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Detection of Hemizygous Chromosomal Copy Number Variants in Williams-Beuren Syndrome (WBS) by Duplex Quantitative PCR Array: An Unusual Type of WBS Genetic Defect

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We have developed a dual probe quantitative PCR (qPCR) mini array enabling a more accurate analysis of the relationship between copy number variants (CNVs) and other genomic features in specific areas. We used it to map hemizygous microdeletion on human chromosome 7 around the elastin gene (ELN), which is the molecular basis of the Williams-Beuren syndrome (WBS). In two WBS patients, the haploid content of the elastin gene was ascertained previously by the fluorescence in-situ hybridization (FISH). Our dual-color qPCR assay used this information to normalize for DNA content in all tests. We mapped the extent of the deleted area using 10 loci spanning over 4 Mb. A border region containing the GTF2I gene, usually deleted in most cases, was found about 10 times amplified in both patients, suggesting an unusual type of the WBS genetic defect. This 10-WBS-loci-specific qPCR assay could be an affirmative diagnostic tool alternative to FISH. Due to low cost, it could be used as a screening test that would not only facilitate research on CNVs, but also allow early diagnosis of the disease, as well-timed diagnosis would benefit WBS children with earlier proper health-care measures.