IN THIS ISSUE

Genetic conditions are common basis for pediatric hospital admission

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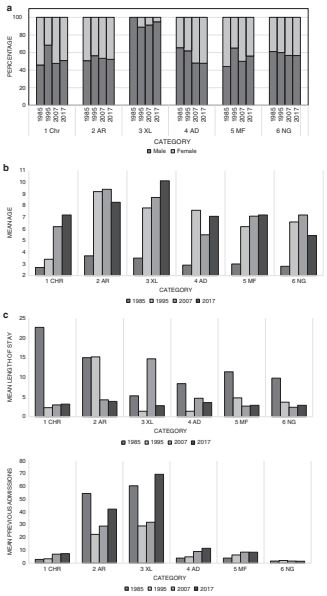

Since 1978, when the results of a study estimated that 4.5% of pediatric hospital admissions were due to monogenic conditions, several groups have undertaken similar investigations. However, methodological differences yielded variability in results and conclusions across the studies. In a descriptive study published in this issue, Gjorgioski and colleagues assessed the genetic contribution to hospital admissions at the Royal Children's Hospital in Melbourne, Australia, between 1985 and 2017. The researchers reviewed electronic health records of all patients younger than 18 years discharged from the hospital during 2 weeks in 2017. They then compared these admissions with similar reviews undertaken in 1985, 1995, and 2007. Admissions were assigned to six categories of causality: chromosomal, autosomal recessive (AR), X-linked, autosomal dominant (AD), multifactorial, and nongenetic. In total, the researchers assessed more than 6500 admissions. Multifactorial conditions contributed about half of admissions in each of the four study periods, increasing from 45% in 1985 to 54% in 2017, while the proportion of admissions due to nongenetic conditions followed a downward trend from 1995 to 2017. Nearly 16% of 2017 admissions were for single-gene and chromosomal conditions compared with 13% of admissions in 1985 and 9% and 10% in 1995 and 2007, respectively. Although admissions for AR conditions dropped from 9% in 1985 to less than 5% in 2017, they have risen since 1995. Likewise, admissions for AD conditions rose from 1% to almost 6% between 1985 and 2017. The authors conclude that hospital admissions for genetic and chromosomal conditions are common in the pediatric setting and that the increasing prevalence of AR, AD, and multifactorial conditions are important considerations for allocating future service resources. —*V. L. Dengler, News Editor*

Distinguishing apparent de novo variants from low-level somatic mosaicism

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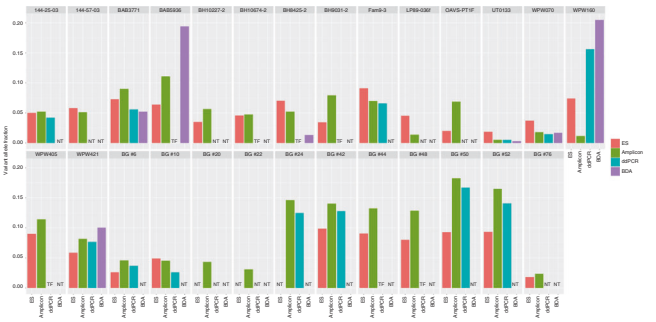

Somatic mosaicism has been implicated in a range of genetic conditions from seizures to cancer. Although research studies and clinical analyses utilize exome sequencing (ES) extensively, standard ES variant calling pipelines are typically unable to detect variants with variant allele fractions (VAFs)—the proportion of alternate allele reads relative to the total number of reads at a variant position—lower than 10%. As a result, standard ES pipelines may miss low-level somatic mosaicism. Now, Gambin and colleagues have developed an approach to identify low- and very low–level parental somatic mosaicism from ES samples, and they show that apparent de novo variants in affected probands can have parental origins. The researchers analyzed family trio ES data from two cohorts: the Baylor-Hopkins Center for Mendelian Genomics (BHCMG) and Baylor Genetics (BG). To identify candidate mosaic variants, they used a two-step filtering process to select rare, unique single-nucleotide variants (SNVs) with VAFs above 30% but less than 70% in probands and less than 10% in one of the parents. The team validated candidate variants by amplicon-based next-generation sequencing, droplet digital polymerase chain reaction (ddPCR), or blocker displacement amplification. The computational approach identified 71 candidate SNVs missed by typical ES analyses from the BHCMG cohort. The average VAF was 3% but ranged from less than 1% to 9%. The validation analyses confirmed somatic mosaicism in 33% of samples from the BHCMG cohort and 20% of samples from the BG cohort. In total, 26% of validated candidates from the two data sets were found to be low- or very low–level mosaic. The authors conclude that the computational approach described is able to efficiently and robustly detect low-level mosaicism from ES samples, which is critical for accurately determining recurrence risk. —*V. L. Dengler, News Editor*