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Expression and regulation of xenobiotic-metabolizing cytochrome P450 (CYP) enzymes in human lung.

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ABSTRACT:

Pathogenesis of lung diseases, such as lung cancer and chronic obstructive pulmonary disease, is tightly linked to exposure to environmental chemicals, most notably tobacco smoke. Many of the compounds associated with these diseases require an enzymatic activation to exert their deleterious effects on pulmonary cells. These activation reactions are mostly catalyzed by cytochrome P450 (CYP) enzymes. Interindividual differences in the *in situ* activation and inactivation of chemical toxicants may contribute to the risk of developing lung diseases associated with these compounds. This review summarizes in detail the expression of individual CYP forms in human pulmonary tissue and gives a view on the significance of the pulmonary expression of CYP enzymes. The localization of individual CYP enzymes in various cell types of human lung and the emerging field of regulation of human pulmonary CYP enzymes are discussed. At least CYP1A1 (in smokers), CYP1B1, CYP2B6, CYP2E1, CYP2J2, and CYP3A5 proteins are expressed in human lung, and also other CYP forms are likely to be expressed. Xenobiotic-metabolizing CYP enzymes are mostly expressed in bronchial andbronchiolar epithelium, Clara cells, type II pneumocytes, and alveolar macrophages in human lung, although individual CYP forms have different patterns of localization in pulmonary tissues. Problems in animal to human lung toxicity extrapolation and several specific aspects requiring more detailed assessmentare identified.

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