Pharmacogenomics in the Oceania region: Precision medicine challenges

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Oceania comprises the large islands of Australia, New Zealand and Papua New Guinea (PNG) and a very large number of islands comprising Melanesia, Micronesia and Polynesia. There are few pharmacogenomic studies and results cannot be readily predicted from one region to another. For example, CYP2C19 genotypic poor metabolisers (*2,*3) comprise almost 70% of the Melanesians in Vanuatu, less than 10% in Maori populations and less than 5% in Aboriginal Australians, and in the latter population, the gain of function *17 results in 17% rapid metabolisers, half that of Caucasians. Such large differences are in contrast to CYP2D6 poor metabolisers (*4,*5) which comprise less than 1% in most of the regions studied. In PNG, most studies have focused on infectious diseases pharmacogenomics. The frequency of CYP2B6*6 is 60% compared to 20% in Caucasian and Asian populations. Efavirenz is metabolized by CYP2B6 and poor metabolizer status is associated with CNS/Psychiatric effects; in 52 subjects, only drowsiness was related to *6 carrier status. For CYP2D6, the *5 frequency was 5% and *1/N duplication 12%, both having implications for p.vivax treatment with primaquine. Minimal data are available on drug transporters in Oceania, however in PNG subjects the frequency of the C3435T variant was 67%, with almost 90% of subjects being either homozygous variant or heterozygotes. The implications of this finding for the efficacy and adverse effects to many medicines, especially those used for infections diseases, is noteworthy. For NAT2 and acetylator status, no genomic studies have been conducted in PNG but almost all are rapid acetylators, and therefore the incidence of isoniazid-induced hepatotoxicity is rare. The phenytoin HLA B*13:01 is associated with severe hypersensitivity reactions prevalent in several Asian countries and with a frequency of almost 25% in PNG and in Aboriginal Australians from Northern Australia. The implications for precision medicine in Oceania are several. Although the frequency of some important pharmacogenes are markedly different to Caucasian and Asian populations, the frequencies are not widespread across the region; many important genes, and genotype-phenotype correlations, have not been assessed and clinical relevance and translation need to be viewed in relation to limited resources.