ABSTRACT
In the course of embryo implantation extensive interaction of the trophoblast with uterine tissue is crucial for adequate trophoblast invasion. This interaction is highly controlled, and it has been pointed out that a specific glycocode and changes in glycosylation may be important for successful implantation and maintenance of pregnancy. Both uterine and trophoblast cells have been shown to express cell surface glycoconjugates and sugar binding proteins, such as mucins (MUC) and galectins (gals). An increasing number of studies have investigated potential candidates interacting in this process. However, knowledge about the biochemical nature of the interactions and their importance for trophoblast cell function, and, consequently, for pregnancy outcome are still lacking. This review is aimed at deliberating the possibility that mucins, as heavily glycosylated proteins, might be among the functionally relevant galectin ligands in human trophoblast, based on both published data and our original research.

KEYWORDS
adhesion; extravillous trophoblast; galectin-1; interaction; migration; mucin

Introduction
The presence of MUC1 on luminal epithelium of the uterus has been widely accepted to direct blastocyst attachment to areas free of its hindering effect. Expression of mucins has also been recorded on human trophoblast cells of fetal origin, from which they can be co-isolated with the endogenous lectin, gal-1. On the other hand, gal-1 has been shown to influence adhesive, migratory and invasive behavior of trophoblast cells in vitro, through interactions with glycoconjugates. This review is aimed at deliberating the possibility that mucins, as heavily glycosylated proteins, might be among the functionally relevant galectin ligands in human trophoblast.

Expression and functions of mucins
Some of the major components of surface epithelia in respiratory, gastrointestinal and reproductive tracts are heterogeneous highly glycosylated proteins known as mucins. Thus far, 20 mucin family members have been identified (MUC1-MUC20). Although they are encoded by different genes, their protein structure shares some characteristic similarities. Mature mucin protein is processed in the Golgi apparatus, where it can be glycosylated, sialylated and sulfated, typically in a cell-type specific manner. According to their cellular localization mucins are classified into 2 distinct categories, membrane-bound or secreted mucins. The secreted mucins are gel-forming components of viscoelastic mucus, which lubricates and protects underlying epithelia, with expression restricted to secretory organs and cell types. On the other hand, membrane-bound mucins belong to the group of type-1 membrane anchored proteins, defined by the presence of a long extracellular domain with many sites for O-glycosylation and fewer for N-glycosylation. Their expression on the apical side of epithelial cells enables interaction with secreted mucins and anchors the mucus layer to the epithelium. Secreted variants of membrane-bound mucins, can be released from the plasma membrane either by enzymatic cleavage or result from alternative splicing. Together with their protective role, membrane mucins are also recognized as sensors of the extracellular environment that can transmit signals, and as molecules involved in cell-cell and cell-matrix interactions.

Different tissues normally express unique combinations of mucins, but in neoplasia this pattern is frequently altered. Aberrant glycosylation is probably responsible for many differences between carcinomas and normal
epithelial tissue.\textsuperscript{10} In addition to their very complex functional roles in both normal and malignant cells, changes in both amounts and forms of mucins may influence cellular growth, differentiation, transformation, adhesion and invasion.\textsuperscript{11-14} Considerable research data have shown that overexpression of MUC1 is associated with invasive and metastatic tumors of the gall bladder, colon, pancreas and oral epithelium.\textsuperscript{14-16} Also, it was found that MUC3, i.e. its cysteine-rich domain, can promote cell migration, accelerate wound healing and inhibit apoptosis.\textsuperscript{17} Therefore, mucins are hypothesized to contribute to tumor cell invasion by simultaneously disrupting existing interactions between neighboring cells (anti-adhesion) and establishing new ligands for interaction between the invading cell and adjoining cells (adhesion).\textsuperscript{10}

