Human Lectins, Their Carbohydrate Affinities and Where to Find Them

Cláudia D. Raposo 1,*, André B. Canelas 2 and M. Teresa Barros 1

1 LAQV-Requimte, Department of Chemistry, NOVA School of Science and Technology, Universidade NOVA de Lisboa, 2829-516 Caparica, Portugal; mtb@fct.unl.pt
2 Glanbia-AgriChemWhey, Lisheen Mine, Killoran, Moyne, Co. Tipperary E41 R622, Ireland; canelasab@gmail.com
* Correspondence: piccfa@gmail.com; Tel.: +351-212948550

Abstract: Lectins are a class of proteins responsible for several biological roles such as cell-cell interactions, signaling pathways, and several innate immune responses against pathogens. Since lectins are able to bind to carbohydrates, they can be a viable target for targeted drug delivery systems. In fact, several lectins were approved by Food and Drug Administration for that purpose. Information about specific carbohydrate recognition by lectin receptors was gathered herein, plus the specific organs where those lectins can be found within the human body.

Keywords: human lectins; carbohydrate specific recognition; biological applications; targeted drug delivery systems; protein expression

1. Introduction

Lectins are an attractive class of proteins of non-immune origin that can either be free or linked to cell surfaces, and are involved in numerous biological processes, such as cell-cell interactions, signaling pathways, cell development, and immune responses[1]. Lectins selectively recognize carbohydrates and reversibly bind to them as long as the ligands are oriented in a specific manner. Some of the commonly occurring carbohydrates that are found in Nature are D-fructose, D-galactose, L-arabinose, D-xylene, D-mannose, D-glucose, D-glucosamine, D-galactosamine, L-fucose, various uronic acids, sialic acid, and their combinations to form other di- and oligosaccharides, or other biomolecules (Figure 1) [2].

Figure 1. Structures of the carbohydrate building blocks found in Nature.

Lectins in vertebrates can be classified either by their subcellular location, or by their structure. Division based on their location includes integral lectins located in membranes
as structural components, or soluble lectins present in intra- and intercellular fluids, which can move freely.

Division according to lectin structure consists of several different types of lectins, such as C-type lectins (binding is Ca²⁺ dependent), I-type lectins (carbohydrate recognition domain is similar to immunoglobulins), galectin family (or S-type, which are thiol dependent), pentraxins (pentameric lectins) and P-type lectins (specific to glycoproteins containing mannose 6-phosphate) [3].

Different lectins have high similarity in the residues that bind to saccharides, most of which coordinate to metal ions, and water molecules. Nearly all animal lectins possess several pockets that recognize molecules other than carbohydrates, meaning that they are multivalent and can present 2 to 12 sites of interaction, allowing the binding of several ligands simultaneously. The specificity and affinity of the lectin-carbohydrate complex depends on the lectin, which can be very sensitive to the structure of the carbohydrate (e.g., mannose versus glucose, Figure 1), or to the orientation of the anomeric substituent (α versus β anomer, e.g., in Figure 2), or both. Lectin-carbohydrate interactions are achieved mainly through hydrogen bonds, van der Waals (steric interactions), and hydrophobic forces (example is given in Figure 3) [3,4].

**Figure 2.** Structures of α- and β-D-glucose.

**Figure 3.** Asialoglycoprotein receptor (Protein Data Bank entry 1DV8, gene symbol ASGR1) binding interactions with N-acetylgalactosamine: (a) ligand conformation inside the binding site; (b) specific interactions are hydrogen bonds (blue dashed lines) and steric interactions (red dashed lines).

It has been shown that the majority of lectins are conserved through evolution, suggesting that these proteins play a crucial role in the sugar-recognition activities necessary for the living process and development [5,6].

Although lectins are present in animals, plants, lichens, bacteria, and higher fungi [3], this review focuses only on human lectins for targeted drug delivery[7] purposes, their specificity towards carbohydrates and the organs where they are expressed. When referring to gene expression (or RNA expression), one means that those specific organs or cells have that specific gene coded. If active, it produces the respective protein, and one
says that the protein is expressed in that organ or cell. In this review, we focus only on protein expression, since that information is the only relevant one for the development of targeted drug delivery systems. More information about carbohydrate-based nanocarriers for targeted drug delivery systems can be found elsewhere[8–10]. Since lectins are able to recognize and transport carbohydrates and their derivatives, lectin targeting can be relevant in research and development of new medicines [7,11,12]. The metabolism of cancer cells, for example, is different from normal cells due to intense glycolytic activity (Warburg effect) [13]. Cancer cells require glucose and/or glucose for cell growth, and glucose transporter isoforms 1 and 2 (gene symbols GLUT1 and GLUT2, respectively) showed an increase in activity in several tumors (gastrointestinal carcinoma, squamous cell carcinoma of the head and neck, breast carcinoma, renal cell carcinoma, gastric and ovarian cancer)[14,15].

The herein adopted lectin nomenclature is in accordance with the Human Genome Group (HUGO) Gene Nomenclature Committee. However, most common designated aliases (non-standard names) are also included (and appear first). The expression data for all lectin-coding genes was compiled from The Human Protein Atlas [16,17] and GeneCards [18] databases.

2. C-Type Lectins

C-type lectins are involved in the recognition of saccharides in a Ca2+-dependent manner but exhibit low affinities to carbohydrates, requiring multiple valencies of carbohydrate ligands to mediate signaling pathways, such as DC-SIGN2 which gene symbol is CLEC4M (Most genes carry the information to make proteins. The gene name is often used when referring to the corresponding protein). MINCLE (gene symbol CLEC4E), on the other hand, shows high affinity and can detect small numbers of glycolipids on fungal surfaces [19,20]. Most of the lectin-like domains contain some of the conserved residues required to establish the domain fold, but do not present the residues required for carbohydrate recognition [21]. The amino acid residues known to be involved in calcium-dependent sugar-binding are the EPN motif (mannose-binding), the QPD motif (for galactose binding), and the WND motif (for Ca2+-binding) [22]. More information about glycan affinity and binding to proteins can be found elsewhere [23]. A comprehensive list of C-type lectins is presented in Table 1, divided by subfamilies that differ in the architecture of the domain [22,24], along with the carbohydrates that they recognize and the human tissues where they are expressed.

Table 1. C-type superfamily, their carbohydrate ligands and protein expression in human organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|----------------------------------|---------------------------------|
| Proteoglycans or lecticans            |             |                                  |                                 |
| Aggrecan                             | ACAN        | Hyaluronic acid [25]             | Cartilage, soft tissue          |
| Brevican                             | BCAN        | Hyaluronic acid [26,27]          | Brain                           |
| Neurocan                             | NCAN        | Hyaluronic acid [28]             | Brain                           |
| Versican                             | VCAN        | Hyaluronic acid [29]             | Brain                           |
| FRAS1 related extracellular matrix 1  | FREM1       | [b]                             |                                   |
|                                      |             |                                  | Adrenal gland, appendix, colon, duodenum, epididymis, kidney, lung, pancreas, placenta, rectum, salivary gland, small intestine, stomach, testis, tonsil, thyroid gland |

Type II transmembrane receptors

| Blood Dendritic Cell Antigen 2 (C-type lectin domain family 4 member C) | CLEC4C | Gal-β-(1-3 or 1-4)-GlNAc-β-(1-2)-Man trisaccharides [30,31] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| DC-SIGN (CD209 molecule) | CD209 | High N-linked d-Mannose- | Bone marrow, lung |
| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|----------------------------------|----------------------------------|
| Dectin-2 (C-type lectin domain containing 6A) | CLEC6A | Mannose, fucose and weakly interacts with N-acetylgalcosamine | Bone marrow, spleen, lung |
| Dendritic cell immunoreceptor (DCIR) (C-type lectin domain family 4 member A) | CLEC4A | N-acetylgalacosamine, mannose, N-acetylgalacosome, fucose. Note that OH-3 and OH-4 should be free for recognition, and preferentially equatorial. | Lymph node, bone marrow, spleen, appendix, tonsil, skin |
| Fc fragment of IgE receptor II | FCER2 | Terminal β-D-galactose and N-acetylgalacosamine units | Stomach, liver, gallbladder |
| Hepatic Asialoglycoprotein Receptor 1 | ASGR1 | Terminal β-D-galactose and N-acetylgalacosamine units | Liver |
| Hepatic Asialoglycoprotein Receptor 2 | ASGR2 | Terminal β-D-galactose and N-acetylgalacosamine units | Liver |
| Kupffer Cell receptor (C-type lectin domain family 4 member F) | CLEC4F | Galactose, fucose, and N-acetylgalacosamine | Liver |
| Langerin (CD207 molecule) | CD207 | N-acetylgalacosome showed less affinity; thereby axial derivatives should be avoided. Sulfated mannosylated glycans, keratan sulfate and β-glucans | Lymph node, tonsil, skin, spleen |
| Liver sinusoidal epithelial cell lectin (LSECtin) (C-type lectin domain family 4 member G) | CLEC4G | Mannose, N-acetylgalcosamine and fucose | Lymph node, brain, colon, kidney, liver, testis |
| Macrophage Asialoglycoprotein Receptor | CLEC10A | Terminal galactose and N-acetylgalacosamine residues | Bone marrow, brain, lymph node, oral mucosa, Trehalose 6,6-dimyclolate, α-D-mannans18 | Liver |
| Macrophage C-type Lectin (MCL) | CLEC4D | α-D-mannans18 (however it was suggested that MCL is not a carbohydrate-binding lectin) | Bone marrow, lung, lymph node, spleen, tonsil |
| MINCLE (C-type lectin domain family 4 member E) | CLEC4E | α-mannose, trehalose-6,6-dimyclolate, glucose | α |

