

Sialylated antigen biosynthesis and hepatocarcinoma progression

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The metastasis of hematogenous cancer cells is associated with abnormal glycosylation such as sialyl lewis antigens. The human hepatocellular carcinoma tissues, HBx transgenic mice and HBx-transfected cells were used to check the correlation of expressions between HBx and Sialyl lewis antigen for cancer metastasis. To investigate whether expression levels of glycosyltransferases induced in HBx-transfected cells are specifically associated with sialyl lewis A synthesis, which enhances metastasis by interaction of liver cancer cells with endothelial cells, ShRNA and siRNAs targeting specific glycosyltransferases were used. Although the hepatitis B virus X protein (HBx) plays important role in liver disease, the precise function of HBx on aberrant glycosylation for metastasis remains unclear. In this study, HBx expression in liver cancer region of HCC is associated with the specific synthesis of sialyl lewis A. Furthermore, the sialyl lewis A was specifically induced both in liver tissues from HBx-transgenic mice and in *in vitro* HBx-transfected cells. Among sialyltransferase and fucosyltransferase genes, HBx increased transcription levels and activities of ST3Gal III, FUT III and VII genes, which were specific for sialyl lewis A synthesis. The sialyl lewis A increased by HBx in liver cells interacted with E-selectin expressed in TNF- α -stimulated endothelial cells, allowing dramatic cell-cell adhesion for metastatic potential. ST3Gal III, FUT III and FUT VII siRNAs, suppressing sialyl lewis A synthesis, resulted in the inhibition of HBx-transfected cell adhesion to TNF- α -treated endothelial cells. Interestingly, HBx specifically induced expression of β 1-3GalT gene associated with the initial synthesis of sialyl lewis A, but not β 1-4GalT. The β 1-3GalT shRNA suppressed sialyl lewis A expression by HBx, blocking the adhesion of HBx-transfected cells to the endothelial cells. Moreover, β 1-3GalT silencing suppressed lung metastasis of HBx-transfected cells in *in vivo* lung metastasis system. From the results, it was concluded that HBx targets the glycosyltransferases for the sialyl lewis A synthesis and this process regulates hematogenous cancer cell adhesion to endothelial cells for cancer metastasis.

Biography

Cheorl-Ho Kim has completed his Ph.D. at the age of 28 years from The University of Tokyo and Senior Scientist Studies from Korea Research Institute of Bioscience and Biotechnology. He is a professor of Molecular Glycobiology, SungKyunKwan University, Korea, a leading organization of Korea, which is cooperated with the Samsung Group. He has published more than 320 papers in reputed journals and serving as an editorial board member, executive editor and editor-in chief of the international journals.

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