The human female reproductive tract, including ovaries, oviduct, uterus, cervix and vagina, expresses several different mucins.\textsuperscript{18} The earliest studies focused on mucin expression in the uterus, especially on membrane-bound MUC1, because of its dominant presence in human endometrium.\textsuperscript{19-21} MUC1 has characteristics of an integral membrane protein with a large extracellular domain, a transmembrane domain and a short cytoplasmic sequence.\textsuperscript{8} The long extracellular domain contains a variable number of tandem repeats (VNTR) rich in serine and threonine, potential sites of glycosylation. Throughout the menstrual cycle MUC1 is expressed at the apical surface of both luminal and glandular epithelium (Fig. 1) and is secreted into the uterine cavity, while some of the glycoepitopes are phase of cycle dependent.\textsuperscript{19,20} MUC1-associated glycans in the endometrium constitute at least 40\% of the mucin molecular mass. Using different antibodies, highly sulfated lactosaminoglycans and sialokera- tan sulfate epitopes have been detected on endometrial MUC1.\textsuperscript{1} Moreover, several sialoepitopes are expressed on endometrial MUC1, e.g. Sialyl-Tn antigen (STn, Neu5AcO2-6GalNAc) and the carbohydrate adhesion ligands, Sialyl-LewisX (SLeX) and Sialyl-LewisA (SLeA).\textsuperscript{22,23} Endometrial MUC1 is also known to bear the Thomsen-Friedenreich antigen (TF antigen, Galβ1-3GalNAc).\textsuperscript{24} Much evidence clearly points to hormonal regulation of MUC1 expression in the endometrium, with cyclically regulated expression of core protein and glycan sialylation, where maximum levels occur in the secretory phase of the menstrual cycle.\textsuperscript{25} Specific MUC1 structures and the abundance of sialic acid and sulfate residues may subsequently inhibit interaction between the embryo and maternal apical adhesion molecules during implantation. Thus, the high density of MUC1 molecules must be lost from the implantation site if embryo implantation is to occur. Local loss of MUC1 could result from production of downregulating factors by blasto- cysts,\textsuperscript{26} or binding by carbohydrate binding proteins (lectins) from the blastocyst cell surface specific for MUC1-associated glycans.\textsuperscript{27} The latter possibility indicates that involvement of the selectin-adhesion mechanism may be critical for embryo implantation, implying the importance of lectin-carbohydrate recognition/binding in initial adhesive interactions.

Mucins are thought to play important roles in many cellular processes, including cell signaling, cell proliferation and tumor progression, and also to mediate immune eva- sion.\textsuperscript{19} Due to abundant glycosylation, mucins and MUC1 in particular, have either pro- or anti-adhesive properties and influence cell-cell and cell-extracellular matrix (ECM) interactions,\textsuperscript{28-30} depending on the cell type. Thus, sialomucin CD34 inhibited adhesion of HEK293T cells, hematopoietic stem and progenitor cells,\textsuperscript{31,32} but increased murine hematopoietic cell adhesion to human bone marrow stromal cells.\textsuperscript{33} Another membrane-bound mucin, MUC16, promoted the formation of multicellular aggregates of ovarian carcinoma cells \textit{in vitro} and may play a role in ovarian carcinoma progression.\textsuperscript{34}

**Trophoblast mucins**

Mucins are also expressed by the trophoblast. To date, only membrane-bound mucins have been investigated. Thus, at the protein level MUC1 and MUC15 (Fig. 1), as well as mRNA for MUC1, MUC3, MUC15 and MUC20 have been detected in human placenta.\textsuperscript{35,36} The presence and localization of MUC1 was studied using different antibodies specific for various epitopes on the molecule. These antibodies detected either MUC1 epitopes within the VNTR region or MUC1-associated glycans, indicating the significance of glycosylation of the core protein.\textsuperscript{35,36} MUC1 has been observed in human and macaque placenta, choriocarcinoma cell lines and isolated trophoblast, but findings regarding the distribution and staining intensity of this glycoprotein are discordant.\textsuperscript{28,36-38} Using antibodies specific for underglycosylated and hypoglycosylated MUC1, Shyu et al. showed that expression of MUC1 increases with gestational age, with dominant expression by the syncytiotrophoblast (ST) and to a lesser extent by a subset of extravillous trophoblast (EVT) cells (Fig. 1).\textsuperscript{36} Other distinct glycoepitopes carried by trophoblast MUC1, CA 15-3 and CA 19-9, were detected in extravillous trophoblast, while CA 19-9 was also present in surrounding decidual cells. Moreover, it has been shown that invasive trophoblast of the first and second trimester of pregnancy expresses CA 15-3 (Fitzgerald clone M411149), in keeping with the study of Shyu et al.,\textsuperscript{36} regarding the intensity of staining (relatively weak) and the relative number of stained trophoblast cells. In contrast, using polyclonal anti-bovine submaxillar mucin antibodies (anti-BSM) we recently
demonstrated moderate to strong MUC1/mucin(s) staining of first trimester placental villi (Fig. 1), while Jeschke et al. reported strong MUC1 expression in human first and second trimester placenta. Expression of MUC1 has also been observed in isolated trophoblast cells, as well as in JAr and BeWo choriocarcinoma cells. The MUC1 staining pattern is consistent with plasma membrane/cytoplasmic localization in rhesus monkey trophoblast cells and in freshly isolated trophoblast. Strong membrane staining was obtained using either antibodies specific for the cytoplasmic MUC1 domain or for carbohydrate MUC1 epitopes. Kumar et al. recently detected the MUC1 extracellular domain in nuclear speckles and in spliceosomes in rhesus monkey trophoblast cells using 3 different antibodies specific for MUC1 VNTR. Nucleus associated staining was also seen in JAr choriocarcinoma cells and in MCF7 breast cancer cells. Clearly, the staining pattern strongly depends on the antibody used, and this must be considered in the light of variability of MUC1 glycosylation in different cells and the influence of glycosylation on epitope recognition by MUC1 extracellular domain specific antibodies.

