The -104G nucleotide of the human CYP21 gene is important for CYP21 transcription activity and protein interaction

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Abstract

CYP21 gene encodes the steroid 21-hydroxylase (P450c21) that is involved in steroidogenesis in the adrenal cortex. Mutations occurring on CYP21 which convert it to the neighboring pseudogene, CYP21P, are found in patients with congenital adrenal hyperplasia (CAH), an autosomal recessive disease. We previously reported that the CYP21P pseudogene had lower transcription activity when compared with the active CYP21 gene. The sequences determining the basal transcription activity of the human CYP21 gene are located within the 166 bp region upstream from the transcriptional start site. Within this region, only 4 nucleotides are different between the active CYP21 and the CYP21P pseudogene; they are located at the -117, -104, -101 and -94 positions from the start site of the gene. Here, we report that the CYP21 gene-specific G nucleotide sequence at the -104 position is required for its basal transcription activity driven by the native TATA box of the human CYP21 gene. When this single nucleotide is changed to the CYP21P sequence, the basal transcription activity decreases by ~80% in transient transfection assay. In addition, our data from gel retardation assay show that this sequence is also critical for interaction with nuclear proteins from adrenal cells. These results therefore suggest that the single G sequence of the human CYP21 gene is crucial for the expression of its basal transcription activity, and this may be influenced by the interaction with specific nuclear proteins from the adrenal gland.