ALTERED SIALYLATION AND SIALYLTRANSFERASE EXPRESSION IN GYNECOLOGIC CANCERS

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SUMMARY
Sialic acids and their derivatives are ubiquitous at the terminal positions of the oligosaccharides of glycoproteins that play roles in a variety of biologic processes, such as cell–cell communication, cell–matrix interaction, adhesion, and protein targeting. Altered sialyltransferase (ST) expression plays an important role in oncogenesis, tumor progression, and lymph node metastases. For example, in squamous cell carcinoma of the cervix, α2,6-ST I shows positive correlation not only with oncogenesis, but also with tumor metastases to the pelvic lymph node. The over-expression of α2,6-ST I is due to reactivation of the hepatic form of the promoter. With advanced metastases, α2,3-linkage also dramatically changes, and this change more accurately predicts pelvic lymph node metastases in squamous cell carcinoma of the cervix. This laboratory successfully cloned α2,3-, α2,6-, and α2,8-ST genes to screen a powerful anti-ST reagent, soyasaponin I (SsaI). SsaI is not cytocidal but, in contrast, has a cytostatic effect on cancer cells, mainly slowing cell growth and division. It also modifies the invasive behavior of cancer cells such as migration and adhesion. Thus, altered glycosylation is important in gynecologic cancers, especially squamous cell carcinoma of the cervix. In future, the functional roles of ST in cancer pathogenesis may be elucidated. For example, specific anti-ST inhibitors could clarify the role of changing sialylation in cancer behavior, monoclonal antibodies to certain glycosylated epitopes will help diagnosis of such tumors and, most importantly, both these techniques will offer therapeutic avenues designed to attack tumor cells via their glycans in the near future. [Taiwanese J Obstet Gynecol 2004;43(2):53–63]

Key Words: neoplasms of the cervix, prognosis, sialic acid, sialyltransferase

Introduction
Glycosylation is one of the most frequently occurring co- or post-translational modifications made to proteins and lipids in the secretion machinery of the cell [1]. More than half of known protein sequences contain the requisite sequence for N-glycosylation (AsnXxxSer(Thr); Xxx ≠ Pro), and any serine (Ser) or threonine (Thr) residue can potentially be glycosylated [2,3]. The resultant carbohydrate side chains often have very complex oligosaccharide sequences and concomitant structural diversity [1–3]. There are two major types of glycosylation: O-glycosylation, where the sugar is bound to the hydroxyl of a serine or a threonine residue, and N-glycosylation, where the sugar is attached to the amide function of an asparagine in the consensus sequence Asn-X-Ser/Thr, where X is any residue but a proline [3]. While the protein sequence is completely encoded by the genome, the sequence and structure of the sugar moiety, or glycan, only depend on the action of highly specific and precisely located enzymes known as glycosyltransferases and glycosidases. Thus, the glycan structure is determined not only by the nature of the protein it is bound to, but also by the tissue or cell where it is made [3]. These carbohydrate side chains modulate...
the interaction of a protein with its environment, influencing its solubility, activity, and biologic fate. The function of the glycans covers a wide spectrum, from relatively trivial to crucial for the growth, development, and survival of cells and organisms. However, sugars are often overlooked, compared to the extent of research on genes and proteins [3]. This is mainly due to their complexity, which makes them difficult to sequence and study. Glycan structures cannot be readily obtained because they cannot be amplified as nucleic acids can, they generally come as a highly heterogeneous mix of different species bound to a single protein, they are non-linear molecules, and there is no universal method to precisely determine the structure of a glycan species without making assumptions regarding the biologic system [4]. Of particular importance are the sialic acids and sialic acid derivatives that are ubiquitous at the terminal positions of the oligosaccharides of glycoproteins [5–7], which determine the half-lives of many circulating glycoproteins. The biosynthesis of these molecules may act as a coding system, since they are able to interact with high specificity and selectivity with carbohydrate-binding proteins including lectins [8], antibodies, receptors, and enzymes. These molecules are also involved in cell communication such as cell–cell and cell–matrix interactions and molecular recognition during tumor development, differentiation, and progression [1,9,10], which is catalyzed by enzymes of the sialyltransferase (ST) family [9].

