

# Glycobiology of Cancer: Targeting Glycan Structures for Precision Medicine

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## DESCRIPTION

Cancer, a complex and multifaceted disease, is driven by various genetic, epigenetic, and environmental factors. Over the past few decades, our understanding of cancer has expanded beyond mutations in DNA to include alterations in other cellular processes, such as glycosylation. Glycosylation, the process by which sugar molecules are covalently attached to proteins, lipids, and other biomolecules, plays a crucial role in cellular signaling, protein folding, and cell-cell interactions. Aberrant glycosylation patterns are a hallmark of cancer, and the study of these changes known as cancer glycobiology has unveiled new insights into the disease's biology and opened the door to potential therapeutic strategies, particularly in the realm of precision medicine.

## Role of glycosylation in cancer

Glycosylation is a post-translational modification that adds carbohydrate structures, or glycans, to proteins and lipids. These glycan structures are essential for cellular functions such as protein stability, cell signaling, and immune recognition. In cancer cells, however, these glycosylation patterns are often altered, influencing tumor growth, metastasis, and immune evasion.

There are several key types of glycosylation that play significant roles in cancer, including N-linked glycosylation, O-linked glycosylation, and the glycosylation of glycolipids. Each type of glycosylation can impact different aspects of cancer cell behavior. For instance, N-linked glycosylation (where sugar molecules are attached to the nitrogen atom of asparagine residues) plays a central role in protein folding and trafficking. In cancer, the enzymes that regulate N-linked glycosylation, such as N-acetylglucosaminyl transferases, are often dysregulated, leading to the production of abnormal glycan structures. These altered structures can, in turn, affect cell adhesion, migration, and immune recognition, processes that are crucial for cancer progression.

In particular, the expression of tumor-associated glycans has become a focus of cancer glycobiology. These glycans are not

typically found on normal cells but are overexpressed or altered in cancer cells. For example, sialylated glycans (sugar structures containing sialic acid) are often found on the surface of tumor cells and contribute to the evasion of immune detection. Tumor cells that express certain glycan structures, such as Thomsen-nouveau (Tn) antigens or sialyl Lewis X, can evade immune surveillance and enhance their ability to metastasize.

## Glycans as biomarkers for cancer diagnosis

The unique glycosylation patterns expressed by cancer cells have made glycans promising candidates for diagnostic biomarkers. Unlike traditional cancer markers, which often rely on protein expression levels, glycan-based biomarkers are capable of identifying cancer-specific changes at the cellular level. For instance, the sialylated glycan markers, such as sialyl Lewis X and sialyl Tn antigen, are overexpressed in a variety of cancers, including colorectal, breast, and pancreatic cancers. These glycan alterations can be detected in blood, serum, or tumor biopsies, offering a non-invasive method for early detection, monitoring disease progression, and assessing response to treatment.

Recent advances in glycomic profiling have enabled the identification of cancer-specific glycan signatures. By mapping the glycan composition of cancer cells, researchers can distinguish between cancerous and normal cells, providing a new avenue for personalized cancer diagnostics. This has the potential to transform early cancer detection and help stratify patients for tailored therapeutic approaches, improving patient outcomes.

## Targeting glycan structures in cancer therapy

One of the most promising aspects of cancer glycobiology is the potential to target glycan structures as part of cancer therapy. Glycans are often involved in key cancer processes such as tumor growth, metastasis, and immune evasion. By targeting the glycan modifications that drive these processes, scientists are developing new therapeutic strategies aimed at disrupting cancer cell biology.

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**Enzyme inhibition:** One approach to targeting glycosylation in cancer is the inhibition of glycosyltransferases and other enzymes involved in glycan biosynthesis. By blocking the enzymes responsible for abnormal glycan formation, researchers can reduce the expression of tumor-associated glycans and potentially inhibit tumor growth and metastasis. For instance, sialyltransferase inhibitors have been shown to decrease the levels of sialylated glycans on cancer cells, which in turn impairs their ability to evade immune detection and limits tumor progression.

**Monoclonal antibodies:** Another approach involves the use of monoclonal antibodies that specifically target cancer-associated glycans. These antibodies can be designed to recognize and bind to specific glycan structures on the surface of tumor cells. Once bound, the antibodies can trigger immune-mediated cell death or block the interactions between tumor cells and their surrounding microenvironment, which are essential for tumor growth. For example, anti-Tn antibody therapy is being explored as a way to target Tn antigens, a glycan structure often overexpressed in epithelial cancers.

**Lectin-based therapies:** Lectins are proteins that specifically bind to certain carbohydrate structures. By exploiting lectin-glycan interactions, researchers are developing lectin-based therapies that can be used to target cancer cells. Plant-derived lectins or engineered lectins could be utilized to selectively bind to and kill cancer cells by inducing apoptosis or inhibiting key signaling pathways. These therapies may also be combined with other treatments, such as chemotherapy or immunotherapy, to enhance their efficacy.

**Glycan-based vaccines:** In addition to directly targeting tumor glycans, glycan-based vaccines are being investigated to elicit an immune response against cancer cells. These vaccines work by introducing cancer-specific glycan epitopes to the immune system, triggering the production of antibodies and activating T-cells to attack cancer cells that express the same glycan structures. For example, vaccines targeting tumor-specific glycoproteins or glycolipids, such as the gangliosides GD2 and GM2, have shown promise in clinical trials, particularly for cancers like neuroblastoma and melanoma.

## CONCLUSION

Glycosylation is an essential process in normal cell function, but its dysregulation is a hallmark of cancer. Aberrant glycosylation patterns play a crucial role in tumor growth, immune evasion, and metastasis, making glycans a promising target for precision cancer therapies. By targeting glycan structures with enzyme inhibitors, monoclonal antibodies, lectins, or glycan-based vaccines, researchers are paving the way for new, more effective cancer treatments. However, challenges such as glycan heterogeneity and specificity must be overcome for these therapies to reach their full potential. As research in cancer glycobiology continues to evolve, the hope is that these innovative strategies will ultimately lead to more personalized, targeted treatments that improve the prognosis and survival rates of cancer patients.