

Stereochemistry

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Regio- and stereospecific hydroxylation reactions catalyzed by human cytochrome P450 enzymes

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Human cytochrome P450 (CYP) enzymes are involved in the biotransformation of endogenous compounds and in the Phase I metabolism of xenobiotics in humans. Examples of exogenous CYP substrates are drugs, polycyclic aromatic hydrocarbons, and plant products, while physiological substrates include steroid hormones and fatty acids. Most human CYP enzymes are localized in the smooth endoplasmic reticulum of liver or other organs and function as the terminal oxidases of an electron transport chain in which one atom of oxygen from molecular oxygen is incorporated into the substrate and the other atom is reduced to water. The second protein in the microsomal electron transport chain is the flavoprotein CYP reductase (CPR or POR). CYP as the terminal oxidase of the chain is the enzyme active site, the oxygen- and substrate-binding site and the determinant of substrate specificity. CYP enzymes contain a heme prosthetic group in the form of iron protoporphyrin IX, which is essential for enzymatic activity and in most CYP enzymes is bound noncovalently at the fifth coordination site of iron to the sulfur atom of a cysteine residue located close to the C-terminus of the enzyme. A water molecule normally occupies the sixth coordination site of the heme iron but is replaced by molecular oxygen in the course of the reaction cycle. Binding of substrates in a defined orientation in the active center of CYP enzymes enables them to carry out regio- and stereospecific hydroxylations of both endogenous steroids and steroidal doping compounds.

Biography

Matthias Bureik has completed his PhD at the age of 29 years at Saarland University and, after postdoctoral studies and habilitation, served as CEO of a biotech startup company for four years. Since 2014 he is professor of biochemistry at Tianjin University. He has published more than 40 papers in reputed journals and serves as an editorial board member for several journals.

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