EDITORIAL

Genome sequencing—do you know what you are getting into?

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Various forms of documentation and "consent" forms are used to record evidence of permission to undertake paediatric genome or exome sequencing. But how fully do parents and caregivers understand the implications of such testing? Gereis et al. report a systematic review examining these issues [1]. They find parents/caregivers may over estimate the benefits of such testing, and have limited understanding of the potential for variants of uncertain significance, the negative impacts of secondary findings and privacy/data sharing concerns. The evidence base also raised concerns about the depth and detail of understanding. Clearly this is an important area of research—how best to design information resources so that people can opt for genome/exome sequencing in an informed manner?

In this issue we print papers providing further evidence of the diagnostic utility of exome and genome sequencing. Sironi et al. use combinations of array comparative genomic hybridisation and next generation sequencing to identify a novel RAI1 intra-genic deletion in a case of Smith-Magenis syndrome [2]. Neurofibromatosis type 1 is clinically diagnosed and in 95% or more a loss-of-function variant can be found in neurofibromin. What accounts for the mutation negative cases? Alesi et al. report a novel mechanism for neurofibromin loss-of-function: gene inversions [3]. Perplexing phenotypes, with multiple organ involvement, are the signature of rare diseases. Gargello et al. report that CTCF variants explain the link between intellectual disability and Wilm's tumour [4]. Koprulu et al. report a novel cutaneous disorder associated with Keratin-17 mutations [5] and Robles-Bolivar et al. describe heterozygous CENPP variants in autosomal deafness [6]. Of course, once causal genes are identified the phenotype must be fully defined in order to inform clinical practice. Guo et al. report a novel cohort of people with KBG syndrome to help define the phenotype [7].

Appropriate utilisation of next generation sequencing depends to an extent upon clinician attitudes. Haider reports a qualitative study of Canadian genetic health professionals attitudes to non-invasive prenatal testing [8]. They favour use of these techniques for monogenic disease but not indications such as paternity testing. Rapid exome sequencing for critically ill neonates is common, but genetics professionals report barriers to offering appropriate follow up. Mainstreaming Clinical Genetics - that is allowing non-genetics clinicians to request genomic tests and manage results is the current strategy to increase uptake of testing. Quinn and Mazur report the experiences of genetic counsellors working in mainstream clinical genetics in the United Kingdom and suggestions to improve working practices [9]. In many countries, there are protections around people who have had genetic testing having to disclose the results to finance companies. Dowling et al. describe the Australian experience of such a moratorium [10].

Genetic testing to aid in clinical diagnosis is relatively non-controversial. Using genetic testing more widely in the general population for screening is less accepted. Van Steijvoort et al. report mixed views on reproductive carrier screening in the general population [11]. Baribeau et al. report that genetic testing for physical health concerns can identify a condition with an unexpected developmental delay [12]. Careful patient counselling is required in all settings before genetic testing.

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AUTHOR CONTRIBUTIONS

AM conceived and wrote this article.

COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

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