

Correspondence

Reply

To the Editor:

Professors Upham and Pritchard¹ raise 2 very interesting and interrelated questions about our recent work published in the Journal.² The first concern relates to the perceived lack of information in Fig 4 regarding the source of cells used in the coculture experiments in which we measured cytokine responses of T cells activated with monocyte-derived dendritic cells. We should note that the data presented in Fig 4 are based on coculture of the conditioned monocyte-derived dendritic cells (the source of which is described in Fig 3) and autologous T cells; thus, the source of T cells and monocyte-derived dendritic cells is the same patient for each coculture. To avoid redundant information, we did not give demographics of T cells because they are identical to the source of cells shown in Fig 3 and instead described monocyte-derived dendritic cell-induced T-cell activation in the Methods section. We hope that this information clarifies any confusion regarding the source of cells used in Fig 4. Regarding differences in the assays performed in Figs 3 and 4 between control subjects and subjects with chronic obstructive pulmonary disease, none were observed, which is why we combined results from the 2 groups.

The second concern raised relates to the viral specificity of the T_H2 immune skewing in acute exacerbation of chronic obstructive pulmonary disease in comparison to other microbial causes. Our study was not powered to analyze data separately from Figs 1 and 2 according to individual culture results. Moreover, we did not examine *in vitro* the immune responses to other potential microbial causes of chronic obstructive pulmonary disease exacerbation such as *Haemophilus influenzae*.³ This is because previous studies have convincingly shown that extracts of this organism induce a highly polarized T_H1 immune response, even in atopic subjects.^{4,5} Instead, we analyzed the immune response to rhinoviral proteinases *in vitro* and *in vivo* as a means of assessing whether these enzymes are specifically capable of inducing a T_H2 immune bias. In this regard and entirely in support of our main hypothesis, our data show that human rhinovirus (HRV) proteinase 2A can induce T_H2 differentiation via activation of dendritic cells. It is thus clear that proteinases from diverse sources including plants,⁶ fungi,⁷ and now viruses⁸ are all capable of triggering robust T_H2-biased

immune responses. This observation further provides molecular support for the experimental observation that rhinovirus airway infection induces allergic inflammation.⁹ Although airway hyper-responsiveness induced by rhinovirus-triggered T_H2 responses may produce a temporary change in the respiratory rate or slight wheezing in healthy subjects, in those with significant respiratory compromise, the added airway narrowing may be enough to precipitate respiratory failure.

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