A role for dendritic cells in bleomycin-induced pulmonary fibrosis in mice?

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Résumé en anglais	RATIONALE: Lung dendritic cells (DCs) have been shown to accumulate in human fibrotic lung disease, but little is known concerning a role for DCs in the pathogenesis of fibrotic lung. OBJECTIVES: To characterize lung DCs in an in vivo model of bleomycin-induced pulmonary fibrosis in mice. METHODS: We characterized the kinetics and activation of pulmonary DCs during the course of bleomycin-induced lung injury by flow cytometry on lung single-cell suspensions. We also characterized the lymphocytes accumulating in bleomycin lung and the chemokines susceptible to favor the recruitment of immune cells. MEASUREMENTS AND MAIN RESULTS: We show, for the first time, that increased numbers of CD11c(+)/major histocompatibility complex class II(+) DCs, including CD11b(hi) monocyte-derived inflammatory DCs, infiltrate the lung of treated animals during the fibrotic phase of the response to bleomycin. These DCs are mature DCs expressing CD40, CD86, and CD83. They are associated with increased numbers of recently activated memory T cells expressing CD44, CD40L, and CD28, suggesting that fully mature DCs and Ag-experienced T cells can drive an efficient effector immune response within bleomycin lung. Most importantly, when DCs are inactivated with VAG539, a recently described new immunomodulator, VAG539 treatment attenuates the hallmarks of bleomycin lung injury. CONCLUSIONS: These findings identify lung DCs as key proinflammatory cells potentially able to sustain pulmonary inflammation and fibrosis in the bleomycin model.
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