ラット肝実質細胞中のリソソームタンパクに及ぼすプリマキンの効果

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The Effect of Primaquine on Lysosomal Protein in Cultured Rat Hepatocytes

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ABSTRACT: We previously reported that chloroquine disrupted lysosomes, but not the shift to low-density lysosomes. In the present study, the effects of primaquine on lysosomal integrity in cultured rat hepatocytes were studied by measuring lysosomal enzyme β-glucuronidase (β-G) or lysosomal membrane glycoprotein (lamp-1) in the cytosolic fraction obtained from cells permeabilized by digitonin, and in the cytosolic fraction obtained by conventional cell fractionation or in Percoll density gradient fractions. The percentage disruption of lysosomes in living cells by 50 μM or 100 μM of primaquine was 1% or 4%, respectively, and lysosomes disrupted by homogenization or centrifugation during cell fractionation by 50 μM or 100 μM of primaquine were 2% or 7%, respectively. The decrease of β-G and lamp-1 in lysosome fractions (fractions 16 to 18) on a Percoll density gradient (1 to 18 fractions) in 50 μM or 100 μM primaquine-treated cells was 9% or 19% for β-G, and 16% or 24% for lamp-1, respectively. The decrease of β-G and lamp-1 in the lysosome fraction was higher than the disruption of lysosomes in living cells or by homogenization or centrifugation during cell fractionation by 50 μM or 100 μM of primaquine. Also, the peak fraction numbers of the subcellular distribution of β-G and lamp-1 on a Percoll density gradient by 50 μM primaquine-treated cells were fraction 17 (high density) and 4 (low density), while those by 100 μM primaquine-treated cells were fraction 6 (low density) or 4 (low density). From these data, we infer that the main effect of primaquine is to cause a shift of lysosomal protein to low density, and then to cause differences in the proportion of membrane and luminal proteins of lysosomes in low-density fractions, although the main effect of chloroquine was the disruption of lysosomes.

抄録　我々は以前、クロロキンがリソソームの崩壊を引き起こすことを明らかにした。今回は、クロロキンの類似物質であるプリマキンを用いて実験を行った。その結果、プリマキンの主要効果は、高密度画分に存在するリソソームタンパクを低密度画分へシフトすることであり、その時、低密度画分中においてリソソーム内タンパクと膜タンパクの比率が異なることを明らかにした。