Regulation of glutathione S-transferase Ya subunit gene expression: identification of a unique xenobiotic-responsive element controlling inducible expression by planar aromatic compounds.

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We have identified a region in the 5' flanking sequence of the glutathione S-transferase (RX:glutathione R-transferase, EC 2.5.1.18) Ya subunit gene that contains a unique xenobiotic-responsive element (XRE). The regulatory region spans nucleotides -722 to -682 of the 5' flanking sequence and is responsible for part of the basal level as well as inducible expression of the Ya subunit gene by planar aromatic compounds such as beta-naphthoflavone (beta-NF) and 3-methylcholanthrene. The DNA sequence of this region (beta-NF-responsive element) is distinct from the DNA sequence of the XRE found in the cytochrome P-450 IA1 gene. In addition to the region containing the beta-NF-responsive element, two other regulatory regions of the Ya subunit gene have been identified. One region spans nucleotides -867 to -857 and has a DNA sequence with identity to the hepatocyte nuclear factor 1 recognition motif found in several liver-specific genes. The second region spans nucleotides -908 to -899 and contains a DNA sequence with identity to the XRE found in the cytochrome P-450 IA1 gene. The XRE sequence also contributes to part of the responsiveness of the Ya subunit gene to planar aromatic compounds. Our data suggest that regulation of gene expression by planar aromatic compounds can be mediated by a DNA sequence that is distinct from the XRE sequence.