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Editorial

From CoVID-19 to Hong Kong Genome Project

I wish to thank the Chief Editor for inviting me to write the editorial of this issue of Hong Kong Journal of Paediatrics (HKJP). As I am writing this editorial, we are still in the midst of the CoVID-19 pandemic, and it is timely to have an article in this issue in which colleagues from the Princess Margaret Hospital, the first government-funded infectious disease centre in Hong Kong, have shared their valuable experience in fighting the pandemic.[1] Their experience sharing is not only important to us in fighting the ongoing battle against CoVID-19, but will also prove important for future generations to be better prepared for the next epidemic or pandemic. Compared to one year ago when WHO just announced CoVID-19 a pandemic, today we seem to see the light at the end of the tunnel because of the availability of vaccines. Vaccination against CoVID-19 has become the talk of the town. Almost everyone is asking, or is asked of. Should I get a shot? Which one should I choose? Are there any risks? From the perspective of a geneticist, there are now two main categories of CoVID-19 vaccines, one produced by traditional technology and the other by new genomic technologies, the latter including one that delivers into the human body synthetic mRNA molecules encoding the CoVID-19 antigen, and another that incorporates CoVID-19 DNA in an adenovirus that acts as a vector. I am not here to provide a simple answer as to which one is superior to the others, not to mention that I really don't have a simple answer. But from the emergence of such RNA or DNA vaccines, one cannot but realise that genetic and genomic technologies have already infiltrated our lives, unknowingly, before the general public can comprehend what they are, how they work, and what long term effects or side effects they can bring about.

Undoubtedly, we are living in the genomic era. The applications of genetic and genomic technologies can be seen everywhere, from the diagnosis of hereditary disorders, providing guidance to the treatment of cancers and informing prognosis, to the detection and prevention of CoVID-19. There are quite a few examples in this issue of the HKJP, especially with respect to disease diagnosis. Qiao et al studied the genetic defects of 32 Wilson disease patients in southern China and identified *ATP7B* mutations that are particularly prevalent in this region.[2] The results provide valuable information for possible fine-tuning of molecular diagnostic strategy in Wilson disease, particularly in places where next generation sequencing platform is not readily available. Wang et al reported the clinical course and the biochemical and genetic findings of four cases of infantile citrin deficiency, another autosomal recessive inborn error of metabolism that is relatively common in this locality, and highlighted the importance of early genetic testing so as to inform prognosis and management.[3] In one of the case reports, Poon et al presented a case of alternating hemiplegia of childhood due to de novo mutation of the *ATP1A3* gene.[4] I congratulate the clinicians for this early diagnosis because this disorder is so rare and the clinical presentation can mimic other epileptic disorders. It requires astute clinical sense and prior knowledge

of the disorder before one can confirm the diagnosis by targeted analysis of the disease genes. In this day and age, it is more likely and easier for clinicians to seek for whole exome sequencing much earlier on. Liu et al published their results of a genetic study on neonatal hearing loss.[5] They looked for a defined set of hearing loss-associated genetic mutations using MALDI-TOF Mass Spectrometry in over two hundred neonates who failed the neonatal hearing screening and compared the findings with a control group. Expectedly, the frequency of hearing-loss associated genetic mutations is significantly higher in the hearing loss group than in the control group. Besides providing assistance in disease diagnosis and prognostication, the application of genetics and genomics is increasingly important in informing treatment options. In this issue, Akin-Bali et al studied the somatic mutations involving the RAS/RAF/MEK/ERK signaling pathway in paediatric patients with leukaemia and detected genetic variants in over 90% of patients.[6] Their findings have shed light on the potential use of RAS/RAF/MEK/ERK pathway inhibitors in the treatment of high-risk leukaemia.

The pervasive applications of genetics and genomics seen today, especially in the healthcare setting, are not possible without the availability of the human reference genome released in 2003 after the decade-long Human Genome Project (HGP). Soon after the release of the human reference genome, people foresaw that personalised medicine would come into being. However, the first human reference genome was only based on a few individuals. To make personalised medicine possible, there is a long way to go. First, we need to understand human genome variations, particularly those present in our population, in relation to health and disease. Our genome carries a lot of variations, now estimated to be at least 0.5% between two randomly picked individuals, both at the single nucleotide and structural levels.[7] It is these variations that make every human being unique, but it is also these variations that confer different disease susceptibilities to everyone. Thanks to other post-HGP projects, like the 1000 Genomes Project, HapMap Project, and countless disease specific genome-wide association studies (GWAS), we had a glimpse of the association between genotype and different diseases, but personalised medicine is still a remote possibility. We need genome sequencing endeavors of much larger scale. With the advent of next generation sequencing technology and its gradually decreasing cost, large-scale genome sequencing is both possible and affordable now. In the 2018 Policy Address, the Chief Executive announced that a genome project, now known as the Hong Kong Genome Project (HKGP), will be launched.[8] It is a six-year research project with a target of sequencing 50,000 genomes. The genome data may provide immediate healthcare benefits to a fraction of participants, in terms of more specific diagnosis and new treatment options, but, more importantly, it serves as a foundation for future genome researches that might benefit the bigger local population, not just in terms of personalised treatment of diseases, but also in terms of personalised health promotion and prevention of disease. I am excited to know that a lot of preparations are in progress and patient recruitment will commence soon in the middle of this year. This will be an important milestone in the healthcare system of Hong Kong. We used to say HGP provided the blueprint of mankind. Now, with the HKGP to be kick-started shortly, I look forward to a blueprint that belongs to Hongkongers.

IFM Lo
Guest Editor

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