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Review Article

Role of Glycan-Lectin Interaction in Diseases: A Review

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Abstract

The glycans are carbohydrate present with other macromolecules where it could act as ligand for glycan-binding protein called lectin. This glycan-lectin interaction plays important role in cell and organ functioning and immune regulation in both animals and humans. Glycan-lectin interaction is also utilized in viral pathogen interaction which is encoded through host genome or own genome replication and enhancement of infection. Current advancement in glycobiology investigations had revealed interaction between glycan and lectins mediating prominent interaction between host and virus which regulates spread of virus and activation of immune system. Carbohydrates are also found to be involved in viability and growth of cells. Glycosylation process occurs in the cells for regulated processing of secondary protein in the cells, it had an integral functioning in multiple processes ultimately to apoptosis. Glycan with glycan binding protein or solely could convey intracellular signals or extracellular signal control process which leads to initiation, execution of apoptosis program. Glycans and its binding proteins are important cell death machinery, glycan-lectin interactions could alter the spread of viral infections either profitable for virus or host. The interaction of glycan-lectin could be useful as can be used as a diagnostic or prognostic tool in tumor because it had ability of controlling cell apoptosis or cell functioning. This interaction also play prominent role in ocular infection associated pathogenesis and its immune response. The viral disease recently known had been spread in entire world cause due to coronavirus this interaction provide help in forming antiviral agents and gave various thoughts in field of vaccination for this virus. Therefore, all these findings reveled that glycan-lectin interactions are advantageous for various disease and also multiple process of our body.

Keywords: Glycans, Lectins, Glycobiology, Diseases.

INTRODUCTION

Glycans

Glycan and polysaccharide can be used synonymsly which means compound containing large number of monosaccharides linked glycosidically [1]. Also glycan are associated in denoting the carbohydrate portion of glycoconjugate which are named accordingly lipid, protein named glycoplipid, glycoprotein or proteoglycan and carbohydrate present in glycoconjugates are generally oligosaccharides [2]. Glycan could be of similar or different unit and linear or branched with O-glycosidic linkage generally. They are present usually at outer cell surface can be O-linked or N-linked glycans are found exclusively in eukaryotes than in prokaryotes.

N-Linked Glycosylation

This is basically a process by which oligosaccharide (carbohydrates with many sugar molecules also named as glycan) attachment of nitrogen atom to amino acid asparagines residue of protein occurs known as N-glycosylation [3]. This attachment is important for both types of aspects structural and functional in some eukaryotic proteins [4]. This process occurs both in eukaryotes and prokaryotes and widely archaeabacteria, N-linked glycan are determined through cell or protein in which it had been expressed [5]. Different organism species consist distinct N-linked glycan types these glycan are attached with cell organelle endoplasmic reticulum through asparagine nitrogen in side chain with sequence of Asparagine-X-threonine (X= any amino acid) beside proline due to its

structural conformation. Glycan can be composed of galactose, N-acetylgalactosamine, neuramic acid, N-acetylglucosamine, mannose and other monosaccharide. These types of glycan are very crucial for appropriate folding of proteins in eukaryotes for this there are proteins named chaperone found in endoplasmic reticulum serve in proper folding of protein to which glycans are attached. N-linked glycan play role in interaction between two cells, tumor cell forms N-linked glycan and recognized from CD337 receptor found on natural killer cells as indication that cells are normal or cancerous. Lysosomal destruction is also one of the processes executed by this glycosylation. In discriminating self or non-self-cells, N-linked glycan play important role which can ultimately prevent various autoimmune diseases [6].

O-Linked Glycosylation

The binding of carbohydrate to the oxygen of amino acid serine or threonine of protein is known as O-linked glycosylation. It is one type of modification which happens after synthesis of protein or named post translational modifications. In eukaryotes it takes place in cell organelles endoplasmic reticulum, Golgi apparatus and few times in cytoplasm but in prokaryotes it always occurs in cytoplasm. O-linked glycosylation performs many functions so they play important role in various diseases like cancer, Alzheimer diabetes and many more this glycosylation occurs in all types of species eukaryotes, prokaryotes, archaeabacteria. Glycosylation O-linked helps in various processes like in leukocyte circulation at the time of fertilization, protecting from any foreign pathogens by providing defensive immune response [7, 8]. The O-linked attached sugar are commonly present on membrane and provides help in enhancing the stiffness of the place near membrane so that membrane protein remains far from the surface of membrane like seen in less density protein protruding from cell surface through place stiffed by O-linked glycosylation [9]. Mucins a highly O-linked glycosylated protein present at outer lining of respiratory and gastrointestinal tract for protecting these place from infections, protein mucin are negatively charged and allows them to interact with water and prevent from evaporation. It ultimately leads to providing shielding effect function as it lubricates the tract so bacteria could not bind and nor infects the body. Mucin associated alterations are involved in many diseases.

