オルトバナジン酸ナトリウムによる培養ラット肝細胞からの肝性リパーゼ活性の分泌促進：サイクリックＡＭＰ量の急速な増加

森田哲生、坂田幸治、金川麻子、植木　寛

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Stimulatory Release of Hepatic Lipase Activity from Cultured Rat Hepatocytes by Sodium Orthovanadate: Rapid Increase in Cyclic Adenosine Monophosphate Content

Tetsuo MORITA, Kouji SAKATA, Asako KANAGAWA, and Hiroshi UEKI

The release of hepatic triacylglyceride lipase [EC3.1.1.3] has been examined in isolated hepatocytes in primary culture. The stimulatoly release of activity from the hepatocytes into the medium by sodium orthovanadate (vanadate) was observed in a time- and dose-dependent manner. However, insulin failed to have this stimulatory action.

Moreover, vanadate rapidly increased the cyclic adenosine monophosphate(cyclic AMP) content in hepatocytes in a time- and dose-dependent manner.

The treatment of hepatocytes with H-89, which is a potent cyclic AMP-dependent protein Kinase inhibitor, decreased the stimulatory release of hepatic lipase activity by vanadate. The vanadate-stimulated release of the enzyme activity was suppressed by uncouplers. In addition,the incorporation of [^{3}H]leucine into protein was increased in the presence of vanadate. Under the marked inhibition of protein synthesis by cycloheximide, vanadate still showed a full effect on the release of the enzyme activity. These results suggest that the vanadate-stimulated release of hepatic lipase activity from the cultured hepatocytes is associated with a rapid increase in intracellular cyclic AMP content,probably due to an activation of cyclic AMP-dependent protein kinase which requires a metabolic energy process rather

than an elevation in enzyme molecule synthesis.

初代培養ラット肝細胞系における肝性リパーゼは、オルトバナジン酸ナトリウム（バナデート）によって、時間の経過並びにその濃度の増加に伴って、分泌が促進された。更に、バナデートは、肝細胞中のcyclic AMP準位を、急速且つ一過的に増加させた。一方、cyclic AMP依存性プロテインキナーゼの強力な阻害剤H-89共存下、バナデートの肝性リパーゼの分泌促進効果は、大きく阻害された。又、脱共役剤や蛋白合成阻害剤によるバナデートの作用の挙動から、肝性リパーゼの分泌が、酵素蛋白分子の合成亢進より、むしろ、代謝エネルギーを必要とするcyclic AMPの増加とそれに伴うプロテインキナーゼの上昇に密接に関与していることが示唆された。