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Activated Oligoclonal CD4⁺ T Cells in the Lungs of Patients with Severe Emphysema

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Rationale: Within the lungs of patients with severe emphysema, inflammation continues despite smoking cessation and is characterized by the presence of T lymphocytes (T cells). Disease severity has been associated with increasing numbers of T cells within the small airways and alveolar walls of patients with chronic obstructive pulmonary disease (COPD). At present, the role of the T cell in this persistent inflammation remains unknown. One important question is whether these T cells are accumulating in the lung in response to an antigen or are being nonspecifically recruited. The aim of this study was to determine

if T cells recruited to the lungs of subjects with severe emphysema are composed of oligoclonal T-cell populations, suggesting their accumulation in response to conventional antigenic stimuli. **Methods:** Lung T-cell receptor (TCR) V β repertoire from seven patients with emphysema was evaluated at the time of tissue procurement (*ex vivo*) and after 2 weeks of culture with interleukin-2 (*in vitro*). Junctional region nucleotide sequencing of expanded TCR V β subsets was performed.

Results: No significantly expanded TCR V β subsets were identified in *ex vivo* samples. However, T cells grew from all emphysema (n = 7) but no control (n = 4) lung samples when exposed to interleukin-2. Within the cultured CD4⁺ T cells, a total of six major TCR V β subset expansions were identified in four of the seven patients with emphysema. Importantly, these T-cell expansions contained T-cell clones that had already been expanded *in vivo*.

Conclusion: From the lungs of subjects with severe emphysema, oligoclonal CD4⁺ T-cell populations were identified that preferentially proliferated in culture. Oligoclonal populations of T cells within the lungs of patients with severe emphysema suggest that response to an antigen plays an important role in the continuing inflammation characteristic of severe COPD.

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Mechanisms of Autoimmune Emphysema

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Although cigarette smoking is implicated in the pathogenesis of emphysema, the precise mechanisms of chronic progressive alveolar septal destruction are not well understood. Here we show in a novel animal model (1) that immune competent, but not athymic, nude rats injected intraperitoneally with xenogeneic endothelial cells produce antibodies against endothelial cells and develop emphysema. Anti-endothelial cell antibodies cause endothelial cell apoptosis *in vitro*. TUNEL assay and activated caspase-3 Western blot and immunostaining showed more cells undergoing cell death in immunized animal lungs than in control rat lungs. There is a significant up-regulation of matrix