**Collectins**

| Common Name | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|-------------|-------------|----------------------------------|----------------------------------|
| Collectin-K1 (collectin subfamily member 11) | COLEC11 | High mannoseline oligosaccharides with at least α-(1-2)-mannose residue | α |
| Collectin-L1 (collectin subfamily member 10) | COLEC10 | Galactose, mannoseline, fucose, N-acetylgalacosamine | α |
| Mannose-binding lectin 2 | MBL2 | Mannose, fucose, N-acetylgalacosamine | Liver |
| Pulmonary surfactant protein 1 (surfactant protein A1) | SFTPA1 | Mannose, glucose, poorly to galactose. Preferentially oligosaccharides | α |
| Pulmonary surfactant protein 2 (surfactant protein A2) | SFTPA2 | N-acetylgalacosamine, 1-fucosyl, mannoseline, glucose, poorly to galactose | α |
| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|----------------------------------|---------------------------------|
| Pulmonary surfactant protein B (surfactant protein B) | SFTPB | Galactose. Preferentially oligosaccharides [47] | Lung |
| Pulmonary surfactant protein C (surfactant protein C) | SFTPC | Lipopolysaccharides [47] | Lung |
| Pulmonary surfactant protein D (surfactant protein D) | SFTPD | Maltose, glucose, mannose, poorly to galactose. Preferentially oligosaccharides [47] | Lung |
| Scavenger receptor with CTLD (SRCL) (collactin subfamily member 12) | COLEC12 | D-galactose, L- and D-fucose, N-acetylgalactosamine (internalizes specifically in nurse-like cells), sialyl Lewis X, or a trisaccharide and asialo-orosomucoid (ASOR). May also play a role in the clearance of amyloid-beta in Alzheimer disease [48] | Brain, lung, placenta |
| Selectin E | SELE | Sialyl Lewis x, a [49] | Bone marrow, colon, nasopharynx |
| Selectin E | SELL | Sialyl Lewis x [50] | Appendix, bone marrow, lymph node, spleen, tonsil |
| Selectin P | SELP | Sialyl Lewis x [49] | Bone marrow, colon |
| Selectins | | | |
| C-type lectin domain family 2 member L | CLEC2L | Fucose, mannose, N-acetylgalactosamine, N-acetylmuramic acid-β(1-4)-N-acetylgalactosamine [51] | Brain, skeletal muscle |
| C-type lectin domain containing 5A | CLEC5A | | Blood |
| CD72 molecule | CD72 | | Appendix, bone marrow, lymph node, spleen, tonsil |
| Killer cell lectin-like receptor G1 | KLRG1 | Mannose [52] | Appendix, cervix (uterine), colon, duodenum, small intestine, stomach, tonsil |
| Killer cell lectin-like receptor G2 | KLRG2 | | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| CD69 molecule | CD69 | Fucoidan (weak), N-acetylamide was reported but not supported by a second report. Does not bind glucose, galactose, mannose, fucose or N-acetylgalactosamine [53] | Appendix, bone marrow, lymph node, spleen, tonsil |
| Killer cell lectin-like receptor F1 | KLRF1 | Predicted to not bind carbohydrates [54] | Blood |
| | | | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, proximal digestive tract, skin |
| C-type lectin domain family 2 member B | CLEC2B | Known to bind to KLRF1 | |
| Oxidized low-density lipoprotein receptor 1 | OLR1 | Predicted to not bind to carbohydrates[55] α-(2-3)-linked NeuAc on multi-antennary N-glycan, heparin, sulfate-containing polysaccharides [56] | |
| Killer cell lectin-like receptor D1 | KLRL1 | Predicted to not bind to carbohydrates [57] | |
| | | | |
| C-type lectin domain family 1 member A | CLEC1A | | |
| C-type lectin domain family 1 member B | CLEC1B | | |
| C-type lectin domain family 12 member B | CLEC12B | | |
| C-type lectin-like 1 | CLEC1L | Predicted to not bind to carbohydrates [21] | |
| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|-------------------------------------|-------------|----------------------------------|---------------------------------|
| C-type lectin domain family 12 member A | CLEC12A | Specific interactions were not discovered yet, although it is known that this lectin binds to α-actin filaments and β-spectrin [59] | Bone marrow, lung, spleen |
| DNGR (C-type lectin domain containing 9A) | CLEC9A | β-(1,3)- and β-(1,6)-Gal-Glycans (neither mono- or short oligosaccharides/polymers are recognized) [60] | Blood, bone marrow |
| C-type lectin domain family 2 member A | CLEC2A | | Skin |
| Dectin-1 (C-type lectin domain containing 7A) | CLEC7A | Terminal Gal-α-(1,3)-Gal, N-acetyllactosamine, [62] Sucrose octasulphate [63] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Killer cell lectin-like receptor B1 | KLRB1 | α-(2-3)-NeuAc-containing N-glycans[64], heparin, heparan sulfate [56] | Appendix, lymph node, spleen, tonsil |
| Killer cell lectin-like receptor C1 | KLRC1 | Terminal Gal-α-(1,3)-Gal, N-acetyllactosamine, [62] Sucrose octasulphate [63] | Colon, duodenum, small intestine, stomach, tonsil |
| Killer cell lectin-like receptor C2 | KLRC2 | | |
| Killer cell lectin-like receptor C3 | KLRC3 | | |
| Killer cell lectin-like receptor C4 | KLRC4 | | |
| Killer cell lectin-like receptor K1 | KLRK1 | | |

**Macrophage Mannose Receptor (MMR)**

- **Endo180 (Mannose receptor C type 2)**
  - MRC2
  - Mannose, fucose, N-acetylgalactosamine [65]
- **Lymphocyte antigen 75**
  - LY75
  - Predicted to not bind carbohydrates [65]
- **Mannose receptor C-type 1**
  - MRC1
  - Mannose, fucose, glucose, N-acetylgalactosamine [66] (C-type 4-O-sulphated GalNAc (R-type) Predicted to not bind carbohydrates [65] but known to bind collagen
- **Phospholipase A2 receptor**
  - PLA2R1
  - |t|

**Free C-type Lectin Domains (CTLDs)**

- **C-type lectin domain containing 19A**
  - CLEC19A
  - Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin
- **Lithostathine-alpha (Regenerating family member 1 alpha)**
  - REG1A
  - Duodenum, pancreas, small intestine, stomach
- **Lithostathine-beta (Regenerating family member 1 beta)**
  - REG1B
  - Duodenum, pancreas, small intestine, stomach
- **Regenerating family member 3 alpha**
  - REG3A
  - Peptidoglycan (binding affinity increases with the length of the carbohydrate moiety) [67]
- **Regenerating family member 3 gamma**
  - REG3G
  - Peptidoglycan [67]
- **Regenerating family member 4**
  - REG4
  - Mannans, heparin [67]

**Type I receptors**

- **Chondrolectin**
  - CHODL
  - Adipose and soft tissue, bone marrow and
- **Layilin**
  - LAYN
  - Hyaluronan [69]
| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|---------------------------------|
| Tetranectin Cartilage-derived C-type lectin domain family 3 member A | CLEC3A | Expected to bind sulfated polysaccharides such as heparin [70] | lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Stem cell growth factor (SCGF) (C-type lectin domain containing 11A) | CLEC11A | Expected to bind galactosyl and glucosyl residues. Might bind oligosaccharides with mannosyl moieties [71] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas, proximal digestive tract, skin |
| Tetranectin (C-type lectin domain family 3 member B) | CLEC3B | Sulfated polysaccharides such as heparin [70] | |
| Polycystin Polycystin 1 like 3, transient receptor potential channel interacting | PKD1L3 | Predicted to not bind carbohydrates | |
| Polycystin 1, transient receptor potential channel interacting | PKD1 | Predicted to bind galactosyl and glucosyl residues. Might bind oligosaccharides with mannosyl moieties [71] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas, proximal digestive tract, skin |
| Attractin Attractin | ATRN | Expected to bind carbohydrates | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas, proximal digestive tract, skin |
| Attractin-like 1 | ATRNL1 | Expected to bind carbohydrates | |
| CTLD/acidic neck CD302 molecule | CD302 | Heparin [72] | |
| Proteoglycan 2, pro eosinophil major basic protein | PRG2 | Heparin [73] | Bone marrow, placenta |
| Proteoglycan 3, pro eosinophil major basic protein 2 | PRG3 | | Bone marrow |
| Endosialin CD93 molecule | CD93 | | Bone marrow, brain, colon, kidney, lung, spleen Appendix, brain, cervix (uterine), colon, duodenum, esophagus, gallbladder, heart muscle, kidney, lung, pancreas, prostate, rectum, skin, small intestine, stomach, testis |
| C-type lectin domain containing 14A | CLEC14A | | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas, proximal digestive tract, skin |
| Endosialin (CD248 molecule) | CD248 | | |
| Thrombomodulin | THBD | | |
| Others C-type lectin domain family 18 member A | CLEC18A | Fucoidan, β-glucans, β-galactans [74] | |
| Prolectin (C-type lectin domain containing 17A) | CLEC17A | Terminal α-D-mannose and fucose residues [75] | Appendix, lymph node, spleen, stomach, tonsil |
| DiGeorge syndrome critical region gene 2 | DGR2 | | Pancreas |
| FRAS1 related extracellular matrix 1 | FREM1 | | Adrenal gland, appendix, colon, duodenum, epididymis, kidney, lung, pancreas, placenta, rectum, salivary gland, small intestine, stomach, testis, tonsil, thyroid gland |

* Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases. ** Carbohydrate moieties recognized by this protein have not been discovered yet. ^ FDA-approved drug target.
3. Chitolectins (or Chilectins)

There are two types of proteins that are able to recognize chitin: chitinases and chitolectins. The first ones are active proteins that bind and hydrolyze oligosaccharides, whereas the latter ones are able to bind oligosaccharides but do not hydrolyze them [76,77] and are presented in Table 2.

Table 2. Human chitolectins (also called chilectins), their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|---------------------------------------|-------------|-----------------------------------|---------------------------------|
| Chitinase 3 like 1                    | CHI3L1      | Chitin [78]                        | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, proximal digestive tract |
| Chitinase 3 like 2                    | CHI3L2      | Chitooligosaccharides (GlcNAc) and (GlcNAc)s showed the highest affinities [79] | Fallopian tube |
| Oviductin (Oviductal glycoprotein 1)  | OVGP1       | Chitin [80]                        |                                |
| Stabilin-1 interacting chitinase-like protein | CLP | GalNAc, GlcNAc, ribose, mannose. Prefers to bind oligosaccharides with a four-sugar ring core [81] |                                |


a) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases.

4. F-Type Lectins

F-type lectins, also called fucolectins, are characterized by an α-L-fucose recognition domain and display both unique carbohydrate- and calcium-binding sequence motifs [76]. F-type lectins are immune-recognition proteins and are presented in Table 3. Fucose is recognized by specific interactions with O5 (pyranose acetal oxygen), 3-OH and 4-OH [82], the reason why these atoms must be available to form these interactions after the synthesis of fucose derivatives.

Table 3. Human f-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|---------------------------------------|-------------|-----------------------------------|---------------------------------|
| Coagulation factor V                  | F5          | Fucose [83]                        | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| APC, WNT signalling pathway regulator | APC         | Fucose [83]                        | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |

a) FDA-approved drug target. b) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases. c) Carbohydrate moieties recognized by this protein have not been discovered yet.

