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Center for COPD Research
Odense, Denmark

SDU

Surfactant protein D deficiency aggravates cigarette smoke-induced inflammation

Bartosz Pilecki[1], Helle Wulf-Johansson[1], Christian Støttrup[1], Patricia T. Jørgensen[1], Anders Schlosser[1], Søren Hansen[1], Jørgen Vestbo[2], Howard Clark[3], Nades Palaniyar[4,5], Uffe Holmskov[1], Grith L. Sørensen[1]

[1]Department of Cancer and Inflammation Research, Institute of Molecular Medicine, University of Southern Denmark, Odense, Denmark; [2]Department of Respiratory Medicine, Odense University Hospital, Odense, Denmark; [3]Department of Child Health, Sir Henry Wellcome Laboratories, Academic Unit for Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK; [4]Program in Physiology and Experimental Medicine, Lung Innate Immunity Research Laboratory, Sick Kids Research Institute, Toronto, Canada. [5]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

BACKGROUND

Surfactant protein D (SP-D) is a pulmonary collectin mediating host defence through opsonization of phagocytes and apoptotic cells and modulation of alveolar macrophage phenotype. SP-D-deficient mice (SP-D KO) develop pulmonary emphysema accompanied by lipid and macrophage accumulation. SP-D levels increase after exposure to cigarette smoke (CS), the main risk factor for chronic obstructive pulmonary disease (COPD).

AIM AND METHODS

We hypothesized that SP-D protects from CS-induced inflammation and can be used as a local therapeutic to alleviate the disease.
We exposed male C57BL/6N WT and SP-D KO mice to CS subchronically (5 days/week for 12 weeks) or acutely (daily for 3 days) to investigate the effects of SP-D deficiency on CS-induced lung disease. Recombinant fragment of human SP-D (rfhSP-D) was given intranasally 1 h prior to each acute exposure.

RESULTS

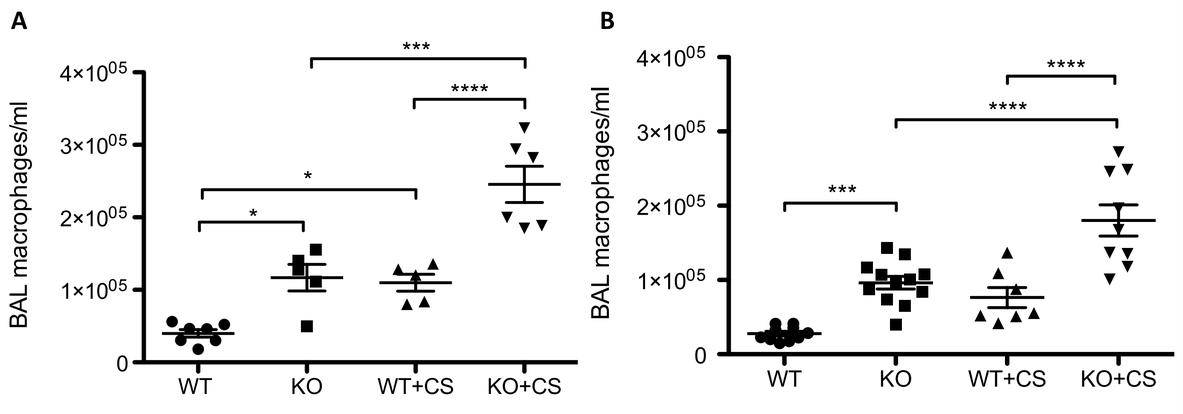

Figure 1. SP-D deficiency exacerbates macrophage-rich inflammation after CS exposure. Graphs show macrophage numbers in bronchoalveolar lavage (BAL) after subchronic (A) or acute (B) exposure to CS. *p < 0.05, ***p < 0.001, ****p < 0.0001, calculated by one-way ANOVA/Bonferroni's test.

