EDITORIAL

Expanding what we know about rare genetic diseases

European Journal of Human Genetics (2023) 31:1091–1092; https://doi.org/10.1038/s41431-023-01453-2

In this issue, we have a selection of papers describing the genotypes and phenotypes of a range of rare (and ultra rare) diseases. Terradas et al. provide important confirmation that heterozygous variants in MBD4 are not associated with colorectal cancer [1]. Smith et al. provide a second report of PRORP variants being associated with a mitochondrial phenotype, confirming the clinical entity [2]. ALDH1A3 variants account for around 10% of severe inherited ocular conditions. Kesim and colleagues expand the phenotype by reporting neurodevelopmental phenotypes in affected individuals [3]. Hadar et al. provide insights into a novel genetic cause of haemolytic uraemic syndrome [4]. Ganapathi et al. update us on the clinical spectrum associated with NR2F2 variants [5].

Genome sequencing to identify genetic variants predisposing to cancer is well established in adult practice. Schroeder et al. report the role of trio genome sequencing in paediatric cancers [6]. A high proportion of paediatric cancer patients were found to have a genetic variant in a cancer predisposition gene. When these were inherited from an apparently unaffected parent it could have implications for their health and potential cancer screening.

To support genomic testing for rare diseases an adequate genetic counsellor workforce is required. Zakaria et al. review trends in research in genetic counselling [7]. They note an increasing amount of research being published in this area; with access to genetic services and workforce issues recurrent themes in the research area. Yanes et al. report a novel initiative to embed a genetic counsellor in an inherited metabolic disease clinic [8]. This was found to improve access to genomic testing.

Detailed discussion of the pros and cons of genome sequencing is required to enable a person or a child's parents to consent to such testing. But what is the critical information required to be given in this process? A North American study of clinical genetics clinicians suggests that a core set of information can be defined for various scenarios and that totally comprehensive or exhaustive discussions may not be required [9].

Despite technological advances, many patients remain undiagnosed after exome or genome sequencing. Periodic reanalysis has been suggested as a strategy to uplift diagnostic rates. In this issue, an increased diagnostic rate with a 5-yearly reanalysis is reported [10]. The emergence of novel gene-disease associations was seen as crucial to increasing the proportion of solved cases.

Studying large cohorts of patients helps to improve genomic diagnostic strategies. Kim et al. report the diagnostic utility of a nationwide genomics diagnosis program in the Republic of Korea [11]. A large clinical series of over 600 people with Niemann-Pick Type C identified novel genotype-phenotype correlations [12].

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AUTHOR CONTRIBUTIONS

AM conceived and wrote this editorial

FUNDING

There is no funding to report.

COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

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