Journal of Glycobiology
ISSN: 2168-958X

Yu, J Glycobiol 2013, S1
DOI: 10.4172/2168-958X.S1-e001

Editorial Open Access

Glycosylation Change in Cancer as Therapeutic Target: Opportunities and Challenges

Lu-Gang Yu*

Department of Gastroenterology and Centre for Glycobiology, Institute of Translational Medicine, University of Liverpool, Liverpool L69 3GE, UK

Alterations in cell surface glycosylation are common features in cancer. Many of these glycosylation changes result in expression of cancer-associated carbohydrate antigens such as Tn (GalNAcα-Ser/Thr), sialyl-Tn (sialic acid-β1,6GalNAcα-Ser/Thr), TF(Galβ1,3 GalNAcα-Ser/Thr) and Lewis-related carbohydrate structures. These glycosylation changes have offered multiple opportunities for potential therapeutic treatment of cancer.

Over 90% of all types of human cancers express Tn, sialyl-Tn or TF antigens while these short chain carbohydrate structures rarely occur in normal tissues. The high specificity of these cancer-associated carbohydrate antigens attracted many earlier studies to investigate the possibility of using those short carbohydrate structures as targets of vaccination in cancer immunotherapy. Immunization with Tn or TF carbohydrate structures showed to be capable of eliciting cross-reactive antibodies in mice in the earlier studies. However, the immunological response induced by such glycans is poor due to lack of ability of the carbohydrates to induce T-cell-dependent immune reactions. Subsequent attempts to improve the carbohydrate immunogenicity and promote long-lasting immune responses were made by conjugating the carbohydrate antigens with immunogenic proteins or peptides. The resulting carbohydrate antigen-protein/peptide conjugates did demonstrate improved immunological responses in mice and a number of such conjugates successfully progressed into clinical trials. However, the immune response elicited against such carbohydrate conjugate vaccines was not effective enough to improve patient survival in subsequent clinical trials. One of the technical challenges facing such approaches is the lack of tight control of the coupling reactions between the carbohydrate antigens and proteins/peptides to produce consistent and unified conjugates. Other drawbacks in those approaches are the production of undesired antibodies against the protein/peptide carrier and the carrier-induced epitopic suppression. Recently, a number of peptide sequences have been found to be able to mimic the tumour-associated carbohydrate antigens and shown to induce sustained immune responses in mice. As peptide mimics are able to overcome immunological tolerance and induce a T cell-dependent response instead of the T cell-independent response typically attributed to carbohydrate antigens, the carbohydrate mimicking peptides may significantly improve immunogenicity. It remains to be seen whether an improved immunogenicity by such carbohydrate mimicking peptides can be transferred to patient benefit in clinical trials.

Changes of cell surface glycosylation in cancer often cause altered interaction of the cancer cells with carbohydrate-binding proteins (i.e. lectins) expressed on adjacent cells or in the cancer microenvironment. Increasing evidence has shown that many of these altered carbohydrate-lectin interactions in cancer are actively involved in promoting cancer progression and metastasis and are therefore potential therapeutic targets for development of novel anti-metastasis drugs. One such interaction occurred between cancer-associated TF antigen and galectin-3 has attracted particular attention over the past few years. Galectin-3 is galactoside-binding protein and is over expressed in many types of cancer cells. The concentration of galectin-3 is increased up to 30-fold in the blood circulation of cancer patients. An increased interaction of galectin-3 with cancer-associated TF in cancer, as a result of the increased occurrence of TF and increased expression of galectin-3 by cancer cells, increases tumour cell metastatic spread to remote sites by enhancing disseminating tumour cell adhesion to the blood vascular endothelium and also by increasing tumour cell homotypic aggregation for the formation of tumour emboli that prolongs the survival of tumour cells in the circulation. Several laboratories are currently exploring the possibility of using galectin-3 binding inhibitors from natural or synthetic sources or using TF-mimicking peptides to prevent/reduce cancer metastasis. Several galectin-3 binding inhibitors (e.g. modified citrus pectins) have shown to be able to reduce metastasis in animal models and have proceeded or about to proceed to clinical trials. As galectin-3 knockout mice grow normally, targeting the galectin-3 actions in cancer may represent a promising therapeutic approach to reduce metastasis.

Alterations of cellular glycosylation in caner are the consequence of malfunction of the cell glyco-biosynthesis machinery. These include changes of the expression, localization and activity of specific glycosyltransferases, nucleotide sugar transporters, molecular chaperons or Golgi ATPases in the multi-stepped, sequential, glyco-biosynthesis process. The defects in the glyco-biosynthesis machinery in cancer therefore also represent potential points of intervention in cancer therapy. However, as the same glyco-biosynthesis machinery is essential for molecule glycosylation in ordinary cells for maintaining normal cell function, specifically targeting the defects of glyco-biosynthesis machinery in cancer cells while maintaining the glyco-biosynthesis machinery intact in normal cells is enormously challenging with the current technology.

So, alterations in the cell surface glycosylation in cancer represent a class of attractive but challenging therapeutic targets in cancer therapy. With increased understanding of the functional importance of cellular glycosylation in cancer development and progression and with further advance of new technologies, targeting the cancer-associated glycosylation changes likely will attract more and more attention for the development of novel therapeutic strategies for cancer treatment.

***Corresponding author:** Lu-Gang Yu, Department of Gastroenterology and Centre for Glycobiology, Institute of Translational Medicine, University of Liverpool, Liverpool L69 3GE, UK, Tel: + 441517946820; Fax: +44 151 7946825; E-mail: lgyu@liv.ac.uk

Received May 26, 2013; **Accepted** May 27, 2013; **Published** May 30, 2013

Citation: Yu LG (2013) Glycosylation Change in Cancer as Therapeutic Target: Opportunities and Challenges. J Glycobiol S1: e001. doi:10.4172/2168-958X.S1-e001