Classification of Sialyltransferases

Altered sialylation, which occurs during certain pathologic processes such as tissue inflammation, oncogenesis, and metastasis, is associated with either enhanced or decreased activity of different STs, including glycoprotein-specific α2,3-, α2,6-, and α2,8-linkage transferring enzymes and glycolipid-specific α2,3- and α2,8-linkage transferring enzymes [11–26]. These STs are classified into four families according to the carbohydrate linkages they synthesize: the ST3Gal (α2,3-ST), ST6Gal (α2,6-ST), ST6GalNAc, and ST8Sia families [27]. Every family can be further classified into many subtypes. The ST3Gal family includes at least seven subtypes, ST3Gal I to ST3Gal VI and ST3Gal VI ubiquitous. The ST6 family includes two large subtypes, ST6Gal and ST6GalNAc, each of which is further separated into many types: the ST6Gal family comprises ST6Gal I, II, and III, and the ST6GalNAc family is further classified into ST6GalNAc I to ST6GalNAc VI. The primary structures deduced from cloned sialyltransferase cDNAs suggest a putative domain structure with a type II transmembrane topology. There are no significant amino acid sequence similarities among these STs, except in two sialyl motifs, L and S, which are proposed to be the cytidine monophosphate-sialic acid recognition and/or catalytic sites [28]. The α2,3 sialic acid linkages to Gal residues seem to be the most widely expressed, followed by the α2,6 linkage to Gal or GalNAc [29]. Among these, Thomsen-Friedenreich (TF)-related blood group antigens, such as TF (Galβ1-3GalNAcα1-RL), Tn (TF precursor, GalNAcα1-RL), and their sialylated variants, are oncofetal carbohydrate structures. Increases in β-1,6-branched, sialyl-Lewis epitopes, and sialyl-Tn antigen (sialylα2,6-GalNAc-Ser/Thr), or general increases in sialylation of cell surface glycoproteins, are commonly observed in N-linked and O-linked oligosaccharides in carcinoma cells [12,23,30], and these are correlated with tumor prognosis and metastasis. Carbohydrate changes have been noted in breast cancer [21,31–33], colorectal cancer [5,18,30,34–38], lung cancer [39,40], hepatic carcinoma [41,42], gastric carcinoma [43], head and neck squamous cell carcinoma (SCC) [44], brain tumor [45,46], choriocarcinoma [47], prostate cancer [48], and SCC of the cervix [19,49,50]. These changes in glycoprotein expression may play important roles in tumor grade, invasion, metastatic ability, and clinical outcome [13,18,21,30,32–34,38–40,42,44,46,49–51].

Altered Sialylation in SCC of the Cervix

This laboratory has demonstrated that, in SCC of the cervix, altered expression of α2,3- and α2,6-STS, which modify cell-surface glycosylation, correlates directly with poor prognosis and lymph node metastasis [19,49,51]. Expression of α2,6-STGal I was highest in cancers with more malignant behaviors such as poor differentiation, deep stromal invasion, lymphovascular space involvement, and lymph node metastases [49]. Similarly, α2,3-ST III is highly expressed in cancers with lymph node metastases: although initial expression can be down-regulated [19], during disease progression with lymph node metastases, expression of α2,3-ST III is paradoxically up-regulated. The positive correlation between α2,3-ST III and lymph node metastases is more specific than that between α2,6-STGal I and lymph node metastases, because only lymph node metastasis can predict increased α2,3-ST III mRNA expression, but nearly all conventional poor prognostic factors, including poor differentiation, deep stromal invasion, and lymphovascular space involvement, can predict increased α2,6-STGal I mRNA expression [49]. Together, these data suggest that an early event in oncogenesis of
SCC of the cervix is up-regulation of α2,6-STGal I, and its positive feedback control is associated with tumor growth and spread. A following event might be over-expression of α2,3-ST III, which shows a significant association with lymph node metastasis in International Federation of Obstetrics and Gynecology (FIGO) IB1 cervical SCC patients. Using this biologic model for monitoring lymph node metastases, this laboratory highlighted the possibility that finding factors to overcome the progressive stage of cancer could lead to changes in the first therapeutic approach [49].

