

Correspondence

The crucial task of defining a healthy immune response toward respiratory infections

To the Editor:

In a recent publication, King et al¹ obtained heterogeneous populations of total primary lung cells from patients with chronic obstructive pulmonary disease (COPD) and smokers with normal lung function and stimulated them *ex vivo* with a common bacterium in COPD, that is, nontypeable *Haemophilus influenzae* (NTHi). These assays mainly showed that resident lung T cells of patients with COPD produce more TNF- α and IL-13 than do those of smokers without COPD, albeit similar IFN- γ .¹ The authors conclude that this type of T-cell-derived cytokine response promotes inflammation and impedes bacterial clearance in COPD. However, some issues are worth commenting on.

First, most of the T cells that reside in the lungs are memory T cells, which respond more rapidly and vigorously to their cognate antigens than do naive T cells.² NTHi is a common bacterium in COPD, and NTHi-specific memory T cells, expected to exist in the lungs of patients with COPD but not in the lungs of healthy subjects, will be stimulated by NTHi only in patients with COPD. Second, the lungs of patients with COPD contain higher numbers of antigen-presenting cells (APCs), such as macrophages, B cells, and langerin⁺ dendritic cells, than do the lungs of healthy subjects.³ The higher APCs-to-T cells ratio in patients with COPD may cause increased cytokine production by lung T cells. This bias could be overcome if lung T cells were isolated and stimulated by NTHi at a single APC-to-T cell ratio for all subjects.

Despite the fact that the study designed by King et al was biased toward increased stimulation of lung T cells in COPD, the master effector cytokine of T helper cells, that is, IFN- γ , was produced at similar levels between patients with COPD and smokers without COPD. This was unexpected, as the numbers of IFN- γ expressing T_H1 cells are higher in COPD. However, experimental respiratory rhinoviral infection induces lower pulmonary IFN- γ levels in patients with COPD than in healthy smokers and secondary bacterial infection.^{4,5} Furthermore, animal emphysema models and *in vitro* functional immunologic assays suggest that cigarette smoke possesses proinflammatory, yet immunosuppressive properties.⁶ Taken together the data obtained by King et al with these

data underscore the notion that antigen-specific lung T-cell responses are less efficient in clearing pathogens in patients with COPD than in healthy subjects.

But the question that we as respiratory physicians are really interested in answering is “Do patients with COPD get sicker because their lung T-cell responses toward respiratory pathogens fail to clear pathogens?” A scanty immune response would increase vulnerability to pathogens, yet an overly immune response could cause damage.⁷ Whether scanty T cell-mediated antigen-specific immune responses in patients with COPD are “unhealthy” or whether they represent a mechanism used by the respiratory system to reduce the impact of persistent/frequent respiratory infections would be an excellent area of future research.

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Disclosure of potential conflict of interest: M. Tsoumakidou declares that she has no relevant conflicts of interest.

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<http://dx.doi.org/10.1016/j.jaci.2013.01.038>