the Main Phase. I am happy to share that we completed the Pilot Phase covering undiagnosed diseases and hereditary cancer in mid-2022, and commenced the Main Phase right away with scopes expanded to include cases related to genomics and precision health.

We have published several papers during this journey including the experiences we had and learnt from in the process. Our comprehensive meta-analysis proves that there is a clear advantage for patients of having a human genome project in place.

As an example projects like Genomics England had 100,000 genome sequences. Do you have a target number, or are you just processing patients as they arrive at the clinic?

Under the Hong Kong Genome Project, our target is to recruit 20,000 cases. The genome sequencing amount could be more as results are better as a trio, that is to say the patient and their parents. So, it could be more like sequencing 40,000 â?? 50,000 genomes in the end.

Overall, we have four strategies focused on the human genome project. Firstly, to integrate genomic medicine into clinical care. Secondly, to advance research in genomic science. Thirdly, to nurture talents in genomic medicine. And finally, to enhance public genomic literacy and engagement and to this effect we are working on showing the Hong Kong population exactly what we are doing and how it can benefit them.

One of the areas of medicine that is most heavily impacted by genetic testing is rare diseases. How is this area integrated into the Hong Kong Human Genome Project?

When we planned the project, we had a few challenges and they were under three themes, with one of them being undiagnosed diseases. Rare or orphan diseases are very difficult to diagnose as they are not as prevalent, and doctors do not have experience with these conditions. This is a problem not just for Hong Kong, but for the rest of the world.

Therefore, starting in the pilot phase, we chose patients with undiagnosed diseases, and we were able to see the benefit of gene sequencing in the acceleration of diagnosis of these patients. This is one key reason countries should have their own gene objects as genetic differences exist across population groups.

A lot of studies are predominantly done with Caucasian European participants, so in Hong Kong this project will shine a light on the Asian population. If we just rely on US or European data, then we would see results that might not be the same as here. Human genome projects in each territory will have implications on the treatment and management of conditions.

In fact, we have seen patients that have been undiagnosed for more than ten years, correctly diagnosed and able to manage their symptoms by simply changing their diet. A lot of diseases have a genetic basis and understanding the gene sequence that causes these conditions is the first step in developing treatments, and in fact there is a field of medicine that uses genetic information to predict the effect of drugs on patients, pharmacogenomics.

For example, with the changes of the genetic makeup of a person that will metabolise a drug in a certain way. If they metabolise it too quickly, the drug will not stay in their body long enough, and so we must increase the dose. If the opposite occurs, and it stays in their body too long, they will get symptoms, and we must lower the dose. So, in fact we are using genomics as a guidebook to administer therapies, and again, every country must have their own program as the genetic make-up changes depending on the race of the person and knowing the genome will only be beneficial for patients and doctors.

Part of the interest in genomics is coming from the pharmaceutical industry. How are you collaborating with the industry to drive genomics forward in Hong Kong?

We understand that to build the genomic ecosystem in Hong Kong, we need not only patients, doctors, hospitals, and universities, but all stakeholders, and that includes the pharmaceutical industry whom we have conversations with as a part of our engagement work. In fact, I am a member of a thinktank on personalised medicine with the Hong Kong Association of the Pharmaceutical Industry (HKAPI).

Clinical trials are costly, and many of them are stopped at phase II and III, and these drugs never reach the market. There have been studies to find a reason for the success or failure of a clinical trial, and one of the largest contributing factors is genetic data. The industry understands the contribution of genetics and genomics for the success of their drug development, and this is why they are proactive in wanting to work with us.

Throughout the world there are examples of collaboration between the public sector and private industry. For example in the UK, the UK Biobank collaborates with companies in different formats to promote genomics and their clinical application. As I mentioned, all stakeholders need to move in the same direction to build the genomics ecosystem. This is true of Hong Kong as well.

There has been a lot of talk in Hong Kong about taking advantage of the large population of the Greater Bay Area (GBA). Is this a concept that is impacting your operations?

While we are excited about all the global networks and collaborations we have cultivated, we are also keen to establish closer ties with clinical and academic experts and scientists across the border. Given its close proximity to Hong Kong, the Greater Bay Area is undoubtedly an area we are looking into.

For instance, we have engaged with the University of Hong Kong-Shenzhen Hospital for case discussion and sharing of clinical experience on undiagnosed diseases, as well as paediatric cancer

genomics and multi-omics studies. These exchanges and potential collaborations in the pipeline are particularly important for the study of disorders commonly found in Chinese populations. They will also have a key role to play in addressing a long-standing challenge the scientific and medical community around the world has been facing â?? the under-representation of the Southern Chinese populations in the global genomic database.

What resources will you need to continue moving forward on the project?

Continued support from our stakeholders on all fronts will be the driving force that takes us further. Over the last two years, we have benefited tremendously from the close relationships built with universities, hospitals, and patients, and we are very grateful for that. Moving forward we must continue to nurture these partnerships and interactions.

Furthermore, we must work closely with professional bodies and universities to nurture future talent. Just earlier this year, HKGI joined hands with the Hong Kong Academy of Medicine (HKAM) to set up the â??HKAM-HKGI Research Excellence Grants in Genomic Medicineâ?• to encourage and inspire research in genetics and genomics. We also partnered with HKAM to host a one-day symposium, inviting experts from the UK, Australia and Singapore to discuss applications, research and professional training of genomic medicine. Collaborations with authoritative bodies like HKAM will remain vital to HKGIâ??s work in driving professional training and development for healthcare professionals. Support from the younger generation is also what we need to build up a talent pool for Hong Kong. Therefore, we have also set up scholarships with leading local universities to attract talent and inspire interest among students.

We must always look to stay updated on the latest technology in the field so we can benefit patients as much as possible. Also, we are looking toward multi-omics, which entails not just genomics, but transcriptomics, proteomics, and epigenomics. Gathering data from each separate area and integrating it will allow us to get a better idea on the complex biology of a disease, which will provide in the long run better diagnosis and treatment of patients.

What is your final message to the broader healthcare community?

Genomics is very important. It is the future of medicine and it is worthwhile exploring as it increases the chances of more accurate diagnosis, success in clinical trials, and therefore the development of better treatments and disease prevention plans.

For example, in oncology therapy development the inclusion of patients in clinical trials does not only include the histology of the cancer, but the genetic makeup of the formation of the tumour, which is called a basket clinical trial. So, in this trial the patients may have various cancers, such as liver, brain or lung, and although they seem to be different due to where they are located in the body, they are the same genetic mutation, just in different locations. This means the trial needs to look at the genetics of tumours and the patients.

I am a great supporter of collaborations, and I regard them as key to success. By coming together â?? patients, authorities, hospitals, researchers, scientists, universities, the pharmaceutical industry and so on, our work at HKGI, and that of our partners and stakeholders, can contribute to the diversity of human genomic data. This can be translated into health benefits for millions of people.

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