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The Regulation of Hepatic Microsomal Triglyceride Transfer Protein Activity by Calcium ion

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Microsomal triglyceride (TG) transfer protein (MTP) is involved in the secretion of TG-rich very low-density lipoprotein (VLDL) containing apolipoprotein B (apoB) from liver and hepatocyte. Which is the cause of the hypertriglyceridemia and atherosclerosis. At the present, what is the regulatory factor has not been proved. We found that hepatocellular calcium ion is deeply associated with the MTP activity. Exogenous $CaCl_2$, calcium ionophore (A23187), and calmodulin increased the MTP activity *in vivo* and *in vitro*. However, these activities were reduced in response to the calmodulin antagonist N-(6-aminohexyl)-5-chloro-1- naphthalene sulfonamide (W-7, K_i = 25 μM), the intracellular Ca^{2+} chelator BAPTA-AM, and the extracellular Ca^{2+} chelator EDTA. The inhibition of MTP activity by these calcium antagonists resulted in hypotriglyceridemia and hypolipoproteinemia in serum and hepatocytes culture medium. These results suggested that there might be a very close association between high MTP activity and high Ca^{2+} level in the liver or hepatocytes. In conclusion, the MTP activity and the secretion of both TG and apoB are very closely associated with the level of hepatic Ca^{2+}. Thus, our findings might provide a new perspective regulatory effect of Ca^{2+} on MTP activity that toward to hyperlipidemia. [This work was supported by the MRC program of MOST/KOSEF(grant # : R13-2005-013-01003-0), Korea]

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Inhibitory Effect of Cnidii Rhizoma on Cytokines-induced Nitric Oxide Production in Human Colorectal Adenocarcinoma HT-29 Cell

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The present study investigates the increase of nitric oxide (NO) production and inducible nitric oxide synthase (iNOS) expression in human colorectal adenocarcinoma HT-29 cells with the treatment of pro-inflammatory cytokines. The effect of water extract from Cnidii Rhizoma on pro-inflammatory cytokines-induced NO production and iNOS expression was also tested. The pro-inflammatory cytokines IFN-γ (100 U/mL), IL-1α (10 ng/mL), and TNF-α (50 ng/mL), added alone to HT-29 cells did not affect NO generation. The minimal requirement for enhanced NO production was the combination of IFN-γ/IL-1α, while other pairs of cytokines were ineffective. Different concentrations of TNF-α (0-50 ng/mL) in the presence of the combination IFN-γ (100 U/mL)/IL-1α (10 ng/mL) induced a concentration-dependent enhancement of NO production. Pretreatment of the cells with Cnidii Rhizoma (0.1-5 mg/mL) had inhibitory effect on cytokines-induced NO production. Cnidii Rhizoma reduced cytokines-induced iNOS expression in a dose-dependent manner. This study shows that pro-inflammatory cytokines induce NO production and iNOS expression in human colorectal adenocarcinoma HT-29 cells. Cnidii Rhizoma pretreatment inhibited cytokines-mediated NO production and iNOS expression. These results provide sufficient information for the further development of Cnidii Rhizoma as an antitumor agent against colon cancer. [This work was supported by the Korea Research Foundation Grant funded by the Korea Government (MOEHRD, Basic Research Promotion Fund) (KRF-2005-075-C00024)]