Differential Expression of
*N*-Acetylglucosaminyltransferase-III and -V Activities in
Human Hepatoma Cells and Colon Cancer
Cells: Implication of Cancer Specific-Glycoantigen
Synthesis in Malignant Transformation

Jae-Kyoung Shim · Chun Park · Eun-Young Song · Young-Choon Lee ·
Tae-Wha Chung and Cheol-Ho Kim

Department of Biochemistry and Molecular Biology, College of Oriental Medicine, Dongguk University,
Kyungju 780-714, Korea; Division of Molecular and Cellular Biology, Korea Research Institute of Bioscience
and Biotechnology, KIST, Taejon 305-600, Korea

Abstract

UDP-*N*-Acetylglucosamine:α-6-D-mannoside β-1,6*N*-Acetylglucosaminyltransferase-III (GlcNAc-transferase-III)
and UDP-*N*-Acetylglucosamine:α-6-D-mannoside β-1,6*N*-Acetylglucosaminyltransferase-V (GlcNAc-transferase-V)
activities were determined in human hepatoma cell lines of Hep3B and HepG2, and also compared with those
of normal liver tissues and primary hepatocytes. GlcNAc-transferase-III activities were higher than those of
GlcNAc-transferase-V in hepatic carcinomacells. In contrast, the two enzyme activities were assayed in highly
metastatic colon cancer cells, GlcNAc-transferase-V activities were much higher than those of GlcNAc-transferase-
III. When GlcN, GlcN-biant-PA and UDP-GlcNAc were used as substrates, the enzymes displayed different kinetic
properties between hepatic and colon cancer cells, depending on their metastatic potentials. Normal cells of two
origins are characterized by a very low level of GlcNAc-transferase- III and -V activities, whereas hepatoma and
colon cancer cells contain high activities. These data were supported by reverse transcription-polymerase chain
reaction results, showing that expression of the GlcNAc-transferase-III and V mRNAs increased in proportion to
the enzymatic activities. Although the mechanism underlying the induction of this enzymes is unknown, lectin
blot analysis showed that oligosaccharides in many glycoproteins were observed in cancer cells. Thus, this is the
first demonstration of GlcNAc-transferase-III and V activities in human hepatoma and colon cell lines. Molecular
aspects of two GlcNAc-transferases in tumorigenesis and metastasis will be extensively discussed.

Key words: *N*-acetylglucosamine (GlcNAc), GlcNAc-transferase-III, GlcNAc-transferase-III hepatoma, colon
cancer, metastasis, expression.

* Corresponding author
Introduction

The carbohydrate structures of glycoproteins and glycolipids on the cell surface are associated with development, differentiation, and transformation\(^2\). Carbohydrate structures are mainly determined by glycosyltransferases and glycosidases. Since the synthesis of oligosaccharides requires one enzyme for one glycosidic linkage, more than one hundred kinds of glycosyltransferases seem to exist. Until now we have cloned several glycosyltransferases from human GlcNAc-transferase-III\(^3\), Galβ1,3GlcNAc 2,3sialyltransferase\(^4\), mouse Galβ1,3(4)GlcNAc 2,3sialyltransferase\(^5\), Galβ1,4(3)GlcNAc 2,3sialyltransferase\(^5\), human α2,8sialyltransferase\(^6\) and GlcNAc-transferase-V (unpublished result).

The asparagine-N-linked oligosaccharides found on the cell surface of liver cirrhotic and hepatoma tissues differ in size and structure from those found on the cell surface of normal liver cells\(^5\). Mizoguchi and co-workers\(^6\) suggested that these changes are due to a changed expression of GlcNAc-transferases, involved in the biosynthesis of tri- and tetraantennary N-linked chains, bisected structures and elongated chains. The formation of the branches is governed by the activities of a set of GlcNAc-transferase-I - VII\(^7\). To obtain more insight into the enzymatic basis for the tumor-dependent structural alterations, we assayed the activities of GlcNAc-transferase-III and GlcNAc-transferase-V (Fig. 1) in human hepatoma cell lines of Hep3B and HepG2, and also in human colon cancer cells of SW620 and HTB39.

GlcNAc-transferase-III produces a bisecting GlcNAc residue in the β-linked mannose of the trimannosyl core of the oligosaccharides. GlcNAc-transferase-III activity was observed in a variety of tissues and cell lines such as rat liver during hepatocarcinogenesis\(^8-12\), human serum from hepatoma patients\(^7\), rat kidney\(^13\), human B lymphocytes\(^14\), HL60 cells\(^15\), Novikoff ascites tumor cell\(^16\), CaCO-2 cells\(^17\), and HuH-6 cells

Fig. 1. The oligosaccharide chain structures of GlcN,GlcN-biant-PA, GlcN,(GlcN),GlcN-biant-PA and GlcN,GlcN,GlcN-biant-PA.

GlcN,(GlcN),GlcN-biant-PA and GlcN,GlcN,GlcN-biant-PA are the reaction products of GlcNAc-transferase-III and GlcNAc-transferase-V, respectively, when GlcN,GlcN-biant-PA as acceptor substrate and UDP-GlcNAc as donor substrate were used.