EDITORIAL

Clinical genetics—it's polygenic

European Journal of Human Genetics (2021) 29:1037; https://doi.org/10.1038/s41431-021-00931-9

The contribution of deleterious genetic variants to severe disease phenotypes is well established. In this issue of EJHG we publish further examples. Buelow et al. report novel *SPTBN4* variants that cause a neurodevelopmental disorder with hypotonia, neuropathy and deafness [1]. Knapp et al. establish bi-allelic variants in MCM3 and MCM7 as a cause of Meier-Gorlin syndrome [2]. Genome sequencing of large cohorts is fundamental to identifying and characterizing disease causing genetic variation. Runolfsdottir uses this approach to identify the allele frequency of genetic variants causing adenosine phosphoribosyltransferase deficiency [3]. Importantly they provide evidence that this condition is not likely to be underdiagnosed. Despite decades of work linking variation in single genes to disease phenotypes, the extensive phenotypic variation in many of these conditions remains unexplained. Mosaicism for genetic variants could explain some phenotypic variants. Angelini et al. describe the example of mosaicism for *SPAST* variants in spastic paraperesis [4]. Modifying genetic variants could also explain phenotypic heterogeneity. Whitworth et al. describe digenic variation in *SDHA* and *PALB2* in an unusual cancer [5]. For more common phenotypic traits and disorders the contribution of polygenic variation is becoming better understood. Aguirre presents a novel analysis of polygenic risk scores to enable finer scale investigation of genetic drivers of complex traits [6]. Andersen reviews the contribution of polygenic variation to a common heart disease—atrial fibrillation [7]. We hope you find this month's edition informative and an enjoyable read.

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COMPETING INTERESTS

Dr Alisdair McNeill is Editor-in-Chief of the European Journal of Human Genetics.

ADDITIONAL INFORMATION

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Published online: 16 July 2021