

PIKfyve activity regulates reformation of terminal storage lysosomes from endolysosomes.

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Abstract

The protein complex composed of the kinase PIKfyve, the phosphatase FIG4 and the scaffolding protein VAC14 regulates the metabolism of phosphatidylinositol 3,5-bisphosphate, which serves as both a signaling lipid and the major precursor for phosphatidylinositol 5-phosphate. This complex is involved in the homeostasis of late endocytic compartments, but its precise role in maintaining the dynamic equilibrium of late endosomes, endolysosomes and lysosomes remains to be determined. Here, we report that inhibition of PIKfyve activity impairs terminal lysosome reformation from acidic and hydrolase-active, but enlarged endolysosomes. Our live-cell imaging and electron tomography data show that PIKfyve activity regulates extensive membrane remodeling that initiates reformation of lysosomes from endolysosomes. Altogether, our findings show that PIKfyve activity is required to maintain the dynamic equilibrium of late endocytic compartments by regulating the reformation of terminal storage lysosomes.

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