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## Crystalline silica is a negative modifier of pulmonary cytochrome P-4501A1 induction.

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### Abstract

Polycyclic aromatic hydrocarbons (PAHs) are products of incomplete combustion that are commonly inhaled by workers in the dusty trades. Many PAHs are metabolized by cytochrome P-4501A1 (CYP1A1), which may facilitate excretion but may activate pulmonary carcinogens. PAHs also stimulate their own metabolism by inducing CYP1A1. Recent studies suggest that respirable coal dust exposure inhibits induction of pulmonary CYP1A1 using the model PAH beta-naphthoflavone. The effect of the occupational particulate respirable crystalline silica was investigated on PAH-dependent pulmonary CYP1A1 induction. Male Sprague-Dawley rats were exposed to intratracheal silica or vehicle and then intraperitoneal beta-naphthoflavone, a CYP1A1 inducer, and/or phenobarbital, an inducer of hepatic CYP2B1, or vehicle. Beta-naphthoflavone induced pulmonary CYP1A1, but silica attenuated this beta-naphthoflavone-induced CYP1A1 activity and also suppressed the activity of CYP2B1, the major constitutive CYP in rat lung. The magnitude of CYP activity suppression was similar regardless of silica exposure dose within a range of 5 to 20 mg/rat. Phenobarbital and beta-naphthoflavone had no effect on pulmonary CYP2B1 activity. Both enzymatic immunohistochemistry and immunofluorescent staining for CYP1A1 indicated that sites of CYP1A1 induction were nonciliated airway epithelial cells, endothelial cells, and the alveolar septum. Using immunofluorescent colocalization of CYP1A1 with cytokeratin 8, a marker of alveolar type II cells, the proximal alveolar region was the site of both increased alveolar type II cells and decreased proportional CYP1A1 expression in alveolar type II cells. Our findings suggest that in PAH-exposed rat lung, silica is a negative modifier of CYP1A1 induction and CYP2B1 activity.

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