We thank Fattori et al. (1) for their positive comments on our report (2). Their letter (1) contains much useful information on possible additional biological effects of IL-33. However, the publications discussed in the text and figure 1 in the Fattori et al. (1) letter do not directly address our findings.

Moreover, the data in our report came only from human cultured mast cells (2), while the studies in the letter (1) discuss mostly experiments in rodents that do not reflect human inflammatory conditions (3, 4).

We are taking this opportunity to highlight the importance of substance P (5) and IL-33 in human diseases (6). New findings presented include the facts that: (i) mast cell-derived tryptase can cleave extracellular IL-33 into mature active forms (7); (ii) such IL-33 isoforms may have additional abilities to activate mast cells, thus promoting inflammation (8); and (iii) human mast cells stimulated by either antigen or IL-33 can also release soluble ST2, which may modulate the biological effect of IL-33 (9).

The ability of the natural flavonoid tetramethoxyluteolin to inhibit mast cells stimulated by either IL-33, substance P, or their combination (2), which we report in our paper, has now been validated in a pilot clinical trial: a skin lotion containing tetramethoxyluteolin was shown to reduce skin inflammation in patients with atopic dermatitis and psoriasis (10).


