

Cytochrome P450 1B1 expression in rat esophageal tumorigenesis promoted by gastric and duodenal reflux

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Abstract

Cytochrome P450 1B1 (CYP1B1) mRNA is constitutively expressed in most normal extra-hepatic tissues; however the protein is not detectable in these tissues but is expressed in a wide variety of tumors. CYP1B1 is responsible for the activation of a number of carcinogens present in tobacco smoke and food. A surgical model of rat esophageal tumorigenesis, promoted by gastric or duodenal reflux was used to determine CYP1B1 expression in premalignant esophageal tissue. Immunohistochemistry was performed using a modified amplified fluorescein tyramide protocol. CYP1B1 was not observed in normal esophageal mucosa, submucosa, or muscularis mucosa. Animals exposed to gastric reflux developed mild hyperplasia. Varying degrees of hyperplasia were observed in the duodenal reflux group. All regions of hyperplasia showed moderate or strong CYP1B1 immunoreactivity. Duodenal reflux induced a small number of premalignant changes: immunoreactivity was absent from the epithelium of squamous dysplasia (0/10), Barrett's esophagus (0/7), and majority of dysplastic Barrett's esophagus (1/4). Moderate or strong immunoreactivity was observed in the majority (7/8) of squamous cell carcinomas (SCCs) in situ. Immunoreactivity was also observed in the lamina propria and submucosa in association with inflammation, regardless of the severity of inflammation. The expression of CYP1B1 in hyperplasia, SCCs in situ, or in association with inflammation may increase the production of carcinogenic metabolites, which may promote esophageal tumorigenesis. © 2008 Wiley-Liss, Inc.