Cigarette Smoke induced Inflammation and Cytotoxicity in viable lung tissue

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common leading cause of death worldwide, often developed due to cigarette smoke (Cs) inhalation. It is characterised by degradation of airways, inflammation and mucus hypersecretion. Mechanisms that underlie various components of COPD can be modelled in vitro, specifically using cigarette smoke with fresh human lung tissue. The aim of the study is to establish pathological changes of COPD in vital lung tissue by using Cs and cigarette smoke condensate (Csc).

Materials and Methods

Precision-Cut Lung Slices (PCLS) prepared from rodent, rhesus and human lungs were exposed to Csc in a submers culture or to Cs in an Air-Liquid Interface (ALI) for up to 96 h. Tissue viability (WST-1, Live/Dead staining) and cytotoxicity (LDH) were assessed. Pro-inflammatory cytokines and matrix metalloproteinases (MMPs) were determined by ELISA. Dexamethasone was used to inhibit inflammatory responses of tissue to Cs.

Results

Csc induced concentration dependent cytotoxicity in rat, rhesus and human PCLS after 24 h submersion exposure. EC₅₀ values were determined by WST-1 assay (Fig. 2) (curves not shown). Pro-inflammatory cytokines interleukin α and β (IL-1α/β) were significantly increased in all species after 24 h Csc exposure of lung tissue. Dexamethasone inhibited Csc induced production of pro-inflammatory cytokines (Fig. 2C).

Exposure of viable rat, rhesus and human lung tissue to Cs increased release of pro-inflammatory cytokines (Fig. 6). High concentrations of Cs induced an anti-inflammatory effect in IL-1α production in human PCLS (Fig. 6E). Matrix metalloproteinase-9 is increasingly released after Cs exposure in human PCLS as well as after Csc exposure in rhesus and human PCLS (Fig. 6D and data not shown).

Conclusions

Csc and Cs induced tissue damage and early biomarkers of inflammation in rodent, rhesus and human PCLS. The exposure of lung tissue to the complex mixture of whole cigarette smoke closely reflects the in vivo situation in PCLS. Therapeutical intervention of inflammatory responses can be studied in PCLS.

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