Another studied member of the class of membrane-bound mucins is MUC15, which is abundantly expressed in placenta. MUC15 is predominantly found at the apical ST membrane, while it is absent from EVT cells (Fig. 1). Interestingly, as previously shown for MUC1, MUC15 is differentially expressed in human placenta through gestation, with the highest levels at term, for both MUC15 protein and mRNA.

It is well known that there is tissue specific glycosylation of MUC1, despite almost identical transcripts. For example, pancreatic MUC1 is larger and more glycosylated than that from breast or endometrium. While endometrial MUC1 glycotopes have been the subject of many studies, data regarding carbohydrates associated with placental mucin molecules are incomplete. Most of the results were obtained from histochemical studies and lectin-blotting, by combining antibodies specific for different mucin glycotopes with different plant lectins to decipher glycotope specificities. These data suggest the probable presence of short mucin-type O-glycans, such as TF and Tn (GalNAc) antigens. Some of these glycotopes terminate with sialic acid, mainly linked by the α2,3 bond and less by the α2,6 bond, as indicated by binding of lectins from Maackia amurensis (MAA) and Sambucus nigra (SNA). Some of these glycans could vary during pregnancy or be engaged by their...
binding partners, which may further affect the functional properties of MUC1.

In recent years, the functional properties of MUC1/mucins expressed by the trophoblast have also been investigated. Adhesion of HTR-8/SVneo EVT cells to ECM components, such as collagen type IV, fibronectin and laminin was negatively affected by MUC1 overexpression. In our study HTR-8/SVneo enhanced cell aggregation was also observed (Fig. 2A) when bovine submaxillary mucin (BSM), similar to MUC1 with respect to the presence of defined glycotopes such as TF and STn, was added to cell culture. Under similar culture conditions the presence of BSM reduced HTR-8/SVneo cell migration, which could be prevented by a specific antibody (Figs. 2B and 2C).

In the macaque, EVT cell adhesion and transendothelial migration were mediated by MUC1 involving intercellular adhesion molecule-1 (ICAM-1). However, the finding that endothelial ICAM-1 is one of the counterreceptors for trophoblast MUC1 does not exclude potential additional MUC1 ligands on the trophoblast or other uterine cell types. It has been suggested that both MUC1 and MUC15 could have active roles in trophoblast invasion, since overexpression of each suppressed invasion of choriocarcinoma cells. Consistent with this finding, overexpression of MUC1 also reduced invasion of HTR-8/SVneo cells. Since MUC1 overexpression inhibited β1-integrin activity and downstream signaling, invasion may be suppressed mainly by modulation of β1-integrin signaling.

