Endosomal compartments interact with the exocytic organelles Weibel Palade Bodies in a Rab27-dependent manner

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ABSTRACT

Endocytosis is a process that takes up molecules from the plasma membrane and the extracellular space and delivers them to the endosomes and lysosomes. Besides its role in degrading internalised molecules in the lysosomes, endocytosis of growth factor receptor/ligand complexes plays fundamental role in controlling the nature, intensity and duration of the signaling process.

The exact opposite route of endocytosis is the pathway of exocytosis, which delivers molecules to the plasma membrane or secrets them to the extracellular space. This route plays critical role in central cellular functions, such as immune response, neurotransmission, blood clot formation, differentiation, cell migration, etc. Especially in endothelial cells, the exocytic organelles Weibel-Palade bodies (WPBs) are of vital importance, as they secrete the homeostatic protein von Willebrand factor (vWF) and other cargo proteins that contribute to hemostatic plug formation, inflammation, angiogenesis, and tissue repair[1]. To accomplish secretion of their cargo molecules, WPBs undergo maturation, transport and fusion with the plasma membrane. Although a number of molecules have been found to be involved in these steps, Rab GTPases are the most critical in controlling the specific targeting and fusion with the plasma membrane[2].

Given the opposite direction of endocytosis and exocytosis, these two pathways have been studied so far separately, as independent processes. However, these two pathways may not be as independent as they were initially considered, since, for example, specialised cargo molecules may get transferred from endocytic to exocytic organelles, and vice-versa. Here we tested the possibility that endosomes interact with WPBs, in endothelial cells. We show that early endosomes that are positive for EEA1 interact with WPBs (revealed by the cargo molecule vWF). Since EEA1 is a surface marker of early endosomes, we also tested whether this interaction is also seen when lumenal cargo markers are internalised. Indeed, internalised GFP (as a fluid phase marker) revealed contact points between early endosomes and WPBs. Given that Rab27a has a major role in WPBs maturation and exocytosis[3], we tested the role of this GTPase in the formation of contacts between EE and WPBs. Interestingly, knockdown of Rab27a increased 17-fold the number of contacts between these organelles, suggesting an involvement of this Rab in the formation of the contact sites.

Altogether, these data unravel a novel crosstalk between the endocytic and exocytic organelles and suggest an involvement of Rab27 in this communication process.

REFERENCES

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