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No role of Protected Region B of Human Cytochrome P4501A2 Gene (*CYP1A2*) As an AP-1 Response Element

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Cytochrome P4501A2 (CYP1A2) is a member of the cytochrome P450 family of isozyme involved in the phase I drug metabolism in vertebrates. CYP1A2 is responsible for the activation of a number of the aromatic amines to mutagenic and carcinogenic forms. Thus, the level of CYP1A2, which varies among the populations, may determine individual susceptibility by these chemicals.

We have previously reported on the importance of a *cis* element named PRB (protected region B) in the regulation of human Cytochrome P4501A2 (CYP1A2) gene. It appeared that this element acts as a positive regulatory element. Close examination of the PRB sequence (-2218 to 2187 bp) revealed a putative AP-1 binding site, TGACTAA, at -2212 bp (Chung and Bresnick, 1997). To elucidate the role of AP-1 in *CYP1A2* regulation, we transiently overexpressed c-Jun and c-Fos transcription factors in a human hepatoma HepG2 cells, and examined their influence on the CYP1A2 promoter activity by reporter gene assays. Cotransfection of c-Jun and c-Fos expression vectors induced transactivation by five to six fold from CYP1A2 promoter constructs. However, deletion of PRB element did not affect the degree of activation by c-Jun and c-Fos. Thus, it is not likely that c-Jun and c-Fos activates the CYP1A2 promoter through this AP-1 consensus-like sequence in PRB region.