Title:	RUFY1 binds Arl8b and mediates endosome-to-TGN CI-M6PR retrieval for cargo sorting to lysosomes
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Keywords:	RUFY1 binds Arl8b mediates endosome-to-TGN cargo sorting to lysosomes
Issue Date:	2022
Publisher:	Journal of Cell Biology
Citation:	Journal of cell biology, 222(1), 2108001.
Abstract:	Arl8b, an Arf-like GTP-binding protein, regulates cargo trafficking and positioning of lysosomes. However, it is unknown whether Arl8b regulates lysosomal cargo sorting. Here, we report that Arl8b binds to the Rab4 and Rab14 interaction partner, RUN and FYVE domain-containing protein (RUFY) 1, a known regulator of cargo sorting from recycling endosomes. Arl8b determines RUFY1 endosomal localization through regulating its interaction with Rab14. RUFY1 depletion led to a delay in CI-M6PR retrieval from endosomes to the TGN, resulting in impaired delivery of newly synthesized hydrolases to lysosomes. We identified the dynein-dynactin complex as an RUFY1 interaction partner, and similar to a subset of activating dynein adaptors, the coiled-coil region of RUFY1 was required for interaction with dynein and the ability to mediate dynein-dependent organelle clustering. Our findings suggest that Arl8b and RUFY1 play a novel role on recycling endosomes, from where this machinery regulates endosomes to TGN retrieval of CI-M6PR and, consequently, lysosomal cargo sorting.
Description:	Only IISERM authors are available in the record
URI:	https://doi.org/10.1083/jcb.202108001 (https://doi.org/10.1083/jcb.202108001) http://hdl.handle.net/123456789/4799 (http://hdl.handle.net/123456789/4799)
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