Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Role of NF-κB Pathway on Platelet Activation

To the Editor:

I have read with great interest the review by Rondina et al[1] on "Platelets as Cellular Effectors of Inflammation in Vascular Diseases" recently published in the *Circulation Research* Journal.[1] Although I consider that it is a detailed and updated review on the role of platelets in the inflammatory and immune response, I am surprised by the vague and partial information about the expression and nongenomic role of the nuclear transcription factor-kappa B (NF-κB) in platelets.

The authors mention that platelets express several NF-κB proteins and that a complex of NF-κB, inhibitor of κB, and protein kinase A was reported to exert negative feedback activities that modulate cytoskeletal reorganization and aggregation in platelets stimulated by thrombin or collagen. The references for this concept are the articles of Gambaryan et al[2] and Spinelli et al.[3,4]

Remarkably, the study of Spinelli et al,[3] instead of showing a negative regulatory effect of NF-κB, claims the opposite. In fact, in the last sentence of the abstract, it is written "On the basis of these data, NF-κB is also identified as a new target to dampen unwanted platelet activation." The second article of Spinelli et al is just an editorial comment of the article published by Gambaryan et al.[2]

More important still, there is no mention of 7 other articles,[5–11] including a pioneer work from our group,[5] describing an opposite effect of NF-κB activation in platelets. In fact, using different strategies (including IkB kinase β knockout mice), these studies show that activation of NF-κB pathway promotes platelet activation.

Furthermore, the study of Wei et al[9] shows an interesting dual regulatory role of NF-κB on platelet activation. Although NF-κB activation initiates platelet activation, it also seems to be necessary for activated platelets to shed their surface glycoproteins. More specifically, NF-κB activation promotes a disintegrin and metalloprotease domain 17 (ADAM17)-mediated glycoprotein Ibα (GPIbα) shedding, limiting platelet interactions with leukocytes.

Simultaneously with the publication of the review by Rondina et al,[1] Karim et al,[12] using IkB kinaseβ knockout mice, show that IkB kinase phosphorylation of synaptosomal associated protein (SNAP)-23 controls platelet secretion. Collectively, all these data support the notion that NF-κB activation is increasingly recognized as a new signaling pathway in the regulation of platelet biology. However, it is clear that the underlying mechanisms of NF-κB function still remain to be established.

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