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Mini Review

Cellular Glycans and their Binding Proteins

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Abstract

Glycans are one of the fundamental classes of molecules which make up the living system, along with nucleic acids, proteins, and lipids. Glycans include glycoproteins, glycolipids, proteoglycans which are displayed on every cell surface. However, display of glycans differs between mammals and microbes. Glycan binding proteins can distinguish these differences. Glycan-binding proteins recognize specific glycans and translate these recognitions in to functions. There are different methods to evaluate carbohydrate-protein interactions. These evaluations help in understanding interactions between the glycans and proteins in host defense and microbial pathogenesis. The aim of this mini-review is to give general information about glycans, glycan binding proteins and evaluation of carbohydrate-protein interactions.

Keywords: *Glycans; Glycan-Binding Proteins; Carbohydrate-Protein Interactions*

Abbreviations

Siglesc: Sialic Acid-Binding Immunoglobulin-Type Lectins

Introduction

Every cell carries a rich glycan coat on its surface, which facilitates the interaction of the cell with its environment [1]. Glycans are found in bacteria, archaea, and eukaryotes. Cell surface sugars exist as glycoproteins, glycolipids, proteoglycans, which are commonly referred to as glycans [2]. They play vital roles in many cellular processes such as cell recognition and signal transduction [3]. The sum of all the diverse glycan structures on each cell is called the glycome [4]. Each cell type has its distinct glycome, which is determined by the metabolic state of the cell [5]. Specific enzymes such as glycosyltransferases and glycosidases alter carbohydrates on the cells. Altered oligosaccharides change specific cellular functions of cells [6]. Glycan-binding proteins recognize sugars on the cell surface (Figure 1). Thus, many specific biological roles of glycans are mediated via glycan-binding proteins [7]. Organisms that serve as a host must distinguish between microbial cells and their cells [8]. Glycans displayed on the mammalian cell can markedly differ from the ones on the microbial surface; thus, glycans can serve as a microbial cellular ID. Furthermore, glycans are ideal structures for isolation, characterization and identification of different cell population [9]. Microbial cell glycans perform multiple functions such as protecting the cell from osmolality, desiccation and mediates adhesion of cells to the surfaces or the cells in its environment [10]. Moreover, they can help in escaping host immune surveillance, thereby allowing microbes to survive [11]. Thus, evaluating of microbial glycan- host glycan-binding protein interactions can help in developing new strategies to control microbial infections. This review gives general information about the glycans, glycan binding proteins and evaluation of carbohydrate-protein interactions.

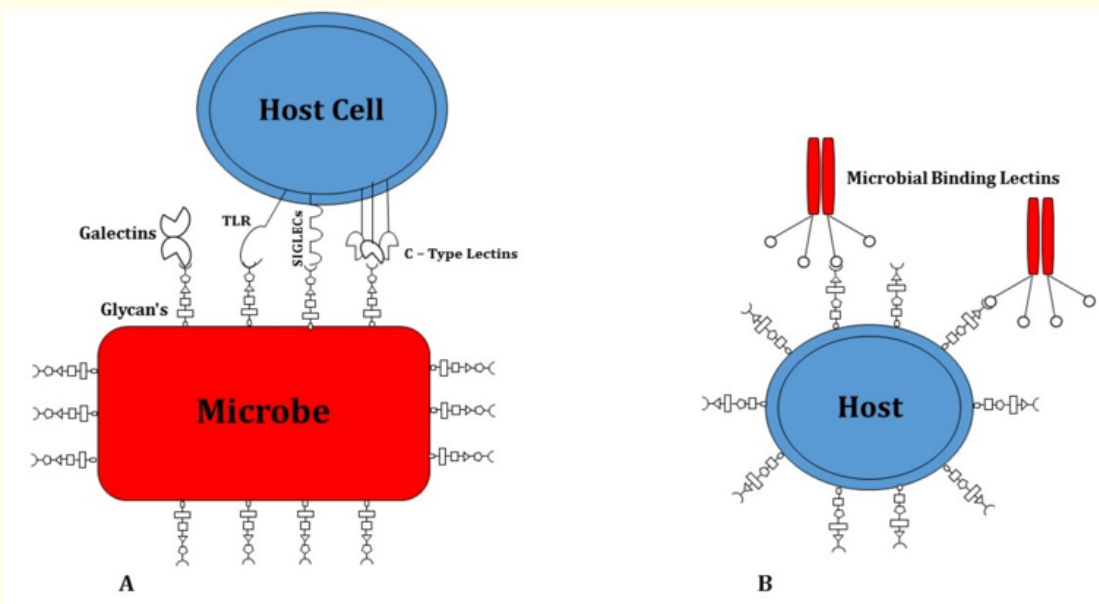

Figure 1: *Recognition of glycans by glycan-binding proteins. A) Host glycan binding proteins are recognizing microbial glycans. B) Microbial glycan binding proteins are recognizing host glycans.*