**Cell Surface Sialic Acid Levels Mainly Controlled at Sialyltransferase mRNA Levels**

Cell surface sialic acid levels are mainly controlled at the mRNA level of ST genes [52]. Northern blotting has revealed that each ST gene is expressed in a tissue-specific manner, suggesting that transcription of the specific ST genes is also regulated in a tissue-specific manner [52–53]. For example, in humans, α2,6-STGal I is expressed by many tissues, but at dramatically different levels [54–56]. Changes in α2,6-STGal I expression have been observed in cancerous tissues and cells, and regulation of its expression is achieved transcriptionally through tissue-specific promoters that lead to the production of mRNA species which diverge in the 5'-untranslated region [35,57–64]. Multiple promoters are found in the α2,6-STGal I, α2,3-ST IV, α2,3-ST V (GM 3 synthase), and α2,3-ST VI genes. These promoters may respond to different physiologic signals and stimuli in different cell types. Cell type-specific transcriptional regulation of α2,6-STGal I has been studied most thoroughly. Three major mRNA species have been cloned from human sources [37,54]. The first, from a placenta cDNA library, contains the 5'-untranslated exons Y and Z (placental or Y+Z form: 250 bp) and is thought to represent the basal or housekeeping expression of the gene [59–62]. A second species lacks exons Y and Z but contains a specific sequence in front of exon I and represents the major liver transcript (hepatic or H form: 446 bp) [57,59,62]. The hepatocyte-specific promoter P1 (part of the liver transcript) has hepatocyte nuclear factor-1 (HNF1), activator protein 2 (AP2), and nuclear factor-interleukin 6 (NF-IL6) binding sites [57]. HNF1 consists of liver-enriched factors that are thought to participate in the hepatocyte specificity of P1 promoter activity. Xu et al characterized the P1 promoter region, which regulates Form 1 mRNA expression, using luciferase assays, and showed that the nt-156 to -1 region, which contains the HNF1 recognition element, is important for the transcriptional activity of the α2,6-STGal I gene in colon adenocarcinoma cell lines, because mutation of the HNF1 site reduced luciferase activity by about 80% compared with the wild-type construct [65]. The third form, specific to B-lymphocytes, lacks exons Y and Z but contains the 5'-untranslated exon X (X form or X transcript: 128 bp) [56,58,64]. The mature B lymphocyte cell line-specific promoter P2 (part of the X transcript) has NF1-κB, C/EBP (CCAAT enhancer binding protein), AP2, and NF-IL6 binding sites [57]. These factors may be important for B cell-specific regulation of the α2,6-STGal I gene, suggesting that cell type-specific regulation of the α2,6-STGal I gene is controlled by both specific promoter utilization and cell type-specific transcriptional factors, which allows quantitative regulation of α2,6-STGal I expression [63]. Wang et al found that in SCC of the cervix, enhanced α2,6-STGal I mRNA expression is not only associated with more invasive characteristics, such as deep stromal involvement, poor differentiation, and presence of lymphovascular invasion [19], but is also more frequently associated with lymph node metastases than with FIGO IB1 disease without lymph node metastases [49]. In SCC of the cervix, the presence of at least two different transcripts of ST6Gal I mRNA indicates that the gene may be transcribed through the use of both the “constitutive” promoter (Y+Z form) and the “hepatic” promoter in both normal and cancerous cervical tissue. However, the hepatic transcript is significantly enhanced during cancer transformation. Over-expression of the hepatic transcript might contribute to the general increase in α2,6-STGal I mRNA in cancerous cervical tissue, although Dall'Olio and colleagues reported that both the Y+Z and hepatic transcripts contribute to the total pool of α2,6-STGal I mRNA in normal and cancerous tissues [66]. The hepatic transcript shows a higher translational efficiency in vitro [55], so reactivation of the hepatic transcript in cancer transformation will permit a higher yield of α2,6-STGal I mRNA, especially in cervical cancer.

**Complexity of Individual Sialyltransferase mRNA Forms**

The original structures and chromosomal location of α2,3-ST IV genes have been determined [67,68]. Multiple mRNA forms that differ only in the 5'-untranslated region have also been identified for α2,3-ST IV. The mRNAs of α2,3-ST IV in the human placenta and a keratinocyte cell line consist of many isoforms, A1, A2, B1, B2, B3, and BX [68,69]. These transcripts are produced by a combination of alternative splicing and promoter use, which suggests that the transcriptional
regulation of α2,3-ST IV depends on the use of alternative promoters [70]. The α2,3-ST IV mRNAs are transcribed from different promoters, pA, pB1, pB2, pB3, and pBX, respectively [51]. Type B mRNAs are expressed in several cells, whereas type A mRNAs are specifically expressed in the testis, ovary, and placenta, suggesting that pA promoter activity is especially high in these tissues [52]. Taniguchi and Matsumoto suggest that the epithelial cell-specific regulation of the α2,3-ST IV gene is mediated by specific interaction between AP2 and the up-stream nt -520 to -420 element [69]. AP2 belongs to transcription factors involved in epithelium cell-specific gene expression [71,72]. Grahn et al cloned and sequenced human α2,3-ST III gene transcripts from human peripheral blood leukocytes, covering the coding region of the gene, and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety in and isolated 19 different transcripts with a wide variety

