Duplication of 111 bases in exon 1 of the CYP21 gene is combined with deletion of CYP21P-C4B genes in steroid 21-hydroxylase deficiency

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Abstract

Congenital adrenal hyperplasia (CAH) is a common autosomal recessive disorder mainly caused by defects in the steroid 21-hydroxylase (CYP21) gene. A 9.3-kb fragment generated by NdeI and AseI digestion by Southern blot analysis indicated that a consequence of deletion of the C4-CYP21 repeat module was the production of a distinct chimeric CYP21P/CYP21 molecule. In the present study, we report a novel CYP21 genotype in two CAH families in which the gene appeared as 9.4- and 3.3-kb fragments by TaqI digestion, rather than as a chimeric gene. From the analysis of PCR amplification patterns and DNA sequencing, we found that there was a duplication of 111 bases from codons 21 to 57 inserted at codon 58 in exon 1 of the CYP21 gene. In addition, codon 21 in the repeated sequence changed from TGG to AGG. Furthermore, this novel CYP21 gene present in both CAH families showed no mutations at IVS2-12A/C>G, 707-714delGAGACTAC, and P30L. Interestingly, the 5' end region of these two CYP21 genes showed the sequence of the CYP21P gene at nucleotides (nt) -103, -110, -123, and thereafter. Our data suggest that these two CYP21 genes are caused by deletion of the CYP21P, XA, RP2, and C4B genes. Possibly, the additional 111-base duplicated coding sequence may be generated by multiple intergenic recombinations, while there seems to be no relationship with deletion of the CYP21P-C4B regions.