Increase in Serum and Tissue Glycosyltransferases and Glycosidases in Tumor-bearing Rats

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SUMMARY

In this report, both galactosyltransferase and sialyltransferase were examined in the serum, liver, and tumor of rats with either 7,12-dimethylbenz(a)anthracene-induced mammary tumors that grew slowly or the transplantable Walker carcinomas 256 that grew rapidly. In rats bearing the 7,12-dimethylbenz(a)anthracene-induced mammary tumors, a twofold elevation in serum sialyltransferase activity was seen only when the tumor weight was in excess of 15 g. This was accompanied by an increase of about 60% in the liver sialyltransferase. No change in the levels of serum and liver galactosyltransferase was detected in these animals. In contrast, the increase in both serum and liver sialyltransferase and galactosyltransferase in rats bearing the transplantable Walker carcinomas paralleled the weight of the growing tumor mass. Moreover, the magnitude of increase of both enzymes in this group was significantly higher than that in rats carrying a similar load of 7,12-dimethylbenz(a)anthracene-induced mammary tumors. Examination of the substrate specificity of sialyltransferase in different tissues from tumor-bearing rats suggested that the serum enzyme resembled more closely the host liver enzyme. In addition, β-galactosidase and sialidase activities were found to be elevated only in the serum of rats carrying the Walker carcinomas, although there was no relationship between the increment of enzyme levels and the tumor mass in these animals. Thus, it seems that tumor growth rate could be one of the factors in determining the levels of serum glycosyltransferase and glycosidase activities.

INTRODUCTION

Neoplastic transformation of cells has been known to be accompanied by changes in the composition of plasma membrane glycoproteins. One example of such an alteration is an elevation in the level of sialic acid on the cell surface (26, 28). The importance of cell-surface glycoproteins is underscored by the increasing recognition of their role in modulating many membrane-mediated functions, such as cell-cell adhesion and agglutination, antibody-antigen interaction, hormone binding, etc. (7, 8). It is conceivable that changes in the glyocalyx could affect the behavior and therefore the invasive nature of the cancer cells. Another phenomenon that is related to the appearance of neoplasia is the detection of certain newly acquired serum glycoproteins that are associated with some human cancers. These include carcinoembryonic antigen of the digestive tract (10), α-fetoprotein for hepatic carcinoma (17), and specific antigens in human ovarian (2) and breast cancer (11). The use of these glycoprotein antigens as a diagnostic marker for cancer and disease recurrence has been widely investigated.

Glycoprotein synthesis is initiated by the sequential addition of individual monosaccharides to the protein core, catalyzed by a group of enzymes collectively known as glycosyltransferases. These enzymes are primarily located in the Golgi apparatus (22); however, recent ultrastructural evidence shows that they are also present on the cell surface (20). Presumably those in the Golgi are involved in the synthesis of glycoproteins or glycolipids that may either be secretory or subsequently translocated to the cell surface as structural or functional components of the plasma membrane. On the other hand, the respective formation of specific "ectoglycosyltransferases" and the appropriate glycoconjugate acceptors on the cell membrane have been implicated in the mechanism of cell adhesion and recognition (21).

In this report, we have examined 2 glycosyltransferases (sialyltransferase and galactosyltransferase) and 2 glycosidases (sialidase and β-galactosidase) in the serum, liver, and tumor of rats bearing either the DMBA3-induced mammary tumors or the Walker 256 carcinoma. The objective of this study is to determine whether measurement of enzymes in different tissues that are involved in glycoprotein metabolism may serve as an indicator of tumor proliferation.

MATERIALS AND METHODS

Materials. UDP-[U-14C]galactose (specific activity, 274 mCi/mmmole) and CMP-[4,5,6,7,8,9-14C]sialic acid (specific activity, 197 mCi/mmmole) were purchased from New England Nuclear, Boston, Mass. Fetuin was purchased from Grand Island Biological Co., Grand Island, N. Y. Ovine submaxillary mucin, lactose, N-acetylneuraminic lactose, and α-nitrophosphorylgalactopyranoside were obtained from Sigma Chemical Co., St. Louis, Mo.

