

Correspondence

Reply

To the Editor:

We read with great interest the report by Bratke et al¹ stating that thrombomodulin expression is increased on bronchoalveolar lavage plasmacytoid dendritic cells (pDCs) after segmental allergen challenge in people with mild asthma. These observations extend our recent finding of allergen-induced thrombomodulin (BDCA3, CD141) expression on myeloid dendritic cells (mDCs) and its association with a T_H2-polarized response.²

It is well established that several blood dendritic cell antigens (BDCAs) can be used to define human pDC and mDC subsets.³ Thrombomodulin (BDCA3) is highly expressed on and used to define a minor subset of mDCs that lack CD1c, and are referred to as mDC2s. However, thrombomodulin is also expressed, albeit at much lower levels, on some mDC1s and on all pDCs (defined by BDCA1/CD1c and BDCA2, respectively). In our study of atopic asthmatic teenagers and healthy control subjects,² we reported that both mDC2 numbers and the intensity of thrombomodulin expression were increased in subjects with atopic asthma compared with that seen in nonatopic control subjects, whereas total mDC1 numbers (BDCA1/CD1c⁺) were similar in all groups.

Prompted by the observations of Bratke et al,¹ we have re-examined the mDC1 data from our study.² Interestingly, both thrombomodulin-positive mDC1 numbers ($P = .037$; Fig 1, A) and the intensity of thrombomodulin expression ($P = .007$; Fig 1, B) were significantly increased in atopic asthmatic subjects compared with those seen in the nonatopic group. However, the number of thrombomodulin-positive pDCs (Fig 1, C) and the intensity of thrombomodulin expression (Fig 1, D) on pDCs were similar in all groups.

Although there are differences in the experimental approaches used by ourselves and Bratke et al,¹ our 2 studies are indeed complementary, both pointing to a previously unappreciated role for thrombomodulin on multiple dendritic cell subsets in the pathogenesis of allergic asthma. Further studies are clearly needed to examine the mechanisms regulating thrombomodulin in allergic inflammation, including the role of microenvironmental factors within the airway epithelium, because bronchoalveolar lavage fluid pDCs show enhanced thrombomodulin expression compared with blood pDCs,¹ suggesting that pDCs might upregulate thrombomodulin when recruited into the airways.

We reported increased thrombomodulin expression in response to house dust mite allergen *in vitro*² and have questioned whether other allergens would have a similar effect. The current report¹ goes some way to addressing this issue by using both house dust mite ($n = 6$) and birch allergen ($n = 4$) airway challenges. Although it does appear that all patients had increased thrombomodulin expression on bronchoalveolar lavage fluid pDCs, irrespective of the allergen challenge, this preliminary report will need to be confirmed in a larger study so that the separate effects of various allergens on thrombomodulin can be statistically analyzed. Overall, the study of Bratke et al¹ supports our initial finding of allergen-induced thrombomodulin expression, extending it to include pDCs within the lung. This highlights an important and novel role for thrombomodulin expression on multiple dendritic cell subsets in the pathogenesis of asthma, a story that is just beginning to emerge.

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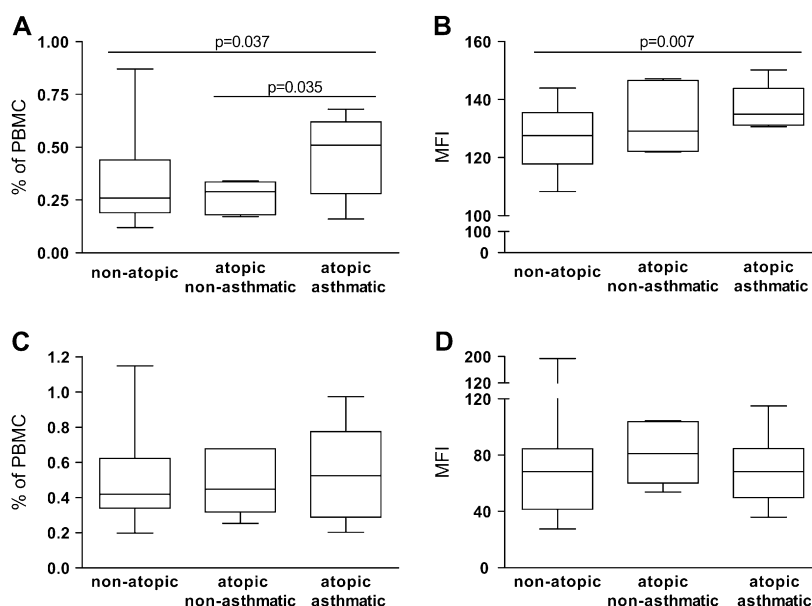


FIG 1. Thrombomodulin expression on blood mDC1s and pDCs. Data are from nonatopic control subjects ($n = 19$), atopic nonasthmatic subjects ($n = 6$) and atopic asthmatic subjects ($n = 11$). **A**, Number of thrombomodulin-positive mDC1s. **B**, Thrombomodulin mean fluorescence intensity (MFI) on mDC1s. **C**, Number of thrombomodulin-positive pDCs. **D**, Thrombomodulin MFI on pDCs. Box and whisker plots are shown. P values were determined by using the Mann-Whitney U test.

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