Lectin

Lectins are proteins which binds to carbohydrate specifically and reversible without any modification in them and perform agglutinations property in cells [10]. They are ubiquitous in nature present in all plants, animals, fungi. Its interaction with glycolipid, oligosaccharides make it prone towards cell-cell communication process also they play important role in decrypting the glycan code [11]. Lectin is found abundantly in plants where it provides protection against pathogen [12]. Its role in animals includes glycoprotein trafficking immune defense and other [13].

Lectin in pathogenic microorganism are associated in recognizing the host and tissue adhesion [14]. As all of the organism consist free or covalently attached glycans interacting with receptor present on cell surface and microorganism. Glycans have wide range of structural variation correlated with monosaccharides configuration and variation in between monosaccharide units in inclusion of branching points [15]. Pathogen associated infection strategies are interaction with its higher specificity with host glycans and many time with multivalency. Interference with artificial compounds mimics the natural oligosaccharides constructively competing with binding site is strategy resulting in anti-infectious environment which is found to be so attractive [16]. It had been now developed in various glycochemistry laboratories.

It plays important part in identification at cellular and molecular level which has various biological cell recognition process associated with cells, carbohydrate and proteins [17, 18]. Lectins are known to be present everywhere in nature and function in attachment and binding of bacteria, fungi and viruses at its target. It is also present in various foods among which few vegetables like beans grains which are need to be cooked for reducing lectin content. Few of the lectin are fruitful like C-type lectin containing domain 11A (CLEC11A) it stimulates bone growth also some can work as potent toxin like ricin [19].

Lectin are known to be disabled through any particular oligosaccharides and monosaccharides which could bind to engulfed lectins through legumes, grains, night shades plants etc. This process could prevent its attachment to carbohydrate in the cell membrane. The selection processes of lectins depends on its observation of blood type and it has been established as potentially useful in forming pest resistant plants through genetic engineering of crops.

Interaction between Lectin and Glycans

Glycan protein interactions are class of bimolecular interactions which occurs among free or conjugated glycan and their binding conjugated macromolecules. Intramolecular interaction occurs in between glycan and proteins to which they are covalently attached with. Also this interactions play essential role in cell-cell interactions and host cell interactions like known in ongoing disease of COVID-19. It is engaged in spike protein binding to receptor ACE2 permitting its entrance in host cells. The spike protein is trimeric and N-glycosylated site is found at each subunit forming it more prone towards the target of vaccine.

This interaction plays very important role in immune system of all eukaryotes either animals or humans. Current glycobiology advancement reveled that glycan and lectin mediates key interactions in between virus and host interaction by regulating the viral spread and stimulation of immune system against it. As this interaction is mainly involved in any pathogen and host interaction though, bacterial surface are enriched with glycoconjugates which are mainly present at outer layer and play essential role in interaction with innate immune system of host. As innate immune system is primary barrier for any pathogen through conserved pattern recognition receptors. Innate immune cells express lectin which is a prominent class of pattern recognition molecule receptor have the ability of recognizing the carbohydrates. In innate immune system among various lectins few are majorly known type of lectins that are C-type lectins having antiviral ability, galectins involve in inflammatory response, sialic acid binding immunoglobulin type lectin (siglecs) responsible as receptor-glycan functioning in cell signaling and all the other processes within cells. These lectins participate primarily in recognition of bacterial glycan sand providing early immune response against bacterial infections but can also destructed from bacteria during escape from immune response.

