

Sialo-oncology: Hematogenous cancer cell adhesion to endothelial cells through E-selectin-Sialyl lewis A/X interaction

Tae-Wook Chung^{ab}, Hee-Jung Choi^{ab}, Seok-Jo Kim^{ab} and Cheorl-Ho Kim^{ab}

^aGlycobiology and Glycomics Research Center (GGRC) and ^bMolecular and Cellular Glycobiology Unit, Department of Biological Science, SungKyunKwan University, 300 Chunchun-Dong, Jangan-Gu, Suwon City, Kyunggi-Do 440-746, Korea. www.glycobio.org

Email: chkimbio@skku.edu, Tel: +82-31-290-7002, Fax: +82-31-290-7015

Malignant transformation is associated with abnormal glycosylation, resulting in the synthesis and expression of altered carbohydrate determinants. Expression of carbohydrate determinants such as sialyl lewis A and sialyl lewis X is markedly enhanced in cancer cells. Sialyl lewis A and sialyl lewis X are involved in selectin-mediated adhesion of cancer cells to vascular endothelium, and these determinants play important roles in hematogenous metastasis of cancer cells.

Human HBV induces acute and chronic hepatitis, and is closely associated with the incidence of human liver cancer. Among the four proteins that originate from the HBV genome, HBx is a multifunctional regulatory protein and has been reported to be associated with hepatocellular carcinogenesis. Moreover, HBx induces liver cancer in transgenic mice. Recently, we have found that HBx causes the progression of liver cancer through down-expression of PTEN, known as a tumor suppressor gene. Furthermore, we have reported that the enhanced expression of MMP-9 through activation of PI-3K/AKT and ERKs signals by HBx is eventually associated with the invasive potential of liver cells. Therefore, previous studies show that HBx is potentially associated with hepatocellular carcinogenesis and invasion. However, the precise function of HBx in the metastasis of liver cancer remains unclear at this time.

In this study, we investigated whether HBx induces the expression of sialyl lewis X/A in liver cells, HBx-transgenic mice and liver cancer tissues of HBV-infected patients. Additionally, we examined whether HBx has an effect on the liver cancer cell adhesion to endothelial cells for metastatic step. We have shown for the first time that HBx plays important role in the induction of metastatic potential by modulating the expression of carbohydrate ligand for E-selectin of cytokines-stimulated endothelial cell surface.