apoptosis is still unclear. In the present study, we determined if p38 MAP kinase was involved in ceramide-induced cell death. Treatment with SB203580, a p38 MAP kinase inhibitor, protected HL-60 cells from ceramide-induced cell death, which is in accordance with phosphorylation of p38 MAP kinase induced by ceramide. Ceramide elevated caspase-3 and -9 activities and induced translocation of Bax from cytosol to mitochondria. Treatment with SB203580 diminished caspase-3 and -9 induction and blocked Bax translocation induced by ceramide. These results demonstrate that p38 MAP kinase may play an important role in ceramide-mediated cell death in HL-60 cells.

[PC3-8] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Activation of hypoxia-inducible factor-1a in hepatocarcinogenesis by Hepatitis B virus X protein

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Hepatitis B viruse x (HBx) protein has been directly involved in development of hepatocellular carcinoma (HCC), highly vascularized solid tumors. However, the molecular function of HBx remains controversial. We previously reported that HBx increases the expression of vascular endothelial growth factor (VEGF) mRNA in HBx-expressed cells lead to stimulate angiogenesis in vivo mouse Matrigel plug assay. It is well known that hypoxia-inducible factor-1a (HIF-1a) is major regulator of VEGF expression under hypoxia. Herein, We examined the expression of HIF-1a in the liver of transgenic mice expressing the HBx gene. HBx and HIF-1a proteins are highly expressed in the HBx-transgenic liver, in contrast, these proteins are rare or no expressed in normal liver. Also, VEGF protein is highly expressed in HBx-transgenic liver. HBx induces HIF-1a and VEGF protein level in HEK 293 cells in normoxic condition. We further show that HBx blocks the ubiquitination of HIF-1a in normoxia mediated by down-regulation of p53. Our results suggest that HBx induce expression of HIF-1a in the HBV-infected liver and then stimulates angiogenesis, result in development of HCC.

[PC3-9] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Determination of interaction between a novel biotinylated biocompatible polymer and a hepatoma cell line (HePG2)

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Nanoparticles can be delivered to specific sites in the body by size-dependent passive targeting or by active targeting using receptor-mediated interactions. For developing a potential liver cancer targeting system, we attempted to design a receptor-mediated delivery system using biotinylated pullulan acetate (PA/biotin 500). The interactions between the RITC-labeled nanoparticles [pullulan acetate (PA) and PA/biotin 500] and HepG2 cells were quantified by a microplate fluorescence reader and flowcytometer. PA/biotin 500 showed stronger adsorption to HepG2 cells than PA. We investigated the changes of fluorescence intensity as a function of concentration and cultivation time of PA and PA/biotin 500. The fluorescence intensity of HepG2 cells linearly increased with the concentration of PA and PA/biotin 500. The cultivation time of HepG2 cells for the time also affected the fluorescence intensity in similar way. To clarify the specific interaction between RITC-labeled nanoparticles and HepG2 cells, we attempted to use confocal laser microscopy. HepG2 cells were strongly luminated by specific interactions with PA/biotin 500 while the luminescence of PA was a little observed. Therefore, It is suggested that the PA/biotin 500 has a specific interaction with HepG2 cells by ligand-receptor recognition. In conclusion, PA/biotin 500 is a potential drug delivery system for the treatment of liver cancer. The carrier may induce the immunological enhancement activity in the body and attach to hepatoma cell (HepG2) by ligand-