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Surface sugars of cancer cells: The sweeter the deadlier?

In tumorigenesis and metastasis of tumours, although factors such as protease production and organ-specific microenvironment have been implicated in target selection, recent evidences assign a decisive role to oligosaccharide structures on cell-surface glycoconjugates, interaction of which with sugarspecific molecules on other cells or on extracellular matrix governs cell sociology. For example, in reactivity the carbohydrate-binding towards proteins (lectins) from peanut (peanut agglutinin, PNA), soybean (soybean agglutinin, SBA) and Ulex europeus (Ulex europeus agglutinin-1, UEA-1), primary subcutaneous tumours induced in rats using Lewis lung carcinoma cells had the phenotype PNA, SBA, UEA-1⁻, while its liver and lung metastases were PNA⁺, SBA⁺, UEA-1⁻, and PNA⁺, SBA⁺, UEA-1⁺ respectively¹. Penno et al.² observed in in vitro studies that galactosylation in general, and that of a 110-kDa cell-surface glycoprotein in particular, correlates with invasiveness of a murine adrenal carcinoma cell line. In more detailed investigations by Dennis and colleagues³, using the highly metastatic lymphoreticular tumour cell line MDAY-D2 and its non-metastatic glycosylation mutants, two events have been shown to enhance metastatic potential: (i) sialylation of oligosaccharides and (ii) addition of $\beta 1 \rightarrow 6$

branched N-acetylglucosamine (GlCNAc) to which galactose is also attached as part of a tri- or tetra-antennary structure in N-linked ogligosaccharides. The above conclusion is supported by earlier in vitro tests that showed that natural-killer (NK)-cell attachment to cells is inversely proportional to their sialylation and to masking of mannose groups by substitution such as by $\beta 1 \rightarrow 6$ GlcNAc branching⁴. Also, swainsonine, an alkaloid that inhibits oligosaccharide processing, has been found to reduce growth and increase susceptibility to NK cells of tumour cells in vitro⁵. MDAY-D2, unlike its undersialylated mutants or its desialylated derivative, adhered very weakly to plastic surfaces coated with fibronectin, laminin or collagen type IV, thus providing an explanation for its mobility and metastasis⁶.

Recent results suggest that endogenous lectins, as complementary molecules or receptors to oligosaccharide groups, may be most effective, though glycosidases and anticarbohydrate antibodies may be operative. Many animal tissues contain a β -galactoside-binding lectin (galaptin)⁷. Galaptins are easily solubilized from tissue by soluble galactosides, indicating their association in vivo with complementary glycoconjugates.

Lotan and Raz⁸ also demonstrated

two β -galactoside-binding lectins in human and murine tumour cells. Interestingly, both the β -galactoside-containing glycopeptides from asialofetum and monoclonal antibodies to the lectins could inhibit tumour-cell aggregation as well as attachment to the substratum. Further evidence for an active role of glycoconjugate-lectin interaction in growth regulation was provided by the recent results of Sanford and Harris-Hooker⁹, who found that rat-lung galaptin was mitogenic towards pulmonary arterial cells and smooth-muscle cells in culture (as measured by incorporation of radiolabelled thymidine) in a sugar-dependent manner.

Changes in oligosaccharide structures $vis-\dot{a}-vis$ their corresponding lectins is a popular topic in cancer research today. Inasmuch as a tumour is regarded as a retrogression to the embryonic stage, it will be interesting to examine if reexpression of differentiation antigens, like the stage-specific embryonic antigen [Gal $\beta 1 \rightarrow 4$ (Fucal $\rightarrow 3$) GlcNAc-R] or oversially lated form of neural cell adhesion molecule, and their recognition by lectins facilitate tumour mobility and anchorage.

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