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Fab1p PtdIns(3)P 5-Kinase Function Essential for Protein Sorting in the Multivesicular Body

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Abstract

Sorting of signal-transducing cell surface receptors within multivesicular bodies (MVBs) is required for their rapid down-regulation and degradation within lysosomes. Yeast mutants defective in late stages of transport to the vacuole/lysosome accumulate MVBs. We demonstrate that the membrane glycoprotein carboxypeptidase S and the G protein-coupled receptor Ste2p are targeted into the vacuole lumen, and this process requires a subset of *VPS* gene products essential for normal endosome function. The PtdIns(3)P 5-kinase activity of Fab1p, which converts the product of the Vps34p PtdIns 3-kinase PtdIns(3)P into PtdIns(3,5)P₂, also is required for cargo-selective sorting into the vacuole lumen. These findings demonstrate a role for phosphoinositide signaling at distinct stages of vacuolar/lysosomal protein transport and couple PtdIns(3,5)P₂

synthesis to regulation of MVB sorting.



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