Glycan lectin interaction in virus

This interaction are advantageous for host membrane involved host (lectin) could trap and destroy the virus, lectin is found to be essential for animals host immune defense. Certainly various membrane associated host of immune system and lectin play role in recognizing pathogen molecules which could bind to pathogen and initiates signaling pathway for pathogens for further destruction and presenting to cells for acquired immune response leading to pathogen specific adaptive immune response. On the other side, pathogen attached to this type of cell surface lectins probably presented directly to the nearby immune cells in trans a processes seems particularly remarkable at a place with higher immune cell density (lymph nodes). Therefore, viral pathogen binding to the lectins associated with membrane could lead to the destruction and clearance. It can be understood through the prominent example of human immunodeficiency virus type-1 and langerin mainly C-type lectin present on Langerhans cells. Human immunodeficiency virus (HIV) type1 interaction with langerin (type A II integral transmembrane protein, C-type lectin receptor on Langerhans cells) through greater mannose containing glycans on gp120 protein is eventually engulfed into birbeck granules through receptor mediated endocytosis causing destruction of virus.

The mannose binding C-type lectin like dendritic cell specific intercellular adhesion molecule grabbing non-integrin (DC-SIGN) particularly expressed on dendritic cells which are mainly associated in adaptive immune response and perform destruction of HIV-1 virions through phagocytosis and stimulates both major histocompatibility complex-II (MHC-II) and exogenous MHC-I constricted presentation of HIV- 1 antigens.

Similarly many membrane associated host lectin could help in providing immune response in defense of pathogens. Therefore evolving evidences demonstrates that many of these lectins in inclusion of DCSIGN are also being destructed by viruses for gaining entry to the target cells and providing the viral spread.

Glycans and lectins shield as important role in virology its interplay frequently shapes the interaction in between host and virus. Usually glycan and lectin nature and their particular environmental conditions in which interaction of glycan lectin occurs determines resultant incidence of binding and direct the specific fate of virus. According to the recent knowledge it is transparently known that viral infection is facilitated through viral lectin and its spread. Beside this, it may be instinctive that host lectin associated pattern recognition receptors (PRRs) and further lectins of immune system entirely give protection to host also there are facts which disagreed it. There are various host lectin associated in inducing the effective defense against pathogen and viruses which could exploit the lectins for promoting the infection. Interestingly, various studies associated with lectins role as a host in viral infections reveled that it is dispersible host lectins found to be involved in antiviral activity. On other side, membrane associated host lectins plays more uncertain role and are frequently incriminate in both pro-viral along with antiviral mechanism.

Glycan-lection interaction role in Ocular Infection

Lectin- glycan interaction is present in various diseases among which corneal pathology is one. As the outer surface cornea epithelium consist an unusual barrier against any foreign particles and microorganism which is involved in penetrating the eye. The protective layer of eye consist mucins highly glycosylated proteins emerge from rigid folds of plasma membrane which is an important unit of the protective layer. This layer consist single pass membrane region with extracellular domains of 100nm from cell surface and other glycans in glycocalyx [20].

Investigations over decades had revealed a process through which mucin facilitate protection to corneal epithelial by galectins interference. Analysis through microarray technique have revealed that MUC1 and 16 altogether with galectin-3 are highly expressed glycoprotein at ocular surface [21]. These two mucin binds to galectin-3 in relation of carbohydrate, mucin-galectin3 association is important for maintaining galectin3 at outer membrane for preserving transport from the cell membrane forming barrier function of

corneal epithelial cells [22]. Their involvement masks mediators of virus entry on epithelial glycocalyx of corneal [23]. The core 1O-glycans are known to be the main constituent on mucin transmembrane at ocular surface. The experiments involving c1galt1 as a target which is a glycotransferase needed for core 1O glycan synthesis reveling the participation of this modulation in enhancing surface confinement of galectiin-3 stabilizing the barrier function. Though, synthetic glycan microarray technique had revealed that galectin-3 represents highest capability of binding for N-glycan in comparison of O-glycan [24]. Suggesting mucin N-glycans role associated with stabilization of epithelial glycocalyx inspite of lower abundance than O-glycans. Currently evidences are there for supporting this scenario, organizational data revealed the abundance of mucin-N-glycan in complicated type of structure which associated with galectin-3 and enhancing integrity of barrier [25]. Decrypting the relevant contribution and biological importance of distinct groups of mucins glycans when interrelated with galectins can be crucial target for subsequent investigations on mucosal surfaces. The cause is viral, fungal, bacterial pathogen colonization of the eye is a prominent reason of myopia in entire world. Various findings gives strong proof for lectin-glycan interactions which plays dominant part in pathogenesis and immune defense associated with eye infection.

