EDITORIAL

Genotyping arrays, population genetic studies and clinical implications

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Studying genomics at a population level is accepted to be vital both to understanding human variation, and the cause of human disease. Genotyping arrays are crucial tools for such studies. In this issue, Verlouw et al. compare the properties of 28 different genotyping arrays [1]. Not all arrays are created equal and some are better suited to different studies with different research questions. Such technology enabled Mattingsdal to study the genetic architecture of Norway for the first time [2]. They trace routes of immigration into Norway and provide evidence that diversification of genomic background in the South of the country is due to geographic isolation and restricted gene flow. This has implications for variant interpretation in clinical contexts, since the frequency and type of population variants will differ due to geographic considerations.

Variant classification not only helps diagnose human disease, but can define prognosis and management. Matsumoto et al. systematically review the literature to identify clinical correlates of different genetic variants in *FLCN* [3]. *FLCN* variants are associated with Birt-Hogg-Dube syndrome; which can present with skin lesions, renal carcinoma and pneumothorax. Data are presented to suggest that certain *FLCN* variants may cause pneumothorax but not other clinical features. This has important implications for clinical screening and follow up of these individuals.

The fetal phenotypes of genetic disease are being identified through prenatal genomic testing. In a single family, a *COL4A2* variant was shown to segregate with hemiplegic cerebral palsy in a parent and prenatal intra-cerebral haemorrhage [4]. This underscores the clinical variability associated with *COL4A2* with important implications for genetic counselling. Another example of clinical variability is provided by Haag et al. [5]. Heterozygous *WDR11* variants are associated with hypogonadotrophic hypogonadism. In this issue, patients with bi-allelic *WDR11* variants and a neurodevelopmental disorder are described. Ascertainment bias can also cloud our view of genotype–phenotype correlation [6]. Initially *TAB2* variants were associated with congenital heart disease and cardiomyopathy. Engwerda et al. describe a larger cohort of individuals with *TAB2* variants, some ascertained in a 'genotype-first' manner [7]. They confirm a syndromal phenotype with non-cardiac manifestations.

Neurofibromatosis is one of the more common 'rare diseases', and clinically well recognised. However, there is still an unmet need for treatment. The treatment priorities of stakeholders were identified in a Delphi study [8]. Malignant peripheral nerve sheath tumours and glioma were identified as treatment priorities for research.

Implementation science concerns itself with the study of how to move scientific and clinical advances into clinical practice. O'Shea et al. use an implementation science approach to investigate barriers to mainstreaming genetic testing for cancer in Australian Oncology clinics [9]. They identify a perceived lack of knowledge and confidence to discuss and consent for such testing as a barrier to implementation. The preferences of patients and families should also be taken account of when implementing and developing genetic services. This Australian study describes preferences towards rapid genome sequencing for critically ill children.

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COMPETING INTERESTS

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ADDITIONAL INFORMATION

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