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Title:	Role of small GTPase Arl8b and its effector proteins in regulating cargo trafficking to lysosomes
Authors:	Khatter, D. (/jspui/browse?type=author&value=Khatter%2C+D.)
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Abstract:	<p>Eukaryotic cells have an elaborate endocytic system that is specialized to take up materials from the environment and route it to the lysosomes for degradation. The endocytic pathway is marked by multiple fusion and fission events whose regulation involves an interplay of small GTPases, tethering factors and SNAREs. Homotypic fusion and Protein Sorting (HOPS) complex is an evolutionarily conserved multisubunit tethering factor that mediates vesicle fusion with lysosomes. The mechanism of mammalian HOPS action and its crosstalk with other lysosome proteins is only beginning to be understood. In the first part of this thesis, we demonstrate that the small GTPase Arl8b interacts with, and recruits HOPS complex to lysosome membranes. Depletion of HOPS subunit Vps41 results in defects in cargo trafficking to lysosomes that were rescued upon expression of wild-type but not an Arl8b-binding-defective mutant, suggesting that Arl8b-dependent localization of HOPS complex to lysosomes is required for cargo degradation. Since the discovery of Arl8b, an ever-increasing number of its interaction partners have come into light, inclusive of the RUN domain-containing proteins. In the second section of the thesis, we have identified that Arl8b interacts with the RUN and FYVE (RUFY) domain-containing proteins, Rabip4' and Rabip4/RUFY1, via their RUN domains. Arl8b depletion results in striking displacement of endogenous Rabip4(s) from the endosomal membranes to the cytosol that can be rescued upon expression of siRNA-resistant Arl8b. Future studies will be useful to gain insights into how Arl8b regulates the membrane localization of Rabip4(s) and significance of Rabip4(s) interaction with Arl8b in membrane trafficking.</p>
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