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REPLY TO LETTER TO THE EDITOR

Allergen-stimulated production of intracellular ROS in neutrophils: Yes but questions remain

We thank Drs. Monteseirin and Vega for their Letter (in this issue), and we agree the absence of extracellular reactive oxygen species (ROS) production in response to anti-IgE in our study [1] is not inconsistent with their finding of intracellular ROS production [2]. The use of different methods by us (reduction of cytochrome c) and by Drs. Monteseirin and Vega (luminol-based luminescence) to measure ROS production provides a plausible explanation for the two sets of results, as described in their letter. Indeed, Drs. Monteseirin and Vega provided good evidence for NADPH-dependent production of intracellular ROS in response to stimulation by anti-IgE or specific allergen extract in their study [2]. We did not assess intracellular ROS production, but instead used their findings as a rationale in our study [1] to assess release of extracellular ROS.

The larger question that remains for us is if and how liganded IgE mediates ROS production, either intracellularly or extracellularly. Drs. Monteseirin and Vega speculated previously [3] that allergens triggered intracellular (luminol-dependent) ROS production via a galectin-3-IgE interaction. Our study focused, instead, on assessing a role for IgE-liganded FcεRI in neutrophil activation [1]. The finding that the levels of both neutrophil FcεRI expression and neutrophil-bound IgE were at or near background levels [1] creates uncertainty regarding a role for IgE-liganded FcεRI, or bound IgE in general, in neutrophil activation. The methodology we used suggested no statistically significant signal but to be fair about the limits of the method for some samples, we estimated an upper bound of 1500 molecules/neutrophil. This consideration is particularly relevant to allergen-induced ROS production. Though the levels of allergen-specific IgE as a percentage of total IgE vary widely among the population, allergen-specific IgE constitutes, on average, 1% of total IgE [4,5]. With this as a typical value, there might be, at best, only 15 molecules of antigen-specific IgE per cell. An ability to respond to this level of aggregation would make the neutrophil considerably more sensitive to this route of stimulation than a basophil.

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