5. F-Box Lectins

F-box proteins are the substrate-recognition subunits of the SCF (Skp1-Cul1-F-box protein) complex. They have an F-box domain that binds to S-phase kinase-associated protein 1 (Skp1) [84]. The F-box proteins were divided into three different classes: Fbw5 are those that contains WD-40 domains, Fbls containing leucine-rich repeats, and Fbxs that have either different protein-protein interaction modules or no recognizable motifs [85]. Although F-box proteins are a superfamily of proteins, only five are known to recognize N-linked glycoproteins [84] as presented in Table 4.
### Table 4. Human F-box lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|---------------------------------|
| Cyclin F                             | CCNF        | N-acetylgalactosamine disaccharide chitobiose | Appendix, bone marrow, lung, lymph node, skin, spleen, tonsil |
| F-box protein 2                      | FBXO2       |                                   | Breast, ovary, pancreas         |
| F-box protein 3                      | FBXO3       |                                   |                                 |
| F-box protein 4                      | FBXO4       |                                   |                                 |
| F-box protein 5                      | FBXO5       |                                   | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| F-box protein 6                      | FBXO6       | High-mannose glycoproteins [87]   | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| F-box protein 7                      | FBXO7       |                                   | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| F-box protein 8                      | FBXO8       |                                   | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| F-box protein 9                      | FBXO9       |                                   |                                 |
| F-box protein 10                     | FBXO10      |                                   | Cervix (uterine), colon, duodenum, endometrium, fallopian tube, lung, prostate, rectum, seminal vesicle, small intestine, testis |
| F-box protein 11                     | FBXO11      |                                   |                                 |
| F-box protein 15                     | FBXO15      |                                   |                                 |
| F-box protein 16                     | FBXO16      |                                   | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| F-box protein 17                     | FBXO17      | Sulfated and galactose-terminated glycoproteins [88] |                                 |
| F-box protein, helicase, 18          | FBXO18      |                                   | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| LIM domain 7                        | LMO7        |                                   |                                 |
| F-box protein 21                     | FBXO21      |                                   |                                 |
| F-box protein 22                     | FBXO22      |                                   |                                 |
| Tetraspanin 17                      | TSPAN17     |                                   |                                 |
| F-box protein 24                     | FBXO24      |                                   |                                 |
| F-box protein 25                     | FBXO25      |                                   |                                 |
| F-box protein 27                     | FBXO27      |                                   |                                 |
| F-box protein 28                     | FBXO28      |                                   |                                 |
| F-box protein 30                     | FBXO30      |                                   |                                 |
| F-box protein 31                     | FBXO31      |                                   |                                 |
| F-box protein 32                     | FBXO32      |                                   |                                 |
| F-box protein 33                     | FBXO33      |                                   |                                 |
| F-box protein 34                     | FBXO34      |                                   |                                 |
| F-box protein 36                     | FBXO36      |                                   |                                 |
| F-box protein 38                     | FBXO38      |                                   |                                 |
| F-box protein 39                     | FBXO39      |                                   |                                 |
| F-box protein 40                     | FBXO40      |                                   |                                 |
| F-box protein 41                     | FBXO41      |                                   |                                 |
| F-box protein 42                     | FBXO42      |                                   | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |

Carbohydrate preferential affinity: 86: N-acetylgalactosamine disaccharide chitobiose; 87: High-mannose glycoproteins; 88: Sulfated and galactose-terminated glycoproteins.
Table 5. Human ficolins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|---------------------------------|
| Ficolin 1 (FCN1)                     |             | GlcNAc, GalNAc; sialic acid [89]   | a)                              |
| Ficolin 2 (FCN2)                     |             | GlcNAc (acetyl group); β-(1-3)-D-glucan [89] | a) |
| Ficolin 3 (FCN3)                     |             | N-acetylgalactose, fucose, lipopolysaccharides [89] | a) |

a) Carbohydrate moieties recognized by this protein have not been discovered yet. b) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases.

6. Ficolins

Ficolins play an important role in innate immunity by recognizing and binding to carbohydrates present on the surface of Gram-positive and Gram-negative bacteria [89]. There are three human ficolins and they are presented in Table 5.

7. I-Type Lectins

I-type lectins are a subset of the immunoglobulin superfamily that specifically recognizes sialic acids and other carbohydrate ligands. Most of the members of this group of lectins are siglecs, which are type I transmembrane proteins, and can be divided into two groups: the CD33-related group that includes CD33 (siglec3) siglecs5–11, and siglec14 while the other group includes siglec1, CD22 (siglec2), MAG (siglec4) and Siglec15 [90,91]. CD33-related groups possess between 1 and 4 C-set domains and feature cytoplasmic tyrosine-based motifs involved in signaling and endocytosis. Siglec1 possesses 16 C-set domains, CD22 has 6 C-set domains and MAG presents 4 C-set domains. MAG is the only siglec not found on cells of the immune system. Members of this I-type superfamily are presented in Table 6 along with their carbohydrate ligands and protein expression. An example of a drug delivery system was developed by Spence, Greene and co-workers who developed polymeric nanoparticles of poly(lactic-co-glycolic acid) decorated with sialic acid [92,93].
Table 6. Human I-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|----------------------------------|
| Siglec11 (Sialic acid binding Ig like lectin 1) | SIGLEC1 | α-(2-3)-Sialic acid, α-(2-6)-Sialic acid, α-(2-8)-Sialic acid [94] | Bone marrow, lung |
| Siglec2 (CD22 molecule) | CD22 | α-(2-6)-Sialic acid [95,96] | Appendix, lymph node, spleen, tonsil |
| Siglec3 (CD33 molecule) | CD33 | α-(2-6)-Sialic acid, α-(2-3)-Sialic acid | Appendix, bone marrow, lung, lymph node, skin, spleen, tonsil |
| Siglec4a, MAG (Myelin associated glycoprotein) | MAG | α-(2-3)-Sialic acid [98] | Brain |
| Siglec5 (Sialic acid binding Ig like lectin 5) | SIGLEC5 | α-(2-3)-Sialic acid, α-(2-6)-Sialic acid, α-(2-8)-Sialic acid [99] | Bone marrow, lymph node, placenta, spleen, tonsil |
| Siglec6 (Sialic acid binding Ig like lectin 6) | SIGLEC6 | α-(2-6)-N-acetylgalactosamine (Sialyl-Tn) [100] | Placenta |
| Siglec7 | SIGLEC7 | α-(2-3)-Sialic acid, α-(2-6)-Sialic acid, α-(2-8)-Sialic acid [101] and disialogangliosides [102-104] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Siglec8 | SIGLEC8 | α-(2-3)-Sialic acid, α-(2-6)-Sialic acid [105] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Siglec9 (Sialic acid binding Ig like lectin 9) | SIGLEC9 | α-(2-3)-Sialic acid, Sialyl Lewis x, α-(2-6)-Sialic acid, α-(2-8)-Sialic acid [106] | Appendix, bone marrow, lymph node, soft tissue, spleen, tonsil |
| Siglec10 (Sialic acid binding Ig like lectin 10) | SIGLEC10 | α-(2-3)-Sialic acid, α-(2-6)-Sialic acid [107] | Appendix, bone marrow, lung, lymph node, spleen, tonsil |
| Siglec11 (Sialic acid binding Ig like lectin 11) | SIGLEC11 | α-(2-8)-Sialic acid [101] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Siglec14 (Sialic acid binding Ig like lectin 14) | SIGLEC14 | Sialic acid-α-(2-6)-N-acetylgalactosamine (Sialyl-Tn), N-acetylnexaminic acid [108] | Appendix, bone marrow, brain, endometrium, fallopian tube, kidney, lung, lymph node, spleen, testis, tonsil |
| Siglec15 (Sialic acid binding Ig like lectin 15) | SIGLEC15 | Sialyl-Tn [109] | Appendix, lymph node, spleen, tonsil |
| CD2 molecule | CD2 | N-glycans with fucose [110] | Appendix, bone marrow, lung, lymph node, spleen, tonsil |
| CD83 molecule | CD83 | Sialic acid [111] | Appendix, bone marrow, brain, endometrium, fallopian tube, kidney, lung, lymph node, spleen, testis, tonsil |
| Intercellular adhesion molecule 1 | ICAM1 | Hyaluronan [112] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, proximal digestive tract, skin |
| L1 cell adhesion molecule | L1CAM | α-(2-3)-Sialic acid [113] | Bronchus, esophagus, fallopian tube, small intestine, soft tissue, stomach, testis |
| Myelin protein zero | MPZ | SOc-3GlucA-β-(1-3)-Gal-β-(1-4)-GlcNac (HNK-1 antigen) [101] | Brain, colon, heart muscle, pancreas, smooth muscle, soft tissue, thyroid gland |
| Neural cell adhesion molecule 1 | NCAM1 | High N-linked d-mannose [114] | Brain, bronchus, colon, duodenum, gallbladder, ovary, rectum, small intestine, soft tissue, testis |
| Neural cell adhesion molecule 2 | NCAM2 | | |

a) FDA-approved drug target. b) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases. c) Carbohydrate moieties recognized by this protein have not been discovered yet.

8. L-Type Lectins

L-type lectins are distinguished from other lectins on the basis of tertiary structure, not the primary sequence, and are composed of antiparallel β-sheets connected by short loops and β-bends, usually lacking any α-helices [115]. Members of this family of lectins present different glycan-binding specificities as presented in Table 7. L-type superfamily
includes Pentraxins [116,117] that require Ca\(^{2+}\) ions for ligand binding. Both LMAN1 and LMAN2 also require Ca\(^{2+}\) ions for their binding activity [115].

Table 7. Human L-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|---------------------------------|
| Calnexin                             | CANX        | Non-reducing glucose residues in an oligosaccharide (Glc(Man)(GlcNAc)\(_2\)) [118] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Calreticulin                         | CALR        | Non-reducing glucose residues in an oligosaccharide (Glc(Man)(GlcNAc)\(_2\)) [119] | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas |
| Calreticulin 3                       | CALR3       | \(\alpha\)-(1-2) mannans with free OH-3, OH-4 and OH-6 [120] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Lectin, mannos-binding 1             | LMAN1       | High \(\alpha\)-(1-2) mannans, Low affinity for D-glucose and N-acetylglucosamine [121] | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, pancreas |
| Lectin, mannos-binding 1 like        | LMANIL      | \(\alpha\)-(1-2) trimannose [122] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Lectin, mannos-binding 2             | LMAN2       | \(\alpha\)-(1-2) trimannose [122] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Adhesion G protein-coupled receptor D1| ADGRD1      | Heparin, dextran sulfate proteoglycans [123] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Adhesion G protein-coupled receptor D2| ADGRD2      | Gal-\(\alpha\)-(1-4)-GalNAc, other phosphate-containing ligands [124,125] | Liver, gallbladder, soft tissue |
| Amyloid P component, serum           | APCS        | Galactose 6-phosphate, Gal-\(\beta\)-(1-3)-GalNAc, Gal-\(\beta\)-(1-4)-Gal-\(\beta\)-(1-4)-GalNAc, Gal-\(\beta\)-(1-3)-GalNAc, Gal-\(\beta\)-(1-4)-GalNAc, other phosphate-containing ligands [124,125] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| C-reactive protein                   | CRP         | Gal-\(\beta\)-(1-4)-GalNAc, Gal-\(\beta\)-(1-3)-GalNAc, other phosphate-containing ligands [124,125] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |

\(\alpha\) Carbohydrate moieties recognized by this protein have not been discovered yet. \(\beta\) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases.

9. M-Type Lectins

M-type family of lectins consists of \(\alpha\)-mannosidases, which are proteins involved in both the maturation and the degradation of Asn-linked oligosaccharides [127]. Members of this family, their binding affinities and protein expression are presented in Table 8.
Table 8. Human M-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name                                      | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs                                                                 |
|--------------------------------------------------|-------------|-----------------------------------|--------------------------------------------------------------------------------------------------|
| Mannosidase alpha class 1A member 1              | MAN1A1      | α-(1-2)-mannans [128,129]         | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Mannosidase alpha class 1A member 2              | MAN1A2      | α-(1-2)-mannans [128,129]         | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Mannosidase alpha class 1B member 1              | MAN1B1      | α-(1-2)-mannans [128,129]         | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Mannosidase alpha class 1C member 1              | MAN1C1      | α-(1-2)-mannans [128,129]         | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |

10. P-Type Lectins

P-type lectins constitute a two-member family of mannose-6-phosphate receptors (Table 9) that play an essential role in the generation of functional lysosomes. The phosphate group is key to high-affinity ligand recognition by these proteins. Furthermore, optimal ligand-binding ability of M6PR is achieved in the presence of divalent cations, particularly Mn$^{2+}$ cation [130,131].

