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The Role Of Serotonin Homeostasis In Airway Oxidative Stress And Inflammation In Airway Epithelial Cells

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Background: Chronic obstructive pulmonary disease (COPD) is a slowly progressive age-related disease characterized by chronic airflow limitation that is not fully reversible and chronic airway inflammation. Cigarette smoking is the major risk factor in the development of COPD. Elevated plasma levels of serotonin (5-hydroxytryptamine, 5-HT) were present in patients with COPD, but the role of serotonin homeostasis in developing airway oxidative stress and inflammation is not clear. We hypothesize that serotonin homeostasis plays a role in airway oxidative stress and inflammation.

Methods: Human primary bronchial and tracheal epithelial cells (HBEC and HTEC), and human bronchial epithelial cell line (BEAS-2B) were used in the study. All cells were cultured to 80% confluence before starving overnight and challenged by cigarette smoke medium (CSM), 5-HT or serotonin creatinine sulfate monohydrate (SCSM; a 5-HT analog) for 24 hours. Expression of 5-HT2A receptors in BEAS-2B cells was analyzed by immunohistochemistry. Intracellular reactive oxygen species (ROS) production was measured by dichlorofluorescein diacetate (DCFH) assay. Protein expressions of antioxidant enzymes, quinone oxidoreductase 1 (NQO1) and heme oxygenase-1 (HO-1) in cell lysates were detected by Western blot analysis. Releases of pro-inflammatory markers [interleukin (IL)-6, IL-8 and monocyte chemoattractant protein (MCP)-1] in supernatants were measured by ELISA.

Results: In BEAS-2B cells, CSM caused a concentration-dependent upregulation of 5-HT2A receptors. We also observed dose-dependent elevation of ROS production after exposure to CSM, 5-HT and SCSM. In support, CSM also caused a concentration-dependent increase in NQO1 and HO-1 protein expression in all three different airway epithelial cells. On the contrary, SCSM caused only upregulation of NQO1 protein expression in BEAS-2B and HBEC. For cytokine release, CSM, 5-HT and SCSM caused elevation of IL-8 and MCP-1 in BEAS-2B, and IL-6 and IL-8 in HBEC and HTEC.

Conclusion: Our data suggest that CSM and 5-HT analog may play differential role in modulating inflammatory responses via oxidative stress in airway epithelial cells in vitro.

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