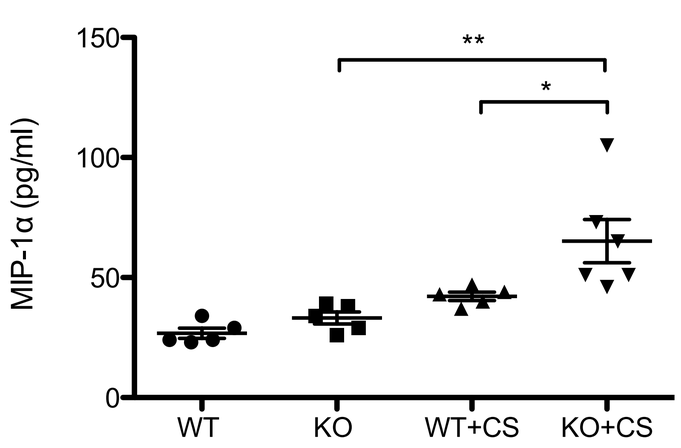

Figure 2. SP-D deficiency promotes chemokine release after subchronic CS exposure. BAL levels of macrophage inflammatory protein 1-α (MIP-1α) were significantly increased in CS-exposed SP-D KO mice compared to WT littermates. *p < 0.05, **p < 0.01, calculated by one-way ANOVA/Bonferroni's test.

RESULTS

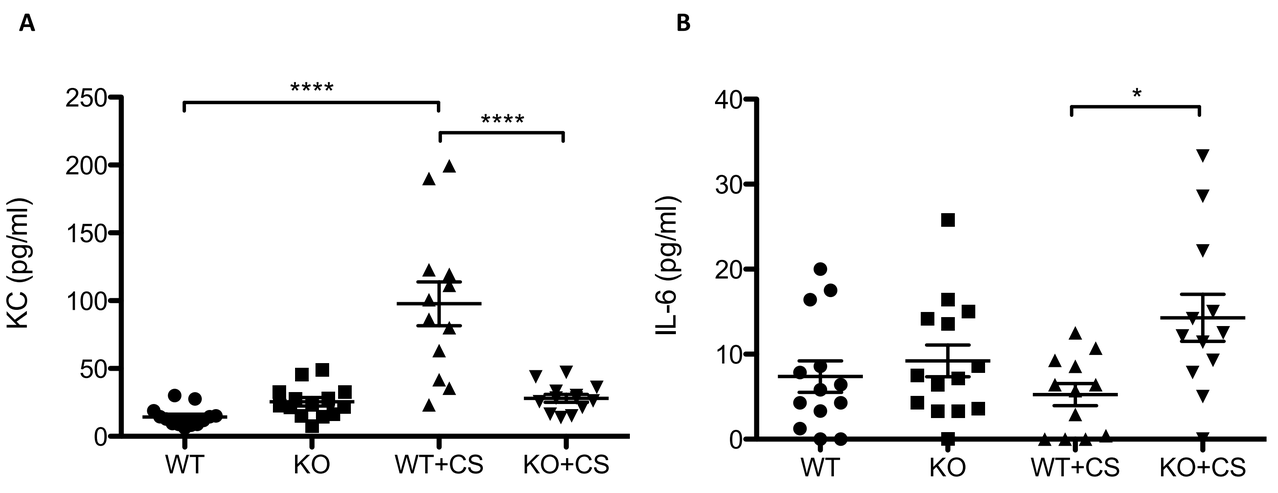

Figure 3. Modulation of CS-induced cytokines by SP-D deficiency. BAL levels of (A) keratinocyte-derived chemokine (KC) are decreased and (B) IL-6 are increased in SP-D KO mice compared to WT littermates. . *p < 0.05, ***p < 0.001, ****p < 0.0001, calculated by one-way ANOVA/Bonferroni's test.

