EDITORIAL

Managing genetic information sharing at family and population level

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The process by which the "at risk" relatives of a person with a genetic condition should be notified of the possible need for them to have genetic testing has long been controversial. At present, it is common practice to request the proband to inform relatives of the genetic condition, treatment and testing options. Uptake of cascade testing is generally low, and dissemination of the genetic information within families is a major barrier. Tiller et al. explore the views of the Australian public on healthcare practitioners directly informing relatives of their genetic risk [1]. In a survey of over 1000 Australians, there was broad support for this approach, with some reservations around privacy issues. End of life care is understandably focussed on the comfort of the affected individual. However, palliative care may provide an important opportunity to make diagnoses of a genetic condition or inform relatives of their risk. White et al. highlight barriers to integrating genetic testing into palliative care [2].

Screening of the general population using genomic based testing, to identify individuals at increased risk of neoplasia or cardiac disease who carry variants in actionable genes, is possible. There has been little research into the impact of uninformative results on participants. Rao et al. studied a group of adults who had negative genomic screening, there was no real evidence of psychosocial harm and around 10% planned to make changes to health related behaviours [3]. In support of such population screening, Klemenzdottir et al. report a genomic prevalence of Marfan syndrome in Iceland of 1/6600 as opposed to a clinical prevalence of 1/10,000 [4].

Parijs et al. characterise the influence of maternal or paternal inheritance of 15q11-q13 duplications on phenotype [5]. They do this by utilising genome wide DNA sequencing data from non-invasive prenatal screening. They find that maternally inherited duplications are always associated with a neurodevelopmental phenotype. Paternally inherited duplications had a more variable phenotype. This has important implications for genetic counselling.

It is common for many large scale genomic studies to run for years. Ongoing engagement with participants is crucial for consent to remain valid. "Dynamic consent", using web based platforms has been proposed as a mechanism to address this. Haas et al. report the initial evaluation of the Australian CTRL dynamic consent platform [6]. Only 15% registered to use CTRL; but there was no particular evidence that demographic features influenced this. Few changes were made to the initial consent given. Web based platforms are feasible for dynamic consent, but their true value require further study. Smit et al. review legal measures which might permit use of personal data in data intensive medical research [7]. Bernier et al. consider how to reconcile transnational biomedical research with the demands of GDPR [8]. A Finnish study of the impact of neurofibromatosis type 1 illustrates the value of such data at the population level [9]. This study found that neurofibromatosis type 1 reduces employment prospects and identifies mechanisms and mediators.

Genomic technologies have revolutionised our ability to characterise the genetic architecture of disease. Proximal spinal muscular atrophy (SMA) is most commonly caused by SMN1 variants. In this paper a series of proximal SMA cases are characterised with exome sequencing [10]. DYNC1H1 was an unexpectedly common genetic cause. Genomic technologies also help us understand population structures. Gagnon et al. exploit the unique availability of genealogies in Quebec to help understand the population structure [11].

Again in this month's edition of EJHG we publish reports characterising novel genetic conditions. Yap et al. report bialleic ATP2B1 variants in a novel neurodevelopmental condition [12]. A child with a complex neurodevelopmental phenotype and primary hypoparathyroidism was identified to have biallelic ATP2B1 loss of function variants. There were some similarities noted with mouse models of ATP2B1 mutations. ATP2B1 has also been reported to cause a neurodevelopmental condition in the heterozygous state; providing a further example of a gene causing both a dominant and a recessive condition. Uctepe et al. describe lissencephaly in association with biallelic CASP2 variants. CASP2 interacts with CRADD and PIDD1 as part of the PIDDosome [13]. There are overlapping clinical and neuroimaging features.

The COVID-19 pandemic may be behind us, in this month's EJHG there is a review of disease mechanisms in COVID-19, lest we forget [14].

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