Table 9. Human P-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name                                      | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs                                                                 |
|--------------------------------------------------|-------------|-----------------------------------|--------------------------------------------------------------------------------------------------|
| Mannose-6-phosphate receptor, cation dependent a) | M6PR        | Mannose-6-phosphate residues [132,133] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Insulin-like growth factor 2 receptor b)         | IGF2R       | Mannose-6-phosphate residues [132,133] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |

a) FDA-approved drug target. b) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards[18] databases.

11. R-Type Lectins

R-type lectins are protein-UDP acetylgalactosaminyltransferases that contain an R-type carbohydrate recognition domain, which is conserved between animal and bacterial lectins[135]. Members of this superfamily recognize Gal/GalNAc residues and are expressed in several tissues as presented in Table 10.

Table 10. Human R-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name                                      | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs                                                                 |
|--------------------------------------------------|-------------|-----------------------------------|--------------------------------------------------------------------------------------------------|
| Polypeptide N-acetylgalactosaminyltransferase 1   | GALNT1      | GalNAc [136]                      | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 2   | GALNT2      | GalNAc [136,137]                 | Bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 3   | GALNT3      | GalNAc [136]                      | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, muscle tissues, pancreas, proximal digestive tract, skin |

Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, male tissues, muscle tissues, pancreas, proximal digestive tract, skin
| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|----------------------------------|
| Polypeptide N-acetylgalactosaminyltransferase 4 | GALNT4 | GalNAc, GalNAc-glycosylated substrates [136,138] | gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 5 | GALNT5 | GalNAc [136] | Appendix, bronchus, cervix (uterine), colon, duodenum, esophagus, gallbladder, lung, oral mucosa, rectum, salivary gland, small intestine, stomach, tonsil, vagina |
| Polypeptide N-acetylgalactosaminyltransferase 6 | GALNT6 | GalNAc [136] | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 7 | GALNT7 | GalNAc, GalNAc-glycosylated substrates [100] | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 8 | GALNT8 | GalNAc [139] | Bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 9 | GALNT9 | GalNAc [140] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 10 | GALNT10 | GalNAc [141] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 11 | GALNT11 | GalNAc [142] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 12 | GALNT12 | GalNAc [143] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 13 | GALNT13 | GalNAc [144] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 14 | GALNT14 | GalNAc [145] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 15 | GALNT15 | GalNAc [146] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 16 | GALNT16 | GalNAc [147] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 17 | GALNT17 | GalNAc [148] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase 18 | GALNT18 | GalNAc [149] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Polypeptide N-acetylgalactosaminyltransferase like 5 | GALNTL5 | o [150] | Testis |

a) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases. 
b) FDA-approved drug target. c) Carbohydrate moieties recognized by this protein have not been discovered yet.

### 12. S-Type Lectins

S-type lectins are known nowadays as galectins and are a superfamily of proteins that show a high affinity for β-galactoside sugars (Table 11). Formerly called S-type lectins because of their sulphhydryl dependency, galectins are the most widely expressed
class of lectins in all organisms. Human galectins have been classified into three major
groups according to their structure: prototypical, chimeric and tandem-repeat [151–153].

Galectins play important roles in immune responses and promoting inflammation. They are also known for having a crucial role in cancer-causing tumor invasion, progression, metastasis and angiogenesis [154–156].

Table 11. Human S-type lectins, their carbohydrate ligands and protein expression in the organs.

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|-----------------------------------|---------------------------------|
| Galectin 1                           | LGALS1      | β-δ-galactosides, poly-N-acetyllactosamine-enriched glycoconjugates [157,158] | Bone marrow, brain, cervix (uterine), endometrium, lymph node, ovary, parathyroid gland, placenta, smooth muscle, skin, spleen, testis, tonsil, vagina Appendix, colon, duodenum, gallbladder, kidney, liver, lymph node, pancreas, rectum, small intestine, spleen, tonsil |
| Galectin 2                           | LGALS2      | β-δ-galactosides, lactose [159]    |                                  |
| Galectin 3                           | LGALS3      | β-δ-galactosides, LacNAc [160]     | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract |
| Galectin 3 binding protein           | LGALS3BP    | β-δ-galactosides, lactose [161]    | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, proximal digestive tract, skin |
| Galectin 4                           | LGALS4      | β-δ-galactosides, lactose [162]    | Appendix, colon, duodenum, gallbladder, pancreas, rectum, small intestine, stomach |
| Galectin 7                           | LGALS7      | Gal, GalNAc, Lac, LacNAc [163]     | Cervix (uterine), esophagus, oral mucosa, salivary gland, skin, tonsil, vagina |
| Galectin 8                           | LGALS8      | β-δ-galactosides. Preferentially binds to 3′-O-sialylated and 3′-O-sulfated glycans [164] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Galectin 9                           | LGALS9      | β-δ-galactosides. Forsmann pentasaccharide, lactose, N-acetyllactosamine [165] | Adipose and soft tissue, bone marrow and lymphoid tissues, brain, endocrine tissues, female tissues, gastrointestinal tract, kidney and urinary bladder, lung, male tissues, muscle tissues, pancreas, proximal digestive tract, skin |
| Galectin 9B                          | LGALS9B     | β-δ-galactosides [166]             | Appendix, bone marrow, breast, lymph node, spleen, tonsil |
| Galectin 9C                          | LGALS9C     | β-δ-galactosides [166]             | Appendix, bronchus, colon, duodenum, gallbladder, lung, pancreas, spleen, stomach, tonsil |
| Galectin 10                          | LGALS10     | Binds weakly to lactose, N-acetyl-δ-glucosamine and δ-mannose [167] | Lymph node, spleen, tonsil |
| Galectin 12                          | LGALS12     | β-δ-galacto and lactose [168,169]  |                                  |
| Galectin 13                          | LGALS13     | N-acetyllactosamine, mannose and N-acetyllactosamine [170]. Contrary to other galectins, Galectin 13 does not bind β-δ-galactosides [171] | Kidney, placenta, spleen, urinary bladder |
| Placental Protein 13 (Galectin 14)   | LGALS14     | N-acetyllactosamine [172]         | Adrenal gland, colon, kidney |
| Galectin 16                          | LGALS16     | N-acetyllactosamine, β-δ-galacto and lactose [172] | Placenta |

a) Only RNA expression data available in The Human Protein Atlas [16,17] and GeneCards [18] databases.
13. X-Type Lectins

Intelectins (Table 12) were classified as X-type lectins because they do not have a typical lectin domain, instead, they contain a fibrinogen-like domain and a unique intelectin-specific region [173].

| Common Name (HUGO Name if Different) | Gene Symbol | Carbohydrate Preferential Affinity | Protein Expression in the Organs |
|--------------------------------------|-------------|----------------------------------|---------------------------------|
| Intelectin 1 (ITLN1)                 |             | Terminal acyclic 1,2-diol-containing structures, including β-d-galactofuranose, d-phosph glycerol-modified glycans, d-glycero-d-talo-oct-2-ulosonic acid, 3-deoxy-d-manno-oct-2-ulosonic acid [174] | Appendix, colon, duodenum, rectum, small intestine |
| Intelectin 2 (ITLN2)                 |             |                                  | Appendix, colon, duodenum, rectum, small intestine |

* Carbohydrate moieties recognized by this protein have not been discovered yet.

14. Orphans

Orphan lectins are those that do not belong to known lectin structural families [175]. Proteins that bind to sulfated glycosaminoglycans are usually not considered as lectins [101], however, the specific binding of these proteins to sulfated glycosaminoglycans can provide a valuable tool to develop targeted drug delivery systems. Glycosaminoglycan binding interactions with proteins were described in detail by Vallet, Clerc and Ricard-Blum [176] which information is outside of the scope of this review.

**Author Contributions:** conceptualization, C.D.R.; methodology, C.D.R. and A.B.C.; resources, M.T.B.; writing—original draft preparation, C.D.R.; writing—review and editing, A.B.C. and M.T.B.; visualization, C.D.R.; supervision, M.T.B.; funding acquisition, M.T.B. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was funded by Fundação para a Ciência e a Tecnologia, grant number PD/BD/109680/2015. This work was also supported by the Associate Laboratory for Green Chemistry, LAQV, which is financed by national funds from FCT/MEC (UID/QUI/50006/2013 and UID/QUI/50006/2019) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265).