**Trophoblast galectin-1**

Galectins are small soluble proteins defined by an affinity for β-galactosides and significant sequence similarity of the carbohydrate recognition domain (CRD) among family members. Due to their capacity to modulate cellular functions, they are involved in diverse processes, including immunomodulation, cell differentiation and death, proliferation, adhesion, migration and invasion. Several lines of evidence suggest that human galectins play important roles in implantation, angiogenesis, maternal-fetal immunotolerance and placentation. For example, gal-1 expression by the trophectoderm and inner cell mass of human preimplantation embryos, points to involvement in attachment to the uterine epithelium, even though gal-1 null mice implant normally. Among the 16 human galectins, gal-1, -3, and

---

**Figure 2.** Effect of BSM on adhesion and migration of HTR-8/SVneo extravillous trophoblast cells. (A) Cell adhesion after 2 h in the presence of BSM (100 μg/ml) in culture medium. A representative micrograph shows aggregation of trophoblast cells in the presence of BSM. (B) Representative images of the bidirectional migration of HTR-8/SVneo monolayers following wounding. Cells were grown with or without (control) BSM in culture media. Cell migration was reduced in the presence of BSM. (C, D) Statistical analyses of wound healing assays. (C) BSM (100 μg/ml and 200 μg/ml) reduced cell migration, which was prevented in the presence of anti-BSM antibodies (25 μg/ml). (D) Supplementation of culture media with 5 μg/ml of CS-gal-1 or Ox-gal-1 (2 molecular forms of biologically active recombinant human gal-1) prevented inhibition of HTR-8/SVneo cell migration by BSM (100 μg/ml). The data are expressed as a percentage of the value for the untreated control ± SEM, n = 6. *p < 0.05; **p < 0.01; ***p < 0.001. Methad details available in Supplemental material.
-8 were detected in EVT differentiating along the invasion pathway. Since they are expressed by the EVT of the anchoring villi, these galectins could be involved in the organization of the ECM, modulating cell adhesion through interaction with glycans of the cell column and the placental bed ECM. Galectin-1 was the first to be isolated, purified and cloned from human placenta. It is immunolocalized in the syncytiotrophoblast, cytotrophoblast of middle and distal cell columns, and abundantly in the endometrium and decidua of early gestation (Fig. 1). Galectin-1 is also expressed by isolated cytotrophoblast in culture and trophoblast cell lines. This protein has an important role in maintenance of pregnancy in mice, with a high fetal loss rate in gal-1 deficient animals, preventable by treatment with recombinant gal-1. In the human, in addition to its proposed involvement in immunomodulation leading to non-rejection of the fetus, gal-1 level was found to be positively correlated with pregnancy success in vivo, and contributes to trophoblast invasiveness in vitro. Blocking the extracellular function of endogenous gal-1 of primary trophoblasts and HTR-8/SVneo extravillous cells reduced invasion substantially, while supplementation with recombinant gal-1 enhanced it.

**Mucins and galectin-1**

Specialized structural features of the mucin protein backbone and the abundant glycosylation lead to interaction with distinct protein partners. There are multiple ways for both secreted and membrane mucins to interact, with secreted, membrane bound and transmembrane proteins, including mucins, some of which initiate signaling cascades or influence the availability of the proteins involved. Mucin-binding partners are found in the extracellular space in different tissues, most of them being detected in saliva. However, as carbohydrate binding proteins, galectins are so far the only known extracellularly located mucin-binding partners of non-salivary origin. Several biochemical studies have provided direct evidence of interaction between mucins and galectins. As shown by histochemistry, gal-1 binds mucin and epithelial surface glyocalyces of the gastrointestinal mucosa. Glycans associated with both soluble and membrane-bound CA125 (MUC16) present in HeLa cells are specifically and preferentially recognized by gal-1, as opposed to gal-3. Although the exact biological significance of this interaction is currently not known, it has been proposed that CA125 might be a factor regulating gal-1 export to the surface of these cells. It has been shown that MUC1 and MUC16, both membrane-bound mucins, interact with gal-3 on the apical surface of ocular epithelial cells. This interaction is abrogated in the presence of competitive carbohydrate inhibitors of galectin binding, which leads subsequently to reduced gal-3 at the cell membrane. Galectin-3 from the sera of cancer patients also interacted with MUC1 present on the cancer cell surface, i.e., with TF antigen. This interaction promoted strong adhesion of tumor cells to the endothelial surface, thus enabling cancer metastasis.

