LETTER TO THE EDITOR

Platelet-derived microparticles cause CD154-dependent activation of dendritic cells

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To the Editor

Platelets represent an important linkage between inflammation, thrombosis and atherosclerosis [1]. Platelet-induced chronic inflammatory processes at the vascular wall result in development of atherosclerotic lesions and atherothrombosis [2]. In addition, accumulating evidence from recent studies indicates an additional role in modulating adaptive immune responses [3, 4]. Platelets express many immune mediators such as cytokines and chemokines. Furthermore, only a few researchers have suggested that platelet-derived CD154 has the ability to promote protective adaptive immune responses [5].

Dendritic cells (DCs) sense immune adjuvants through pathogen sensors and are critical for linking innate and adaptive immunity [6, 7]. In humans, myeloid DCs and plasmacytoid DCs represent two major subsets of DCs. They play distinct roles in innate and adaptive immune responses through expression of their specialized cytokines and molecules [8].

Platelet activation by various agonists or shear stress results in the shedding of platelet-derived microparticles (PDMPs) [9]. Early studies showed that PDMPs are an important source of integrins and selectins for leukocyte attachment to endothelial cells, which is a process that is important for recruitment to and transmigration at sites of injury [10, 11]. In addition, platelets and PDMPs are known to modulate the activity of cells with which they interact, including monocytes, neutrophils, and endothelial cells [9–11]. However, the role of PDMP on DC activation is poorly understood. We investigated the effect of PDMPs in DC activation focusing on the adaptive immune responses properties of PDMPs.

Human peripheral blood DC subsets (plasmacytoid DCs and myeloid DCs) were isolated from peripheral blood mononuclear cells from healthy adult donors, as described previously [12]. We examined whether DC subsets are activated in the presence of thrombin receptor activating peptide (TRAP)-stimulated platelets or PDMPs. DC subsets were cultured with TRAP-stimulated platelets or PDMPs for 24 h, and the expression of some molecules such as CD40, CD80, CD83, CD86 and HLA-DR was analysed by flow cytometry.

We found that, although TRAP-stimulated platelets could induce up-regulation of some molecules such as CD40, CD80, CD83, CD86 and HLA-DR to some extent, the addition of PDMPs further increased this expression compared with expression induced by TRAP-stimulated platelets or PDMPs for 24 h, and the expression of some molecules such as CD40, CD80, CD83, CD86 and HLA-DR was analysed by flow cytometry.

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Several reports have suggested that T cell-derived CD154 contributes to the modulation of adaptive immunity. For example, CD154 is crucial for the development of T cell-dependent humoral immune responses during CD4+ T cell-mediated activation of B cells [13]. However, immune responses in platelet-related CD154 are poorly understood. A report by...
Sprague et al. [5] has partially resolved this problem. They reported the modulation of adaptive immunity by PDMP-derived CD154 using B cells and T cells. Many immunologists countenance the participation of CD154 for immune responses [4]. Despite such a common understanding, the role for DC function of platelet-related CD154 remains unclear. In this report, we suggest that CD154 derived from both platelets and PDMPs can cause DC activation, although we could not demonstrate the role of soluble CD154 and the effect of CD function such as the production of cytokines by platelet-related CD154. Our findings on DC activation by PDMP-derived CD154 contribute to the understanding of adaptive immune responses by platelets.

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Notes: Plt, unstimulated platelets; Act Plt, TRAP-activated platelets; PDMP, platelet-derived microparticles; NC, no change; ↑, enhancement (10–30%); ↑↑, enhancement (>31%).

References