All around CYP106A2:
The Many Faces of Molecular Modelling

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The application of Cytochrome P450 enzymes allows the selective hydroxylation of hydrocarbon skeletons that are otherwise difficult to synthesize. The necessary electron transport to the cytochrome can be achieved by a variety of ferrodoxins. Although 3D-structures and amino acid sequences are highly conserved between bacterial and mammalian ferredoxins, they give rise to different product distributions when used for the hydroxylation of progesterone by CYP106A2. [1, 2] Protein-Protein docking of bovine Adrenodoxine and the corresponding Electron transport protein 1 (Etp1) from yeast to CYP106A2 indicates that these differences are not only due to the lower redox potential of Etp1, but are also caused by subtle structural differences that lead to different binding modes of both redox enzymes. Moreover, molecular dynamic simulations of 15β-OH-progesterone in the binding pocket of CYP106A2 showed that reorientation occurs within 100ns, which suggests that the rate of electron transfer strongly influences the amount of polyhydroxylated products being formed. Likewise, rearrangement of intermediately formed radicals can influence the rate of turn-over: Despite dexamethasone exhibits a higher binding affinity compared to prednisone, it was found to be hydroxylated much slower. Semiempirical AM1 calculations of the conceivable radicals showed that migration to the more stable but unproductive radical in position 16 is responsible for the slow hydroxylation. [3]

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