Since gal-1 preferentially recognizes type I and type II N-acetyllactosamine residues on all complex N-linked and many O-linked glycoproteins, its direct connection with trophoblast invasion is probably a consequence of recognition and interaction with β-galactoside containing ligands on the cell surface or in the ECM. It is well known that oncofetal fibronectin and laminin function as physiological ligands of gal-1 in human placenta, but there are also data to support binding to TF antigen expressed on either MUC1 or other glycoproteins in the trophoblast. Co-localization of both trophoblast mucin(s) and gal-1 at the plasma membrane of EVT cells suggested mutual interaction (Fig. 3). Mucin(s) and gal-1 were co-isolated from trophoblast cells in culture, confirming that these molecules indeed interact in these cells. Furthermore, the molecular interaction between MUC1/mucin(s) and gal-1 was reduced in the presence of lactose, pointing to the relevance of gal-1 lectin activity. Interestingly each of these proteins was shown to affect trophoblast cell invasion in vitro. Our own and other published data point to an inverse effect on this process, MUC1 decreasing it and gal-1 inducing an increase. It was interesting to speculate whether disturbing the balance between trophoblast mucin(s) and gal-1 would in any way affect trophoblast cell functional characteristics. Preliminary test results for cell migration under conditions in which both exogenous molecules were added to culture medium support the possibility that gal-1 and mucin(s) interact in such a way that the presence of gal-1 restores cell migration (Fig. 2D), originally decreased by added BSM (Figs. 2B and 2C). This suggests that a reduced presence of mucins, either by previous binding and thus diminished availability for other yet unspecified interactions, or by silencing, promotes the adhesive and invasive capacity of the trophoblast, since silencing MUC15 restored trophoblast cell migration/invasion, while overexpression of MUC1 and MUC15 downregulated it.

Based on the previously mentioned data, the potential cellular effects resulting from various possible interactions of trophoblast galectin-1 and MUC1 are diverse, depending on the cellular localization of this interaction, other participating molecules, or downstream targets. Translated gal-1 (Fig. 3A) can be translocated into the nucleus (Fig. 3B), where it may associate with
ribonucleoproteins (RNP), participate in spliceosome assembly, or it can accumulate in the cytoplasm where it may interact with cytosolic binding partners through protein-protein interactions (Fig. 3C). Gal-1 is transported outside the cells via non-classical protein export. In the extracellular space (E) this lectin binds several ECM glycoproteins, and (F) can form homogeneous lattices at the cell surface and activate signaling cascades. (G) Gal-1 can bind to cell surface glycoconjugates and crosslink them with ECM, (H) or promote cell-cell adhesion. MUC1 may act as a binding partner of gal-1, in a carbohydrate-dependent manner. (I) A fragment of the cytoplasmic tail of MUC1 may be transported to the nucleus and regulate gene expression, (J) or might sequester some cytosolic proteins. (K) Binding of gal-1 to trophoblast MUC1 and crosslinking with other transmembrane glycoproteins could trigger signal transduction. (L) Hypothetical molecular interactions of exogenous recombinant human gal-1 (CS-gal-1 and Ox-gal-1) and MUC1-like molecules of BSM in trophoblast cell culture.

Figure 3. Schematic representation of cellular effects resulting from interactions of gal-1 and MUC1. (A) Cytoplasmic gal-1 can be translocated into the nucleus, (B) where it can associate with ribonucleoproteins (RNP) and participate in spliceosome assembly, or it can accumulate in the cytoplasm (C) where it may interact with cytosolic binding partners. (D) Gal-1 is transported outside the cells via non-classical protein export. In the extracellular space (E) this lectin binds several ECM glycoproteins, and (F) can form homogeneous lattices at the cell surface and activate signaling cascades. (G) Gal-1 can bind to cell surface glycoconjugates and crosslink them with ECM, (H) or promote cell-cell adhesion. MUC1 may act as a binding partner of gal-1, in a carbohydrate-dependent manner. (I) A fragment of the cytoplasmic tail of MUC1 may be transported to the nucleus and regulate gene expression, (J) or might sequester some cytosolic proteins. (K) Binding of gal-1 to trophoblast MUC1 and crosslinking with other transmembrane glycoproteins could trigger signal transduction. (L) Hypothetical molecular interactions of exogenous recombinant human gal-1 (CS-gal-1 and Ox-gal-1) and MUC1-like molecules of BSM in trophoblast cell culture.

