Aberrant Glycosylation in Biology : Current Progress and Prospects

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The carbohydrate structures of glycoproteins and glycolipids on the cell surface are associated with development, differentiation, and transformation. *N*-glycans contribute to the folding, stability and biological activity of glycoproteins. UDP-N-Acetylglucosamine:-D-mannoside -1,4N-acetylglucosaminyltransferase III (GnT-III) catalyses the attachment of a GlcNAc residue to mannose in (1-4) configuration in the region of N-glycans and forms a bisecting GlcNAc. The HBx plays a major role on HCC. ApoB is an important glycoprotein for transportation of VLDL and LDL. The pathophysiological role of dysregulated glycosylation mediated by transgenic mice hyperexpressing the human GnT-III in the liver has been investigated. The triglyceride level in GnT-III transgenic mice was significantly decreased without any differences in the levels of cholesterol, albumin, total bililubin and total protein. Large amounts of Apo B were specifically detected in the intracellular liver of transgenic mice. The accumulated Apo B was severely glycosylated, causing a decrease in the release of lipoproteins and accumulations of Apo B in the liver. The transgenic mice resulted in numerous lipid droplets in liver tissues and the obesity. In in vitro experiment, hepatic overexpression of HBx protein interfered with the hepatic secretion of apo B by upregulation of GnT-IIIexpression. HBx transfected liver cells inhibit secretion of Apo B by intracellular accumulation of aberrantly glycosylated apo B. These cells also increase accumulation of intracellular triglyceride and cholesterol. Furthermore, inhibition of secretion of apo B as well as intracellular accumulation of triglyceride and cholesterol were also shown in GnT-IIItransfected liver cells. Moreover, overexpression of GnT-III and HBx in liver cells down-regulate transcriptional level of microsomal triglyceride transfer protein (MTP), which regulates the assembly and secretion of apo B.

Therefore, it was suggested that GnT-III increase intracellular lipid accumulation by elevating the expression of GnT-III and HBx governs GnT-III expression. On the other hand, sialic acid containing glycosphingolipids (gangliosides) have been proposed to play a role in the regulation of a variety of biological phenomena, including cell differentiation. The role of ganglioside GD3 will be reported in the acceleration of erythroid differentiation in K562 cells and modulation of the recruitment of transglutaminase 2 (TG2) into membranes. Increase of GD3 by GD3 synthase overexpression potentates PI3K/Akt signaling that was confirmed by the phosphorylation of CREB, one of the Akt substrates, as well as RT-PCR analysis of several marker genes related to erythroid lineage. GD3 synthase-transfected cells accelerated the erythroid differentiation, as evidenced by benzidine positive staining and hemoglobination. The membrane recruitment of TG2, as well as its ability to be photoaffinitylabeled with [-32P]GTP, was increased in GD3 synthase-transfected cells, indicating that GD3 is involved in the recruitment of GTP-bound TG2 to membranes. Furthermore, membranebound TG2 in GD3 synthase, as well as TG2-transfected cells, was co-immunoprecipitated with GD3 and the localization of GD3 in the membrane was also increased as evidenced by an immunofluorescence study. Therefore, the recruitment of TG2 into membranes by the endogenous ganglioside GD3 might play an important role in the regulation of differentiation and survival in K562 cells. In this limited seminar, general aspects of glycobiology including relationships between artherosclerosis, oncogenesis, xenotransplantation, leukemic differentiation and glycan will be discussed for the new prospects of this specific field.