Glycan- lectin interaction in Tumor and role of glycan in diagnosis and prognosis of cancer

The development of cancer requires various events in ordered and sequential manner to be completed. As metastatic is one of the events which leads to cancer invasiveness this process of metastatic require interaction of many cell surface glycans and its interaction with lectins. Abnormality in glycosylation is a one of the prominent feature for malignant transformation and glycan associated in adhesive interaction of cancerous cells frequently provides advantageous environment for dispersal of tumor. This invasiveness of tumor mainly involves glycans present on cell surface and its involvement with intrinsic lectins, prominently E cadherins, laminin, integrins and cell surface marker CD-44 are found to involve in invasion and metastasizing tumor cells from the connective tissue and ultimately forms tumor cells from early lesions of tumor. Angiogenesis is one of the processes found in transformed cells forming new blood vessels in this process one of the glycan named heparan sulfate and lectin C- or S type interacts with vascular system. Glycan potent role is seen in cancer cell invasion in association of immune system its role in cancer causation had been seen since almost 6 decades. The abnormality in cancer cells are formed due to glycosylation this has been known but its acknowledgment is very minute in context of relationship with survival rates [26]. Although, monoclonal antibody emergence had revealed glycan as a tumor specific antibody target and currently glycans in cancer research are mainly focused and have significant advancement providing enhanced understanding of tumors glycoprotein and advantages of glycosphingolipids alterations [27]

Tumor cells shows distinct types of glycoprotein abnormalities in comparison of healthy cells present next to altered cells. Protein glycosylation enhances the variability in its functions during the time few modifications are seen in structure of cells. Alteration in glycosylation specificity in normal cells were found distinct from glycosylated cancerous cells and also other factor are associated in alterations of cancerous cells [28]. Glycosylation process could also happen even if there occur any abnormality in glycotransferase responsible for catalyzing the carbohydrate addition on protein at genetic level or from abnormalities in Golgi apparatus place at which assembly of this process occurs [29, 30]. Dysregulation of chaperons could also lead to change in malignant cells [31]. Commonly changes seen in cancerous cells are glycosylation, sialyation, branching glycans either N or O linked and fucosylation. Various epigenetic and other conditional component are known to be associated with alterations in malignant tumor cells. [32].

Glycans not only involve in cause of tumor or cancer but also in diagnosis of cancer it is an prominent factor involve against ever-evolving disease with potent role in acting as non-invasive biomarkers which could diagnose cancer before it become invasive and help in diagnosis of malignant transformation and accurately predicting the diagnosis.

Biomarker alpha-fetoprotein (AFP) is a glycoprotein formed at the time of embryogenesis and development of fetus which had been currently utilized in detection of liver cancer [33].Beside this various other biomarkers mainly alcohol family members named glycol biomarker could diagnose early stages cancer this leads to lower the cancer associated mortality rate and give more accurate rate of data regarding prognosis and diagnosis of cancer further provide the ease in differentiating the types of cancer [34].

Cancer is known to be a disease group which involves dysregulation of cell development and capability of occupying other areas of body. In both cancer and normal cells post translation modification (PTMS) which includes (N-acetylation, glycosylation, phosphorylation) are associated in maintenance of proteins functioning, these all PTMS are commonly found in glycosylation and are involved in various biological process [35].

In biosynthesis glycan have an important role as a precursor and in structural elements as glycoprotein or glycolipids depending on attachment of lipid or protein to glycan. Therefore it is a crucial factor for

understanding distinct cancer process, diagnostic and therapeutic strategies. It had also potential in regulatory process of various physiological process leading to any disease [36]. The aberration in glycosylation are associated in forming tumor cell to transformed cells which had been seen while comparing cancerous cells and non-transformed complements this fact have been known many years before from various investigations.

Currently new strategies are to be urgently required for convenient detection, severity assessment and cancer treatment. Though glycan are found as a potential source for forming new biomarkers. Glycoprotein is commonly utilized serological biomarkers for observation of invasiveness, diagnosis and recurrence of disease in cancer [37]. Various types of prominent biomarkers are used in different cancers these biomarkers had reveled abnormality in cancerous cell. The utilization of biomarker for diagnosis and screening should not be of low specificity it would lead to drastic consequences. Therefore new research for greater specificity of biomarkers are essential for pre-diagnosis of cancer like α-fetoprotein AFP is one of the biomarker involve in diagnosis of liver disease and its certified protein for liver cancer diagnosis.

