The many abilities of omalizumab and the unbeaten path

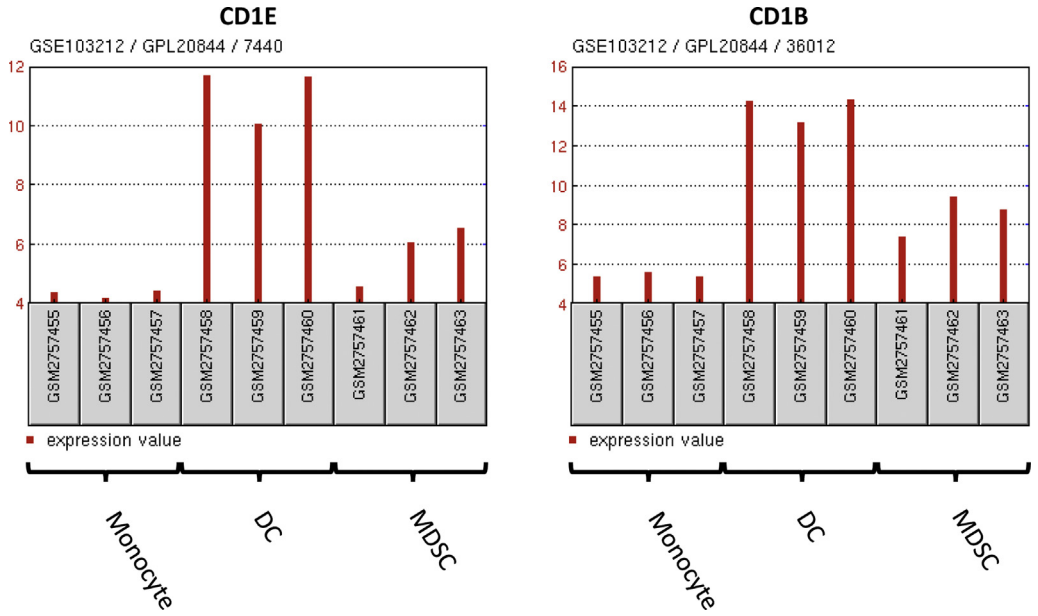

FIG 1. Gene expression levels of CD1E and CD1B in monocytes, DCs, and MDSCs from GSE103212 displayed using GEO2R.

approach when considering deconvolution and to incorporate as many cell types as possible. Finally, we would suggest that because deconvolution is a method of statistical inference, a compelling approach to confirm, refute, or extend our results would be to consider cell sorting and/or single-cell analyses informed by deconvolution results.

The readers' second question states that because our samples were not collected simultaneously, the length of time and/or condition of storage of the RNA could affect the results. Because all RNA samples were stored at −80°C, and all samples had been stored for between 7 and 9 years when the RNA was extracted, we are doubtful whether there was a major differential effect introduced by differing lengths of storage on RNA quality or measured expression levels. Nevertheless, if there were an effect because of the length of storage, this is balanced across the 4 outcome groups in our study so would not be a source of bias in our comparisons. Finally, we did observe that the timing of sample collection was a source of variability in RNA expression but not RNA quality, so we concluded that there was technical variability across time in PBMC stimulations as opposed to RNA preservation. We did therefore account for timing of sample collection in our analyses, and so if there was a subtle effect on data variability from the length of time of storage, we have already accounted for it in our analysis.

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The many abilities of omalizumab and the unbeaten path

To the Editor:

We appreciated the article by Cardet and Casale,[1] who focused on the current status of omalizumab treatment in its authorized applications (ie, severe allergic asthma not controlled by standard therapy and chronic spontaneous urticaria not controlled by antihistamines), as well as off-label use in a number of other IgE-mediated or non–IgE-mediated diseases.

Severe uncontrolled asthma remains the major indication for omalizumab treatment, which was long ago added to step 5 therapy in the Global Initiative on Asthma (GINA) guidelines. In the GINA 2017 update, also sublingual immunotherapy with registered dust mite tablets was added as an option in steps 3 and 4

in adult patients with mite allergy "who have exacerbations despite ICS [inhaled corticosteroids], provided FEV_1 is > 70% of predicted lung function."[2] Indeed, uncontrolled asthma is a contraindication to allergen immunotherapy,[3] and therefore omalizumab, based on its capacity to control asthma in patients not responding to standard drug treatment, is a candidate to overcome such a contraindication and to work as a synergic agent when immunotherapy is indicated. In fact, Cardet and Casale[1] included "Facilitation of subcutaneous immunotherapy to aeroallergens" in the indications by quality of supportive evidence.[1]

A recent review analyzed the available literature, which comprises only open studies, on the use of omalizumab as an adjunct to allergen immunotherapy. Omalizumab was able to improve the safety of immunotherapy, but the authors claimed larger, randomized, placebo-controlled trials aimed at identifying patients with the highest response to omalizumab treatment, optimal dosing strategies, and the duration of treatment.[4] Actually, despite reports of some persistence of the efficacy of omalizumab after stopping treatment,[5] there is no evidence on the optimal duration allowing withdrawal. Clear evidence is available instead for allergen immunotherapy, with a duration of 3 to 5 years being agreed upon in consensus documents.[6] This crucial outcome is produced by the mechanisms of allergen immunotherapy, which substantially reverse the immune response typically occurring in allergic subjects toward tolerance.[7] Hence it is surprising that the ideal sequence for treating patients with severe allergic asthma was overlooked thus far. Such a sequence would consist of an initial treatment with omalizumab to achieve disease control, thus allowing, when the contraindication is overcome, immunotherapy. Once asthma control is achieved through immunotherapy, omalizumab could be withdrawn to finally complete the treatment when the optimal duration of immunotherapy is reached.

Notably, use of immunotherapy is now supported by the updated GINA guidelines, at least in patients with asthma induced by dust mites,[2] which are the most common cause of respiratory allergy worldwide. We believe that studies addressing the synergy of omalizumab in combination with allergen immunotherapy to achieve long-term effectiveness are warranted to prove the rationality of this model.

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Reply

To the Editor:

Incorvaia et al[1] have commented that "studies addressing the synergy of omalizumab in combination with allergen immunotherapy to achieve long-term effectiveness are warranted to prove the rationality of this model."

We agree with the correspondents that additional studies are needed to clarify the optimal conditions and patient selection for the combination of allergen immunotherapy with omalizumab. As stated in Table I of our article,[2] there is only moderate-quality data to support the facilitation of subcutaneous immunotherapy to aeroallergens.

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Corrigendum

With regard to the article in the January 2019 issue entitled "Anti–IL-5 treatments in patients with severe asthma by blood eosinophil thresholds: Indirect treatment comparison" (J Allergy Clin Immunol 2019;143:190-200.e20), the authors report that in Table II (summary of baseline characteristics), the exacerbation data for the benralizumab studies (SIROCCO and CALIMA) were incorrectly reported as not available. The omission of these baseline data from the paper did not impact the analysis, results or conclusions of this paper. The error has been corrected in the online version of the article. The authors apologize for the error.