Conclusion
The data presented here have been selected with the aim of contributing to our understanding of the complex interactions between diverse proteins that are both associated with the trophoblast cell membrane, as well as present in the
extracellular space, such as MUC1/mucins and gal-1. Individually, both proteins have been found to affect the adhesive and invasive properties of trophoblast cells in culture. Since these proteins co-isolate from human trophoblast cells, but their effects on the trophoblast may be opposite, the question arises how any change in their level would affect the adhesive and migratory functions of these cells. This is obviously a complex task to address, due to the shared specificity of galectins, of which at least 3 are expressed by extravillous trophoblast on the one hand, while multiple mucin (glyco) forms are likely to be present in these cells on the other. Interaction between MUC1/mucin(s) and galectin-1 may balance pro- and anti-migratory effects, while high expression of decidual gal-1 may shift the balance favoring migration/invasion, explaining trophoblast invasion in vivo. One way to further our understanding of this complex field would be to selectively silence or otherwise inhibit multiple of the proposed interacting proteins, in the context of the large number of other functionally relevant interactions of these molecules documented in the literature.

On the other hand, while the relevance of MUC1 glycosylation in tumor progression has been thoroughly studied, much less is known about trophoblast mucin glycosylation. A combination of several approaches is needed to provide insights into how glycan structures and probable changes during pregnancy affect functional properties of the trophoblast. Deciphering the trophoblast mucin glycocode would open up the possibility of identifying the exact nature of the interaction between gal-1 and MUC1/mucin(s). This might help explain the roles of trophoblast mucin and galactin-1 in vivo, since both individually and jointly affect trophoblast function in vitro.

**Abbreviations**

- BSM: bovine submaxillary mucin
- CRD: carbohydrate recognition domain
- ECM: extracellular matrix
- EVT: extravillous trophoblast
- gal: galectin
- ICAM-1: intercellular adhesion molecule-1
- MAA: *Maackia amurensis* lectin
- MUC: mucin
- SLeA: Sialyl-LewisA
- SLeX: Sialyl-LewisX
- SNA: *Sambucus nigra* lectin
- ST: syncytiotrophoblast
- Tn: Tn antigen (GalNAc)
- STn: Sialyl-Tn antigen (Neu5Acα2,6GalNAc)
- TF antigen: Thomsen–Friedenreich antigen (Galβ1,3GalNAc)
- VNTR: variable number of tandem repeats.

**Disclosure of potential conflicts of interest**

No potential conflicts of interest were disclosed.

**Funding**

This study was funded by grant No. 173004 from the Ministry of Education, Science and Technological Development of the Republic of Serbia.

**References**

[1] Aplin JD, Hey NA, Graham RS. Human endometrial MUC1 carries keratan sulphate: characteristic glycoforms in the luminal epithelium at receptivity. Glycobiol 1998; 8:269-76; http://dx.doi.org/10.1093/glycob/8.3.269

[2] Bojić-Trbojević Z, Jovanović Krivokuća M, Kolundžić N, Petronijević M, Vrzić- Petronijević S, Golubović S, Vićovac LJ. Galectin-1 binds mucin in human trophoblast. Histochem Cell Biol 2014; 142:541-53; PMID:24854997; http://dx.doi.org/10.1007/s00418-014-1229-7

[3] Kolundžić N, Bojić-Trbojević Z, Kovačević T, Stefanoska I, Kadoya T, Vićovac LJ. Galectin-1 is part of human trophoblast invasion machinery - a functional study in vitro. PLoS One 2011; 6:e28514; PMID:Can’t; http://dx.doi.org/10.1371/journal.pone.0028514

[4] Theodoropoulos G, Carraway KL. Molecular signaling in the regulation of mucins. J Cell Biochem 2007; 102:1103-16; PMID:17957706; http://dx.doi.org/10.1002/jcb.21539

[5] Lang T, Hansson GC, Samuelsson T. Gel-forming mucins appeared early in metazoan evolution. Proc Natl Acad Sci USA 2007; 104:16209-14; PMID:17911254; http://dx.doi.org/10.1073/pnas.0705984104