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2 To whom requests for reprints should be addressed, at Roswell Park Memorial Institute, 666 Elm Street, Buffalo, N. Y. 14263.
3 The abbreviation used is: DMBA, 7,12-dimethylbenz(a)anthracene.
Sialic acid-free fetuin for sialytransferase assay was prepared by mild acid hydrolysis (24). The removal of terminal sialic acid was confirmed by the thiobarbituric acid assay (27). Sialic acid and galactose-free fetuin for galactosyltransferase assay were prepared by the periodate oxidation-borohydride reduction method described by Spiro (25). N-[^3H]Acetylneuraminic acid of α₁-glycoprotein for sialidase assay was prepared according to the method described by Schauer et al. (23). The radioactive α₁-glycoprotein had a specific activity of 15 μCi/mg and was tested against Clostridium perfringens sialidase (Sigma). The amount of radioactivity released (in the form of N-[^3H]acetylneuraminic acid analog) was proportional to the quantity of the purified bacterial enzyme added, showing that the modified α₁[^3H]glycoprotein could be used as the appropriate substrate for the sialidase assay.

Tumors. Mammary tumors were induced in female Sprague-Dawley rats by a single injection i.v. of 5 mg DMBA in an emulsion when the animals were 55 to 60 days old. The lipid emulsion of DMBA was prepared by Dr. Paul Schurr of the Upjohn Company, Kalamazoo, Mich. The DMBA-induced mammary tumors grew relatively slowly, with a latent period of about 2 months before the tumors became palpable. In some rats, multiple tumors could be found. Walker 256 carcinomas were obtained by injecting a homogeneous mince of Walker tumor (suspended in Eagle's medium) s.c. in female Sprague-Dawley rats. The Walker tumors grew rapidly as a solid mass, attaining a size of from 30 to 40 g in about 3 weeks.

Serum Collection and Tissue Extraction. Rats were anesthetized with ether, and blood was collected in 10-ml syringes via heart puncture without anticoagulant. RBC were removed by centrifugation, and serum samples were stored at −70° until ready for assay.

Liver and tumor samples were dropped in liquid nitrogen immediately after excision from the animals. They were then pulverized with a Thermovac pulverizer and stored at −70°. Prolonged storage of tissues at this temperature for 3 to 4 months had no effect on the activities of either sialytransferase or galactosyltransferase. On the day of the enzyme assay, the pulverized tissue was homogenized in approximately 10 volumes of ice-cold 0.9% NaCl solution with a Potter-Elvehjem homogenizer. The crude homogenate was centrifuged at 1200 × g for 10 min to remove cell debris and nuclei. The supernatant fraction thus obtained was used for enzyme assays. Protein in serum and tissue extract was determined by the method of Lowry et al. (16).

Enzyme Assays. For the determination of sialytransferase, the assay mixture contained 50 μl of serum or the same quantity of liver homogenate or tumor extract, 500 μg of desialated fetuin (sialic acid-free-fetuin), 1 nmole of CMP-[^4C]sialic acid (444,000 dpm), 10 mM MnCl₂, and 20 mM Tris buffer (pH 7.4) in a final volume of 150 μl. For the determination of galactosyltransferase, the assay mixture contained 20 μl of serum or tissue extract, 250 μg of sialic acid and galactose-free-fetuin, 3 nmoles of UDP-galactose (22,000 dpm of UDP-[^4C]galactose + unlabeled UDP-galactose), 10 mM MnCl₂, and 20 mM Tris-maleate buffer (pH 6.8) in a total volume of 100 μl. In the case of liver and tumor samples, the presence of Triton X-100 in a final concentration of 0.1% was required for optimal assay condition. It should be noted here that for the assay of serum glycosyltransferases, the addition of a nonionic detergent (both Triton X-100 and Tergitol NPX were tested) to the incubation medium had no beneficial effect in either the control or the experimental samples from tumor-bearing rats. To determine endogenous activities in both enzyme measurements, the respective exogenous glycoprotein acceptor was omitted in the reaction mixture.

Tubes for sialytransferase and galactosyltransferase assays were incubated at 37° in a Dubonhoff shaker for 1 and 0.5 hr, respectively. Conditions for each enzyme assay were chosen so that linearity of the reaction was achieved with respect to time and enzyme concentrations. The reaction was terminated by the addition of 2 ml of ice-cold 5% trichloroacetic acid-2% phosphotungstic acid in 0.5 N HCl, and the tubes were centrifuged at 2600 × g for 10 min. The resultant pellet was washed 2 times with the same acid solution and once with ethanol: diethyler (2:1, v/v). The precipitate was dissolved in 1 ml of NCS tissue solubilizer (Amersham/Searle Corp., Arlington Heights, III.) and placed in 10 ml of scintillation cocktail consisting of Spectrafluor (Amersham/Searle): ethylene glycol monomethyl ether: toluene (1:10:14, by volume): 8% naphthalene. Radioactivity was determined by liquid scintillation counting. Both sialytransferase and galactosyltransferase activities are reported under "Results" as calculated exogenous activities, i.e., total (in the presence of exogenous glycoprotein acceptor) minus endogenous (in the absence of exogenous acceptor) activities. Enzyme activities were expressed as pmoles of sialic acid or galactose transferred per mg protein per hr.

