Acute cigarette smoke exposure increases susceptibility to influenza infection by disrupting epithelial barrier function and suppressing the antiviral immune response

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease that affects more than 65 million people worldwide and is predicted to be the third leading cause of death in 2030. Smoking is the major cause for developing COPD. Symptoms include chronic cough, excessive sputum production and breathlessness. Additional occurrence of respiratory viral infections can cause severe exacerbations and are a major cause of death for COPD patients. The mechanisms underlying virus-induced disease exacerbations are not well understood. Therefore, in this study the impact of cigarette smoke exposure on the antiviral immune response of the lower respiratory tract was investigated using H1N1 (California/04/2009) pandemic strain infection of smoke exposed Calu-3 cells and viable human precision-cut lung slices (PCLS).

Methods

Calu-3 cells or human PCLS were cultured at air liquid interface and exposed to high and low dose cigarette smoke for 18 puffs, 35 mL each, using the P.R.I.T ExpoCube®. Controls were exposed to clean air. Afterwards, cells or PCLS were inoculated with 5,000 ffu/well H1N1 (Calu-3) or 10^5 ffu/mL (PCLS) for 1 h and post-incubated for 48 h. The immune response was assessed via analysis of cytokine release by ELISA, and tissue damage was measured by LDH release. The trans-epithelial electrical resistance (TEER) was measured in Calu-3 cells prior to infection and 48 h after the infection (Fig. 1).

PCLS Results

First, ex vivo H1N1 infection in human PCLS was confirmed by immunofluorescence staining. Specific virus infection was confirmed within the airway epithelium ex vivo (Fig 2).

H1N1 infection leads to a loss of cilia after 72 h and indicates a cytopathic effect within the airway epithelium.

Conclusion

This study shows that cigarette smoke disrupted the epithelial barrier function in Calu-3 cells and suppressed the H1N1-induced antiviral immune response in human lung tissue ex vivo. These two events could contribute to the exacerbation occurring during infections in COPD patients. Further research could focus the viral titre and the efficacy of influenza drugs after CS exposure.

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The authors have nothing to disclose.