[6] Silverman HS, Sutton-Smith M, McDermott K, Heal P, Leir S-H, Morris HR, Hollingsworth MA, Dell A, Harris A. The contribution of tandem repeat number to the O-glycosylation of mucin. Glycobiol 2003; 13:265-77; http://dx.doi.org/10.1093/glycob/cwg028

[7] Kufe DW. Mucins in cancer: function, prognosis and therapy. Nat Rev Cancer 2009; 9:874-85; PMID:19935676; http://dx.doi.org/10.1038/nrc2761

[8] Jonckheere N, Van Seuninge I. The membrane-bound mucins: how large O-glycoproteins play key roles in epithelial cancers and hold promise as biological tools for gene-based and immunotherapies. Crit Rev Oncog 2008; 14:177-96; PMID:19935676; http://dx.doi.org/10.1371/journal.pone.0028514

[9] Aplin JD, Hey NA, Graham RS. Human endometrial MUC1 carries keratan sulphate: characteristic glycoforms in the luminal epithelium at receptivity. Glycobiol 1998; 8:269-76; http://dx.doi.org/10.1093/glycob/8.3.269

[10] Holllingsworth MA, Swanson BJ. Mucins in cancer: Protection and control of the cell surface. Nat Rev Cancer 2004; 4:45-60; PMID:14681689; http://dx.doi.org/10.1038/nrc1251

[11] Quin RJ, McGuckin MA. Phosphorylation of the cytoplasmic domain of the MUC1 mucin correlates with changes in cell-cell adhesion. Int J Cancer 2000; 87:499-
The human endometrium expresses the glycoprotein mucin-1 and shows positive correlation for Thomsen-Friedenreich epitope expression and galectin-1 binding. J Histochem Cytochem 2009; 57:871-81; PMID:19506091; http://dx.doi.org/10.1369/jhc.2009.952085

Meseguer M, Pellicer A, Simón C. MUC1 and endometrial receptivity. Mol Hum Reprod 1998; 12:1089-98; http://dx.doi.org/10.1093/molehr/4.12.1089

Meseguer M, Aplin JD, Caballero-Campo P, O’Connor JE, Martin JC, Remohi J, Pellicer A, Simón C. Human endometrial mucin MUC1 is up-regulated by progesterone and down-regulated in vitro by the human blastocyst. Biol Reprod 2001; 64:590-601; PMID:11159362; http://dx.doi.org/10.1095/biolreprod64.2.590

Genbacev OD, Prakobphol A, Foulk RA, Krtolica AR, Ilic D, Singer MS, Yang ZQ, Kiesling LL, Rosen SD, Fisher SJ. Trophoblast L-selectin-mediated adhesion at the maternal-fetal interface. Science 2003; 299:405-8; PMID:12532021; http://dx.doi.org/10.1126/science.1079546

Thirkill TL, Cao T, Stout M, Blankenship TN, Barakat A, Douglas GC. MUC1 is involved in trophoblast transendothelial migration. Biochim Biophys Acta 2007; 1773:1007-14; PMID:17509701; http://dx.doi.org/10.1016/j.bbamcr.2007.04.006

Hilkens J, Wesseling J, Vos HL, Storm J, Boer B, van der Valk SW, Maas MC. Involvement of the cell surface-bound mucin, episialin/MUC1, in progression of human carcinomas. Biochem Soc Trans 1995; 23:822-6; PMID:8654846; http://dx.doi.org/10.1042/bst0230822

Wesseling J, van der Valk SW, Vos HL, Sonnenberg A, Hilkens J. Episialin (MUC1) overexpression inhibits integrin-mediated cell adhesion to extracellular matrix components. J Cell Biol 1995; 129:255-65; PMID:7698991; http://dx.doi.org/10.1083/jcb.129.1.255

Drew E, Merzaban JS, Seo W, Ziltener HJ, McNagny KM. CD34 and CD43 inhibits mast cells adhesion and are required for optimal mast cell reconstitution. Immunity 2005; 22:43-57; PMID:15666418; http://dx.doi.org/10.1016/j.immuni.2004.11.014

Ohnishi H, Sasaki H, Nakamura Y, Kato S, Ando K, Narimatsu H, Tachibana K. Regulation of cell shape and adhesion by CD34. Cell Adh Migr 2013; 7:426-33; PMID:24036614; http://dx.doi.org/10.4161/cam.25957

