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Chemical and Enzymatic Synthetic Methods Used to Produce Glycans and Glycoproteins

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DESCRIPTION

Pure glycans with defined structures are essential research tools in glycobiology. Glycans produced in biological systems are heterogeneous, in contrast to proteins and nucleic acids, which can be obtained in homogeneous form using biological techniques such as recombinant expression or Polymerase Chain Reaction (PCR). Furthermore, the amount that can be extracted from biological systems is rather small. Chemical synthesis can be used to obtain uniform glycans in larger quantities than are available from most cellular production systems. Enzymes can be used in conjunction with chemical methods to further simplify the process of glycan synthesis. This chapter summarizes the chemical and enzymatic synthetic methods used to produce glycans and glycoproteins.

Glycosylation is an essential form of post-translational modification that regulates intra and extracellular processes. Unfortunately, conventional biochemical and genetic methods are often inadequate for glycan studies, as glycan structures are often poorly defined at the genetic level. To address this deficiency, chemists have developed techniques to disrupt glycan biosynthesis, profile system-level presentation, and sense their spatial distribution. These tools have identified potential disease biomarkers and ways to monitor dynamic glycome changes *in vivo*. Nevertheless, glycosylation remains an unexplored frontier in many biological systems. This report highlights work in our laboratory aimed at transforming the study of glycan function from a challenge to a routine practice. In protein and nucleic acid studies, functional studies have often relied on genetic manipulations to disrupt structure. Although we are not directly affected by mutation, we can determine the structure-function relationship of glycans by synthesizing defined glycol-conjugates or altering the native glycosylation pathway. Chemical synthesis of unitary glycoproteins and macromolecular glycoprotein mimics has facilitated the study of individual glycol-conjugates in the absence of glycan micro heterogeneity. Depending on the patient's condition, immune function, treatments used, and therefore the type of malignant brain neoplasm, survival with current radiation and chemotherapy treatments may extend that point from around a year to a year and a half, possibly two, in these cases. Untreated survival is usually limited to a few months. Alternatively, selective inhibition or activation of glycosyltransferases or glycosides may define the biological role of the corresponding glycans. Researchers have developed tools including small-molecule inhibitors, decoy substrates, and genetically engineered proteins to modify glycans in cells. Current approaches provide a level of accuracy approaching that of gene regulation. Genomic and proteomics profiling form the basis of biological discovery. Glycans are also information-rich matrices that rapidly adapt to changing environments. Glycomic and glycol-proteomic analyzes using microarrays and mass spectrometry are beginning to characterize glycan alterations that correlate with disease. Metabolic labels can identify recently synthesized glycans, allowing direct tracking of glycan dynamics. This approach can highlight changes in physiology and environment and is more informative than steady-state analysis. Combining glycomics and metabolic labeling techniques provides a comprehensive description of glycosylation as a basis for hypothesis generation. Direct visualization of proteins by Green Fluorescent Protein (GFP) and its homologues has revolutionized the field of protein dynamics. Similarly, the ability to discern the spatial organization of glycans could change our understanding of the role of glycans in development, infection, and disease progression.

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CONFLICT OF INTEREST

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