A novel direct interaction of endoplasmic reticulum with microtubules

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The positioning and dynamics of organelles in eukaryotic cells critically depend on membrane-cytoskeleton interactions. Motor proteins play an important role in the directed movement of organelle membranes along microtubules, but the basic mechanism by which membranes stably interact with the microtubule cytoskeleton is largely unknown. Here we report that p63, an integral membrane protein of the reticular subdomain of the rough endoplasmic reticulum (ER), binds microtubules in vivo and in vitro. Overexpression of p63 in cell culture led to a striking rearrangement of the ER and to concomitant bundling of microtubules along the altered ER. Mutational analysis of the cytoplasmic domain of p63 revealed two determinants responsible for these changes: an ER rearrangement determinant near the N-terminus and a central microtubule-binding region. The two determinants function independently of one another as indicated by deletion experiments. A peptide corresponding to the cytoplasmic tail of p63 promoted microtubule polymerization in vitro. p63 is the first identified integral membrane protein that can link a membrane organelle directly to microtubules. By doing so, it may contribute to the positioning of the ER along microtubules.
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