Glycosylated form of AFP was known to be a cancer marker which shows advantageous results by comparing the hepatocellular carcinoma (HCC) and chronic liver diseases [38]. Proteins glycosylated and other glycans are associated in various prominent processes biological process of normal tissues and is utmost component of cells. Alteration at genetic level Glycosylation associated modifications occurs because of genetic, epigenetic and environmental process which initiates many biological processes of cancer [39]. The current understanding in glycobiology could give frequent expansion for novel glycoengineered and model platforms.

Lectin Glycan in Cell death

The term program cell death was given by Lockshin and Williams and after several years few investigators identified that the morphological modification mechanism are happening in cells are called as apoptosis. The carbohydrate and its recognition with motif particular carbohydrate and lectin study named glycobiology fall behind the investigations and define the structural and cellular process of cell death. Though lectin are known for its agglutination capability of erythrocyte association with lectin and glycan in program cell death (PCD) was not known at that time. After few decades studies reveled that lectin expressed consequently on macrophages cell surface which could specifically recognize glycans modification enhancing the apoptotic thymocytes surface [40]. Therefore this studies do not revealed the mechanism of lectin-glycan interactions through which apoptosis regulated. So afterwards Griffiths and co-workers identified modification associated in apoptosis in lymphoid tissues after injecting the plant lectins further additional studies were performed [41]. Cell shrinkage and fragmentation of DNA in WBCs by displaying it in vitro to the lectins of plants. This approach provides the therapeutic basis of planning aimed for eliminating abnormality of glycosylated cancer cells.

All most living cells are designed from a complex glycosylated molecules layers which contains biological information. The glycosylation system is associated in assembling the different repertoire of glycan structure named as glycome from sequential act of glycosyltransferase and glucosidases. The given protein associated extent and essence of glycosylation depends on N or O-linked glycosylation site of protein [42]. Lectin present on membrane or soluble are associated in decrypting the glycan constituent and regulating homeostasis of cell by modifying endocytosis cell signaling receptor trafficking [43][44]. Though various processes have been known for lectin-glycan identification systems which play prominent role in initiation of apoptosis.

Glaectin a lectin forms mutimeric complex with glycosylated receptor causing shift in molecule of interactome receptor. The initiation of apoptosis requires CD-45,37 (cluster of differentiation) segregates following binding of galectin to T-cells [45]. CD-45 associated phosphorylation mediates apoptosis through modification in extrinsic pathway of apoptosis affecting downstream signaling mechanism after cell ingestion. Involvement of CD-45 leads activation of caspases kind of protease helps in program cell death and further cleavage from DFF40 an endonuclease performs double strand break. Activation of galectin-1 leads downregulation of T-cells expression of anti-apoptotic protein BCl2 and activation of effector caspases [46]. Galectin-1 also stimulates ceramide release which act as a secondary messenger in performing apoptosis. Further ceramide promotes Jun N-terminal (JNK) activation which leads accumulation and condensed B-cell lymphoma-2 (BCl2) and its elevated phosphorylation forms heterodimer with pro-apoptotic protein Bax. Ultimately, this leads molecular events, activation of caspases-3 and 9 following T-cell death [47].

Another example of glycan-lectin interaction role in disease had been reveled in galectin-8 which is known to be involved in inflammatory response. Its interaction with CD-44 stimulates pro-apoptosis system in joints by stimulating inflammation it depend on soluble CD-44 and fibrinogen [48]. Galectin-1 delivering at infection site promotes T-cell death and attenuation of inflammation in distinct representation of autoimmune disease.

This all findings suggest the association of apoptosis as a therapeutic method persistent inflammation T-cell immunoglobulin mucin domain-3

had been found to be implicated in cell death of T-cells. Galectin-9 binding to TIM-3 stimulates specifically death of TH1 cells [49]. This lectin pro-apoptotic effect is found to associate in forming dimeric structure with 2 carbohydrate recognition domain and requires N-glycan on intended site. Among all of these glycoprotein serving as partners for galectin binding CD29 are prefer to bind with galectin2 and elicits cell death activation of T-cell.

