The International Journal of Biochemistry & Cell Biology 50 (2014) 24–28

Contents lists available at ScienceDirect

The International Journal of Biochemistry & Cell Biology

journal homepage: www.elsevier.com/locate/biocel

Organelles in focus

Extracellular vesicles: New players in cardiovascular diseases

Abderahim Gaceb[a], Maria Carmen Martinez[a], Ramaroson Andriantsitohaina[a,b,*]

[a] INSERM UMR1063, Université d'Angers, Angers, France
[b] Centre Hospitalo-Universitaire d'Angers, Angers, France

ARTICLE INFO

Article history:
Received 15 November 2013
Received in revised form 14 January 2014
Accepted 26 January 2014
Available online 6 February 2014

Keywords:
Extracellular vesicles
Cardiovascular diseases
Vascular cells
Myocardium

ABSTRACT

Extracellular vesicles, particles released by all cell types, represent a new way to convey information between cells such as proteins, second messengers, and genetic information to modify the phenotype and function of the target cells. Recent data suggest that extracellular vesicles play a crucial role in both physiology and pathology, including coagulation, angiogenesis, cell survival, modulation of the immune response, and inflammation. Thus extracellular vesicles participate in the processes of cardiovascular diseases from atherosclerosis, myocardial infarction to heart failure. Consequently, extracellular vesicles can potentially be exploited for therapy, prognosis, and biomarkers for health and disease. This review focuses on the role of extracellular vesicles in the development of cardiovascular diseases, as well as the deleterious and beneficial effects that they may provide in vascular cells and myocardium.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Exchange of information between cells is attained through release of specific soluble signaling molecules or through direct cell-to-cell communication. In addition to these mechanisms, intercellular communication via extracellular vesicles (EV) has recently been identified as a conserved way during the evolution process. EV are particles heterogeneous in size (20–2000 nm) enclosed by a phospholipid bilayer, and released into extracellular medium of practically all cell types, both in vivo and in vitro. Up to now, three groups of EV have been mainly described depending on the mechanism of formation and physical characteristics: exosomes, microparticles and apoptotic bodies. Whereas exosomes are generated from the endosome-derived multivesicular bodies, both microparticles and apoptotic bodies are produced by budding from the plasma membrane (for review see Tual-Chalot et al., 2011; El Andaloussi et al., 2013). EV offer an elegant solution to cells to exchange biomolecules since, in one vesicle, it is possible to found lipids, proteins (receptors and enzymes), second messengers, mRNA, miRNA, and cell organelle fractions or proteins identified by proteomic analysis (Fig. 1). This leads to a new concept of EV as new cell organelles. Despite of these mix of components, EV possess specialized functions and play a key role in several pathologies by regulating coagulation, angiogenesis, cell survival, modulation of the immune response, and inflammation. The content and/or the number of EV depend on the cells they originate, the stimulus of production and the mechanism of vesicle generation. While quantification of the number of EV generated in vitro from a given number of cells is easy, the numeration of EV released by cells in vivo represents a huge challenge. This is particularly the case for non-circulating cells such as endothelial or smooth muscle cells. Nevertheless, Kanazawa et al. (2003) have shown that, in healthy subjects, 10^4 platelets can release 245 ± 11 microparticles whereas 10^4 monocytes release only 46 ± 7 microparticles. Other authors have shown that the number of platelet microparticles is significantly increased in diabetic patients (507 ± 15 per 10^4 platelets) (Ogata et al., 2005). Also, we have shown that the number of microparticles derived from activated leukocytes ($CD62L^+$) is increased in obstructive sleep apnea patients when compared to healthy subjects (being 75 and 45 microparticles released from 5×10^3 leukocytes, respectively) (Priou et al., 2010).

The mechanism of EV biogenesis represents very important criteria commonly used to classify different populations of EV. Thereby, two modes of EV biogenesis, "calcium-dependent" and "calcium-independent biogenesis" can be distinguished.

1.1. Calcium-dependent mechanism

This mechanism includes microparticle and apoptotic body formation. It has been demonstrated that shedding of microparticles from the cell plasma membrane into the extracellular space is initiated by an increase in the cytosolic concentration of calcium

* Corresponding author at: INSERM UMR 1063 "Stress oxidant et pathologies métaboliques", Institut de Biologie en Santé, 4 rue Larrey, F-49933 Angers, France. Tel.: +33 2 44 68 85 80; fax: +33 2 44 68 85 85.
E-mail address: ramaroson.andriantsitohaina@univ-angers.fr (R. Andriantsitohaina).

1357-2725/$ – see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.biocel.2014.01.018

