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Title:	RUFY3 links Arl8b and JIP4-Dynein complex to regulate lysosome size and positioning
Authors:	Chawla, Prateek (/jspui/browse?type=author&value=Chawla%2C+Prateek) Dhiman, Neha (/jspui/browse?type=author&value=Dhiman%2C+Neha) Sharma, Mahak (/jspui/browse?type=author&value=Sharma%2C+Mahak)
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Abstract:	The bidirectional movement of lysosomes on microtubule tracks regulates their whole-cell spatial arrangement. Arl8b, a small GTP-binding (G) protein, promotes lysosome anterograde trafficking mediated by kinesin-1. Herein, we report an Arl8b effector, RUFY3, which regulates the retrograde transport of lysosomes. We show that RUFY3 interacts with the JIP4-dynein-dynactin complex and facilitates Arl8b association with the retrograde motor complex. Accordingly, RUFY3 knockdown disrupts the positioning of Arl8b-positive endosomes and reduces Arl8b colocalization with Rab7-marked late endosomal compartments. Moreover, we find that RUFY3 regulates nutrient-dependent lysosome distribution, although autophagosome-lysosome fusion and autophagic cargo degradation are not impaired upon RUFY3 depletion. Interestingly, lysosome size is significantly reduced in RUFY3 depleted cells, which could be rescued by inhibition of the lysosome reformation regulatory factor PIKFYVE. These findings suggest a model in which the perinuclear cloud arrangement of lysosomes regulates both the positioning and size of these proteolytic compartments.
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