**Acknowledgments:** The authors acknowledge Christopher D. Maycock for having reviewed this manuscript.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. Lepenies, B.; Lang, R. Lectins and Their Ligands in Shaping Immune Responses. *Front. Immunol.* 2019, 10, 2379.
2. Stick, R. *Carbohydrates: The Sweet Molecules of Life*, 1st ed.; Academic Press: New York, NY, USA, 2001.
3. Santos, A.F.S.; Da Silva, M.D.C.; Napoleão, T.H.; Paiva, P.M.G.; Correia, M.T.S.; Coelho, L.C.B.B. Lectins: Function, structure, biological properties and potential applications. *Curr. Top. Pept. Protein Res.* 2014, 15, 41–62.
4. Wang, B.; Boons, G.-J. Carbohydrate Recognition: Biological Problems, Methods and Applications, 1st ed.; John Wiley & Sons, Inc.: Danvers, MA, USA, 2011; ISBN 9780470892076.
5. Hirabayashi, J.; Kasai, K.J. Evolution of Animal Lectins. In *Molecular Evolution: Evidence for Monophyly of Metazoa*; Jeanteur, P., Kuchino, Y., Muller, W.E.G., Paine, P.L., Eds.; Springer: Berlin, Germany, 1998; Volume 19, ISBN 9783642487477.
6. Drickamer, K. Evolution of Ca2+-dependent Animal Lectins. *Prog. Nucleic Acid Res. Mol. Biol.* 1993, 45, 207–232.
7. Himri, I.; Guadaaoui, A. Cell and organ drug targeting: Types of drug delivery systems and advanced targeting strategies. In *Nanostructures for the Engineering of Cells, Tissues and Organs*; Grumezescu, A., Ed.; Elsevier Inc.: Norwich, UK, 2018; pp. 1–66, ISBN 9780128136652.
8. Liu, K.; Jiang, X.; Hunziker, P. Carbohydrate-based amphiphilic nano delivery systems for cancer therapy. *Nanoscale* 2016, 8, 16091–16156.
9. Zhang, X.; Huang, G.; Huang, H. The glyconanoparticle as carrier for drug delivery. *Drug Deliv.* 2018, 25, 1840–1845.
10. Mosiab, T.; Farr, D.C.; Kiefel, M.J.; Houston, T.A. Carbohydrate-based nanocarriers and their application to target macrophages and deliver antimicrobial agents. *Adv. Drug Deliv. Rev.* **2019**, *151–152*, 94–129.
11. Hossain, F.; Andreana, P.R. Developments in Carbohydrate-Based Cancer Therapeutics. *Pharmaceuticals* **2019**, *12*, 1–18.
12. Keshavarz-fathi, M.; Rezaei, N. Vaccines, Adjuvants, and Delivery Systems. In *Vaccines for Cancer Immunotherapy*; Keshavarz-Fathi, M., Rezaei, N., Eds.; Academic Press: Cambridge, MA, USA, 2019; pp. 45–59, ISBN 9780128140390.
13. Warburg, O. On the origin of cancer cells. *Science* **1956**, *123*, 309–314.
14. Chiaradonna, F.; Moresco, R.M.; Airoldi, C.; Gagliò, D.; Palorini, R.; Nicotra, F.; Messa, C.; Alberghina, L. From cancer metabolism to new biomarkers and drug targets. *Biotechnol. Adv.* **2012**, *30*, 30–51.
15. Wesener, D.A.; Wangkanont, K.; McBride, R.; Song, X.; Kraft, M.B.; Hodges, H.L.; Zarling, L.C.; Splain, R.A.; Smith, D.F.; Cummings, R.D.; et al. Recognition of Microbial Glycans by Human Intelectin. *Nat. Struct. Mol. Biol.* **2015**, *22*, 603–610.
16. Knut & Alice Wallenberg Foundation. The Human Protein Atlas. Available online: https://www.proteinatlas.org/ (accessed on 5 September 2020).
17. Uhlén, M.; Fagerberg, L.; Hallström, B.M.; Lindskog, C.; Oksvold, P.; Sivertsson, Å.; Jörnvall, H.; Tammi, M.; et al. Tissue-based map of the human proteome. *Science* **2015**, *347*, 394–403.
18. *Gene Trees, Version: 3.12.404*; Weizmann Institute of Science: Rehovot, Israel, 2015.
19. Furukawa, A.; Kamishikiro, J.; Morí, D.; Toyonaga, K.; Okabe, Y.; Toji, A.; Kanda, R.; Miyake, Y.; Ose, T.; Yamashiki, S.; et al. Structural analysis for glycolipid recognition by the C-type lectins Mincle and MCL. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 17438–17443.
20. Feinberg, H.; Park-snyder, S.; Kolakar, A.R.; Heise, C.T.; Taylor, M.E.; Weiss, W.I. Structure of a C-type Carbohydrate Recognition Domain from the Macrophage Mannose Receptor. *J. Biol. Chem.* **2000**, *275*, 21539–21548.
21. Ryan, E.J.; Marshall, A.J.; Magaletti, D.; Floyd, H.; Draves, K.E.; Olson, N.E.; Clark, E.A. Dendritic Cell-Associated Lectin-1: A Novel Dendritic Cell-Associated, C-Type Lectin-Like Molecule Enhances T Cell Secretion of IL-4. *J. Immunol.* **2002**, *169*, 5638–5648.
22. Cummings, R.D.; McEver, R.P. C-Type Lectins. In *Essentials of Glycobiology*; Varki, A., Cummings, R.D., Esko, J.D., Freeze, H.H., Stanley, P., Bertozzi, C.R., Gerald, H.W., Etzler, M.E., Eds.; Cold Spring Harbor Laboratory Press: New York, NY, USA, 2017.
23. Feinberg, H.; Park-snyder, S.; Kolakar, A.R.; Heise, C.T.; Taylor, M.E.; Weiss, W.I. String reconstruction of glycolipid recognition by the Ctype lectin domain family 4, member C (CLEC4C/BDCA2). *J. Cell Biol.* **2016**, *205*, 695, ISBN 9780128140390.
24. Imperial College Human CTLD Database. Available online: https://www.imperial.ac.uk/research/animallectins/cctl/mammals/humandata updated.html (accessed on 24 December 2020).
25. Olin, A.I.; Mörgelin, M.; Sasaki, T.; Timpl, R.; Heinegård, D.; Aspberg, A. The proteoglycans aggrecan and versican form networks with fibulin-2 through their lectin domain binding. *J. Biol. Chem.* **2001**, *276*, 1253–1261.
26. Jaworski, D.M.; Kelly, G.M.; Hockfield, S. BEHAB, a New Member of the Proteoglycan Tandem Repeat Family of Hyaluronan-binding Proteins That Is Restricted to the Brain. *J. Cell Biol.* **1994**, *125*, 495–509.
27. Yamaguchi, Y.; Brevcik, A. Major proteoglycan in adult brain. *Perspect Dev. Neurobiol.* **1996**, *3*, 307–317.
28. Rauch, U.; Gao, P.; Janetzko, A.; Flaccus, A.; Hilgenberg, L.; Tekotte, H.; Margolis, R.K.; Margolis, R.U. Isolation and characterization of developmentally regulated chondroitin sulfate and chondroitin/keratan sulfate proteoglycans of brain identified with monoclonal antibodies. *J. Biol. Chem.* **1991**, *266*, 14785–14801.
29. LeBaron, R.G.; Zimmermann, D.R.; Ruoslahti, E. Hyaluronate binding properties of versican. *J. Biol. Chem.* **1992**, *267*, 10003–10010.
30. Riboldi, E.; Daniele, R.; Parola, C.; Infuzorio, A.; Arnold, P.L.; Bosisio, D.; Fremont, D.H.; Bastone, A.; Colonna, M.; Sozzani, S. Human C-type lectin domain family 4, member C (CLEC4C/BDCA2-CD303) is a receptor for asialogalactosyl-oligosaccharides. *J. Biol. Chem.* **2011**, *286*, 35329–35333.
31. Jégouzo, S.A.F.; Feinberg, H.; Dungarwalla, T.; Drickamer, K.; Weiss, W.I.; Taylor, M.E. A novel mechanism for binding of galactose-terminated glycans by the C-type carbohydrate recognition domain in blood dendritic cell antigen 2. *J. Biol. Chem.* **2015**, *290*, 16759–16771.
32. Geurtsen, J.; Driessen, N.N.; Appelmelk, B.J. Mannose–fucose recognition by DC-SIGN. In *Microbial Glycobiology*; Elsevier Inc.: Amsterdam, The Netherlands, 2010; pp. 673–695, ISBN 978-0-12-374546-0.
33. Feinberg, H.; Jégouzo, S.A.F.; Rex, M.J.; Drickamer, K.; Weiss, W.I.; Taylor, M.E. Mechanism of pathogen recognition by human dectin-2. *J. Biol. Chem.* **2017**, *292*, 13402–13414.
34. Lord, A.K.; Vyas, J.M. Host Defenses to Fungal Pathogens. In *Clinical Immunology*; Elsevier Ltd.: Amsterdam, The Netherlands, 2019; pp. 413–424.e1, ISBN 9780702068966.
35. Nagae, M.; Ikeda, A.; Hanashima, S.; Kojima, T.; Matsumoto, N.; Yamamoto, K.; Yamaguchi, Y. Crystal structure of human dendritic cell inhibitory receptor C-type lectin domain reveals the binding mode with N-glycan. *FEBS Lett.* **2016**, *590*, 1280–1288.
36. Sun, P.D. Human CD23: Is It a Lectin in Disguise? *Structure* **2006**, *14*, 950–951.
37. Kijimoto-Ochiai, S.; Toshimitsu, U. CD23 molecule acts as a galactose-binding lectin in the cell aggregation of EBV-transformed human B-cell lines. *Glycobiology* **1995**, *5*, 443–448.
38. Meier, M.; Bider, M.D.; Malashkevich, V.N.; Spiess, M.; Burkhard, P. Crystal structure of the carbohydrate recognition domain of the H1 subunit of the asialoglycoprotein receptor. *J. Mol. Biol.* **2000**, *300*, 857–865.
39. Yang, C.Y.; Chen, J.B.; Tsai, T.F.; Tsai, Y.C.; Tsai, C.Y.; Liang, P.H.; Hsu, T.L.; Wu, C.Y.; Netea, M.G.; Wong, C.H.; et al. CLEC4F Is an Inducible C-Type Lectin in F4/80-Positive Cells and Is Involved in Alpha-Galactosylceramide Presentation in Liver. *PLoS ONE* **2013**, *8*, e65070.
40. Stambach, N.S.; Taylor, M.E. Characterization of carbohydrate recognition by langerin, a C-type lectin of Langerhans cell. Glycobiochemistry 2003, 13, 401–410.

41. Liu, W.; Tang, L.; Zhang, G.; Wei, H.; Cui, Y.; Guo, L.; Gou, Z.; Chen, X.; Jiang, D.; Zhu, Y.; et al. Characterization of a novel C-type lectin-like gene, LSECtin: Demonstration of carbohydrate binding and expression in sinusoidal endothelial cells of liver and lymph node. J. Biol. Chem. 2004, 279, 18748–18758.

42. Nollau, P.; Wolters-Eisfeld, G.; Mortezaei, N.; Kurze, A.K.; Klampe, B.; Debus, A.; Bockhorn, M.; Niendorf, A.; Wagener, C. Protein Domain Histochemistry (PDH): Binding of the Carbohydrate Recognition Domain (CRD) of Recombinant Human Glyco receptor CLEC10A (CD301) to Formalin-Fixed, Paraffin-Embedded Breast Cancer Tissues. J. Histochem. Cytochem. 2013, 61, 199–205.

43. Richardson, M.B.; Williams, S.J. MCL and Mincle: C-type lectin receptors that sense damaged self and pathogen-associated molecular patterns. Front. Immunol. 2014, 5, 1–9.

44. Venkatraman Girija, U.; Furze, C.M.; Gingeras, A.R.; Yoshizaki, T.; Ohtani, K.; Marshall, J.E.; Walls, A.K.; Schwaeble, W.J.; El-Mezgueldi, M.; Mitchell, D.A.; et al. Molecular basis of sugar recognition by collectin-K1 and the effects of mutations associated with 3MC syndrome. BMC Biol. 2015, 13, 1–14.

45. Ohtani, K.; Suzuki, Y.; Eda, S.; Kawai, T.; Kase, T.; Yamazaki, H.; Shimada, T.; Keshi, H.; Sakai, Y.; Fukuhou, A.; et al. Molecular cloning of a novel human collectin from liver (CL-L1). J. Biol. Chem. 1999, 274, 13681–13689.

46. Muto, S.; Sakuma, K.; Taniguchi, A.; Matsumoto, K. Human mannose-binding lectin preferentially binds to human colon adenocarcinoma cell lines expressing high amount of Lewis A and Lewis B antigens. Biol. Pharm. Bull. 1999, 22, 347–352.

47. Wright, J.R. Immunoregulatory functions of surfactant proteins. Nat. Rev. Immunol. 2005, 5, 58–68.

48. Coombs, P.J.; Graham, S.A.; Drickamer, K.; Taylor, M.E. Selective binding of the scavenger receptor C-type lectin to Lewis x trisaccharide and related glycan ligands. J. Biol. Chem. 2008, 283, 22993–22999.

49. Erbe, D.V.; Watson, S.R.; Presta, L.G.; Wolitzky, B.A.; Foxall, C.; Brandley, B.K.; Lasky, L.A. P- and E-selectin use common sites for carbohydrate ligand recognition and cell adhesion. J. Cell Biol. 1993, 120, 1227–1236.

50. Ivetic, A.; Green, H.L.H.; Hart, S.J. L-selectin: A major regulator of leukocyte adhesion, migration and signaling. Front. Immunol. 2019, 10, 1–22.

51. Sung, P.S.; Hsieh, S.L. CLEC2 and CLEC5A: Pathogenic Host Factors in Acute Viral Infections. Front. Immunol. 2019, 10, 1–9.

52. Binsack, R.; Pecht, I. The mast cell function-associated antigen exhibits saccharide binding capacity. Eur. J. Immunol. 1997, 27, 2557–2561.

53. Wong, S.; Arsequell, G. Immunobiology of Carbohydrates; Wong, S., Arsequell, G., Eds.; Springer: New York, NY, USA, 2003.

