분류번호	Ⅱ-P-3

Identification of Positive and Negative Regulatory Elements of the Human Cytochrome P4501A2 (*CYP1A2*) Gene

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We previously demonstrated an enhancer-like positive regulatory element within a 259-bp sequence (-2352 to -2094 bp) of the human *CYP1A2* gene in HepG2 cells. Three protein binding sites were identified by DNase I footprint analyses within the 259-bp sequence: protected region A PRA (-2283 to -2243 bp), PRB (-2218 to -2187 bp), and PRC (-2124 to -2098 bp) (I. Chung and E. Bresnick, *Mol. Pharmacol.* 47, 677-685, 1995). In the present study, the functional significance of those protected regions was examined. Transfection experiments with deletion and substitution mutants defined the PRB and PRC as containing positive and negative regulatory elements, respectively. Human breast carcinoma MCF-7 cells were cotransfected with a hepatocyte nuclear factor-1 (HNF-1) expression vector and *CYP1A2* promoter- or thymidine kinase promoter-luciferase remoter gene constructs. HNF-1, which contributes to the liver specificity of genes, enhanced reporter gene activity in a PRC sequence-dependent manner. These results suggested that PRC could exist bound to a repressor which was displaceable by other transcription factors such as HNF-1. Results obtained by transfection of HepG2 hepatoma cells with various PRB substitution mutant-luciferase gene fusion constructs indicated that the entire sequence of PRB was necessary for promoter activity. Consequently, the regulation of *CYP1A2* expression is very complex, requiring a number of both positive and negative regulatory factors.