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α-L-Fucose in Histology: A Part of the Cancer Glycome Hiding in Plain Sight

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Alpha-L-fucose ("fucose") is a 6-carbon deoxy-sugar that is found to be contained in major blood group antigens, in Lewis minor blood group antigens and on many epithelial cells. Fucose is incorporated into numerous tumor-associated carbohydrate antigens, and appears to have important functional significance, as well as biomarker significance, in common human cancers [1,2]. Data suggest that diagnosis and prognosis would be aided by detection of fucosylated molecules in tissue samples. Unfortunately, the names of fucose-containing cancer antigens rarely provide clues that the sugar is, in fact, present. As a result, fucose remains nearly anonymous in the histopathology literature.

Why should one be concerned with fucose? Because two established functional roles for fucose are directly relevant to common cancers. First, fucose serves as an interaction domain which mediates cell-cell adhesion, cell-matrix adhesion, and cell-cell signaling. Fucose is often expressed as the terminal sugar on glycoproteins and glycolipids and is thus well-positioned for interactions with the cell's environment. Fucose's hydroxyl groups have been shown to ligate calcium enabling homotypic cell adhesion as well as cell adhesion to (calcium-dependent) selectin molecules on endothelial cells. This mechanism subserves both normal inflammatory cell recruitment and metastatic adhesion of circulating tumor cells [1]. Simple enzymatic removal of fucose from malignant cells profoundly decreased metastases in a rat mammary carcinoma model [3] and profoundly decreased invasion of human breast cancer cells into complex human extracellular matrix material [4]. Numerous examples of fucose's adhesion/signaling actions are well documented in the literature.

The second major role of fucose is regulation of receptor activity. Fucosylation of the Notch1 receptor is required for optimal sensitivity to its ligands. "Core fucosylated" glycans regulate the biological functions of integrins and cadherins [5], as well as growth factor receptors such as EGFR and TGF-β1 [6]. Again, further examples are well documented elsewhere.

Just as one may speak of a "cancer genome" or a "cancer proteome," the "cancer glycome" of a particular neoplasm encompasses the entire repertoire of biological carbohydrates, or glycans, expressed by the cancer cells, tissues and the organisms. The daunting complexity of this information obscures an important fact: many of the fucose-containing molecules of the cancer glycome are readily detectable without the aid of microarray technology or other specialized apparatus. In fact, fucose-containing tumor antigens are routinely assessed by standard immunohistochemical techniques. For example, the CD15 antibody detects the Lewis X carbohydrate antigen which is composed of 3 sugars including the immunodominant fucose. For another example, the CA 19-9 antibody detects a four-sugar antigen, sialyl Lewis A, which contains fucose. A third example is tumor-associated carcinoembryonic antigen (CEA, or CEACAM5) which is "decorated" with multiple copies of fucose-bearing Lewis X and Lewis Y. Other fucosylated molecules of interest include (among others) EGFR, the Notch1 receptor and possibly the normal cellular prion protein (PrP^C). It is thus possible to glean information about the patient's fucose-related cancer glycome by means of familiar validated technology.

Users of advanced glycobiology techniques, such as glycan microarrays and mass spectrometry, aim to discover new cancer biomarkers and ultimately establish "cancer glycomes" for specific tumors, with diagnostic and prognostic value. It seems reasonable to predict that selected fucose-bearing glycan biomarkers, once identified and validated, might be targeted by immunohistochemical or similar techniques for routine evaluation. Fucose can then be utilized, in plain sight, to help construct and refine the cancer glycome.

References

1. Listinsky JJ, Siegal GP, Listinsky CM (1998) Alpha-L-fucose: a potentially critical molecule in pathologic processes including neoplasia. Am J Clin Pathol 110: 425-440.

2. Miyoshi E, Moriwaki K, Nakagawa T (2008) Biological function of fucosylation in cancer biology. J Biochem 143: 725-729.

3. Wright LC, May GL, Gregory P, Dyne M, Holmes KT, et al. (1988) Inhibition of metastatic potential by fucosidase: an NMR study identifies a cell surface metastasis marker. J Cell Biochem 37: 49-59.

4. Yuan K, Listinsky CM, Singh RK, Listinsky JJ, Siegal GP (2008) Cell surface associated alpha-L-fucose moieties modulate human breast cancer neoplastic progression. Pathol Oncol Res 14: 145-156.

5. Zhao Y, Sato Y, Isaji T, Fukuda T, Matsumoto A, et al. (2008) Branched N-glycans regulate the biological functions of integrins and cadherins. FEBS J 275: 1939-1948.

6. Wang X, Gu J, Miyoshi E, Honke K, Taniguchi N (2006) Phenotype changes of Fut8 knockout mouse: core fucosylation Is crucial for the function of growth factor receptor(s). Methods Enzymol 417: 11-22.

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