The interaction between them leads to initiation, execution and cell death resolution which will provide few example that demonstrate the importance of these processes. Death receptor associated glycosylation regulates the fatal signals of glycans binding proteins either soluble or cell surface which could execute apoptosis directly or indirectly through death receptor interaction or byc ross linking with glycoprotein present on cell surface. Additionally, galectin-glycans modulation enzyme plays important role in execution of apoptosis and autophagy. Their interaction organize destruction of foreign protein interaction and cellular damage and also regulates immune system by inflammatory response. Undesirable presentation of glycans could alter autophagy leads towards severity of disease. Lectins and glycans present intracellularly could perform signal for intent of apoptosis from keep me, eat me or engulf me indications. Currently more of knowledge had made the clear visualizing strategies from which lectin-glycan manipulation in its identification system could contribute program cell death control with interpretative implications in resolving various disease, neurodegenerative disease, autoimmunity and cancer.

Glycan-lectin in Coronaviruses

The Coronaviruses consist glycoprotein which had been known to be involved in invasion, morphogenesis and immune response modulation process. Currently more than sufficient data are available for spike protein. This protein mediates adhesion of virus through ACE2 binding and involved in immune defensive interaction. Dysregulation in their interaction are known to be target for antiviral therapy. Though lectin could inhibit coronavirus adhesion to host cell receptor by targeting envelope glycoprotein. Spike protein has crucial role in adhesion of virus from ACE-2 binding. However, disruption in their interaction can help as attractive antiviral therapy. Few non-mammalian derived lectins are antiviral agents against enveloped viruses because of its potential to identify the glycans found in structural proteins and harm the preliminary step of virus pathogenesis.

The emergence of COVID-19 had leads to various investigations among which one study revealed the interaction of Glycan- lectin. Lectin was isolated from a plant Lablab purpureus[Flt3 receptor interacting lectin (FRIL)]lectin as an antiviral agent also named as DLL-I reveled to be involved in completely inhibiting the cytopathic effect of COVID-19. This action of study was correlated with the potential of FRIL in binding to COVID-19 virus by shielding N-glycan as of spike protein. Investigators reveled that FRIL associated treatment impairs the COVID-19 Nucleocapsid and Spike protein [50].Beside this also other lectins of plants have been known which exhibit the action toward other coronaviruses like mannose binding lectins concanavalin A, Galanthus nivalis, agglutinin [51].

One of the study dominantly showed importance of glycosylation, inhibition of mannosidases in host leads increased antiviral activity of glycans binding lectins. Other than plant derived agglutination other known potent agents against coronaviruses are cyanovirin-N mannose binding lectins and griffithsin protein isolated from red algae which had been observed against two strains of coronaviruses SARS-CoV and MERS-CoV because the protein griffithsin was consisting various sites for these two strains. Therefore, inhibitory activity of griffithsin (GRFT) had been seen as a potent antiviral activity against these two strain as it this protein had various sites for these strains glycoprotein of greater affinity and inhibits entry of virus [53].

Beside this lectins had also decreased the mortality rate and complexity of fatal pulmonary infection which had been reveled after studies performed on the mice due to decrease pro-inflammatory cytokine in infected lungs [54]. Inspite of lectin antiviral feature few restriction are seen in considering it as therapeutic agent frequent destruction of macromolecules which leads to give various dose for maintaining its clinical utilization. These hurdles can be improved by insertion of proteins in conceptualization which will stimulate balanced release and shielding from denaturing agents.

Glycosylation at sites N165,234, 331 and 343 near receptor binding domain (RBD) protect the immune response associated critical region recognition site. Beside provide protection these sites have another role in conformational modulation associated with RBD its presence provides stabilization and RBD increased conformation and facilitates ACE2 binding and deletion in these glycans from N165, N234A abnormalities leads reduction in RBD conformational shift downward not attainable to ACE2 [55]. The spike protein consist oligomannose type of glycan represents 28% of entire weight which is less for other viral glycoproteins and N34 glycoprotein near RBD show Man5- GlcNAc2 type of glycosides [56]. The glycan O-GalNA cglycans are situated in hinge region of RBD and those found near furin site have censorious role in angiotensinogen converting enzyme -2 receptor binding with virus also fusion of membrane required for the infectious. Similarly ACE-2 receptor glycosylation also play influential role in attachment and infection of virus.

