学 位 論 文 の 要 旨

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主論文の題名

Differential role of regulatory T cells in early and late stages of pulmonary fibrosis

主論文の要旨

Introduction

Pulmonary fibrosis is the end-stage of interstitial lung diseases, characterized by an excessive and abnormal extracellular matrix deposition that eventually leads to a progressively lost of pulmonary function.

Background

Deficiency of CD4+CD25+ regulatory T cells (Tregs) and impairment in their suppressive activity has been correlated with clinical parameters of disease severity in Idiopatic Pulmonary Fibrosis (IPF) patients. However the role of Tregs in early stages of IPF remains unclear.

Objetives

To study the role of Tregs in different stages of lung fibrosis in mice.

Experimental design

Lung fibrosis was induced in C57BL/6 female mice by constant subcutaneous infusion of bleomycin (BLM). Tregs were depleted by treatment with anti-CD25+ antibody during the early, intermediate and late phases of the experimental model and the development of lung fibrosis was compared.

Results and discussion

Lungs from mice depleted of Tregs at the early stage of the model presented significantly reduce d levels of the profibrotic parameters Chemokine (C-C motif) ligand 2 (CCL-2) and Transforming Growth Factor beta 1 (TGF-β1), collagen, hydroxyproline and fewer grade of fibrotic changes. Increased secretion of CCL-2 and TGF-β1 from alveolar epithelial cells cocultured with Tregs was confirmed *in vitro*. On the contrary depletion of Tregs at the late stage of the model led to an increased fibrotic changes and increased levels of TGF-β1, CCL-2 and hydroxyproline. Mice depleted from Tregs at the late stage presented Th2 predominance in lugs suggesting that Tregs-regulation of T cells subpopulations would be a mechanism involved in the different outcome of the fibrotic process at the late stage of this model

Conclusion

The results of this study show that Tregs play a detrimental role in early stages but a protective role in late stages of bleomycin-induced pulmonary fibrosis.