COPD is associated with increased pro-inflammatory CD28null CD8 T and NKT-like cells in the small airways

Greg Hodge et al[1]

[1]Affiliation not available

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Abstract

We previously showed increased steroid resistant CD28null CD8+ senescent lymphocyte subsets in peripheral blood from COPD patients. These cells expressed decreased levels of the glucocorticoid receptor (GCR), suggesting their contribution to the steroid resistant property of these cells. COPD is a disease of the small airways. We therefore hypothesized that there would be a further increase in these steroid resistant lymphocytes in the lung, particularly in the small airways. We further hypothesized that the pro-inflammatory/cytotoxic potential of these cells could be negated using prednisolone with low-dose cyclosporin A.

Blood, bronchoalveolar lavage, large proximal and small distal airway brushings were collected from 11 COPD patients and 10 healthy aged-matched controls. The cytotoxic mediator granzyme b, pro-inflammatory cytokines IFNγ/TNFα, and GCR were determined in lymphocytes subsets before and after their exposure to 1μM prednisolone and/or 2.5ng/mL cyclosporin A.

Particularly in the small airways, COPD subjects showed an increased percentage of CD28null CD8 T-cells and NKT-like cells, with increased expression of granzyme b, IFNγ and TNFα and a loss of GCR, compared with controls. Significant negative correlations between small airway GCR expression and IFNγ/TNFα production by T and NKT-like cells (eg, T-cell IFNγ R= -.834, p=.031) and with FEV_1 (R= -890) were shown. Cyclosporine A and prednisolone synergistically increased GCR expression and inhibited pro-inflammatory cytokine production by CD28null CD8- T and NKT-like cells.

COPD is associated with increased pro-inflammatory CD28null CD8+ T and NKT-like cells in the small airways. Treatments that increase GCR in these lymphocyte subsets may improve morbidity in COPD patients.

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