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Mucins: an overview of functions and biological activity

Habibe Gündoğdu [1] Ebru Karadağ Sarı [2]

[1] *Department of Histology and Embryology, Faculty of Medicine, Ataturk University, Erzurum, Türkiye*
[2] *Department of Histology and Embryology, Faculty of Veterinary Medicine, Kafkas University, Kars, Türkiye*

Correspondence: *Habibe Gündoğdu, (habibe.kars@hotmail.com)*

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ABSTRACT

This review aims to provide novel evidence on the function of mucins in defense of epithelia and to spot mucin changes in the epithelial surface.

High molecular weight glycoproteins known as mucins are distinguished by their substantial O-glycosylation. The membrane-bound mucins and in secretion form are divided into two categories mucins. These are among the significant mucins expressed by the surface epithelia. Recent developments in functional assays have evaluated their functions in preserving corneal, conjunctival, respiratory, and digestive epithelia. The presentation includes changes in mucin and mucin O-glycan production in epithelial surface illnesses, including infection, non-autoimmune dry eye, autoimmune dry eye, and allergy.

Mucins are high molecular weight glycoproteins characterized by their extensive O-glycosylation. Recent advances using functional assays have allowed the examination of their roles in protecting epithelial tissues. Alterations in mucin and mucin O-glycan biosynthesis in epithelial surface disorders, including allergy, non-autoimmune dry eye, cancers, and infection, are presented.

Keywords: *Classification of mucins, Functions of mucins, Mucins*

1. Introduction

Mucins (MUC) are a large macromolecular component of mucus composed of glycoproteins. It is dispersed along the epithelial surface of the digestive, respiratory and reproductive systems (Rachagani et al., 2009). The mucin synthesis begins in the granular endoplasmic reticulum and is completed in the Golgi apparatus. Mucins are stained weakly with acidophilic dyes such as hematoxylin-eosin (Bancroft and Gamble 2008). Mucins are structurally and functionally divided into two. These are sekrete mucins and membrane mucins. Mucins that form the secretion are MUC2, MUC5AC, MUC5B, MUC7, and MUC6. Membrane mucins are MUC1, MUC3, MUC4, MUC12, MUC13, MUC16, MUC17, and MUC20 (Fowler et al., 2001; Pang et al., 2022).

MUC1 plays a role in preventing the adhesion of proteins; MUC3 has a role in defending the body against pathogens (Brayman et al., 2004), MUC4 and MUC13 protect epithelial cells (Pelaseyed et al., 2014; Corfield, 2017), MUC12 enables signal transduction (Yakan, 1990), MUC16 facilitates pancreatic cancer progression and metastasis (Aksoy, 2001), MUC17 allows cells to cling to each other on the apical surface of the tissue (Önder, 2012), MUC20 maintains the humidity of epithelial cells on mucosal cell surfaces (Woodward and Argüeso., 2014), MUC5AC supports the balance of bodily fluids in organs such as the colon and stomach (Bonser and Erle, 2017), MUC2 is involved in the diagnosis of ovarian tumors (O'Connell et al., 2002), MUC7 plays a role in the secretion of mucins at a specific limit in the glycosylation mechanism

(Büyük, 2014), MUC5B serves in the acquisition of viscoelastic properties of mucins (Ratan et al., 2021), MUC6 plays a role in protecting organs in the gastrointestinal tract (Fowler et al., 2001; Matte et al., 2019). Finally, MUC19 plays a role in ensuring the humidity of the respiratory tract (Das et al., 2010).

2. Mucins (MUC)

Mucins are among the first glycoproteins identified as biological compounds in the body. It has been reported that mucins are found in the saliva of nesting birds, such as swallows, and play an important role in the function of saliva and that sugars join the structural parts of mucin glycoproteins (Karaçalı, 2003; Corfield, 2017; Dhanisha et al. 2018).

In humans, it is found in the apical cell membranes of tissues such as the digestive, respiratory tract, and urogenital systems. In general, mucus is secreted to protect the respiratory, gastrointestinal, and reproductive tracts (Fowler et al., 2001; Bryd and Bresalier, 2004; Matte et al., 2019).

2.1. Structure of Mucins

Mucins are glycoproteins synthesized by epithelial cells. Its structure contains oxygen-dependent serine/threonine/proline-rich proteins. They are structures that bind with peptides lined up one after the other and have a high oligosaccharide content and high molecular weight. Mucins in a dense glycosylated state are among the macromolecules with viscoelastic properties. Mucins, which make up the main structure of mucus, are compounds that have all the properties of a protein and the properties of sugars under certain conditions (Aksoy, 2001; Joshi et al., 2018; Argüeso, 2022).

Mucins secreted by epithelial cells mature as they move from the base of the crypt of the luminal organs to the lumen. This maturation manifests itself in the form of a decrease in lysosomes, an expansion of the Golgi membranes, and an increase in the endoplasmic reticulum and mucin-secreting vesicles. The peptic core part of the mucin is collected in the ribosomes of the granular endoplasmic reticulum. From here, it is transported by non-granular endoplasmic reticulum channels and comes to the vesicles in the Golgi apparatus. After this stage, glycosylation occurs in the Golgi apparatus (Corfield, 2017; Svensson, 2018).

