*From the authors:*

We thank S. Hart for some important observations about our paper [1], and we concur that while we have postulated that the effect obtained with fluticasone could be related to apoptosis as one possible mechanism, we have not established the initiating mechanism of the interaction between $\beta_2$-adrenoceptor activation and flucticasone. In a prior publication, we used TUNEL assay [2], which showed no effect on apoptosis at 24 h for eosinophils incubated in an identical manner, as for the study in the current paper. Annexin-I synthesis increased at 24 h and further increased at 48 h in that study. We have not tested annexin-V or other potentially more sensitive means of detecting early apoptosis, as this was not the point of the paper. The hypothesis of the paper was that eosinophil adhesion, which is blocked partially (or not at all at low concentrations of fluticasone), would be blocked additively or synergistically by 30 min incubation with salmeterol. The addition of salmeterol for such a short period would not likely accelerate apoptosis in cells already exposed to fluticasone for 24 h. On the contrary, salmeterol has been shown to decrease apoptosis in eosinophils [3].

Rather than early apoptosis, our paper evaluated the ability of three different essential steps for eosinophils adhesion: 1) CD11b upregulation; 2) $cPLA_2$ phosphorylation; and 3) $cPLA_2$ translocation to the nuclear membrane. Neither of the first two processes was affected by fluticasone at 24 h, whereas the third process was blocked selectively. While it is possible that early apoptosis could theoretically cause selective blockade of one of the three major processes regulating adhesion, we think that is unlikely, especially in view of the acute augmentation effect of salmeterol. Nonetheless, we acknowledge that this remains a possibility and we also concur with editorial of Papi [4], suggesting that more work on the upstream mechanism of the anti-adhesive effects demonstrated in our paper is in order.

Finally, we agree that trypan blue and propidium iodide, while used by other investigators to assess "viability" [5], do not exclude apoptosis, which is an effect of fluticasone [6]. As noted above, we have verified previously that eosinophils treated in the presence of interleukin-5 for 48 h demonstrated other indices of retained cellular function, including leukotriene synthetic function. We agree that the term viability is meaningless; likewise it is difficult to make assumptions about cell physiological functions based on histological assessment of early stages of apoptosis. In the event that early apoptosis is the mechanism selectively blocking this single, but critical, step in adhesion, we now know which physiological step is blocked. By assessing cell physiological functions, we now have some notion of where to look upstream to further define the mechanism.

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