This technique was used when other glycoproteins such as desialated ovine submaxillary mucin or desialated α₁-acid glycoprotein were used as the acceptor for the sialytransferase assay. When an acid-soluble molecule such as lactose was used as the acceptor, radioactive CMP-sialic acid (donor) and neuraminlactose (reaction product) were separated by descending paper chromatography as described by Kuhn (15). The N-[[^4C]acetyleneuraminlactose was compared with the nonradioactive reference compound, and the spot was then cut out for counting. N-Acetyleneuraminlactose was detected by spraying the paper with 4% diphenylamine in ethanol:4% aniline in ethanol: syrupy phosphoric acid (5:5:1, by volume), followed by heating at 80° for 10 min.

β-Galactosidase assay was performed by the method described by Bosmann et al. (6). The incubation medium consisted of 0.05 ml of serum or tissue extract, 6 μmoles of p-nitrophenylgalactopyranoside dissolved in 0.9 ml of citrate buffer (0.05 M, pH 4.5), and 0.05 ml of Triton X-100 (final concentration, 0.1%). Reaction was carried out at 37° for 30 min and was terminated by the addition of 0.2 ml each of 0.25 M ZnSO₄ and 0.25 M Ba(OH)₂. One ml of the clear supernatant fraction obtained after centrifugation was transferred to 2 ml of 0.4 M glycine:NaOH, pH 10.5. The intensity of the yellow color developed was measured spectrometrically at 420 nm, and the amount of p-nitrophenylgalactose hydrolyzed was calculated from a p-nitrophenol standard curve.

For the sialidase assay, the reaction mixture consisted of

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200 µl of serum or tissue extract, 100 µl of 0.3 M sodium acetate buffer, pH 4.0 (to adjust final pH mixture to 4.5), 50 µl of a solution of α1-[3H]glycoprotein (approximately 300,000 dpm, corresponding to 4 moles of tritiated N-acetyleneuraminic acid analog) and Triton X-100 (final concentration, 0.1%). The tubes were incubated at 37° for 2 hr and the reaction was terminated with 50 µl of 30% trichloroacetic acid:12% phosphotungstic acid in 3 n HCl. The acid-insoluble precipitate was removed by centrifugation, and 200 µl of the clear supernatant were used for counting in 10 ml of ACS (Amersham/Searle). Results were expressed as pmoles of N-acetyleneuraminic acid analog released per mg protein per hr.

Statistics. Results were given as mean ± S.E. Statistical comparisons were determined by Student’s t test. Differences between means were considered significant when the p value was less than 0.05.

RESULTS

Results in Table 1 show that there was no significant increase in serum sialyltransferase activity in rats bearing the DMBA-induced mammary tumors until the total tumor load in the animals was in the range of 10 to 20 g. The host liver sialyltransferase activity was elevated maximally about 60% in these same rats. The activity of this enzyme was measured in tumors (ranging from 0.5 to 18 g) and was found to be the same, 6.2 ± 0.4 pmoles/mg protein/hr, despite a wide variation in the size of the tumors. For comparison, the lactating mammary gland was also investigated. Although there was an abundance of enzyme activity in the lactating gland, data in Table 1. Examination of galactosyltransferase activities in these same rats bearing the DMBA-induced tumors showed that there was no elevation in the enzyme activities in the serum, liver, and tumor when compared to the control animals.

Results presented in Table 2 disclose a positive correlation between the tumor weight and the increase in sialyltransferase levels in the serum and the liver in rats bearing the Walker 256 carcinomas. Thus, in rats carrying a tumor load of greater than 30 g, there was about a 9- to 10-fold increase in the serum enzyme activity and an increase of about 4-fold in the enzyme level in the host liver. It was interesting to note that as early as 5 days after tumor inoculation, at a time before the tumor became palpable, a slight but significant increase (about 55%) in both the serum and liver sialyltransferase activities was detected. There was no relationship between the specific activity of the enzyme in the tumor and the size of the tumor mass.