**Ovarian Cancers**

Carcinoma of the ovary is still the most lethal female cancer in Taiwan, although it is not the most common disease. The prognosis of ovarian cancer depends on many factors, most of which are based on clinical and histopathologic parameters including stage, differentiation, and cell type [75–80]. Among these factors, the most important is tumor stage [76]. However, the symptoms and signs of ovarian cancer are indolent and nonspecific, which delays accurate diagnosis [75], so more than two-thirds of patients are diagnosed at advanced stages (stages III and IV), for which the 5-year survival rate is less than 20% [75]. The standard treatment for ovarian cancer is optimal debulking surgery followed by postoperative taxol/cisplatin-based chemotherapy [79,80]. Despite intensive treatment, at least half of these patients will suffer from persistent or recurrent ovarian carcinomas, and finally die of the disease [79]. Recent advances in cell and molecular biology have improved our understanding of the possible mechanisms underlying tissue differentiation, malignant transformation, and host-tumor interactions [81]. Elucidation of the pathways of programmed cell death and cell-cycle control has identified several genes that play a central role in maintaining the integrity of the genome and regulating the cell cycle. Specific gene alterations have been associated with sporadic or hereditary tumors and cell response to chemotherapy [82]. Tumor migration, invasion, metastasis, and angiogenesis are being elucidated at a molecular level. The immune response to tumors has also been extensively studied, and particular defects have been identified in patients with established malignancies. This growing bulk of information has allowed the design of specific molecular strategies aimed at suppressing tumor growth and controlling tumor progression. Several approaches have emerged as potentially promising, and some are being tested in the management of epithelial ovarian cancers. However, no evidence so far supports these approaches as better than conventional therapy. Therefore, evaluation of more specific and sensitive biologic targets in ovarian cancers remains of interest. Among these biologic targets, sialic acids may be one of the most promising molecules because they are involved in cell–cell and cell–matrix interactions and cellular recognition [24,25], all of which are closely related to tumor migration, invasion, metastasis, and tumor-host interaction.

**Altered Glycoproteins in Ovarian Cancers**

The antigenicity of one glycoprotein, mucin (MUC1), is altered in ovarian cancer, and anti-MUC1 antibodies can be used as a diagnostic tool to detect the cancer [83]. In addition, cytotoxic T-cells from malignant ovarian tumors target the MUC1 mucin core peptide and can lyse B-cell lines expressing either MUC1 or MUC1 peptides from the tandem repeat region; this lysis is inhibited by antibodies directed against the MUC1 tandem repeat region [84]. The most frequently used serum marker either in screening or post-treatment follow-up of ovarian cancer, CA125 (cancer antigen 125), is a mucin-like glycoprotein that appears in most epithelial ovarian cancers, although it may also be present in benign ovarian disease or endometriosis [83]. CA125 is isolated from OVCAR-3 ovarian cancer cells using a monoclonal antibody, and is rich in O-glycans with core 2 structures and Le^′^ and Le^′^ determinants.
Sialyl-Tn and Tn antigens are highly expressed in ovarian tumors and this seems to be an early event during carcinogenesis [86,87]. Moreover, sialyl-Tn antigen is usually found in tumors but not usually in normal mucosa. Mucins expressing the sialyl-Tn antigen may be secreted from the tumor and appear in the blood. Inoue et al found that serum sialyl-Tn antigen was significantly elevated at a cutoff of 39 U/mL: clinical stage I, 31%; stage II, 29%; and stage III, 69%; the antigen level was also correlated with the effect of treatment [88]. However, the lack of tumor specificity of sialyl-Tn antigen limits its diagnostic value in gynecologic malignancies, although serial measurement appears to be useful for monitoring patients and evaluating therapy [88]. Kobayashi et al found that the presence of sialyl-Tn antigen in the serum of ovarian cancer patients is associated with a poor prognosis [89]. The reasons for elevated sialyl-Tn antigen expression have not been clarified, but several possible mechanisms have been proposed. Enzyme relocalization: if polypeptide α-GalNAc-transferase is present in later Golgi compartments, the synthesis of the core structure may no longer be possible; alternatively, the α6-ST may be localized to early compartments, and its action would block the synthesis of the core structure. Block in core synthesis: human LSC (sub-clone derived from LS174T human colon cancer cells, ATCC number CL-188) colon cancer cell lines have a block in O-glycan core 1 and 3 synthesis and cannot make the core structure 1-4; therefore, GalNAc is available for sialyl-Tn synthesis. Loss of O-acetylation: in the normal colon, changes in sialic acids of mucins are largely O-acetylation decreases, leading to the exposure of free sialic acid and recognition of the sialyl-Tn antigen by antibodies [83].

