EDITORIAL

Happy 30th birthday to the European Journal of Human Genetics!

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It is 30 years since the first issue of the *European Journal of Human genetics* was published. To celebrate this, we publish a series of comments on significant papers published in the journal in the past 30 years and present an online web collection of papers selected by our editorial board. A clinical or laboratory geneticist from 30 years ago would scarcely believe the advances in genomic technologies, and it is important to reflect on how far the field has come.

In this issue, Corbie et al. use an ecological approach to estimate the number of carriers of pathological PRNP variants (associated with Prion diseases) in the UK [1]. They estimate that there are just over 1000 carriers of a pathogenic PRNP variant in the UK and a 1:6000 lifetime risk of developing a prion disease. This has important implications for service planning.

The diagnostic superiority of whole genome sequencing compared to whole exome sequencing remains to be established. Ewans et al. identified that in a cohort of patients with negative exome sequencing, whole genome sequencing identified a causal variant in 34% [2]. However, exome reanalysis of the same cohort identified a diagnostic variant in 18%. This suggests that genome sequencing is the optimal approach for mendelian disease; however, exome sequencing with reanalysis may be more cost effective. Test selection will depend to an extent upon local resource availability.

Novel bioinformatic approaches represent an additional means of improving diagnostic yield of exome sequencing. Eyries and colleagues developed a pipeline to detect mobile element insertions [3]. Using this they identified a mobile element insertion in PALB2, as a cause of breast cancer. Detecting and understanding the effect of unusual gene variants is crucial for improving genomic medicine. A non-coding variant in FOXF1 was shown to increase promotor activity 10 fold [4]. This rescued the effect of a frameshift variant found in trans and explained phenotypic variability in this pulmonary vascular disease. Carter et al. report a heterozygous variant in PAX1 as causing oculo-auriculo-vertebral syndrome [5]. With important implications for clinical testing.

In general, it is recommended that predictive genetic tests are only done in minors for conditions that might require treatment in childhood. Vibert et al. provide evidence that children could be tested for von Hippel-Lindau disease (in the appropriate circumstances) [6]. In 11 children who had predictive testing, 6 tumours were detected during surveillance. This emphasises the clinical benefit to predictive testing and cancer surveillance in this group.

Genomic testing is well established in mendelian disease. However, its clinical role in multifactorial disease is controversial. An interview study found that people with schizophrenia would be interested in genetic testing if it helped identify a cause, but for the most part understood the multifactorial aetiology [7]. A survey of parents of autistic children found that most supported genetic testing to try and find out useful information for their children's health [8]. Using genomic screening for non-treatable disorders is even more controversial. Kalkman and Dondrop discuss the Netherland's perspective [9]. Genomic influences on body mass index are well known. Muller and colleagues identify a novel IGFBP4 variant associated with body mass index and identify molecular mechanisms by which it might act [10]. Returning results from large scale genomic studies to participants is controversial. Lang et al. discuss genetic issues around "direct to participant" genomic studies [11].

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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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