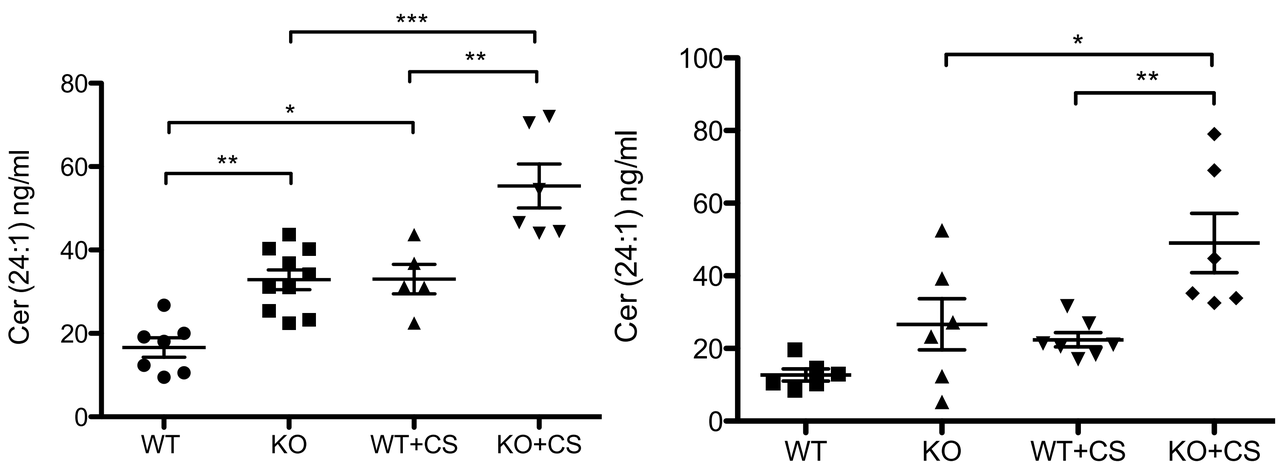

Figure 4. SP-D deficiency results in upregulation of pro-apoptotic ceramides. BAL levels of ceramide (24:1) after subchronic (a) and acute (B) CS exposure are shown. *p < 0.05, **p < 0.01, ***p < 0.001, calculated by one-way ANOVA/Bonferroni's test.

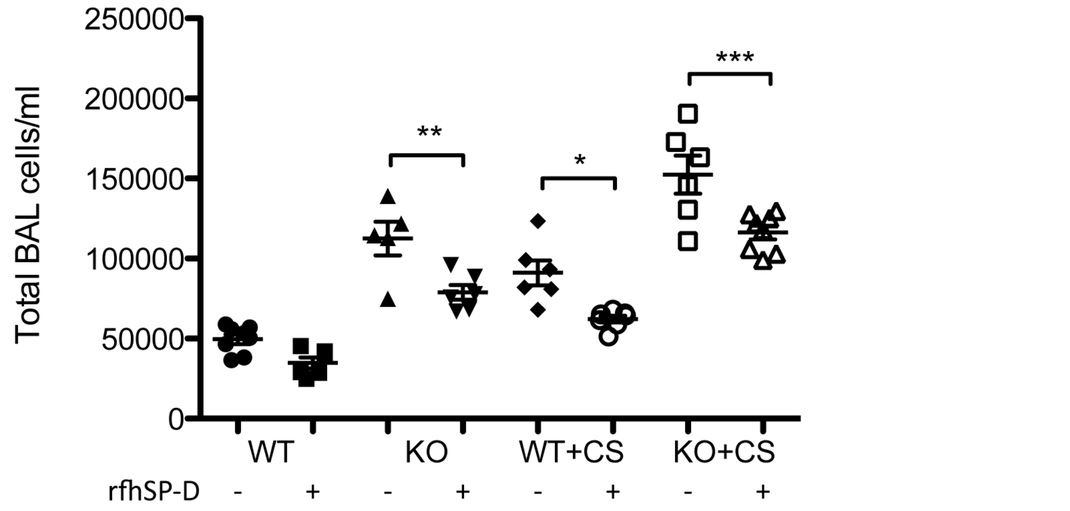

Figure 5. Administration of rfhSP-D alleviates CS-induced airway inflammation. Intranasal rfhSP-D delivery resulted in decrease of BAL cell numbers in all the experimental treated groups. *p < 0.05, **p < 0.01, ***p < 0.001, calculated by one-way ANOVA/Bonferroni's test.

CONCLUSIONS

Our results indicate that SP-D protects from CS-induced pulmonary inflammation and that SP-D-based therapy might be a future potential treatment for COPD.

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Correspondence: bpilecki@health.sdu.dk