EXPANDED CARRIER SCREENING PANELS AND THE PREVENTION OF INHERITED MONOGENIC DISEASES: THE FIRST KEY IN PRECISION MEDICINE EVALUATED USING 1116 HONG KONG CHINESE EXOME SEQUENCING DATA

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Background

Expanded carrier screening (ECS) has been a staple of preconception care in detecting the presence of pathogenic variants for genetic disorders. Comparison between commercially available ECS has, however, only shown partial overlaps in genes offered for screening. Compiled with the inadequate information surrounding carrier frequencies in the Chinese population, we evaluated the carrier status of Hong Kong Chinese using a cohort of 1116 exome sequencing (ES) data.

Methods

A total of 1116 ES (622 males and 494 females) of Hong Kong Chinese were screened for carrier status in 319 genes. The gene list curated for this study was compiled from three ECS panels offered by frequently used commercial companies in Hong Kong. Additional genes from a literature reporting treatable inherited disorders in South East Asia population genomics were included into the gene panel.

Results

There were 180 unique disease-causing variants identified and 41.8% (n = 467) of individuals screened in this study harboured at least one disease-causing variant. Results identified 9 genes with a carrier frequency over 1% including: *GJB2, SLC25A13, SLC22A5, SMN1, ATP7B, SLC26A4, GALC, CFTR*, and *HBB*. Systemic evaluation of the three commercially available ECS panels show that only 37.0% (n = 118) of genes overlap in all panels. The overall number of Hong Kong Chinese carriers missed by commercial ECS panels ranged from 3.8% to 10.7%.

Conclusion

This study showed that secondary analysis of ES data can illustrate the carrier frequencies in the HK Chinese population. Through the comparison of different commercially available ECS panels, we identified room for improvement in the optimization of panels offered as nearly 10% carriers were missed. This deviation could be attributed to population specific variants or founder mutations.

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