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Characterization of a novel interaction partner of lysosomal GTPase Arl8b

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Abstract:

Vesicular trafficking in eukaryotic cells is tightly regulated by various families of small GTP binding proteins, including Rabs, Arfs, and Arf-like (Arl) proteins. Small GTP binding protein Arl8b is known to regulate lysosome motility and function in mammalian cells. Arl8b is recruited onto the lysosomes by BORC, and by interacting with various effectors, it governs essential cellular functions. Interaction of Arl8b with SKIP helps in the motility of lysosomes from minus end to the plus end of the microtubules. Arl8b also helps in late endosome-lysosome as well as autophagosome-lysosome fusion by interacting with proteins like HOPS and PLEKHM1. Since we now know that Arl8b has many effectors, it is crucial to establish novel interaction partners and effectors of Arl8b to better understand lysosome biology. The objective of the study was to characterize a possible novel interaction partner of small GTP binding protein Arl8b. In this study, we determined a novel interaction partner of lysosomal GTPase Arl8b, which is a member of Tre2/Bub2/Cdc16 family of proteins. Our preliminary observations indicate that upon RNAi depletion of this novel interaction partner, LAMP1, Rab14, and Rab7 compartments generally appear enlarged. Immunostaining for M6PR shows more endosomal staining for this cargo; moreover EEA1 also appears to be on enlarged endosomes. Our observations suggest that this protein interacts with Arl8b and may regulate the endo-lysosomal pathway. The detailed cellular roles and mechanism of action of this TBC protein need to be investigated in future studies.

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