54. Roda-Navarro, P.; Arce, I.; Renedo, M.; Montgomery, K.; Kucherlapati, R.; Fernández-Ruiz, E. Human KLRF1, a novel member of the killer cell lectin-like receptor gene family: Molecular characterization, genomic structure, physical mapping to the NK gene complex and expression analysis. Eur. J. Immunol. 2000, 30, 568–576.

55. Ohki, I.; Ishigaki, T.; Oyama, T.; Matsunaga, S.; Xie, Q.; Ohnishi-Kameyama, M.; Murata, T.; Tsuchiya, D.; Machida, S.; Morikawa, K.; et al. Crystal structure of human lectin-like, oxidized low-density lipoprotein receptor 1 ligand binding domain and its ligand recognition mode to OXLDL. Structure 2005, 13, 905–917.

56. Higai, K.; Imaiizu, Y.; Suzuki, C.; Azuma, Y.; Matsumoto, K. NKG2D and CD94 bind to heparin and sulfate-containing polysaccharides. Biochem. Biophys. Res. Commun. 2009, 386, 709–714.

57. Chiffoleau, E. C-type lectin-like receptors as emerging orchestrators of sterile inflammation represent potential therapeutic targets. Front. Immunol. 2018, 9, 1–9.

58. Watson, A.A.; Brown, J.; Harlos, K.; Eble, J.A.; Walter, T.S.; O’Callaghan, C.A. The crystal structure and mutational binding analysis of the extracellular domain of the platelet-activating receptor CLEC-2. J. Biol. Chem. 2007, 282, 3165–3172.

59. Zhang, J.G.; Czabotar, P.E.; Policheni, A.N.; Caminschi, I.; San Wan, S.; Kitsoulis, S.; Tulliet, K.M.; Robin, A.Y.; Brammananth, R.; van Delft, M.F.; et al. The Dendritic Cell Receptor Clec9A Binds Damaged Cells via Exposed Actin Filaments. Immunity 2012, 36, 646–657.

60. Schorey, J.; Lawrence, C. The Pattern Recognition Receptor Dectin-1: From Fungi to Mycobacteria. Curr. Drug Targets 2008, 9, 123–129.

61. Gange, C.T.; Quinn, J.M.W.; Zhou, H.; Kartsogiannis, V.; Gillespie, M.T.; Ng, K.W. Characterization of sugar binding by osteoclast inhibitory lectin. J. Biol. Chem. 2004, 279, 29043–29049.

62. Christiansen, D.; Moultouris, E.; Milland, J.; Zingoni, A.; Santoni, A.; Sandrin, M.S. Recognition of a carbohydrate xenoepitope by human NKRPIA (CD161). Xenotransplantation 2006, 13, 440–446.

63. Kogelberg, H.; Frenkidi, T.A.; Birdsal, B.; Chai, W.; Muskett, F.W. Binding of Sucrose Octasulphate to the C-Type Lectin-Like Domain of the Recombinant Natural Killer Cell Receptor NKRPIA Observed by NMR Spectroscopy. ChemBioChem 2002, 3, 1072–1077.

64. Imaizumi, Y.; Higai, K.; Suzuki, C.; Azuma, Y.; Matsumoto, K. NKG2D and CD94 bind to multimeric α2,3-linked N-acetylgalactosaminic acid. Biochem. Biophys. Res. Commun. 2009, 382, 604–608.

65. East, L.; Rushston, S.; Taylor, M.E.; Isacke, C.M. Characterization of sugar binding by the mannose receptor family member, Endo180. J. Biol. Chem. 2002, 277, 50469–50475.

66. Taylor, M.E.; Bezouska, K.; Drickamer, K. Contribution to ligand binding by multiple carbohydrate-recognition domains in the macrophage mannose receptor. J. Biol. Chem. 1992, 267, 1719–1726.
67. Chen, Z.; Downing, S.; Tzanakakis, E.S. Four Decades After the Discovery of Regenerating Islet-Derived (Reg) Proteins: Current Understanding and Challenges. Front. Cell Dev. Biol. 2019, 7, 1–16.
68. Weng, L.; Smits, P.; Wauters, J.; Merregaert, J. Molecular cloning and characterization of human chondrolectin, a novel type I transmembrane protein homologous to C-type lectins. Genomics 2002, 80, 62–70.
69. Bono, P.; Rubin, K.; Higgins, J.M.G.; Hynes, R.O. Layilin, a novel integral membrane protein, is a hyaluronan receptor. Mol. Biol. Cell 2001, 12, 891–900.
70. Neame, P.J.; Tapp, H.; Grimm, D.R. The cartilage-derived, C-type lectin (CLECSF1): Structure of the gene and chromosomal location. Biochim. Biophys. Acta Gene Struct. Expr. 1999, 1446, 193–202.
71. Pletnev, V.; Huether, R.; Habeberger, L.; Habeberger, L.; Schultz, W.; Duax, W. Rational proteomics of PKD1. I. Modeling the three dimensional structure and ligand specificity of the C3c,1 binding domain of Polycystin-1. J. Mol. Model. 2007, 13, 891–896.
72. Lo, T.-H; Silveira, P.A.; Fromm, P.D.; Verma, N.D.; Vu, P.A.; Kupresanin, F.; Adam, R.; Kato, M.; Cogger, V.C.; Clark, G.J.; et al. Characterization of the Expression and Function of the C-Type Lectin Receptor CD302 in Mice and Humans Reveals a Role in Dendritic Cell Migration. J. Immunol. 2016, 197, 885–898.
73. Swaminathan, G.J.; Myszka, D.G.; Katsamba, P.S.; Ohnuki, L.E.; Gleich, G.J.; Acharya, K.R. Eosinophil-granule major basic protein, a C-type lectin, binds heparin. Biochim. Biophys. Acta 2005, 14412–14158.
74. Huang, Y.L.; Pai, F.S.; Tsou, Y.T.; Mon, H.C.; Hsu, T.L.; Wu, C.Y.; Chou, T.Y.; Yang, W. Bin; Chen, C.H.; Wong, C.H.; et al. Human CLEC18 gene cluster contains C-type lectins with differential glycan-binding specificity. J. Biol. Chem. 2015, 290, 21252–21263.
75. Graham, S.A.; Jégouzo, S.A.F.; Yan, S.; Powlson, J.C.; Brady, J.P.; Taylor, M.E.; Drickamer, K. Prolectin, a glycan-binding receptor on dividing B cells in germinal centers. J. Biol. Chem. 2009, 284, 18537–18544.
76. Zaheer-ul-Haq; Dalal, P.; Aronson, N.N., Jr; Madura, J.D. Family 18 Chitotectins: Comparison of MGP40 and HUMGP39. Biochem. Biophys. Res. Commun 2007, 359, 221–226.
77. Kilpatrick, D.C. Animal lectins: A historical introduction and overview. Biochim. Biophys. Acta 2002, 1572, 187–197.
78. Renkema, G.H.; Boot, R.G.; Au, F.L.; Donker-koopman, W.E.; Strijland, A.; Muijser, A.O.; Heebiek, M.; Aerts, J.M.F.G. Chitotriosidase as a chitinase, and the 39-kDa human cartilage glycoprotein, a chitin-binding lectin, are homologues of family 18 glycosyl hydrolases secreted by human macrophages. Eur. J. Biochem. 1998, 251, 504–509.
79. Boot, R.G.; Blommaart, E.F.C.; Swart, E.; Ghoumsari-van der Vlugt, K.; Bijl, N.; Moe, C.; Place, A.; Aerts, J.M.F.G. Identification of a Novel Acidic Mammalian Chitinase Distinct from Chitotriosidase. J. Biol. Chem. 2001, 276, 6770–6778.
80. Fusetti, F.; Pijning, T.; Kalk, K.H.; Bos, E.; Dijkstra, B.W. Crystal structure and carbohydrate-binding properties of the human cartilage glycoprotein-39. J. Biol. Chem. 2003, 278, 37753–37760.
81. Schimml, M.; Rush, C.L.; Betou, M.; Eggleston, L.M.; Recklies, A.D.; Aalten, D.M.F. V. Human YKL-39 is a pseudo-chitinase with retained chitooligosaccharide-binding properties. Biochem. J. 2012, 446, 149–157.
82. Malette, B.; Paquette, Y.; Merlen, Y.; Bleau, G. Oviductins possess chitinase- and mucin-like domains: A lead in the search for the biological function of these oviduct-specific ZP-associating glycoproteins. Mol. Reprod. Dev. 1995, 41, 384–397.
83. Aronson, N.N.; Kuranda, M.J. Lysosomal degradation of Asn-linked glycoproteins. FASEB J. 1989, 3, 2615–2622.
84. Meng, G.; Zhao, Y.; Bai, X.; Liu, Y.; Green, T.J.; Luo, M.; Zheng, X. Structure of human Stabilin-1 Interacting Chitinase-Like Protein (SI-CLP) reveals a saccharide-binding cleft with lower sugar-binding selectivity. J. Biol. Chem. 2010, 285, 39898–39904.
85. Bianchet, M.A.; Odem, E.W.; Vasta, G.R.; Amzel, L.M. A novel fucose recognition fold involved in innate immunity. Nat. Struct. Biol. 2002, 9, 628–634.
86. Vasta, G.R.; Mario Amzel, L.; Bianchet, M.A.; Cammarata, M.; Feng, C.; Saito, K. F-Type Lectins: A highly diversified family of fucoside-binding proteins with a unique sequence motif and structural fold, involved in self/non-self-recognition. Front. Immunol. 2017, 8, 1648.
87. Yoshida, Y. F-box proteins that contain sugar-binding domains. Biosci. Biotechnol. Biochem. 2007, 71, 2623–2631.
88. Cenciarelli, C.; Chiaur, D.S.; Guardavaccaro, D.; Parks, W.; Vidal, M.; Pagano, M. Identification of a family of human F-box proteins. Curr. Biol. 1999, 9, 1177–1179.
89. Mizushima, T.; Hiro, T.; Yoshida, Y.; Lee, S.J.; Chiba, T.; Iwai, K.; Yamaguchi, Y.; Kato, K.; Tsukihara, T.; Tanaka, K. Structural basis of sugar-recognizing ubiquitin ligase. Nat. Struct. Mol. Biol. 2004, 11, 365–370.
90. Yoshida, Y. A novel role for N-glycans in the ERAD pathway. J. Biochem. 2003, 134, 183–190.
91. Glenn, K.A.; Nelson, R.F.; Wen, H.M.; Mallinger, A.J.; Paulson, H.L. Diversity in tissue expression, substrate binding, and SCF complex formation for a lectin family of ubiquitin ligases. J. Biol. Chem. 2008, 283, 12717–12729.
92. Matsushita, M. Ficolins: Complement-activating lectins involved in innate immunity. J. Innate Immun. 2009, 2, 24–32.
93. Chen, L.; Li, J.; Yang, G. A comparative review of intelectins. Scand J. Immunol. 2020, 92, e12882.
94. Crocker, P.R.; Redelinghuys, P. SiglecCs as positive and negative regulators of the immune system. Biochem. Soc. Trans. 2008, 36, 1467–1471.
95. Varki, A.; Angata, T. SiglecCs – The major subfamily of I-type lectins. Glycobiology 2006, 16, 1–27.
96. Spence, S.; Greene, M.K.; Fay, F.; Hams, E.; Saunders, S.P.; Hamid, U.; Fitzgerald, M.; Beck, J.; Bains, B.K.; Smyth, P.; et al. Targeting SiglecCs with a sialic acid-decorated nanoparticle abrogates inflammation. Sci. Transl. Med. 2015, 7, 1–13.
97. Crocker, P.R.; Kelm, S.; Dubois, C.; Martin, B.; McWilliam, A.S.; Shotton, D.M.; Paulson, J.C.; Gordon, S. Purification and properties of sialoadhesin, a sialic acid-binding receptor of murine tissue macrophages. EMBO J. 1991, 10, 1661–1669.
98. Powell, L.D.; Varki, A. The oligosaccharide binding specificities of CD22f2, a sialic acid- specific lectin of B cells. J. Biol. Chem. 1994, 269, 10628–10636.
99. Kelm, S.; Pelz, A.; Schauer, R.; Filbin, M.T.; Tang, S.; de Bellard, M.E.; Schnaar, R.L.; Mahoney, J.A.; Hartnell, A.; Bradfield, P.; et al. Sialoadhesin, myelin-associated glycoprotein and CD22 define a new family of sialic acid-dependent adhesion molecules of the immunoglobulin superfamily. *Curr. Biol.* 1994, 4, 965–972.

