We appreciate Dr Schattner’s letter and comments on our recent review in Circulation Research outlining facets of platelets as effectors of inflammation in vascular diseases. Unfortunately, we did not have space for an in-depth discussion of all aspects of noncanonical and nongenomic activities of the nuclear family kappa B (NF-κB) pathway in these cells. In the introduction to our article, we noted the necessity of telegraphically profiling topics that had been previously discussed in a comprehensive or integrated fashion in the literature and, throughout the article, we cited recent reviews of many of these topics. One of these was the review of transcription factors in anucleate platelets by Spinelli et al, mentioned in Dr Schattner’s letter. The Spinelli review cites several reports mentioned by Dr Schattner that we did not include in our review because of space limitations.

We agree with Dr Schattner that there is evidence in recent published reports for both positive and negative modulation of specific platelet activation responses by NF-κB signaling. The example that we cited describes a previously unrecognized negative feedback mechanism for fine-tuning of integrin αIIbβ3 activation and aggregation of stimulated platelets by NF-κB–dependent signaling. Spinelli et al also interpreted these observations in this fashion and discussed them in this context. Based on reports cited by Schattner and Spinelli et al, several of which involve inhibitors that block the NF-κB pathway in other cell types, there may also be positive NF-κB–dependent signaling in activated platelets depending on the functional response(s) assayed and the experimental conditions chosen. Spinelli et al commented that additional work and a variety of experimental approaches will be required to fully characterize noncanonical activities of molecular members of the NF-κB pathway in activated platelets. As noted by Dr Schattner, several additional studies have been reported since that time but were not included in our brief synopsis of this topic.

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References
Reply to Schattner
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