Insights into Release of Interleukin-1β from Platelets

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Platelets are key players in the crosstalk between inflammation and thrombosis. Therefore, insights that elucidate the mechanisms of platelet-dependent thromboinflammation are of high interest. Interleukin 1β (IL-1β) is mainly involved in NLRP3 inflammasome complex formation. IL-1β has been found to be an attractive target to suppress chronic vascular inflammation, thus improving prognosis in atherosclerotic disease.[1] Although controversial data exist, it has been proposed that resting platelets contain relevant amounts of preformed IL-1β. Besides their effects on inflammatory cells, IL-1 receptor and IL-1β play a role in megakaryocyte maturation and platelet activation.[2] The work by Pennings et al published in this issue adds to the current knowledge by shedding light on the mechanism of IL-1β release from platelets.[3] The authors convincingly demonstrated that preformed IL-1β protein can be released shortly within minutes after activation of platelets by ADP, protease-activated receptor (PAR)1, and PAR4-activating peptides. The process of IL-1β significantly correlated with the degree of platelet activation. Release of IL-1β was independent of extracellular NLRP3 activation as indicated by missing signals on NLRP3 expression/phosphorylation and caspase-1 activation. Still, it is unclear based on the performed ELISA experiments whether the protein is pro-IL-1β or mature-IL-1β and whether NLRP3 or caspase-1 is involved in the formation of intracellular pro-IL-1β. Although repeatedly demonstrated that platelets despite being anucleate are capable of de-novo protein synthesis, the question about the source of intraplatelet IL-1β is still a matter of debate. The potential translational aspects of the findings warrant further investigation. Besides the role of IL-1β inflammasome activation for leukocyte production and recruitment in atherosclerosis,[4] what is the function of inflammasome-independent platelet IL-1β? Are the detected concentrations high enough to convey substantial cellular signals and to promote alterations in the vascular environment? Experiments in mouse models indicate that IL-1β can induce thrombocytosis, suggesting that platelets could support an inflammatory feedback loop by amplifying IL-1 signaling and triggering platelet biogenesis.[5] Whether platelet-derived IL-1β contributes to this loop in the human system and what clinical impact targeting platelet IL-1β might have require deeper insight.

Conflict of Interest
None declared.

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