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REVIEW ARTICLE

Function and role of microparticles in various clinical settings

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Abstract

Microparticles released from cells (MPs) may play a role in the normal hemostatic response to vascular injury and a role in clinical diseases because they express phospholipids, which function as procoagulants. Although flow cytometry is the most widely used method for studying MPs, some novel assays such as tissue factor-dependent procoagulant assay or the ELISA mothod have been reported. However, the use of MP quantification as a clinical tool is still a matter of debate. Elevated platelet-derived MP, endothelial cell-derived MP, and monocyte-derived MP concentrations are documented in almost all thrombotic diseases occurring in both venous and arterial beds. However, the clear significance of MPs in various clinical conditions remains controversial. For example, it is not known if MPs found in peripheral blood vessels cause thrombosis, or whether they are the result of thrombosis. On the other hand, numerous studies have shown that not only the quantity but also the cellular origin and composition of circulating MPs are dependent on the type of disease, the disease state and medical treatment. In addition, many different functions have also been attributed to MPs. Thus, the number and type of clinical disorders associated with elevated MPs is currently increasing.

Contents

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Introduction

\Microparticles (MPs) are small membrane vesicles that are released from many different cell types by a process of exocytic budding of the plasma membrane [1–3]. During their formation, the symmetry of the plasma membrane lipid bilayer is altered, resulting in the exposure of a phospholipid rich surface. Because MPs disseminate various bioactive effectors originating from the parent cells, they can alter vascular function and may induce biological responses involved in vascular homeostasis [4,5]. Although most MPs in human blood originate from platelets, MPs are also released from leukocytes, erythrocytes and endothelial cells, albeit at much lower numbers [6–10]. Cell membrane MPs have been detected at small amounts in the blood of normal individuals. Elevated platelet-derived MP (PDMP), endothelial cell-derived MP (EDMP), and monocyte-derived MP (MDMP) concentrations are documented in almost all thrombotic diseases occurring in both venous and arterial beds [11–16]. In addition, elevated levels of MPs have been found in a number of conditions associated with inflammation, cellular activation and dysfunction, angiogenesis and transport [17–23]. However, whether MPs directly contribute to disease, or are merely a reflection of disease, remains to be determined. In this review, we will address the function of MPs, and present evidence for a dynamic role of MPs in various clinical settings.

Role of MPs in blood vessels

Composition of MPs

MPs can range in size from 0.02 μm to 0.1 μm, and they have no clear definition. It is unclear whether MPs arise from complete conversion of a few cells or from partial conversion of many or most cells, but it is likely that either process occurs. MP membrane composition reflects the membranous elements of the cell of origin (Table 1). George et al. [24] quantified many different glycoprotein (GP)s on PDMPs and many were present routinely, notably $\alpha_{IIb}\beta_3$ and GPIb/IX/V. Sims et al. [25] characterized PDMPs and reported the presence of $\alpha_{IIb}\beta_3$, GPIb/IX/V and P-selectin. In addition, an activation-dependent epitope of $\alpha_{IIb}\beta_3$ was found on complement-activated platelets but not on PDMPs [26]. Other researchers have also reported differences in the composition of membrane proteins between activated platelets and PDMPs [26–28].

PDMPs contain molecules in addition to GPs, such as platelet-activating factor [29], β-amyloid precursor protein [30], Ca^{2+}-dependent protease calpain [31,32], arachidonic acid [33] and many phospholipids [34–36], which are particularly important because they are involved in the function of PDMPs. Furthermore, it has been reported that

Table 1 Origin and antigens of MPs

Origin	Antigen
Platelet	CD42a (GPIX)
	CD42b (GPIb)
	CD41 (GPIIb/IIIa, $\alpha_{IIb}\beta_3$)
	CD61 (GPIIIa)
	CD62P (P-selectin)
Monocyte	CD14 (Endotoxin receptor)
Endothelial cell	CD31 (PECAM-1)
	CD51 (Vitronectin receptor, $\alpha_v\beta_3$)
	CD54 (ICAM-1)
	CD62E (E-selection)
	CD105 (Endoglin)
	CD144 (VE-Cadherin)
	CD146 (MelCAM)