Title:	The Rab7 effector PLE KHM1 binds Arl8b to promote cargo traffic to lysosomes
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Abstract:	Endocytic, autophagic, and phagocytic vesicles move on microtubule tracks to fuse with lysosomes. Small GTPases, such as Rab7 and Arl8b, recruit their downstream effectors to mediate this transport and fusion. However, the potential cross talk between these two GTPases is unclear. Here, we show that the Rab7 effector PLEKHM1 simultaneously binds Rab7 and Arl8b, bringing about clustering and fusion of late endosomes and lysosomes. We show that the N-terminal RUN domain of PLEKHM1 is necessary and sufficient for interaction with Arl8b and its subsequent localization to lysosomes. Notably, we also demonstrate that Arl8b mediates recruitment of HOPS complex to PLEKHM1-positive vesicle contact sites. Consequently, Arl8b binding to PLEKHM1 is required for its function in delivery and, therefore, degradation of endocytic and autophagic cargo in lysosomes. Finally, we also show that PLEKHM1 competes with SKIP for Arl8b binding, which dictates lysosome positioning. These findings suggest that Arl8b, along with its effectors, orchestrates lysosomal transport and fusion.
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