100. Freeman, S.D.; Kelm, S.; Barber, E.K.; Crocker, P.R. Characterization of CD33 as a new member of the sialoadhesin family of cellular interaction molecules. *Blood* 1995, 85, 2005–2012.

101. Collins, B.E.; Yang, L.J.S.; Mukhopadhyay, G.; Filbin, M.T.; Kiso, M.; Hasegawa, A.; Schnaar, R.L. Sialic acid specificity of myelin-associated glycoprotein binding. *J. Biol. Chem.* 1997, 272, 1248–1255.

102. Cornish, A.L.; Freeman, S.; Forbes, G.; Ni, J.; Zhang, M.; Cepeda, M.; Gentz, R.; Augustus, M.; Carter, K.C.; Crocker, P.R. Characterization of siglec-5, a novel glycoprotein expressed on myeloid cells related to CD33. *Blood* 1998, 92, 2123–2132.

103. Patel, N.; Der Linden, E.C.M.B.; Altman, S.W.; Gish, K.; Balasubramanian, S.; Timans, J.C.; Peterson, D.; Bell, M.P.; Bazan, J.F.; Varki, A.; et al. OB-BP1/Siglec-6 A Leptin and Sialic Acid-Binding Protein of The Immunoglobulin Superfamily. *J. Biol. Chem.* 1999, 274, 22729–22738.

104. Angata, T., Brinkman-Van der Linden E. I-type lectins. *Biochim. Biophys. Acta* 2002, 1572, 294–316, doi: 10.1016/s0304-4165(02)00316-1.

105. Nicoll, G.; Ni, J.; Liu, D.; Klenerman, P.; Munday, J.; Dubock, S.; Mattei, M.G.; Crocker, P.R.; Floyd, H.; Ni, J.; et al. Identification and characterization of a novel Siglec, Siglec-7, expressed by human natural killer cells and monocytes. Siglec-8: A novel eosinophil-specific member of the immunoglobulin superfamily. *Chemtracts* 2000, 13, 689–694.

106. Ito, A.; Handa, K.; Withers, D.A.; Satoh, M.; Hakomori, S. Ii-tiroh Binding specificity of siglec7 to disialogangliosides of renal cell carcinoma: Possible role of disialogangliosides in tumor progression. *FEBS Lett.* 2001, 504, 82–86.

107. Falco, M.; Biassoni, R.; Bottino, C.; Vitale, S.; Sivori, S.; Augugliaro, R.; Moretta, L.; Moretta, A. Identification and molecular cloning of p75/AIRM1, a novel member of the sialoadhesin family that functions as an inhibitory receptor in human natural killer cells. *J. Exp. Med.* 1999, 190, 793–801.

108. Floyd, H.; Ni, J.; Cornish, A.L.; Zeng, Z.; Liu, D.; Carter, K.C.; Steel, J.; Crocker, P.R. Siglec-8 A novel Eosinophil-Specific member of The Immunoglobulin Superfamily. *J. Biol. Chem.* 2000, 275, 861–866.

109. Zhang, J.Q.; Nicoll, G.; Jones, C.; Crocker, P.R. Siglec-9, a novel sialic acid binding member of the immunoglobulin superfamily expressed broadly on human blood leukocytes. *J. Biol. Chem.* 2000, 275, 22121–22126.

110. Munday, J.; Kerr, S.; Ni, J.; Cornish, A.L.; Zhang, J.Q.; Nicoll, G.; Floyd, H.; Mattei, M.G.; Moore, P.; Liu, D.; et al. Identification, characterization and leucocyte expression of Siglec-10, a novel human sialic acid-binding receptor. *Biochem. J.* 2001, 355, 498–497.

111. Angata, T.; Hayakawa, T.; Yamanaka, M.; Varki, A.; Nakamura, M. Discovery of Siglec-14, a novel sialic acid receptor undergoing concerted evolution with Siglec-5 in primates. *FASEB J.* 2006, 20, 1964–1973.

112. Angata, T.; Tabuchi, Y.; Nakamura, K.; Nakamura, M. Siglec-15: An immune system Siglec conserved throughout vertebrate evolution. *Glycobiology* 2007, 17, 838–846.

113. Warren, H.S.; Altin, J.G.; Waldron, J.C.; Kinnear, B.F.; Parish, C.R. A carbohydrate structure associated with CD15 (Lewisx) on myeloid cells is a novel ligand for CD2. *J. Immunol.* 1996, 156, 2866–2873.

114. Scholler, N.; Hayden-Ledbetter, M.; Hellström, K.-E.; Hellström, I.; Ledbetter, J.A. CD83 Is A Sialic Acid-Binding Ig-Like Lectin (Siglec) Adhesion Receptor That Binds Monocytes and a Subset of Activated CD8+ T Cells. *J. Immunol.* 2001, 166, 3865–3872.

115. McCourt, P.A.G.; Ek, B.; Forsberg, N.; Gustafson, S. Intercellular adhesion molecule-1 is a cell surface receptor for hyaluronan. *J. Biol. Chem.* 1994, 269, 30081–30084.

116. Kleene, R.; Yang, H.; Kutsche, M.; Schachner, M. The Neural Recognition Molecule L1 is a Sialic Acid-Binding Lectin for CD24, Which Induces Promotion and Inhibition of Neurite Outgrowth. *J. Biol. Chem.* 2001, 276, 21656–21663.

117. Horstkorte, R.; Schachner, M.; Magyar, J.P.; Vorherr, T.; Schmitz, B. The fourth immunoglobulin-like domain of NCAM contains a carbohydrate recognition domain for oligomannosidic glycans implicated in association with L1 and neurite outgrowth. *J. Cell Biol.* 1993, 121, 1409–1422.

118. Etzler, M.E.; Surulia, A.; Cummings, R.D. L-Type Lectins. In *Essentials of Glycobiology*; Harbor Laboratory Press: New York, NY, USA, 2009.

119. Bottazzi, B.; Garlanda, C.; Teixeira, M.M. The Role of Pentraxins: From Inflammation, Tissue Repair and Immunity to Biomarkers; Frontiers Media SA: Lausanne, Switzerland, 2020; ISBN 9782889633876.

120. Cloé, T.W. Du Pentraxins: Structure, Function, and Role in Inflammation. *ISRN Inflamm.* 2013, 2013, 1–22.

121. Ware, F.E.; Vassilakos, A.; Peterson, P.A.; Jackson, M.R.; Lehman, M.A.; Williams, D.B. The molecular chaperone calnexin binds GlcMan9GlcNAc2 oligosaccharide as an initial step in recognizing unfolded glycoproteins. *J. Biol. Chem.* 1995, 270, 4697–4704.

122. Spirito, R.G.; Zhu, Q.; Bhoyroo, V.; Söling, H.D. Definition of the lectin-like properties of the molecular chaperone, calreticulin, and demonstration of its copurification with endomannosidase from rat liver Golgi. *J. Biol. Chem.* 1996, 271, 11588–11594.

123. Zheng, C.; Page, R.C.; Das, V.; Nix, J.C.; Wigren, E.; Misra, S.; Zhang, B. Structural characterization of carbohydrate binding by LMAN1 protein provides new insight into the endoplasmic reticulum export of factors V (FV) and VIII (FVIII). *J. Biol. Chem.* 2013, 288, 20499–20509.

124. Kamiya, Y.; Yamaguchi, Y.; Takahashi, M.; Arata, Y.; Kasai, K.I.; Ibara, Y.; Matsumo, I.; Ito, Y.; Yamamoto, K.; Kato, K. Sugar-binding properties of VIP36, an intracellular animal lectin operating as a cargo receptor. *J. Biol. Chem.* 2005, 280, 37178–37182.
125. Kamiya, Y.; Kamiya, D.; Yamamoto, K.; Nyfefer, B.; Hauri, H.P.; Kato, K. Molecular basis of sugar recognition by the human L-type lectins ERGIC-53, V1PL, and VIP36. *J. Biol. Chem.* 2008, 283, 1857–1861.

126. Zahedi, K. Characterization of the binding of serum amyloid P to Laminin. *J. Biol. Chem.* 1997, 272, 2143–2148.

127. Köttgen, E.; Hell, B.; Kage, A.; Tauber, R.; Köttgen, E. Lectin specificity and binding characteristics of human C-reactive protein. *J. Immunol.* 1992, 149, 445–453.

128. Lee, R.T.; Lee, Y.C. Carbohydrate ligands of human C-reactive protein: Binding of neoglycoconjugates containing galactose-6-phosphate and galactose-terminated disaccharide. *Glycoconj. J.* 2006, 23, 317–327.

129. Deban, L.; Jarha, H.; Lehtinen, M.J.; Bottazzi, B.; Bastone, A.; Doni, A.; Jokiranta, T.S.; Mantovani, A.; Meri, S. Binding of the Long Pentraxin PTX3 to Factor H: Interacting Domains and Function in the Regulation of Complement Activation. *J. Immunol.* 2008, 181, 8433–8440.

130. Gonzalez, D.S.; Jordan, I.K. The alpha-Mannosidas: Phylogeny and Adaptive Diversification. *Mol. Biol. Evol.* 2000, 17, 292–300.

131. Vallet, S.D.; Clerc, O.; Ricard-Blum, S. Glycosaminoglycan–Protein Interactions: The First Draft of the Glycosaminoglycan Interactome. *J. Histochem. Cytochem.* 2020, doi:10.1369/0022155420946403.

132. Bischoff, J.; Kornfeld, R. The soluble form of rat liver α-mannosidase is immunologically related to the endoplasmic reticulum membrane α-mannosidase. *J. Biol. Chem.* 1986, 261, 4758–4765.

133. Tremblay, L.O.; Dyke, N.C.; Herscovics, A. Molecular cloning, chromosomal mapping and tissue-specific expression of a novel human α1,2-mannosidase gene involved in N-glycan maturation. *Glycosobiology* 1998, 8, 585–595.

134. Dahms, N.M.; Hancock, M.K. P-type lectins. *Biochim. Biophys. Acta Gen. Subj.* 2002, 1572, 317–340.

135. Tong, P.Y.; Gregory, W.; Kornfeld, S. Ligand interactions of the cation-independent mannose 6-phosphate receptor. The stoichiometry of mannose 6-phosphate binding. *J. Biol. Chem.* 1989, 264, 7962–7969.

