SNP array analysis and interpretation

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Abstract/Resumo

Genome wide high resolution SNP-based array analysis has been used in our laboratory for the detection of copy number variations (CNVs) as a first tier diagnostic test since 2009 for patients with intellectual disability (ID) and/or congenital anomalies. Array is also performed prenatally in case of structural ultrasound anomalies or intra uterine foetal death and a normal QF-PCR test result as well as in patients with leukaemia. So far, more than 20,000 samples have been tested by SNP array in our diagnostic laboratory, including 5,400 parental samples.

This diagnostic approach allowed us to reliably identify known and new, recurrent microdeletions and – duplications as well as rare, unique genomic imbalances with great accuracy. Moreover, the routine analysis of SNP genotypes revealed one or more significant stretches of homozygosity in 4 to 6 % of patients. Follow-up testing by either gene mutation analysis or patient-parent trio information analysis subsequently led to the respective identification of pathogenic mutations in recessive disease genes or uniparental disomies (UPD), thereby increasing the diagnostic yield with at least 1%. Using the SNP genotype information also improved the detection of mosaic copy number changes and enabled us to detect clinically relevant, mosaic, copy neutral changes of homozygosity.

Genome-wide high resolution SNP-based array analysis is a suitable and particularly effective technique in genome diagnostics to reliably detect various causes of rare and recurrent disorders including CNVs, UPDs and mosaic imbalances as well as pathogenic mutations in recessive disease genes. By using the right follow-up test procedures after initial SNP array analysis, a higher diagnostic yield and more knowledge of the mechanism underlying the genetic disorder are achieved, thereby enabling more adequate genetic counselling.

Keyword/Palavras-chave: SNP array; CNVs; Genetic counselling

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