A dual role for COOH-terminal lysine residues in pre-Golgi retention and endocytosis of ERGIC-53

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ERGIC-53 (former designation, p53) is a 53-kDa nonglycosylated, dimeric, and hexameric type I membrane protein that has been established as a marker protein for a tubulovesicular intermediate compartment in which protein transport from the endoplasmic reticulum to the Golgi apparatus is blocked at 15 degrees C. Although ERGIC-53 is not a resident protein of the rough endoplasmic reticulum its cDNA sequence carries a double lysine endoplasmic reticulum retention motif at the cytoplasmically exposed COOH terminus. Here we report that overexpression of ERGIC-53 in COS cells saturates its intracellular retention system leading to the appearance of ERGIC-53 at the cell surface. Cell surface ERGIC-53 is efficiently endocytosed by a mechanism that is disturbed when the two critical lysines of the endoplasmic reticulum retention motif are replaced by serines. The results suggest a mechanistic similarity of pre-Golgi retention by the double lysine motif and lysine-based endocytosis.
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