

チオールプロテアーゼ阻害剤ロイペプチン
による培養肝細胞におけるカテプシンLの
細胞内成熟の阻止効果

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Inhibitory Effect of Leupeptin on the Intracellular
Maturation of Lysosomal Cathepsin L in Primary
Cultures of Rat Hepatocytes

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To investigate the intracellular processing event for lysosomal cathepsin L, we examined the effect of leupeptin, a non-covalent cysteine proteinase inhibitor, on the intracellular processing kinetics of cathepsin L as analyzed by pulse-chase experiments with (35 S)methionine in the primary cultures of rat hepatocytes. This revealed that cathepsin L was initially synthesized as a proenzyme of molecular weight 39kDa and the proenzyme was subsequently processed to the mature form of the enzyme, 30 and 25kDa. In the leupeptin-treated cells, the proteolytic conversion of cellular procathepsin L, of molecular weight 39 kDa, to the mature enzyme was significantly inhibited and considerable amounts of proenzyme were found in the cell after 8h chase periods. Furthermore, the subcellular fractionation experiment demonstrated that the intracellular processing of procathepsin L in the high density lysosomal fraction was significantly inhibited and that considerable amounts of the procathepsin L form were still observed in the dense lysosomal fraction after a 2h chase period. These results suggest that leupeptin treatment caused significant inhibition of the intracellular maturation of cathepsin L. These findings show that cysteine proteinase plays an important role in the intracellular

proteolytic processing and activation of lysosomal cathepsin L and that this processing event occurs within the lysosomes.

初代培養肝細胞において、ライソゾーム酵素であるカテプシンLのプロ酵素から成熟酵素への変換をチオールプロテアーゼ阻害剤であるロイペプチンを用いて調べた。カテプシンL 39 KDaのプロ蛋白から、30と25 KDaの成熟蛋白への変換にはチオール酵素が重要な役割をなしており、またその変換場所はライソゾーム顆粒内であることをつきとめた。

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