The peroxin Pex14p is the key component for coordinated autophagic degradation of mammalian peroxisomes by direct binding to LC3-II

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区　　分　：

論　文　内　容　の　要　旨

Pexophagy can be experimentally induced in mammalian cells by removing the culture serum. Pex14p, a peroxisomal membrane protein essential for matrix protein import in docking of soluble receptor Pex5p, is involved in the mammalian autophagic degradation of peroxisomes and interacts with the lipidated form of LC3, termed LC3-II, an essential factor for autophagosome formation, under the starvation condition in CHO-K1 cells. However, molecular mechanisms underlying the Pex14p-LC3-II interaction remain largely unknown. To verify whether Pex14p directly binds LC3-II, I reconstituted an *in vitro* conjugation system for synthesis of LC3-II using recombinant human (h)Atg7, Atg3 and CHO-K1 LC3 mutant with C-terminal Gly exposed in the presence of ATP and phosphotidylethanolamine (PE)-containing liposomes. I show here that Pex14p directly interacts with LC3-II via the transmembrane domain of Pex14p. Pex5p competitively inhibited this interaction, implying that Pex14p preferentially binds to Pex5p under the nutrient-rich condition. Moreover, a Pex5p mutant defective in PTS1-protein import lost its affinity for Pex14p under the condition of nutrient deprivation, thereby more likely explaining why Pex14p prefers to interact with LC3-II under the starvation condition *in vivo*. I also show that another autophagy factor NBR1 is involved in the peroxisomal degradation and interacts with Pex14p and LC3 under the starvation condition. Together, these results suggest that Pex14p is a unique factor that functions in the dual processes in peroxisomal biogenesis and degradation with the coordination of Pex5p in response to the environmental changes.