アラビノガラクタンの初代培養ラット肝細胞における細胞内動態

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Cellular disposition of arabinogalactan in primary cultured rat hepatocytes

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ABSTRACT : To characterize a targeting property of arabinogalactan (AG) as a carrier to the liver, we examined cellular disposition, such as binding and internalization in primary cultured rat hepatocytes, comparing them to those of asialofetuin (AF). A tyramine derivative of AG was synthesized to allow labeling with ^{125}I. Binding of AG to the cells was concentration-dependent and saturable. The number of binding sites (n) of AG on the cell surface was $4.0 \times 10^5 \pm 0.1 \times 10^5$ sites/cell which was about similar to that of AF. The value of K_a of AG was $2.2 \times 10^8 \pm 0.1 \times 10^8$ M^{-1} being sevenfold higher than that of AF. The binding of AG was competitively inhibited by AF and was decreased by calcium depletion. These results indicate that AG can bind strongly to hepatocytes probably through the recognition by the asialoglycoprotein receptor (ASGP-R). Both ^{125}I-labeled AG and fluorescein-labeled AG were internalized into the cells. The rate of internalization of AG was faster than that of AF, indicating that AG is effectively endocytosed. Microscopic observations showed that FITC labeled AG accumulated in granules within the primary cultured rat hepatocytes. Subcellular fractionation indicated that the internalized AG was mainly associated with the lysosomal fraction. However, the internalized AG seemed to remain intact in the hepatocytes. In conclusion, we found that AG is effectively internalized in primary cultured rat hepatocytes. Although AG seems a good candidate for targeting to the liver, due to its high affinity binding and rapid internalization, it remains to be established whether the apparent lack of biodegradation will result in cytotoxic effects at chronic administration *in vivo*.

抄録　初代培養肝細胞系において、アラビノガラクタンがアシアロ糖タンパク質受容体と特異的に結合し内在化を受けることを明らかにした。内在化を受けたアラビノガラクタンはインタクトに近い状態で細胞内のリソソームに分布することが示唆された。アラビノガラクタンはアシアロフェツインに比べて肝細胞へ高い親和性で結合するとともに、より速く内在化されることが速度論的な解析から明らかとなった。以上の知見から、アラビノガラクタンは肝への薬物運搬体として有用であることが示唆された。