Mammalian glycan-binding proteins

Glycan-binding proteins such as lectins recognize different sugars on the cell surface. These glycan binding proteins act as receptors for pathogen-associated molecular patterns and damage-associated molecular patterns [12]. Lectins are grouped into different categories; C-type lectins, galectins (formally S-type lectins), I-type lectins, p-type lectins, F-type lectins, X-type lectins, Rhamnose-binding lectins and Pentraxins [13]. Many C-type lectins and galectins are considered as components of the innate response to pathogens by binding to microbial glycans. They activate the host defense system directly or indirectly, by triggering leukocyte activation, phagocytosis, cytokine production and complement production [14-16]. Selectins (E- P- and L-) are widely expressed in lymphocytes, neutrophils, platelets and endothelial cells and mediate the trafficking of circulating leukocytes to the sites of inflammation [17]. Sialic acid-binding immunoglobulin-type lectins (Siglesc) are cell surface proteins that recognize sialic acid containing glycans as ligands. They are found in white blood cells and are involved in cell signalling through regulatory motifs found in the cytoplasmic domains [18]. Galectins are beta-galactoside-binding proteins. Currently, 15 members of the galectin family have been discovered and they are ubiquitously distributed from sponges, nematode to humans and ruminants [19,20]. some lectins can enhance microbial infection of different hosts, an effect that would seem to be counter-intuitive if lectins are considered to act solely as host defense molecules [12,14,21]. Thus, specific effects of lectins as pro or anti-microbial infection should be considered in context-dependent manner [21]. Every individual has many circulating antibodies against various structures of non-self-glycans [22]. In humans, anti-blood group antibodies are one of the amongst first well studied anti-glycan antibodies [23]. Glycans specific antibodies can be used as research agents are most often produced in mice [24]. New mammalian glycan binding proteins continue to be discovered. Intelectin-1 belongs to the family of X-type lectin found to be bind glycans exclusively found on microbes [25].

Microbial glycan-binding proteins

Microbes can recognize sugars on host cells. The influenza virus haemagglutinin was the first glycan-binding protein isolated from a micro-organism, and it has been demonstrated to bind sialic acid [26]. The specificity of binding can be highly selective based on the species of origin. For example, human influenza virus recognizes distinct linkage compared to avian influenza virus [27]. Most of the virus (e.g. polyomavirus, reovirus, rotavirus) uses sialic acids as linkages in infection [28].

Bacterial glycan-binding proteins fall into two classes 1) Adhesins 2) Secreted toxins. Many of the glycan-binding proteins on the bacterial surface are present in the form of long appendages known as Fimbriae or Pilli. These adhesions facilitate bacterial colonization. However, all interactions between bacterial and host cells are not pathogenic, some of them are beneficial too [29]. Many of the secreted heat sensitive toxins from the bacteria bind to glycan. For example, subtilase cytotoxin secreted by Shiga toxigenic E. coli, bind only to glycans containing 2,4-dihydroxy-5-[(2-hydroxyacetyl) amino]-6-(1,2,3-trihydroxypropyl)oxane-2-carboxylic acid [30].

Evaluation of carbohydrate-protein interactions

Carbohydrate-protein interactions play a crucial role in basic and applied research. However, analysis of carbohydrate-protein interactions *in-vitro* has been a challenging area of science for several reasons. Carbohydrates can be complicated to obtain in large quantities, and molecular recognition is dependent on carbohydrate presentation. There are methods to evaluate carbohydrate-protein interactions such as mono- and oligosaccharide inhibition studies, isothermal calorimetry, surface plasmon resonance, and enzyme-linked lectin assays. However, these methods require more labor and large quantities of each carbohydrate [31]. Array technology overcomes many of these challenges. Carbohydrate arrays are also called glycan arrays and are composed of various oligosaccharides and polysaccharides immobilized on a solid support in a spatially-defined arrangement [31]. However, the major challenge in the array is how to acquire these

In *ex-vivo* studies, binding of structurally different lipopolysaccharides is differentially modulates global gene expression in the blood [32], toll-like receptor and cytokine gene expression in neutrophils [33]. Furthermore, dietary glycans impact gut health and microbial colonization in man [34] and systemic immunity in animals [35]. Thus, carbohydrate-protein interactions influence host health and microbial pathogenesis.

Conclusion

Host carbohydrate binding proteins recognize specific glycans on pathogens, and microbes recognize glycans on host cells. These interactions are important for pathogenesis and host health. The development of new tools to evaluate carbohydrate-protein interactions enhances understanding of these interactions; this will aid in developing new control strategies for diseases. Expanding the glycan array using various distinct carbohydrates structure would provide further elucidation of specificity and interaction of carbohydrate-binding proteins with glycans.

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