[Structure, 4, 33-45 (1996)] [Lab. of Biochemistry]

Crystal Structure of the Ternary Complex of Mouse Lung Carbonyl Reductase at 1.8 Å Resolution: the Structural Origin of Coenzyme Specificity in the Short-Chain Dehydrogenase/Reductase Family.

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The crystal structure of ternary complex of mouse lung carbonyl reductase (MLCR) has been determined at 1.8 Å resolution. This is the first three-dimensional structure of a carbonyl reductase, and MLCR is the first member of the short-chain dehydrogenase/reductase family to be solved in complex with NADPH rather than NADH. Comparison of the MLCR complex with three dimensional structures reported previously for enzymes of the SDR family reveals a pair of basic residues (Lys17 and Arg39) making strong electrostatic interactions with the 2'-phosphate group of NADPH.

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Activation of Human Liver 3 α-Hydroxysteroid Dehydrogenase by Sulphobromophthalein.

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Human liver contains at least two isozymes (DD2 and DD4) of 3 α-hydroxysteroid/dihydrodiol dehydrogenase. The oxidoreductase activities of DD4 were activated more than 4-fold by sulphobromophthalein. Sulphobromophthalein did not stimulate the activities of DD2 and human liver aldehyde reductase. The activation decresed the activation energy in the dehydrogenation reaction for the enzyme, and increased both k_{cat} and K_m values for the coenzymes and substrates. Kinetic analyses with respect to concentrations of $NADP^+$ and (*S*)-indan-1-ol indicated that sulphobromophthalein was a non-essential activatior of mixed type showing a dissociation constant of 2.6 μM.

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Relationship of Human Liver Dihydrodiol Dehydrogenases to Hepatic Bile-Acid-Binding Protein and an Oxidoreductase of Human Colon Cells.

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We previously isolated three dihydrodiol dehydrogenases, DD1, DD2 and DD4, from human liver, and cloned a cDNA (C9) thought to encode DD2. A recombinant enzyme expressed from the cDNA in a bacterial system was purified, and its catalytic properties, bile-acid-binding ability and primary sequence were compared with those of the hepatic dihydrodiol dehydrogenases. The results show that the cDNA encodes DD1. Whereas DD2, showing differences of six amino acid residues from the DD1 sequence, exhibited high-affinity binding for bile acid.