A number of other glycoproteins, including haptoglobin and α1-proteinase inhibitor, are also abnormally glycosylated in ovarian cancers [83]. Haptoglobin contains more fucose (Fuc) residues in patients with ovarian cancer, and this corresponds to higher activities of α2-, α3- and particularly α4-Fuc-transferase [90,91]. There is growing evidence that these molecules act as good markers in ovarian cancer either in screening, diagnosis, or post-therapeutic follow-up. Therefore, it is rational to evaluate the relationship between cell surface sialylation changes or changes in cellular sialyltransferase activity or expression and ovarian disease, progression, invasion, and metastases. Furthermore, it is reasonable to evaluate the possible regulation system that controls these changes in ovarian benign or malignant diseases.

Mucins, the main class of O-glycosylated glycoproteins, are of very large molecular weight, and have Ser/Thr/Pro-rich tandem repeat regions that are heavily O-glycosylated [83]. At least nine human mucins, which can be secreted or membrane-bound, have been characterized [83]. Cancer cells contain membrane-bound mucin-like glycoproteins that have O-glycan-rich domains, and O-glycans play important roles in the attachment and invasion of cancer cells and their survival in the blood stream.

### Altered Sialylation is Related to Tumor Migration and Adhesion

The interactions between tumor cells and endothelial cells, the attachment and invasion of tumor cells through the endothelium via binding of selectins to their ligands, may be an important step in the metastatic process [83]. Tumor cells with mucin type O-glycans and sialyl-Le' ligands readily bind to E-selectins on activated endothelium [92–94]. In several models of metastasis, O-glycans are critical for the formation of metastases [83,95,96]. Inhibition of O-glycan extension by GalNAc-benzyl prevents this binding of human colon cancer cells to E-selectin, and reduces liver metastases of LS174T human cancer cells in nude mice [97]. Since the expression of Lewis antigens can be inhibited with GalNAc-benzyl, these appear to be mainly attached to O-glycans [98,99]. While sialyl-Le' attached to O-glycans may promote cell adhesion and invasiveness, other O-glycan structures may also play important roles on cancer cell surfaces [100]. Compared to primary tumors, the expression of Tn and T antigens is decreased in metastatic colon cancer cells, with a corresponding increase in sialyl-Tn, sialyl-T, sialyl-Le, and sialyl-Le' [101]. The tissue distribution of sialyl-Tn and Le' antigens differs significantly between primary tumors and metastases of cervical cancer [100]. GalNAc-benzyl treatment of B16 L6 melanoma cells increases peanut agglutinin (PNA) binding, probably due to the exposure of the T antigen on its cell surface, which results in enhanced adhesion of tumor cells to activated endothelial cells or platelets mediated by ELAM-1 (E-selectin) or GM P-140 (P-selectin), and reduces sialylation of CD44 while enhancing metastatic capacity [94].

In variants of human KM12 colon cancer cells, the expression of sialyl-dimeric Le' attached to mucin-type chains corresponds to high invasiveness [102]. Sialyl-dimeric Le' is frequently increased in metastatic colon cancer [103,104]. These sialylated Lewis structures may play roles in cancer other than through their selectin-binding properties. Sialic acid has repeatedly been implicated in the metastatic process [105]. Inhibition of sialylation and O-glycan extension and sialylation re-
duces the metastatic potential of cancer cells [97,106]. Metastatic colon cancer cells produce hypersialylated mucins, which appear to play an important role in cell adhesion [107,108]. It is possible that chains carrying sialic acid may regulate the interaction of cancer cells with other cells and with the cell matrix. These chains may therefore be responsible for adhesion as well as anti-adhesion, and for extending the survival times of cancer cells in the blood stream. Sialic acid may also be involved in growth regulation [109]. Because sialylglycoconjugates regulate adhesion and promote motility, they may be important for the colonization and metastatic potential of cancer cells [110-112].

