European Journal of Cell Biology 90 (2011) 189–197

Contents lists available at ScienceDirect

European Journal of Cell Biology

journal homepage: www.elsevier.de/ejcb

Review

Podosome regulation by Rho GTPases in myeloid cells

Suzanne F.G. van Helden*, Peter L. Hordijk

Department of Molecular Cell Biology, Sanquin Research and Landsteiner Laboratory, Academic Medical Centre, University of Amsterdam, Plesmanlaan 125, 1066 CX Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 29 March 2010
Received in revised form 17 May 2010
Accepted 22 May 2010

Keywords:
Podosomes
Rho GTPase
Myeloid cell
Macrophage
Dendritic cell and osteoclast

ABSTRACT

Myeloid cells form a first line of defense against infections. They migrate from the circulation to the infected tissues by adhering to and subsequently crossing the vascular wall. This process requires precise control and proper regulation of these interactions with the environment is therefore crucial. Podosomes are the most prominent adhesion structures in myeloid cells. Podosomes control both the adhesive and migratory properties of myeloid cells and the regulation of podosomes is key to the proper functioning of these cells. Here we discuss the regulation of podosomes by Rho GTPases, well known regulators of adhesion and migration, focusing on myeloid cells. In addition, the regulation of podosomes by GTPase regulators such as GEFs and GAPs, as well as the effects of some Rho GTPase effector pathways, will be discussed.

© 2010 Elsevier GmbH. All rights reserved.

Introduction

The immune system comprises cells from the haematopoietic lineage, which can be subdivided into the lymphoid and the myeloid lineage. The latter derives from a common myeloid progenitor which gives rise to the megakaryocyte/erythrocyte progenitor and the granulocyte/macrophage progenitor (GMP). The GMP gives rise to various types of innate immune cells that form the first line of defense against infections. Neutrophils and monocytes are among the first to be recruited to sites of infection where they, as well as macrophages, phagocytose pathogens and secrete cytokines. Conversely, dendritic cells (DCs) detect and take up pathogens and present antigens to T cells, initiating an adaptive immune response.

A common feature of these cells is that they have to be able to migrate efficiently, from the blood across the endothelium into the tissue and within the stroma and parenchyma. In addition, DCs subsequently have to migrate into the lymphatics. For proper migration, regulated interactions with the endothelium and with the subendothelial extracellular matrix are crucial. As in other cells, integrins play an important role in myeloid cell adhesion and migration. The main integrin-based adhesion structures found in myeloid cells are podosomes. Similar as the functionally related focal adhesions in, e.g., fibroblasts, controlled formation, turnover and loss of podosomes is critical for adhesion and migration. As a result, podosome dynamics is key to the correct functioning of myeloid cells during inflammation and under static state conditions. Rho GTPases have been shown to regulate integrin function, vesicle transport and cytoskeletal dynamics in non-myeloid cells and are therefore excellent candidate regulators of podosomes in myeloid cells. Here, we review recent progress made in the understanding of podosome dynamics by Rho GTPases and their regulators.

Invadosomes

Invadosomes are matrix-degrading cell adhesion structures, such as podosomes and invadopodia. Podosomes and invadopodia share many structural components (Ayala et al., 2006), however, the ability to degrade matrix is more pronounced in invadopodia. It remains to be established whether podosomes and invadopodia are different structures or representations of the same structure in different cell types.

Podosomes

Podosomes are cell–matrix adhesion structures consisting of a bundle of actin perpendicular to the membrane surrounded by a ring-like structure containing integrins and adaptor proteins (Fig. 1 shows examples of ring and core components). Deeper within the cell, the actin bundle connects to radiating actin fibers. Podosomes are about 0.5 μm wide and high and are very dynamic structures with a half-life of less than 10 min. Podosomes are found in myeloid cells, endothelial cells, smooth muscle cells and transformed fibroblasts (David-Pfeuty and Singer, 1980; Kaverina et al., 2003; Marchisio et al., 1984; Moreau et al., 2003; Tarone et al.,

* Corresponding author. Tel.: +31 20 5123213; fax: +31 20 5123474.
E-mail address: s.vanhelden@sanquin.nl (S.F.G. van Helden).

0171-9335/$ – see front matter © 2010 Elsevier GmbH. All rights reserved.
doi:10.1016/j.ejcb.2010.05.008

