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. 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. 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. 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, 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. 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.

References

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