Healy L, May G, Gale K, Grosveld F, Greaves M, Enver T. The stem cell antigen CD34 functions as a regulator of hemopoietic cell adhesion. Proc Natl Acad Sci USA 1995; 92:12240-4; PMID:8618877; http://dx.doi.org/10.1073/pnas.92.26.12240

Giannakourou P, Comamala M, Matte I, Rancourt C, Piché A. MUC16 mucin (CA125) regulates the formation of multicellular aggregates by altering β-catenin signaling. Am J Canc Res 2014; 5:219-30

Shyu MK, Lin MC, Shih JC, Lee CN, Huang J, Liao CH, Huang IF, Chen HY, Huang MC, Hsieh FJ. Mucin 15 is expressed in human placenta and suppresses invasion of trophoblast-like cells in vitro. Hum Reprod 2007; 22:2723-32; PMID:17720698; http://dx.doi.org/10.1093/humrep/dem249

Shyu MK, Lin MC, Liu CH, Shih JC, Lee CN, Chen HY, Huang J, Huang MC, Hsieh FJ. MUC1 expression is increased during human placentation development and suppresses trophoblast-like cell invasion in vitro. Biol
Senapati S, Das S, Batra S. Mucin-interacting proteins: from function to therapeutics. Trends Biochem Sci 2009; 35:236-45; PMID:19913432; http://dx.doi.org/10.1016/j.tibs.2009.10.003

Wasano K, Hirakawa Y. Recombinant galectin-1 recognizes mucin and epithelial cell surface glycoconjugates of gastrointestinal tract. J Histochem Cytochem 1997; 45:275-83; PMID:9016316; http://dx.doi.org/10.1177/002215549704500212

Seelenmayer C, Wegeningel S, Lechner J, Nickel W. The cancer antigen CA125 represents a novel counter receptor for galectin-1. J Cell Sci 2003; 116: 1305-18; PMID:12615972; http://dx.doi.org/10.1242/jcs.00312

Argüeso P, Guzman-Araguez A, Mantelli F, Cao Z, Ricciuto J, Panjwani N. Association of cell surface mucins with galectin-3 contributes to the ocular surface epithelial barrier. J Biol Chem 2009; 284:23037-45; PMID:19556244; http://dx.doi.org/10.1074/jbc.M109.033332

Yu LG, Andrews N, Zhao Q, McKean D, Williams JF, Connor LJ, Gerasimenko OV, Hilkens J, Hirabayashi J, Kasai K, et al. Galectin-3 interaction with Thomsen-Friedenreich disaccharide on cancer-associated MUC1 causes increased cancer cell endothelial adhesion. J Biol Chem 2007; 282:773-81; PMID:17090543; http://dx.doi.org/10.1074/jbc.M606862200

Abbott WM, Hounsell EF, Feizi T. Further studies of oligosaccharide recognition by the soluble 13 kDa lectin of bovine heart muscle. Ability to accommodate the blood-group-H and -B-related sequences. Biochem J 1988; 252:283-7; PMID:3421906; http://dx.doi.org/10.1042/bj2520283

Sparrow CP, Leffler H, Barondes SH. Multiple soluble beta-galactoside-binding lectins from human lung. J Biol Chem 1987; 262:7383-90; PMID:2438278.

Ozeki Y, Matsui T, Yamamoto Y, Funahashi M, Hamako J, Titani K. Tissue fibronectin is an endogenous ligand for galectin-1. Glycobiol 1995; 5:255-61; http://dx.doi.org/10.1093/glycob/5.2.255

Zhou Q, Cummings RD. L-14 lectin recognition of laminin and its promotion of in vitro cell adhesion. Arch Biochem Biophys 1993; 300:6-17; PMID:8380972; http://dx.doi.org/10.1006/abbi.1993.1002

Jeschke U, Karsten U, Wiest I, Schulze S, Kuhn C, Friese K, Walzel H. Binding of galectin-1 (gal-1) to the Thomsen-Friedenreich (TF) antigen on trophoblast cells and inhibition of proliferation of trophoblast tumor cells in vitro by gal-1 or an anti-TF antibody. Histochem Cell Biol 2006; 126:437-44; PMID:16607538; http://dx.doi.org/10.1007/s00418-006-0178-1