136. Tong, P.Y.; Kornfeld, S. Ligand interactions of the cation-dependent mannose 6-phosphate receptor. Comparison with the cation-independent mannose 6-phosphate receptor. *J. Biol. Chem.* 1989, 264, 7970–7975.

137. Gary-Bobo, M.; Nirde, P.; Jeanjean, A.; Morere, A.; Garcia, M. Mannose 6-Phosphate Receptor Targeting and its Applications in Human Diseases. *Curr. Med. Chem.* 2007, 14, 2945–2953.

138. Cummings, R.D.; Schnaar, R.L. R-Type Lectins. In Essentials of Glycobiology; Varki, A., Cummings, R.D., Esko, J.D., Stanley, P., Hart, G.W., Aebi, M., Darvill, A.G., Kinoshita, T., Parker, N.H., Prestegard, J.H., et al., Eds.; Cold Spring Harbor: New York, NY, USA, 2015; pp. 401–412.

139. Clausen, H.; Bennett, E.P. A family of UDP-GalNAc: Polypeptide N-acetylgalactosaminy1transferases control the initiation of mucin-type O-linked glycosylation. *Glycobiology* 1996, 6, 635–646.

140. Iwasaki, H.; Zhang, Y.; Tachibana, K.; Gotoh, M.; Kikuchi, N.; Kwon, Y.D.; Togayachi, A.; Kudo, T.; Kubota, T.; Narimatsu, H. Initiation of O-glycan synthesis in IgA1 hinge region is determined by a single enzyme, UDP-N-acetylα-D-galactomannose: Polypeptide N-acetylgalactosaminy1transferase-7, with specificity for partial GalNAc-glycosylated acceptor substrates. *FEBS Lett.* 1999, 460, 226–230.

141. White, K.E.; Lorenz, B.; Evans, W.E.; Meitinger, T.; Strom, T.M.; Econs, M.J. Molecular cloning of a novel human UDP-GalNAc: Polypeptide N-acetylgalactosaminy1transferase, GalNAc-T8, and analysis as a candidate autosomal dominant hypophosphatemic rickets (ADHR) gene. *Gene* 2000, 246, 347–356.

142. Toba, S.; Tenno, M.; Konishi, M.; Mikami, T.; Itoh, N.; Kurosaka, A. Brain-specific expression of a novel human UDP-GalNAc: Polypeptide N-acetylgalactosaminy1transferase (GalNAc-T9). *Biochim. Biophys. Acta Gene Struct. Expr.* 2000, 1493, 264–268.

143. Cheng, L.; Tachibana, K.; Zhang, Y.; Guo, J.M.; Kakori Tachibana, K.; Kameyama, A.; Wang, H.; Hiruma, T.; Iwasaki, H.; Togayachi, A.; et al. Characterization of a novel human UDP-GalNAc: Polypeptide N-acetylgalactosaminy1transferase, pp-GalNAc-T10. *FEBS Lett.* 2002, 531, 115–121.

144. Boskovski, M.T.; Yuan, S.; Pedersen, N.B.; Goth, C.K.; Makova, S.; Clausen, H.; Brueckner, M.; Khokha, M.K. The Heteroatxy gene, GALNT11, glycosylates Notch to orchestrate cilia type and laterality. *Nature 2013, 504, 456–459.*

145. Guo, J.M.; Zhang, Y.; Cheng, L.; Iwasaki, H.; Wang, H.; Kubota, T.; Tachibana, K.; Narimatsu, H. Molecular cloning and characterization of a novel member of the UDP-GalNAc:Polypeptide N-acetylgalactosaminy1transferase family, pp-GalNAc-T12. *FEBS Lett.* 2002, 524, 211–218.

146. Zhang, Y.; Iwasaki, H.; Wang, H.; Kudo, T.; Kalka, T.B.; Hennett, T.; Kubota, T.; Cheng, L.; Inaba, N.; Gotoh, M.; et al. Cloning and characterization of a new UDP-N-acetylα-D-galactosaminy1transferase, designated pp-GalNAc-T13, that is specifically expressed in neurons and synthesizes GalNAc α-serine/threonine antigen. *J. Biol. Chem.* 2003, 278, 573–584.

147. Wang, H.; Tachibana, K.; Zhang, Y.; Iwasaki, H.; Kameyama, A.; Cheng, L.; Guo, J.M.; Hiruma, T.; Togayachi, A.; Kudo, T.; et al. Cloning and characterization of a novel UDP-GalNAc:Polypeptide N-acetylgalactosaminy1transferase, pp-GalNAc-T14. *Biochim. Biophys. Res. Commun.* 2003, 300, 738–744.

148. Cheng, L.; Tachibana, K.; Iwasaki, H.; Kameyama, A.; Zhang, Y.; Kubota, T.; Hiruma, T.; Tachibana, K.; Kudo, T.; Guo, J.M.; et al. Characterization of a novel human UDP-GalNAc:transferase, pp-GalNAc-T15. *FEBS Lett.* 2004, 56, 17–24.
151. Raman, J.; Guan, Y.; Perrine, C.L.; Gerken, T.A.; Tabak, L.A. UDP-N-acetyl α-d-galactosamine: Polypeptide N-acetylgalactosaminyltransferases: Completion of the family tree. Glycobiology 2012, 22, 768–777.

152. Nakayama, Y.; Nakamura, N.; Oki, S.; Wakabayashi, M.; Ishihama, Y.; Miyake, A.; Itoh, N.; Kurosaka, A. A putative polypeptide N-acetylgalactosaminyltransferase/Williams-Beuren syndrome chromosome region 17 (WBSCR17) regulates lamellipodium formation and macropinocytosis. J. Biol. Chem. 2012, 287, 32222–32235.

153. Li, X.; Wang, J.; Li, W.; Xu, Y.; Shao, D.; Xie, Y.; Xie, W.; Kubota, T.; Narimatsu, H.; Zhang, Y. Characterization of ppGalNAc-T18, a member of the vertebrate-specific y subfamily of UDP-N-acetyl-d-galactosamine:polypeptide N-acetylgalactosaminyltransferases. Glycobiology 2012, 22, 602–615.

154. Takasaki, N.; Tachibana, K.; Ogasawara, S.; Matsuizaki, H.; Hagiuuda, J.; Ishihawa, H.; Mochida, K.; Inoue, K.; Ogonuki, N.; Ogura, A.; et al. A heterozygous mutation of GALNTL5 affects male infertility with impairment of sperm motility. Proc. Natl. Acad. Sci. USA 2014, 111, 1120–1125.

155. Cummings, R.D.; Liu, F.-T. Galectins. In Essentials of Glycobiology; Variki, A., Cummings, R.D., Esko, J.D., Freeze, H.H., Stanley, P., Bertozzi, C.R., Gerald, H.W., Etzler, M.E., Eds.; Harbor Laboratory Press: New York, NY, USA, 2009.

156. Johannes, L.; Jacob, R.; Leffler, H. Galectins. Structure and function of a large family of animal lectins. J. Biol. Chem. 1994, 269, 20807–20810.

157. Barondes, S.H.; Cooper, D.N.W.; Gitt, M.A.; Leffler, H. Galectins. Structure and function of a large family of animal lectins. J. Biol. Chem. 1994, 269, 20807–20810.

158. Chetry, M.; Thapa, S.; Hu, X.; Song, Y.; Zhang, J.; Zhu, H.; Zhu, X. The role of galectins in tumor progression, treatment and prognosis of gynecological cancers. J. Cancer 2018, 9, 4742–4755.

159. Ebrahimi, A.H.; Alalawi, Z.; Mirandola, L.; Rakshshanda, R.; Dahlebeck, S.; Nguyen, D.; Jenkins, M.; Grizzi, F.; Cobos, E.; Figueiredo, J.A.; et al. Galectins in cancer: Carcinogenesis, diagnosis and therapy. Ann. Transl. Med. 2014, 2, 1–7.

160. Chou, F.C.; Chen, H.Y.; Kuo, C.C.; Sytwu, H.K. Role of galectins in tumors and in clinical immunotherapy. Int. J. Mol. Sci. 2018, 19, 430.

161. Cho, M.; Cummings, R.D. Galectin-1, a β-galactoside-binding lectin in Chinese hamster ovary cells. I. Physical and chemical characterization. J. Biol. Chem. 1995, 270, 5198–5206.

162. Di Lella, S.; Ma, L.; Diaz Ricci, J.C.; Rabinovich, G.A.; Asher, S.A.; Alvarez, R.M.S. Critical role of the solvent environment in galectin-1 binding to the disaccharide lactose. Biochemistry 2009, 48, 786–791.

163. Gitt, M.A.; Massa, S.M.; Leffler, H.; Barondes, S.H. Isolation and Expression of a Gene Encoding L-14-II, a New Human Soluble Lactose-binding Lectin. J. Biol. Chem. 1992, 267, 10601–10606.

164. Cederfur, C.; Salomonsson, E.; Nilsson, J.; Halim, A.; Obreg, C.T.; Larson, G.; Nilsson, U.J.; Leffler, H. Different affinity of galectins for human serum glycoproteins: Galectin-3 binds many protease inhibitors and acute phase proteins. Glycobiology 2008, 18, 384–394.

165. Koths, K.; Taylor, E.; Halenbeck, R.; Casipit, C.; Wang, A. Cloning and characterization of a human Mac-2-binding protein, a new member of the superfamily defined by the macrophage scavenger receptor cysteine-rich domain. J. Biol. Chem. 1993, 268, 14245–14249.

166. Huflet, M.E.; Leffler, H. Galectin-4 in normal tissues and cancer. Glycoconj. J. 2003, 20, 247–255.

167. Leonidas, D.D.; Vatzaki, E.H.; Vorum, H.; Celis, J.E.; Madsen, P.; Acharya, K.R. Structural basis for the recognition of carbohydrates by human galectin-7. Biochemistry 1998, 37, 13930–13940.

168. Ideo, H.; Matsuizaki, T.; Nonaka, T.; Sako, A.; Yamashita, K. Galectin-8-N-Domain Recognition Mechanism for Sialylated and Sulfated Glycans. J. Biol. Chem. 2011, 286, 11346–11355.

169. Nagae, M.; Nishi, N.; Nakamura-Tsuruta, S.; Hirabayashi, J.; Wakatsuki, S.; Kato, R. Structural Analysis of the Human Galectin-9 N-terminal Carbohydrate Recognition Domain Reveals Unexpected Properties that Differ from the Mouse Orthologue. J. Mol. Biol. 2008, 375, 119–135.

170. Heusschen, R.; Griffioen, A.W.; Thijssen, V.L. Galectin-9 in tumor biology: A jack of multiple trades. Biochim. Biophys. Acta Rev. Cancer 2013, 1836, 177–185.

171. Su, J. A brief history of Charcot-Leyden crystal protein/galectin-10 research. Molecules 2018, 23, 1–16.

172. Hotta, K.; Funahashi, T.; Matsukawa, Y.; Takahashi, M.; Nishizawa, H.; Kishida, K.; Matsuda, M.; Kuriyama, H.; Kihara, S.; Nakamura, T.; et al. Galectin-12, an Adipose-expressed Galectin-like Molecule Possessing Apoptosis-inducing Activity. J. Biol. Chem. 2001, 276, 34097–34097.