

controls: 50% vs 70%) were found, which is also consistent with our previous report.²

The discrepancies noted between our results and those of Zhang et al^{1,3} are not unique. Contradictory results of TGF- β 1 and Foxp3 expression levels in both healthy and inflamed nasal tissues have been reported in the literature.⁶

Our classification of chronic rhinosinusitis with nasal polyps (CRSwNP) into eosinophilic and noneosinophilic subgroups on the basis of eosinophil count in the polyp tissue,² a commonly used histologic assessment, was questioned by Zhang et al¹ because they assumed that eosinophils identified in CRSwNP samples may not be activated.³ However, we believe that measuring eosinophilic cationic protein levels in tissue homogenates as described in the study by Zhang et al³ may be not a reliable way to confirm the activation state of eosinophils.⁷ First, eosinophilic cationic protein is found not only in eosinophils but also in neutrophils.⁸ Second, such measurement is unable to differentiate between secreted (an indicator of cell activation) and intracellular eosinophilic cationic protein. In additional support of our classification method, using our classification criteria, 2 distinct types of CRSwNP with different immunopathologic phenotypes were revealed.²

With respect to criticisms regarding statistical analysis, although 5 groups were included in Fig 1 in our article,² the comparisons were made only among controls, CRSsNP, and CRSwNP, and among controls, CRSsNP, and noneosinophilic and eosinophilic CRSwNP.

We agree with the comment that our mRNA data need to be confirmed at the protein level. Nevertheless, the weak expression intensity of these markers may represent a significant obstacle to reliable quantitative analysis. To attain a definitive conclusion about TGF- β 1 and Foxp3 in chronic rhinosinusitis, we believe not only that more sensitive protein detection techniques should be used, but also that more proteins need to be assessed in what is obviously a highly complex network.

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Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

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Available online January 11, 2010.
doi:10.1016/j.jaci.2009.10.016

Evaluation of meta-analyses about sublingual immunotherapy in allergic respiratory diseases

To the Editor:

I would like to clarify some points raised by Nieto et al¹ regarding the systematic review by Calamita et al² about the efficacy of sublingual immunotherapy in asthma. In accordance with the Cochrane handbook,³ for analysis of continuous outcome through intention-to-treat methods, it is required that means and SDs are available for all participants; however, this unfortunately did not happen. Although attempts were made to contact the authors to get the necessary information, in some cases no responses were obtained. In these cases, we decided to extract the SDs from *P* values through indirect calculation following guidance from the Cochrane handbook.³ Because of this, in our meta-analyses,² the continuous outcome was performed in relation to the patients who finished the treatment, albeit the categorical outcomes were analyzed according to intention-to-treat methods. Most of the conflicting data among our review² and other studies happened when the SD was indirectly estimated.

I believe, as shown in Fig 2 by Nieto et al,¹ some caution is required in the funnel plot interpretation because the trim and fill method has been proposed to correct the publication bias. The heterogeneity may also lead to funnel plot asymmetry and, in our review,² we found significant heterogeneity among the studies, which in part was explained by the wide variety of scoring systems for outcomes used in different studies.

In conclusion, many discrepancies found by Nieto et al¹ related to our review² may have resulted from the manner the data in articles (mainly the SDs) were obtained. Despite these conflicting data, our review conclusion² points toward the position of Nieto et al¹ in respect to the lack of robustness of evidence on the efficacy of sublingual immunotherapy in asthma and the need for further studies on this subject.

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Disclosure of potential conflict of interest: The author has declared that he has no conflict of interest.

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doi:10.1016/j.jaci.2009.11.021