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BACKGROUND:
D6 is an atypical chemokine receptor involved in chemokine degradation and resolution of acute inflammatory responses in mice. Emerging evidence suggests that D6 might behave differently in human chronic inflammatory conditions. We, therefore, investigated the involvement of D6 in the immune responses in COPD, a chronic inflammatory condition of the lung.
METHODS:
D6 expression was quantified by immunohistochemistry in surgical resected lung specimens from 16 patients with COPD (FEV(1), 57% ± 6% predicted) and 18 control subjects with normal lung function (nine smokers and nine nonsmokers). BAL was also obtained and analyzed by flow cytometry, immunofluorescence, and molecular analysis for further assessment of D6 involvement.
RESULTS:
D6 expression in the lung was mainly detected in alveolar macrophages (AMs). The percentage of D6(+) AMs was markedly increased in patients with COPD as compared with both smoker and nonsmoker control subjects ($P < .0005$ for both). D6 expression was detected at both transcript and protein level in AMs but not in monocyte-derived macrophages. Finally, D6 expression was positively correlated with markers of immune activation (CD8(+) T lymphocytes, IL-32, tumor necrosis factor-α, B-cell activating factor of the tumor necrosis factor family, phospho-p38 mitogen-activated protein kinase) and negatively with lung function (FEV(1), FEV(1)/FVC).
CONCLUSIONS:
D6 is expressed in AMs from patients with COPD, and its expression correlates with the degree of functional impairment and markers of immune activation. Upregulation of D6 in AMs could indicate that, besides its known scavenger activity in acute inflammation, D6 may have additional roles in chronic inflammatory conditions possibly promoting immune activation.