The crosstalk between neutrophils and lung epithelial cells upon endotoxin exposure

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INTRODUCTION

Various lung diseases are characterized by an increased number of polymorphonuclear neutrophils (PMN). It has been discussed that patients suffering from such diseases are more susceptible towards exogenous pro-inflammatory triggers. A possible mechanism underlying this susceptibility may include the influence of this pre-existing neutrophilic inflammation on the airway epithelial defense response.

AIM

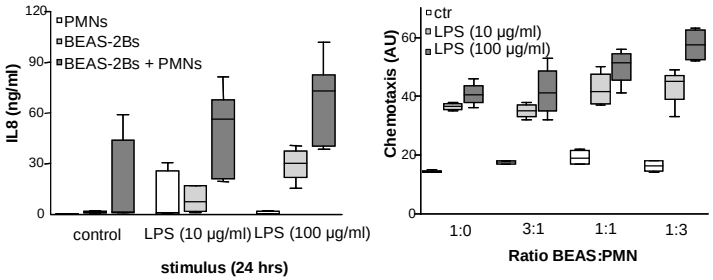
The aim of the present study is to investigate the crosstalk between neutrophils and lung epithelial cells upon exposure to lipopolysaccharide derived from *Escherichia coli* (LPS).

MATERIALS AND METHODS

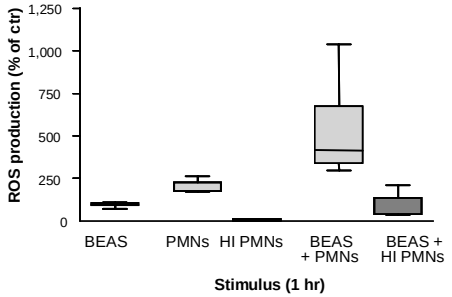
BEAS-2B cells and PMN were co-incubated to mimic the possible crosstalk between these structural and inflammatory cells. The role of neutrophilic NADPH oxidase (NOX2) in this crosstalk was examined by blocking its activity, either temporarily by heat inactivation or indefinite by applying bone-marrow derived neutrophils from either C57BL/6J wildtype or NADPH-oxidase impaired (p47$^{phox-/-}$) mice.

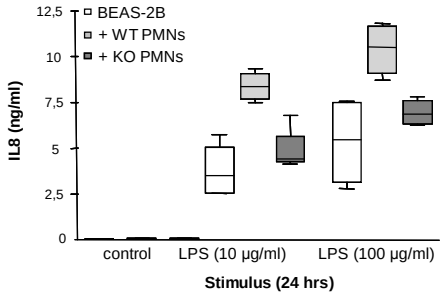
RESULTS

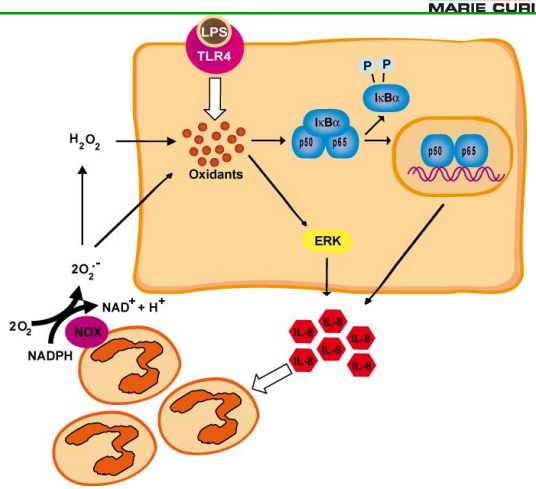
LPS dose-dependently induces a synergistic production of IL-8 and other chemo-attractants in the co-incubations



LPS-induced synergistic ROS generation and IL-8 production are significantly dependent on a functional NOX2







Schematic representation of the proposed crosstalk between lung epithelial cells and neutrophils

CONCLUSIONS

- LPS induces IL-8 production, ERK1/2 and NF-κB activation and ROS generation in lung epithelial cells
- These pro-inflammatory effects of LPS are synergistically amplified when neutrophils are present
- This synergistic crosstalk largely depends on a functional neutrophil NADPH-oxidase

IMPLICATIONS

- Patients suffering from pulmonary neutrophilic inflammation are more susceptible towards exogenous pro-inflammatory triggers.
- Possible therapeutic interventions targeting NOX2 and/or its downstream signaling cascades.