N90 glycosylation partially interrupts with RBD-ACE-2 interaction any abnormality at N90 or T92 eliminate the N-glycosylation sequon at N90 disrupt unglycosylated variant more efficiently for interacting with RBD. N322 has exactly different function it interact tightly with RBD provide strength to ACE-2 – RBC complex [57]. Carbohydrate binding protein is molecule with capability of decoding the glycan information relevant to the biological function. Various virus are enveloped with lectins carbohydrate binding proteins associated in viral infectivity.

Glycobiology had provided defense against COVID-19 infection through host glycans O-GalNAc secreted from mucins are important in protecting and hydrating the urinary, gastrointestinal, and respiratory and eyes outer layer epithelial cells. Mucins traps the microorganism through its O-glycans performing biological mechanism in eliminating mucus entrapped microbes and particles. Also it is associated in providing saliva both types of tissue hard and soft through particular binding and accumulation process and blocks microorganism adherence to oral surface providing microorganism clearance. It also plays prominent role respiratory tract by facilitating as a physical barrier for elimination of pathogen effecting the morbidity and death rate of the lung disease infected patients [58].

Glycan binding proteins are also involved in providing defense against COVID-19 infection and its result provides information for this disease. Innate immune response against virus in humans depends on lectins, interferon, cytokines and antibodies not entirely. If any COVID-19 infected person overcome innate immunity and early phase of infection the person have higher risk of pneumonia complication through viral infection [59]. The mannose binding lectin soluble serum protein with main function innate immune system recognize and binds to microorganism associated terminal mannose glycan. It enhances opsonophagocytosis activation complement pathway and modification in inflammation in defense against COVID-19 infection [60].

These evidences reveled that mannose binding lectin are involve in protection of early stage of COVID-19 infection. Mannose binding lectin (MBL) could also perform recognition of oligomannose type glycan involved in COVID-19 spike protein presenting a susceptible factor for acquiring viral infection. ICAM-3 specific for dendritic cell grabbing non-integrin lectin and Dendritic Cell-Specific Intercellular adhesion molecule-3-Grabbing Non-integrin lectin, (DC-SIGN) specific for lymph node, dermis are the other defensive immune response associated with glycan-lectin interaction [59]. The binding of Mannose (Man), N-acetyl glucosamine (GlcNAc) and N-Acetyl mannosamine (ManAc) revealing a ligand binding licensing. The binding of Mannose N-acetyl glucosamine (GlcNAc) residue enhances DCSIGN associated recognition in various case. DCSIGN recognize the COVID-19 spike protein in glycan depended process. The macrophage of human macrophage galactose lectin (MGL) is a C-type lectin calcium dependent express in tolerogen on dendritic and macrophage performing downregulation of T-cell and inducing programmed cell death of effective T-cell. MGL is basically in autoimmunity disease, consistent inflammation, and inhibition of excessive

CONCLUSIONS

Glycan are carbohydrates mainly present on protein and lipids are basically cell matrix molecules important for maintenance of tissue structure and integrity. These molecules can also consist binding sites for other types of glycans which ultimately helps in overall organization of the matrix. On other side lectin are protein associated in binding to carbohydrate which have greater specificity for sugar groups involved in other molecules and leads to agglutination of particular cells or precipitation of glycans and polysaccharides. Lectins are known to be involved in recognition process of macromolecules and cells and mediates binding of virus, bacteria to their appropriate target site so there is immediate need of studying glycan and its interaction with respective receptors as it is involved in multiple biological process in humans. Therefore it is not possible to avoid future role of glycan lectin interaction in diagnosis and prognosis of disease. Currently, advancement in decoding the knowledge of glycan-lectin interaction had led a comprehension that glycan binding receptor and its interaction perform important part in various disease and biological process. Investigators have unclear glimmer of understanding about glycan role in causing disease or its progression. Further various measures are required about what is known for interaction between protein and polysaccharide for developing effective treatments of diseases for which currently there is not any cures like autoimmune disorders, cancer and many more. Glycan lectin interactions could be utilized as diagnostic or prognostic tool in future due to its role in many processes in our body.

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