

リソソーム膜タンパク質 LAMP-1 の C 末端アミノ酸残基のイソロイシンが効率的なリソソームへの輸送に最適である

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COOH-terminal isoleucine of lysosome-associated membrane protein-1 is optimal for its efficient targeting to dense secondary lysosomes

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ABSTRACT: Lysosome-associated membrane protein-1 (LAMP-1) consists of a highly glycosylated luminal domain, a single-transmembrane domain and a short cytoplasmic tail that possesses a lysosome-targeting signal (GYQTI(382)) at the COOH terminus. It is hypothesized that the COOH-terminal isoleucine, I(382), could be substituted with any other bulky hydrophobic amino acid residue for LAMP-1 to exclusively localize in lysosomes. In order to test this hypothesis, we compared subcellular distribution of four substitution mutants with phenylalanine, leucine, methionine and valine at the COOH-terminus (termed I382F, I382L, I382M and I382V, respectively) with that of wild-type (WT)-LAMP-1. Double-labelled immunofluorescence analyses showed that these substitution mutants were localized as significantly to late endocytic organelles as WT-LAMP-1. However, the quantitative subcellular fractionation study revealed different distribution of WT-LAMP-1 and these four COOH-terminal mutants in late endosomes and dense secondary lysosomes. WT-LAMP-1 was accumulated three to six times more in the dense lysosomal fraction than the four mutants. The level of WT-LAMP-1 in late endosomal fraction was comparable to those of I382F, I382M and I382V. Conversely, I382L in the late endosomal fraction was approximately three times more abundant than WT-LAMP-1. These findings define the presence of isoleucine residue at the COOH-terminus of LAMP-1 as critical in governing its efficient delivery to secondary lysosomes and its ratio of lysosomes to late endosomes.

抄録 リソソーム膜タンパク質 LAMP-1 は C 末端側に細胞質テールを持つ。そのテールには GYQTI のアミノ酸配列のリソソーム標的シグナルが存在する。標的シグナルの C 末端を I 以外の分子量の大きな疎水性アミノ酸で置換した変異体のリソソームへの移行量を細胞分画法で調べた。その結果、野生型 LAMP-1 のリソソームへの移行量は変異体の 3～6 倍であった。この結果、LAMP-1 のリソソームへの輸送には C 末端がイソロイシンであることが重要であることが示された。

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