The galactosyltransferase activities in rats bearing the Walker tumors (Table 3) showed a similar increase in both serum and liver enzyme activities that paralleled the growth of the tumors. Although the pattern of increase in galactosyltransferase was similar to that of the sialyltransferase activities, the magnitude of the increase was not as great.

In order to rule out the possibility that the increase in serum glycosyltransferase activities in rats bearing Walker carcinomas was not due to the presence of an “activator” in the circulation of the host, we performed mixed-assay experiments involving serum samples from both control and experimental animals in the same reaction tube. The data in Table 4 demonstrate that the elevation in serum glycosyltransferase activity is a reflection of an increase in enzyme proteins, since varying mixtures of aliquots of control and experimental samples yielded results that were additive in nature. Dialysis of the serum samples for several hr before the assay also did not alter the enzyme activities.

We also investigated a possible difference in the biochemical characteristics of the sialyltransferases assayed in different tissues and tumors. Experiments with various substrates were carried out to test the property of this particular enzyme. The acceptors for sialyltransferase assay selected for this experiment included the macromolecules α1-glycoprotein, ovine submaxillary mucin, and a low-molecular-weight compound such as lactose. The data are shown in Table 5. It should be pointed out that results for both serum and liver samples from the tumor-bearing rats showed almost identical findings. This suggested that the serum and liver sialyltransferases had the same substrate specificity. Moreover, the serum and enzyme activities from normal control...
rats were found to have similar substrate specificities when compared to those of tumor-bearing rats (results not shown). The sialyltransferase assayed in the DMBA-induced mammary tumors had a lower activity with desialated α-mucin and ovine submaxillary mucin but a much higher activity with lactose when compared to the enzymes in both serum and liver. In contrast, the Walker tumor sialyltransferase seemed to be very active in the sialation of tumors since DMBA-induced mammary tumors grow very fast and metastasize. Bosmann et al. (6) reported higher serum sialyltransferase levels in rats bearing the rapidly growing Novikoff hepatomas in comparison to the slower-growing Reuber H35 hepatomas.

Since both sialyltransferase and galactosyltransferase activities were determined on the basis of the amount of sugars transferred to the appropriate acceptor, changes in sialidase and galactosidase activities could lead to erroneous estimations. For this reason, both of these glycosidase activities were studied in the course of this investigation. It was found that both sialidase and β-galactosidase activities were undetectable at pH's of 7.4 and 6.8, the optimal pH's for the assay of sialyltransferase and galactosyltransferase, respectively. It was therefore concluded that the presence of glycosidases could not possibly interfere with the outcome of the glycosyltransferase assays. However, a different picture emerged when the measurements were carried out at pH 4.5. Results are shown in Table 6.

In rats carrying the DMBA-induced mammary tumors, no change in sialidase or β-galactosidase was detected in the serum and liver of the hosts. The glycosidase activities in the tumor, however, were higher than that found in the mammary gland. In contrast, serum from rats carrying the Walker carcinomas showed an increase in both sialidase and β-galactosidase, although the degree of elevation was not related at all to the tumor mass. Again, no change in liver glycosidases was observed in these animals.

**DISCUSSION**

This study shows that, in rats carrying the DMBA-induced mammary tumors, an increase in serum and liver sialyltransferases is observed only when the tumor mass is above 15 g, thus confirming the results reported earlier by Bosmann and Hilf (5). In contrast, both serum and liver glycosyltransferases as well as serum glycosidases show a marked elevation in rats bearing the transplantable Walker carcinoma. These results suggest that the level of the enzyme activities may be a function of the growth rate of the tumors since DMBA-induced mammary tumors grow very slowly, whereas the transplantable Walker carcinoma is a fast-growing tumor. Bosmann et al. (6) reported higher serum sialyltransferase levels in rats bearing the rapidly growing Novikoff hepatomas in comparison to the slower-growing Reuber H35 hepatomas.

Recently, Bernacki and Kim (1) examined several transplantable mammary tumors, including both metastasizing and nonmetastasizing lesions. They found that rats with metastasizing tumors showed about a 2-fold elevation in their serum sialyltransferase activity compared with the normal rats or rats with various nonmetastasizing tumors. The magnitude of increase of the serum sialyltransferase in rats with either the DMBA-induced mammary tumor or the Walker transplantable carcinoma reported in this paper was much higher, even though both tumors were nonmetastasizing. The discrepancy between these 2 studies could be due to the total tumor burden of the animals. Thus, it is possible that several factors, including tumor load, growth rate, and type of tumor, as well as the metastatic potential of the tumor, could be important in determining the serum glycosyltransferase levels.

