plasma membranes were applied, decreased the rate of DNA synthesis in a low-cell density. (3) The digestive treatment by endoglycosidase F of liver membranes abolished their inhibitory effect on the rate DNA synthesis in a low-cell density. In order to get more direct information of membrane-hepatocyte interactions, we performed experiments of the binding of fluorescence uptaken rat hepatocytes to the plates coated with the liver membranes which were exposed to prior treatment with either glycosidase digestion or purified glycolipids. As a result, we found that adult rat hepatocytes adhered to adult rat liver membranes but weakly to the young ones. Sialidase digestion, however, made the binding potency of young rat liver membranes strengthen to the level observed in adult liver membranes. Moreover, glycoconjugates analogs themselves, such as lactosylceramide and GM3, behaved differently in binding to adult rat hepatocytes. The former markedly adhered to the cells but the latter does not, suggesting the involvement of sialic acid residue in the specificity of binding as well as signaling leading to development and proliferation of hepatocytes.

S.4 DEVELOPMENT AND CANCER

S4.1
Roles of Poly-*N*-Acetyllactosamines in Development and Cancer: A Molecular Approach

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Structural studies on carbohydrates attached to proteins and lipids revealed extreme heterogeneity in those molecules. At the same time, another important finding is that certain types of cells contain only specific sets of carbohydrates. Our assumption is that these cell-type specific carbohydrates play a role in cell-cell interaction. In the past years, we have been particularly interested in the structure, biosynthesis and possible roles of poly-*N*-acetyllactosamines. Because poly-*N*-acetyllactosamines have long side chains, they tend to provide a favorable backbone for cell-type specific modification. In fact, one such modification, sialyl Le^x structure originally discovered on granulocytes by us, was found to be a ligand for E- and P- selectin.

In order to understand the roles of poly-*N*-acetyllactosamines in cell recognition we are taking two different approaches. The first is to focus on the glycoprotein carriers that contain poly-*N*-acetyllactosamines. We found that lysosomal membrane glycoproteins, lamp-1 and lamp-2, are the major carriers for poly-*N*-acetyllactosamines. A small proportion of lamp-1 and lamp-2 can be expressed also on the cell surface and they can provide poly-*N*-acetyllactosaminoglycans at the cell surface (1). Recently our studies demonstrated that highly metastatic colonic tumor cells express more lamp-1 and lamp-2 on the cell surface than low metastatic counterparts (2). Most recently our studies showed that the increased amount of lamp-1, achieved by genetic manipulation of lamp-1 expression, leads to stronger adhesion to E-selectin-expressing cells and this adhesion can be inhibited by soluble lamp-1 containing sialyl Le^x structures (3).

The second approach is to isolate cDNAs that are critical for poly-*N*-acetyllactosamine formation. By using expression cloning procedure, we have succeeded in isolating cDNAs encoding two β-1,6-*N*-acetylglucosaminyltransferases. The first cloned enzyme forms core 2 branches in *O*-glycans which are essential for poly-*N*-acetyllactosamine extension and sialyl Le^x formation in *O*-glycans (4). The second cloned enzyme forms β-1,6-*N*-acetylglucosaminyl branches in poly-*N*-acetyllactosamines, which result in the formation of I-blood group antigens (5). Such formation of branch structures in poly-*N*-acetyllactosamines result in multiple ligand structures in neighboring *N*-acetyllactosaminyl side chains. The availability of cDNAs encoding specific glycosyltransferases now allows us to manipulate the amount of specific oligosaccharide structures by changing the level of expression of the glycosyltransferases, and then examine the functions of those formed oligosaccharides. Furthermore, the roles of specific carbohydrates in development can be addressed by using transgenic mice technology.

These studies will probably reveal the roles of poly-*N*-acetyllactosamines in development and cancer. (Supported by grants CA33000, CA33895, CA48737 and AI33189)

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S4.2
T/Tn Antigen (Ag) Detects Carcinoma (CA) Long Before Biopsy and its Vaccine Prevents Breast CA Recurrence

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Thomsen-Friedenreich (T) and its immediate precursor, Tn, are panCA-associated Ags that elicit strong, specific cellular and humoral autoimmune responses in >90% of CA patients but in <8% of presumably healthy persons and those with nonCA diseases (first visit). Of all 40 subjects we could follow, who reacted repeatedly "falsely" positive in T tests but had persistently negative biopsies/X-rays, 78% developed biopsy-verified CA months to years after the first positive T test. The T tests herald with 80% accuracy clinical CA within 8 yrs, while standard tests are still negative. These added years should allow novel anti-CA therapies and thus prevent appearance of clinical CA. T/Tn EPs uniquely permit CA detection at incipience and throughout. Specific delayed skin hypersensitivity to T (DTHR-T) was detected in 35/41 (85.4%) Tis CA and 84.4% of 454 patients, all stages, with