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Determination of Sites of CYP1B1Mutations in Aligned Sequences of Cytochrome P450 Family Members and 3D Structural Model

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CYP1B1 is a member of the cytochrome P450 superfamily of genes. The protein products of these genes are oxygenases with roles in detoxification reactions. Mutations in the CYP1B1 gene are associated with various types of cancers and glaucoma, an eye disease which accounts for 15 % of blindness worldwide. We have identified 15 CYP1B1 mutations in Iranian glaucoma patients, five of which have not been previously reported (E173K, D291G, G329V, R368C, and I399V).

The amino acid sequences of 21 human cytochrome P450 proteins were aligned using ClustalW and conserved regions were identified. The positions of our 15 mutations and 13 other mutations in the alignment were assessed. As the cytochromes belonged to various families, only 9 positions were strictly conserved. Five of the 21 mutations, including a newly identified mutation, occurred at or adjacent to these sites. Additionally, the known crystalline structure of four cytochrome P450s (cyp2C5, cyp2B4, cyp2C9, and cyp2C8) were used to perform homology modeling using the SWISS MODEL comparative Protein Modeling Server. The sites of the mutations were determined in the 3D-model obtained. Finally, the secondary structure relating to the 3D-model was determined and it was found that the vast majority of the mutations lie in alpha helices.