The identification of CNVs in patients and their association with diseases and phenotypes

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The DNA copy number of a region of a genome is the number of copies of genomic DNA. In humans the normal copy number is two for majority of autosomes. However, discoveries have revealed that many segments of DNA, ranging in size from kilobases to megabases, can vary in copy-number. These DNA copy number variations (CNVs) are common in normal individual and contribute to our uniqueness. These changes can also influence the susceptibility to disease. Many genetic diseases that occur in families result from copy number variations.

Here we report on the phenotypic and genotypic delineation of de novo CNVs in a number of cases with genetic disorders.

Case 1: A 20-year-old male with severe intellectual disability and Marfanoid habitus, cleft palate, facial dysmorphism, microphthalmia and hypermetropia. Cytogenetic investigation showed an unbalanced chromosomal abnormality with an additional un-identified chromosome piece attached to the short arm of chromosome 14. A duplication of the terminal piece of the long arm of chromosome 10 (30.1 Mb) was found.

Case 2: A 9-year-old female with global developmental and speech delay associated with dysmorphic features that includes longitudinal face with prominent forehead, high arched palate, and hypertelorism and alternating isotropia. Prominent fetal pads and bridged simian crease are noted in both hands. Her MRI showed diffuse brain atrophy. A duplication of a segment on the long arm of chromosome 15 as well as a deletion of the terminal part of the short arm of chromosome 8 were detected.

Case 3: A 13-year-old male with mild to moderate mental retardation, obesity, and dysmorphic features that includes but not limited to micropenis, flat occiput, protruding maxilla, and hirsutism. CT scan showed moderate cerebral atrophy. Cytogenetic investigation revealed a 46 XY r(13) p11.2q32. A 20.5 Mb segment deletion on the terminal part of the long arm of chromosome 13 was found.

The cases included demonstrate that CNVs play a role in genetic disorders, birth defects and patterns of malformations. The delineation of the duplicated or deleted material may help in the identification of genes that play a role in developmental processes.