Traffic. 2016 Nov;17(11):1181-1196.

Rab24 interacts with the Rab7/Rab interacting lysosomal protein complex to regulate endosomal degradation.

Celina Amaya, Rodrigo D. Militello, Sebastián D. Calligaris y María I. Colombo

Abstract

Endocytosis is a multistep process engaged in extracellular molecules internalization. Several proteins including the Rab GTPases family coordinate the endocytic pathway. The small GTPase Rab7 is present in late endosome (LE) compartments being a marker of endosome maturation. The Rab interacting lysosomal protein (RILP) is a downstream effector of Rab7 that recruits the functional dynein/dynactin motor complex to late compartments. In the present study, we have found Rab24 as a component of the endosome-lysosome degradative pathway. Rab24 is an atypical protein of the Rab GTPase family, which has been attributed a function in vesicle trafficking and autophagosome maturation. Using a model of transiently expressed proteins in K562 cells, we found that Rab24 co-localizes in vesicular structures labeled with Rab7 and LAMP1. Moreover, using a dominant negative mutant of Rab24 or a siRNA-Rab24 we showed that the distribution of Rab7 in vesicles depends on a functional Rab24 to allow DQ-BSA protein degradation. Additionally, by immunoprecipitation and pull down assays, we have demonstrated that Rab24 interacts with Rab7 and RILP. Interestingly, overexpression of the Vps41 subunit from the homotypic fusion and protein-sorting (HOPS) complex hampered the co-localization of Rab24 with RILP or with the lysosomal GTPase Arl8b, suggesting that Vps41 would affect the Rab24/RILP association. In summary, our data strongly support the hypothesis that Rab24 forms a complex with Rab7 and RILP on the membranes of late compartments. Our work provides new insights into the molecular function of Rab24 in the last steps of the endosomal degradative pathway.