EDITORIAL

Ambivalence and regret in genome sequencing

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The role of genome sequencing in the diagnosis of human disease is well established. Perhaps one of the most challenging clinical scenarios is the utilisation of genomic diagnostics in the neonatal unit. D'Gama and Agrawal provide a timely review of the issues [1]. Ronchi et al. describe a novel neonatal presentation of bi-allelic COX18 variants with cox-IV deficiency and neurology and muscular phenotypes [2].

Consent conversations relating to genome sequencing for children are recognised as being potentially problematic. Given the vast number of potential outcomes of genome sequencing (e.g. no diagnosis, incidental finding), it has been disputed if 'informed' consent can be achieved. A qualitative study of medical geneticists views on consent for genome sequencing in paediatrics provides useful insights [3]. One view was that truly informed consent for genome sequencing in paediatrics is not possible. The need for more genetics professionals and better information resources for families was recognised. A further issue around informed consent in genetics is around that of reuse of genetic information and data in research projects [4].

Peter and colleagues report a survey of participants in the UK 100,000 genomes project [5]. They found variable retention of genomic knowledge/information after the consent conversation. There were, in general, low levels of regret for those who underwent genome sequencing. Kuiper et al. report a multi-site qualitative study of genomics health professionals [6]. They find a high level of ambivalence and uncertainty in the field; surrounding topics such as consent, research-clinical care boundaries and the role of guidelines. Such high levels of ambivalence are perhaps unsurprising when genomics professionals are tasked with offering tests that often have uncertain outcomes and benefits.

Despite this, genomic testing can offer concrete answers in terms of diagnosis and clinical management. Malik et al. use exome sequencing to identify AGPAT3 bi-allelic variants as the cause of a novel neurodevelopmental condition with retinitis pigmentosa and intellectual disability [7]. They support the candidacy of AGPAT3 by reporting neuronal migration defects in a null mouse. Jain and colleagues report 14 new cases of Börjeson–Forssman–Lehmann syndrome [8]. Adding novel phenotype contrasts between females and males. Anomalous pulmonary venous return (APVR) can occur in syndromic and non-syndromic forms. Huth reports a diagnostic yield of 16% for exome sequencing for syndromic APVR [9]. Based on a review of genomic datasets the authors identify three novel disease-gene associations. Tian et al. identify a further case of MAN2B-associated congenital disorder of glycosylation [10]. Adding valuable phenotypic information for this ultra-rare condition. Eiberg et al. report a potential new chromosome locus for ulcerative colitis [11].

What are the barriers to patient-centred care in clinical genetics? A Delphi study of cardiogenetics experts identified that most barriers to patient-centred care are institutional/organisational and not patient level [12].

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AUTHOR CONTRIBUTIONS

AM conceived and wrote this editorial.

COMPETING INTERESTS

The author declares no competing interests.