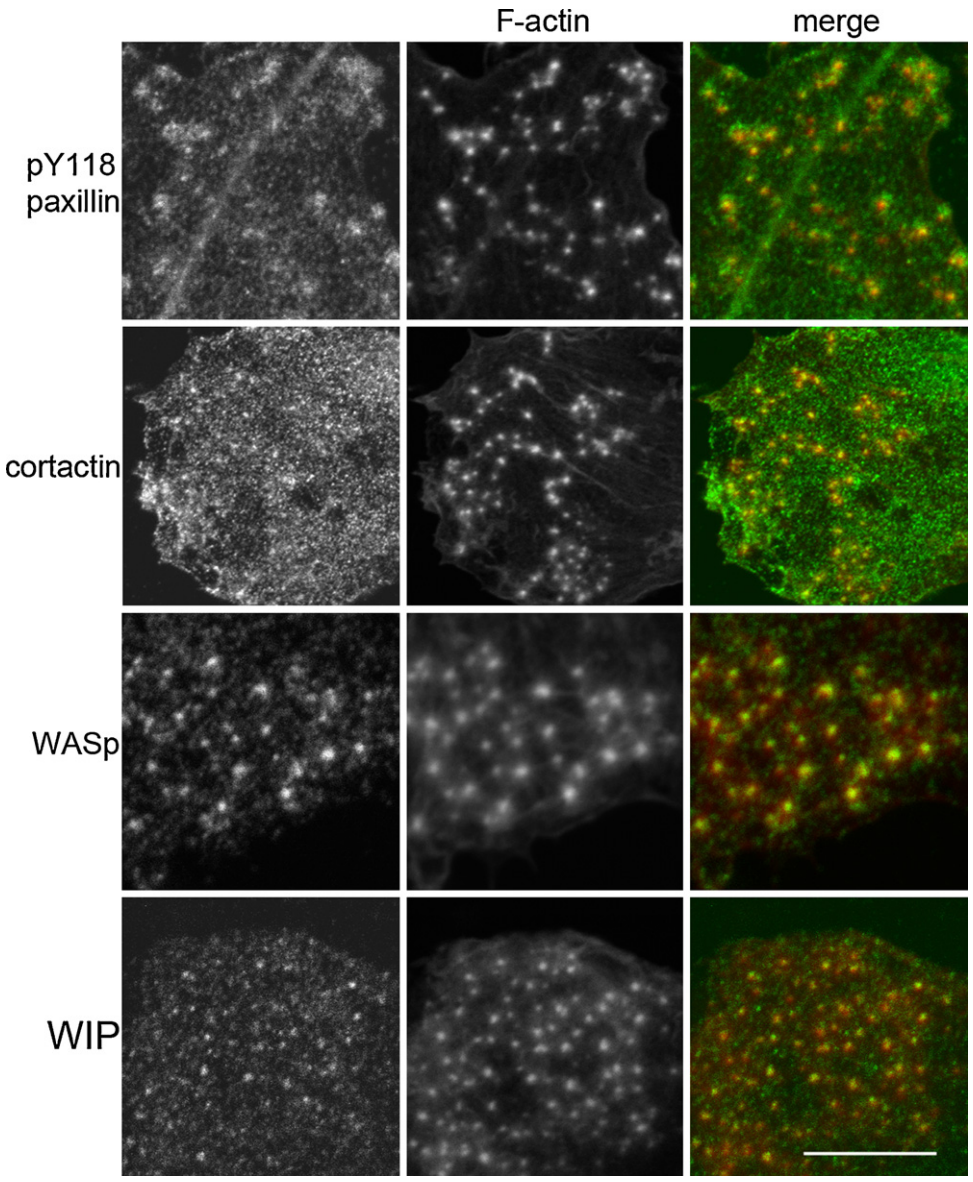

Fig. 1. Localization of podosome components. Immature DCs seeded on fibronectin-coated coverslips were stained with rabbit anti-pY118paxillin (Invitrogen, Praisley, UK), mouse anti-cortactin (Millipore, Billerica, MA), rabbit anti-WASp (Cell signaling, Beverly, MA) or goat anti-WIP (Santa Cruz Biotechnology, Santa Cruz, CA) (green in merge, all secondary antibodies were derived from Invitrogen) and phalloidin-TxRed (Molecular Probes, Invitrogen) to stain F-actin (red in merge). Images were obtained by confocal microscopy using a Zeiss LSM 510-meta microscope with a Plan-Apochromatic 63 × 1.4 NA oil immersion objective (Carl Zeiss, Jena, Germany). Cortactin, WASp and WIP are examples of podosome components that localize to the F-actin containing podosome core, while paxillin, in this case phosphorylated at Y118, localizes to the podosome rings surrounding the cores.

1985). Cells locally degrade the matrix underneath podosomes and this is due to metalloprotease activity, especially MT1-MMP, MMP2 and MMP9 (Cougoule et al., 2010; Mizutani et al., 2002; Nermut et al., 1991; Tatin et al., 2006).

There is scarce information on the pathways and stimuli that drive podosome formation in various cell types. However, Arp2/3 mediated actin nucleation, myosin II-controlled cell contraction and an intact microtubule system are important for podosome regulation (Burgstaller and Gimona, 2004; Clark et al., 2006; Kaverina et al., 2003; Kopp et al., 2006). Src kinase activity is sufficient for podosome formation, as illustrated by the ability of fibroblasts transformed with v-Src to form podosomes, while untransformed fibroblasts are unable to form these structures (David-Pfeuty and Singer, 1980; Tarone et al., 1985). The importance of Src is further underscored by the finding that Src−/− mice have severe osteopetrosis coupled to a lack of podosomes in osteoclasts (Soriano et al., 1991).

Smooth muscle cells can form podosomes in response to PDBu stimulation (Kaverina et al., 2003), which are thought to function in tissue remodeling and repair. In endothelial cells, podosomes form in response to stimulation with phorbol ester (Tatin et al., 2006), TGFβ (Varon et al., 2006), VEGF or TNFα (Moreau et al., 2003; Osiak et al., 2005) and are important for the degradation of basement membrane (Rottiers et al., 2009). Cells of the myeloid lineage are special as these are the only cells capable of podosome formation upon adhesion without additional stimulation or transformation (Burns et al., 2001; Linder et al., 1999; Marchisio et al., 1984). In myeloid cells, podosomes are the main adhesion structures and they are important for adhesive and migratory behavior of these cells.

Download English Version:

https://daneshyari.com/en/article/8470057

Download Persian Version:

https://daneshyari.com/article/8470057

Daneshyari.com