マウスメラノーマ中のコレステロール低下は リソソーム酵素の分泌を引き起こす

道原明宏、戸田　憲、末延道尚、赤﨑健司、辻　　宏

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Decrease of cholesterol in mouse melanoma causes secretion of lysosomal enzymes

Akihiro Michihara, Ken Toda, Michihisa Suenobu, Kenji Akasaki and Hiroshi Tsuji

ABSTRACT: We examined the change in the subcellular distribution of a lysosomal enzyme, *β*-glucuronidase (*β*-G), caused by decreased cholesterol levels in mouse melanoma cells using a HMG-CoA reductase inhibitor, lovastatin, and lipoprotein-deficient serum (LDS). There was a decrease in the cholesterol content of the cells and increased secretion of the mature form of *β*-G located in lysosomes, as documented by Percoll density gradient fractionation, digitonin permeabilization, and immunoprecipitation. Furthermore, another lysosomal enzyme, cathepsin H, was found to be released in the medium from cells treated with lovastatin. Both the precursor and mature forms of cathepsin H were detected in the medium of treated cells. Next, when cells were treated with LDS without lovastatin, concomitantly with the decrease in the levels of cholesterol and *β*-G activity in the cells, *β*-G activity in the medium increased. Also, the ratio of *β*-G (3.2-fold) released in the medium from cells treated with D-MEM containing lovastatin and LDS was higher than that (2.3-fold) on treatment with D-MEM containing LDS without lovastatin. From these results, it was suggested that the exocytosis of mature enzymes from lysosomes into the medium or mis-sorting of the lysosomal precursor forms to the medium was caused by the lovastatin- and/or LDS-induced decrease in the cholesterol content of the cells, although the mechanism of secretion by lysosomal enzymes differed somewhat.

抄録　HMG-CoA 還元酵素であるロバスタチンとリポプロテインを除いた血清を含む培養液でマウスメラノーマＢ１６Ｆ１０細胞を処理したとき、細胞内コレステロールの著しい低下により、リソソーム酵素の前駆体と成熟型が培養液中に放出されることを示した。