

Abstract 55

IDENTIFYING NOVEL MICRODELETION MENTAL RETARDATION SYNDROMES AND CANDIDATE REGIONS FOR AUTOSOMAL MENTAL RETARDATION.

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Genome wide array based Comparative Genomic Hybridization (array CGH) was diagnostically implemented at our department in 2003 for patients with mental retardation with or without multiple congenital abnormalities. So far, more than 2000 patients have been analysed using the 250k Affymetrix SNP array platform (Affymetrix, Inc., Santa Clara, CA, USA). In more than 15% of these patients, a clinically significant copy number variation (CNV) could be detected by array analysis, including CNVs as small as 50 kb. In an additional 4% of patients, one or more "unique" CNVs were detected that were also observed in one of the parents. The clinical significance of these inherited CNVs is as yet unclear. Although the vast majority of all aberrations is non-recurrent, several recurrent aberrations have now been identified. The first novel microdeletion identified through this method is characterized by a 600 kb deletion at 17q21.31 and is associated with a clearly recognizable phenotype^{1,2}. The 17q21.31 region contains several low copy repeats that might act as recombination substrates for non-allelic homologous recombination and a common inversion polymorphism. Other loci at which recurrent genomic aberrations and a recognizable clinical phenotype were identified are 2p15, 2q23.1, 15q24 and 19q13.11. Notably, some recurrent aberrations with incomplete penetrance, such as 1q21.1³ and 15q13.3⁴, seem to elude syndromic classification and could be considered as a (high) risk factor for mental retardation. In conclusion, array CGH technology allows the identification of new candidate regions for autosomal mental retardation and reveals novel recurrent microdeletion mental retardation syndromes.

¹ Koolen DA, et al. Nat Genet 2006;38:999-1001.

² Koolen DA, et al. J Med Genet 2008;45:710-20.

³ Mefford HC, et al. N Engl J Med 2008;359:1685-99.

⁴ Van Bon et al. J Med Genet 2009; Epub ahead of print