The tissue origin of the serum glycosyltransferase remains to be clarified. Kim et al. (14) have suggested that in a normal situation, the majority may originate from blood cells, liver, or mammary gland. Recent evidence presented by Fraser and Mookerjea (9) seems to indicate that the serum galactosyltransferase may be the conversion product of a higher-molecular-weight liver enzyme. On the other hand, the abnormal levels of serum glycosyltransferases and glycosidases in the host with cancer has been attributed to "leakage" of the enzymes from either intact or dying neoplastic cells and/or as a consequence of "shedding" of the tumor plasma membrane (5, 13, 29). In the present investigation, a substrate specificity study showed that, in tumor-bearing rats, the serum sialyltransferase closely resembled the liver enzyme. Although the evidence is far from definitive, it nonetheless raises the possibility that the

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**Table 3**

Tissue galactosyltransferase activities in rats bearing Walker 256 carcinomas

<table>
<thead>
<tr>
<th>Tumor mass</th>
<th>No. of rats</th>
<th>Serum</th>
<th>Liver</th>
<th>Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8</td>
<td>144 ± 9*</td>
<td>866 ± 43</td>
<td></td>
</tr>
<tr>
<td>Nonpalpable</td>
<td>10</td>
<td>184 ± 19</td>
<td>879 ± 92</td>
<td></td>
</tr>
<tr>
<td>&lt; 10 g</td>
<td>5</td>
<td>231 ± 38*</td>
<td>1398 ± 215d</td>
<td>347 ± 39</td>
</tr>
<tr>
<td>10-20 g</td>
<td>6</td>
<td>254 ± 37*</td>
<td>1547 ± 259r</td>
<td>384 ± 45</td>
</tr>
<tr>
<td>20-30 g</td>
<td>8</td>
<td>584 ± 72*</td>
<td>1857 ± 261r</td>
<td>293 ± 35</td>
</tr>
<tr>
<td>30-40 g</td>
<td>8</td>
<td>640 ± 78*</td>
<td>2460 ± 269r</td>
<td>336 ± 31</td>
</tr>
</tbody>
</table>

* pmoles of galactose transferred per mg protein per hr.
* Mean ± S.E.
* Rats were killed 6 days after inoculation of a homogeneous mince of the Walker tumor, at a time before the formation of tumor became apparent.
* Significantly different from the corresponding control value, p < 0.02.
* Significant different from the corresponding control value, p < 0.01.

**Table 4**

Glycosyltransferase activities in mixtures of serum from normal rats and rats bearing Walker carcinomas

<table>
<thead>
<tr>
<th>Enzyme assay</th>
<th>Serum from rats (µl)</th>
<th>Enzyme activity (dpm/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sialyltransferase</td>
<td>Control</td>
<td>Tumor-bearing</td>
</tr>
<tr>
<td>50%</td>
<td>4,458</td>
<td>41,326</td>
</tr>
<tr>
<td>10%</td>
<td>31,365</td>
<td>23,958</td>
</tr>
<tr>
<td>40%</td>
<td>12,614</td>
<td>10,831</td>
</tr>
<tr>
<td>Galactosyltransferase</td>
<td>20%</td>
<td>1,324</td>
</tr>
<tr>
<td>10%</td>
<td>3,988</td>
<td>3,635</td>
</tr>
</tbody>
</table>

* Theoretical values were calculated on a prorated basis, with the use of the observed enzyme activities obtained in assays involving serum samples from either the control rats or tumor-bearing rats.
Table 5
Substrate specificity of sialyltransferase activities of different tissues from tumor-bearing rats

<table>
<thead>
<tr>
<th>Enzyme activities (%)</th>
<th>Rats with DMBA tumors</th>
<th>Rats with Walker tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum</td>
<td>Liver</td>
</tr>
<tr>
<td>Sialic acid-free fetuin</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Sialic acid- and galactose-free fetuin</td>
<td>2.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Sialic acid-free α₂-glycoprotein</td>
<td>89.1</td>
<td>93.2</td>
</tr>
<tr>
<td>Sialic acid-free ovine</td>
<td>14.6</td>
<td>17.5</td>
</tr>
<tr>
<td>Submaxillary mucin</td>
<td>7.2</td>
<td>8.7</td>
</tr>
<tr>
<td>Lactose</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The preparation of these modified glycoproteins was described in “Materials and Methods.”