Monoclonal Antibodies and Lectin: Excellent Tools to Study Change in Cell-surface Carbohydrate-binding Proteins

In pathology, the approach to finding an aberrant antigen expressed in malignant cells is to detect such antigens in paraffin-embedded specimens by histochemical methods, an approach that is very important because pathologists can use archival collections of tissue blocks [113]. To study carbohydrate-binding proteins, the best tool is monoclonal antibodies, which need more complicated preparation. Therefore, various lectins are used as a good alternative to study changes in surface carbohydrates. A lectin is a carbohydrate-binding protein of non-immune origin that agglutinates glycoconjugate polysaccharides, which makes lectin-anti-lectin immunohistochemistry a useful method for detecting specific lectin-binding cell-surface antigens [114-116]. Lectins are widely used in many fields, ranging from medical to chemical research [117]. The carbohydrate targets of several lectins are related to tumor progression and metastasis [113]. Two groups independently reported that Ulex europaeus-I agglutinin (UEA-I) binds to normal colonic epithelium of the right colon but shows no positive staining in material from the left colon or rectum [118-121]. UEA-I lectin not only shows regional distribution in its reactivity, but also positive staining with high frequency in carcinomas of the colon and rectum. In addition, there are differences in molecular weight between UEA-I-binding glycoproteins from normal epithelium from the left colon and from carcinoma tissue, and these molecules are related to carcinomembryonic antigen. UEA-I lectin specifically binds to fucosylated type-II blood group H antigen, and the expression of high-molecular-weight fucosylated glycoprotein detected by UEA-I is increased in carcinoma compared to normal mucosa, but is low in primary tumors that have already produced metastases [121]. Boland et al used several lectins and reported stepwise alteration in the lectin-binding pattern between normal colonic epithelium and carcinomas [122-124]. Boland et al and Cooper and Reuter used PNA, which has specificity for the T antigen (Galβ1-3GalNAcα-O-Ser/Thr), for a lectin-immunohistochemical study of polyps of the colon and rectum [124,125]. Boland et al reported stepwise increases in PNA binding from benign tubular adenoma (7%), benign villo-glandular adenomas (26%), and adenoma-containing cancer (41%) [123]. Cooper and Reuter also reported a stepwise increase in expression of T antigen in the apical cytoplasm and/or glycoconalx of non-mucinous cells of tubular adenoma (25%), villous adenoma (43%), and the adenomatous part of adenoma with in situ carcinoma (60%) [125]. Almost 80% of in situ carcinoma cells express PNA in an apical cytoplasmic and/or glycoconalx pattern. These findings support continuous progression of epithelial malignancies in the colon and rectum. The localization of T antigen is different in the normal colonic epithelium, in adenomas, and in carcinomas, indicating incomplete glycosylation. Irimura and colleagues used another type of lectin, wheat germ agglutinin (WGA), which binds to sialic acid and (GlcNAc)n, and reported that the expression of WGA-binding high-molecular-weight mucin is increased in highly metastatic cell lines relative to parental cell lines, and is increased in metastatic lesions in studies using animal models [126]. There are several reports of metastasis-related lectins [127,128]. These reports imply that altered carbohydrate expression is related to altered biologic function in malignant cells, including tumor progression and metastasis formation. However, a one-to-one correspondence between a lectin and a carbohydrate antigen is sometimes difficult to prove. Lectin binding to oligosaccharide structures in some cases is very specific, but in other cases, it is not as strict as a monoclonal antibody; however, a lectin is more easily and conveniently used than a monoclonal antibody.

Specific Findings Using a Specific Anti-sialyltransferase Inhibitor

Finally, recent studies in this laboratory on the specific cell-permeable anti-sialyltransferase, soyasaponin I (SsaI) [20], showed very impressive findings (unpublished data). SsaI inhibited cellular α2,3-ST activity and expression of cell surface α2,3-sialic acids on MCF-7 breast cancer cells. It also enhanced the adhesion of MCF-7 cells to the extracellular matrix. SsaI had no effect on the migration of MCF-7 cells, but significantly decreased the migration ability of a highly metastatic
breast cancer cell line, MDA-MB-231. We believe that future experiments may elucidate the functional roles of STs in cancer pathogenesis.

Conclusion

Altered sialylation is very common in certain pathological conditions, including cancer transformation and cancer metastasis. Advanced molecular biology techniques allow more insight into the importance of sialylation.

Acknowledgment

The work of the author's laboratory has been supported by grants from the National Science Council (NSC-92-2314-B075-115) and Taipei Veterans General Hospital (93-B-186).

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