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Perspective

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Enzymes Involved in Glycosylation Have Critical Determinants in ER-Golgi Trafficking

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ABSTRACT

All living cells produce a structurally complex and compositionally varied spectrum of glycans and glycoconjugates that are essential for organismal evolution, development, functioning, defence, and survival. GTs accelerate the glycosylation process between activated sugar and acceptor substrate to produce a wide range of glycans. GTs are found in over 130 gene families and have roles in metabolic processes, signal pathways, cell wall polysaccharide formation, cell development, and growth. Glycosylation occurs primarily in the endoplasmic reticulum (ER) and Golgi, where GTs and glycosidases are dispersed to various sites of these compartments and progressively add or cleave various sugars to create glycosylation products.

As a result, delivering these enzymes to the right regions in the cell, the glycosylation sites, is critical and includes multiple secretory route components. This study summarises the current level of knowledge on protein trafficking processes between the ER and the Golgi. It summarises what is known about the fundamental components of protein sorting machinery and trafficking, which are recognition sites on the proteins that are crucial for their interaction with the critical components of this machinery.

Keywords: Glycosyltransferases; ER-Golgi trafficking; mechanism of protein sorting; COPI and COPII complexes; sequences and motifs involved in trafficking.

INTRODUCTION

All living cells produce a structurally complex and compositionally varied spectrum of glycans and glycoconjugates that are essential for organismal evolution, development, functioning, defense, and survival. During normal and stressful settings, the glycans linked to proteins and lipids regulate their activity, solubility, subcellular localization, and structural organization in cells. Glycan-rich cell walls regulate cell development and morphogenesis while also protecting cells from external stressors. Glycosylation is the process by which glycosidic bonds are formed between activated sugar (donor substrate) and acceptor substrate. This process is carried out by a vast range of specialized enzymes known as glycosyltransferases and occurs in most organisms, including yeast, humans, and plants. Because of the variety of sugars and acceptor substrates, the resultant glycosylation products have a great degree of heterogeneity and complexity in structure and function.

Glycosyltransferases (GTs) are found in over 130 gene families. The majority of GTs is type II transmembrane proteins with multiple different domains, including a short N-terminal cytosolic tail, a transmembrane domain (TMD), a flexible stem region, and a large catalytic domain. Another kind of GT consists of integral membrane proteins that include many TMDs and a large catalytic domain that is often found on the cytosolic side of the membrane. GTS is classified as GT-A, GT-B, and GT-C based on the kind of catalytic domain folds. In GT-A folding, two tight / Rossmann domains create a center -sheet and most GT-A-type proteins feature DxD catalytic motifs that collaborate with metal.

The two / Rossmann domains in GT-B are distinct and create a cleft rather than being firmly connected. GT-C proteins, which include numerous hydrophobic helices, are anticipated and discovered based on sequence and structural study. Furthermore, a lysozyme-like domain was discovered in the structure of Aquifex aeolicus peptidoglycan glycosyltransferase. N-glycosylation and O-glycosylation are the two most common kinds of glycosylation in glycoconjugates. N-glycosylation is the creation of a glycosidic bond between an asparagine residue's amino group and the first sugar of the glycan. Although not all Asn residues are glycosylated, asparagine in the Asn-X-Ser/Thr consensus sequence is a candidate for N-glycosylation. N-glycosylation is required for protein solubility, structure, and folding. It also plays an important role in protein localisation and interacts with glycan-binding proteins. The glycan oligosaccharides in N-glycosylated proteins have the same core sugar sequence and structure-Man1-6(Man1–3) Man1-4GlcNAc1-4GlcNAc1-Asn, which can be branched with various sugars depending on the kind of mature glycan produced. N-glycosylation processes occur in the endoplasmic reticulum (ER) and the Golgi.

GTs and glycosidases share a trafficking pathway between the ER and the Golgi that incorporates motifs or particular amino acids in their cytoplasmic tails, TMDs, and catalytic domains. These many variables can work independently or collaboratively by interacting with COP coatomer proteins directly or indirectly, thereby altering the location and transit of GTs and glycosidases (Table 1). The shared trafficking mechanism of GTs and glycosidases is comparable to that of other proteins. Thus, research into other protein trafficking pathways can provide clues to the probable mechanism for GT and glycosidases trafficking. Most GTs and glycosidases have arginine and lysine residues, which can interact directly with cargo receptors and COP coatomers. The arginine and lysine residues' positive charge and branching shape are important in protein–protein interactions with cargo receptors and COP coatomers. The ER-retrieval signal and the Golgi-retrieval signal are two motifs, however the method for identifying and discriminating these two signalling sequences is unknown. One proposed explanation might be that the specific type of retrieval signal is determined by the varied placements of these motifs in the structure of GTs and glycosidases. These motifs are recognised at different places by different isoforms of COP coatomers and cargo receptors. The protein–protein interaction with other GTs or cargo proteins is crucial for the correct localization of GTs that lack the motifs and particular amino acids identified by COP coatomers.