* Enzyme activities were expressed as percentages of an arbitrary reference measurement. The sialyltransferase activity determined with desialated fetuin (sialic acid-free fetuin) as the exogenous acceptor was designated as such a reference measurement and was set as 100%.

Table 6
Tissue glycosidase activities in tumor-bearing rats

<table>
<thead>
<tr>
<th>Rat</th>
<th>Tissue</th>
<th>β-Galactosidase*</th>
<th>Sialidase*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Serum</td>
<td>2.6 ± 0.2</td>
<td>2.2 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>168 ± 12</td>
<td>48.1 ± 3.9</td>
</tr>
<tr>
<td>Postlactating</td>
<td>Serum</td>
<td>2.7 ± 0.3</td>
<td>3.1 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Involuting Mammary Gland</td>
<td>656 ± 59</td>
<td>124 ± 15</td>
</tr>
<tr>
<td>DMBA-treated</td>
<td>Serum</td>
<td>3.1 ± 0.4</td>
<td>2.6 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>149 ± 13</td>
<td>53.5 ± 6.8</td>
</tr>
<tr>
<td></td>
<td>Mammary gland</td>
<td>125 ± 10</td>
<td>31.2 ± 4.7</td>
</tr>
<tr>
<td></td>
<td>Tumor</td>
<td>169-786 (317)</td>
<td>44.5-95.3</td>
</tr>
<tr>
<td>With Walker carcinomas</td>
<td>Serum</td>
<td>5.5-23.8 (12.6)</td>
<td>2.8-8.1 (4.3)</td>
</tr>
<tr>
<td></td>
<td>(352)</td>
<td>(243)</td>
<td>(41.6)</td>
</tr>
</tbody>
</table>

* nmoles of p-nitrophenylgalactose hydrolyzed per mg protein per hr.

* pmole of N-acetylneuraminic acid analog released per mg protein per hr.

* Mean ± S.E.

* Range of values obtained.

* Numbers in parentheses, mean.

rum glycosyltransferases may be “secreted” by the liver. Further confirmation of this would require purification of the enzymes from these 2 tissues.

The data also raise the question of how the growth of a tumor at a distant locus influences the liver function of the host. It is conceivable that the tumor may release an “information molecule” to direct the synthesis of liver glycosyltransferase enzymes. It has been demonstrated that the presence of a tumor elsewhere in the body markedly alters the enzyme profile of host tissue, such as the liver (12). The concept of a circulating “toxohormone” (18) is attractive, but this still remains unconfirmed. Recently, Noguchi et al. (19) have reported evidence of a “protein factor” in the Ehrlich ascites tumor cells that may be responsible for the increase in ornithine decarboxylase activity in the liver of the host mice. Whether the elevation in liver glycosyltrans-

ferases in the tumor-bearing rats observed in this study is due to the same mechanism remains to be investigated.

The physiological significance of these serum enzymes that are involved with the metabolism of glycoconjugates is far from clear. Bosmann et al. (4, 6) have suggested that the increase in glycosyltransferases and glycosidases in the circulation could conceivably lead to changes in the synthesis and degradation of oligosaccharides of glycoconjugates on the cell surface, thus resulting in alterations in cell-cell interaction. However, the hypothesis seems rather unlikely in view of the absence of nucleotide sugars in the extracellular fluid. Since glycosidases operate optimally in an acidic pH environment, the alkaline pH of the blood would most likely render the glycosidases inactive.

Elevated plasma sialyltransferase activity in cancer patients was also reported by Kessel and Allen (13). Recently,
Bhattacharya et al. (3) have demonstrated an increase in serum galactosyltransferase levels in patients with ovarian cancer. Weiser et al. (29) have made the interesting observation of an isoenzyme of galactosyltransferase in the serum in 43 of 58 patients with various types of cancer. Moreover, the quantity of this isoenzyme is significantly higher in patients with widespread metastasis.

Altogether, it seems that the growth of a tumor can lead to other physiological events that are remote from the primary tumor sites, namely, the elevation of certain host liver glycosyltransferases. Moreover, the neoplastic tissues are also characterized by increased glycosidase enzymes. It would be interesting to know whether these changes could affect the immunological response of the host or the invasive nature of the tumor. The use of serum glycosyltransferase and glycosidase as markers of tumor proliferation seems a promising project for further investigation.

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