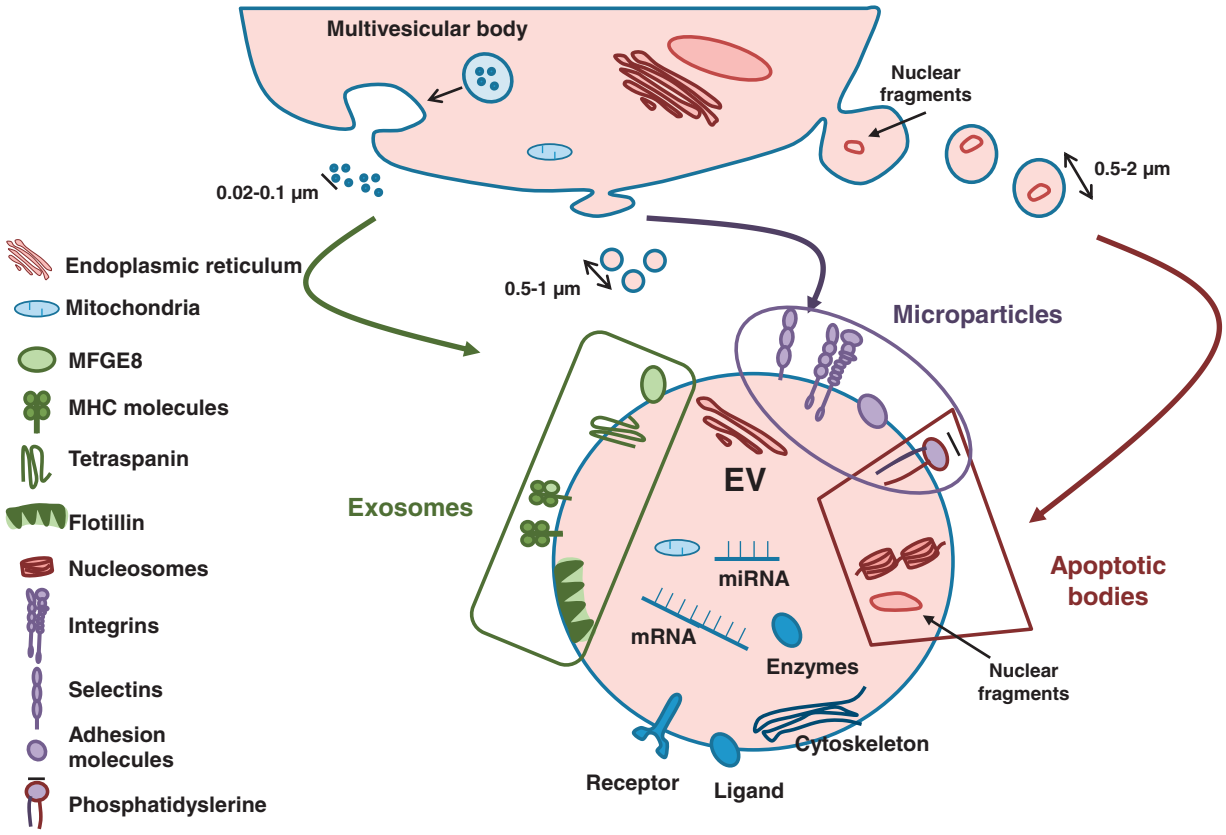

Fig. 1. Biogenesis and content of extracellular vesicles (EV). Exosomes are formed by the inward budding of the multivesicular body membrane, whereas both microparticles and apoptotic bodies are generated from plasma membrane. All three types of EV carry receptors, ligands, active enzymes, cytoskeleton-associated proteins, mRNA and miRNA (in blue). In brown, apoptotic bodies (diameter between 0.5 and 2 μm) are characterized by phosphatidylserine expression and nuclear components (nucleosomes, histones and nuclear fragments). In purple, microparticles (0.5–1 μm) carry phosphatidylserine, integrins, selectins and other adhesion molecules. In green, exosomes (0.02–0.1 μm) express tetraspanins, major histocompatibility complex molecules, flotillin and milk fat globule-epidermal growth factor 8. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

resulting from the influx of extracellular calcium. The increase of calcium ions activates calpain which leads to degradation of various cytoskeleton-associated proteins. Thus, the result of dynamic interplay between phospholipid redistribution and cytoskeleton reorganization leads to the membrane budding and EV release. In addition, microparticle release is often, but not always, preceded by the loss of membrane asymmetry resulting from local perturbation of the bilayer structure leading to phosphatidylserine exposure at the membrane surface that could contribute to plasma membrane destabilization and blebbing (for review see Martinez et al., 2011). Apoptotic bodies are generated during apoptosis resulting from calcium-sensitive factors compartmentalized in various intracellular organelles including endoplasmic reticulum and mitochondria. In this case, membrane blebbing is, in part, mediated, by actin–myosin interaction. Phosphorylation of myosin light chain by Rho kinase I, becomes constitutively active upon cleavage by caspase 3 and induces a net increase in membrane blebbing (Akers et al., 2013).

1.2. Calcium-independent mechanism

Exosomes are originated from the endosomal membrane cell compartment, and their release is subsequent to the exocytosis of multivesicular bodies into the extracellular space, after fusion with the plasma membrane. This mechanism is dependent on cytoskeleton activation, but independent of cytosolic calcium concentration.

Independently of the mechanism implicated in the EV generation, all types of EV are generated from a selective cellular process leading to significantly different selective enrichment of specific proteins, mRNA and miRNA. This is not the case of membrane particles from unspecific cell degradation. For instance, monocytes selectively package and secrete miRNA-150 into exosomes and deliver them to endothelial recipient cells where exmiRNA-150 modulates endothelial cell functions (Zhang et al., 2010). Also, microparticles from activated and apoptotic T cells harbor the morphogen Sonic hedgehog whereas those from apoptotic T cells do not (Martínez et al., 2006). Altogether, these findings illustrate that EVs are easily distinguishable from membrane particles from unspecific cell degradation.

The biological information is transmitted either by direct interaction between the vesicle membrane and the membrane of the recipient cell implicating ligand–receptor binding, fusion of the vesicle and target cell membranes, transfer of membrane constituents without fusion or by internalization of the vesicle content by the recipient cell. Consequently, vesicles can potentially be used for therapy, prognosis, and biomarkers for health and disease.

Here, we summarize the role of EV, independently of their types, on the maintenance of homeostasis of the cardiovascular system as well as their involvement in the development and maintenance of cardiovascular diseases.

2. EV and homeostasis of the cardiovascular system

Although the physiological role of EV is difficult to demonstrate, evidences show that EV possess specific effects due to their intrinsic composition and in addition, they may participate in regulating the

Download English Version:

https://daneshyari.com/en/article/8323596

Download Persian Version:

https://daneshyari.com/article/8323596

Daneshyari.com