2.2. Functions of Mucins

The main function of mucins is to ensure protection and the lubricity of the luminal organs in the body. Mucins contribute to the adhesion of epithelial cells, differentiation, and renewal of cells by providing signal modulation. Membrane-bound mucins function as cell surface receptors for pathogens and help activate intracellular signaling pathways (Bonser and Erle, 2017, Bansil and Turner, 2018).

Mucins are involved in all physiological events as heavily glycosylated proteins, including inflammation, activation of the immune system, and tumor formation (Birchenough et al., 2015; Haugstad et al., 2015; Tassew et al., 2022).

In the glycosylation mechanism, mucins facilitate cell adhesion during tumor metastasis. It regulates the immune system's response, and it has also been reported that mucin can displace proteins according to the functions of proteins in the interaction of carbohydrates (Chaturvedi et al., 2008; Corfield, 2017).

2.3. Classification of Mucins and Areas of Action of Mucins

It has been stated that mucins are divided into membrane-bound mucins and secreted mucins. Secreted mucins are divided into gel-forming and non-gel-forming mucins have also been stated. (Fowler et al. 2001; Cha et al. 2015; Oh et al., 2015).

Table 1. Classification of mucins (Fowler et al. 2001; Cha et al. 2015; Oh et al. 2015).

Mucins		
Secretory Mucins		Membrane Associated
Gel-forming	Non-gel-forming	
MUC 2	MUC 7	MUC1
MUC 5AC	MUC 8	MUC3
MUC 5B	MUC9	MUC4
MUC 6		MUC10
MUC 19		MUC12
MUC 11		MUC13
		MUC16
		MUC17
		MUC18
		MUC20

2.3.1. Membrane-associated mucins

Membrane mucins are mucins in glycoprotein structure containing peptide domains, and it has been stated that they protect epithelial cells by being on the apical membrane of epithelial cells, provide cell interactions and play a role in signal transmission between cells with their cytoplasmic extensions (Van and Strijbis 2017).

Table 2. Histochemical staining for determination of mucins (Alan and Liman 2010).

Paints	Identified Mucin	Color
PAS	Neutral mucins, weak sulfate mucins	Purplish, red
PAS/D	Neutral mucins	Red
AB (ph2,5)	Sulfomucin ve sialomucins	Blue
PAS/AB, PAS	Neutral mucins	Red
(ph 2,5), PAS/AB	Mixture of neutral and acidic mucins	Purple
HID	Sulfomucin	Black/ Dark Brown
HID/AB, AB (ph 2.5)	sialomucins	Blue
(pH 2.5), HID/AB	Mixture Sulfomucin and sialomucins	Bluish brown
AF	Sulfomucin	Purple
AF/AB, AB (ph 2.5)	sialomucins	Blue
(pH 2.5), AF/AB	Mixture Sulfomucin and sialomucins	bluish purple
PAPS	Neutral mucins	No Staining
PAPS	Sialomucins	Purplish Red

PAS: Periodic Acid Schiff, **PAS-D**: Periodic Acid Schiff-Diastase, **AB-PAS**: Alcian Blue-Periodic Acid Schiff, **HID-AB**: High İron Diamine-Alcian Blue, **AF-AB**: Aldehyde Fuchsin-Alcian Blue, **PAPS**: Periodic acid- Phenylhydrazine-Schiff

2.3.1.1. MUC1

It is one of the subunits of the protective family of mucins and one of the mucins that are rich in serine and contain threonine deposits with intense O-glycosylation properties around proteins. They prevent proteins from sticking together. MUC1 is secreted from the apical part of the epithelial cells of many organs. In cancer cells, it occurs not only in the apical but also in the lateral or cytoplasm of the cell membrane (Cheever et al., 2009; Lakshminarayanan et al., 2016; Yousefi et al., 2019).

MUC1 is involved in the protection of cells by providing hydration of cell surfaces. MUC1 is an effective inhibitor in intracellular and extracellular matrix interactions. MUC1 has a highly dynamic structure in normal epithelial cells, which changes in response to the effects of steroid hormones or cytokines. The MUC1 gene is found as heavily glycosylated mucin on the apical surfaces of the simplest epithelial cells, including the urogenital system, GIS (Gastrointestinal system), respiratory system, and some non-epithelial cell types (Sakurai et al., 2007; Wu et al., 2018; Khodabakhsh et al., 2021). Mucins in the lungs have been secreted from goblet cells and mucous and serous cells in the submucosal glands (Kufe, 2009; Bafna et al., 2010; Menon et al., 2015).

2.3.1.2. MUC3

MUC3, one of the membrane-bound transmembrane mucins, is on the apical side of epithelial cells. They are macromolecules that protect epithelial tissues against harmful microorganisms with endogenous and exogenous origin by enveloping the cells in contact with the external environment, like capsules (Ho et al., 2006; Kumar and et al., 2022). MUC3 is present in excess in goblet cells and enterocytes of the small intestine (Lakshminarayana et al., 2016; Ratan et al., 2021).

It has been reported that MUC3 increases in the epithelial part of the appendix in cases of appendix cancer and plays a role as a determining factor in patients with appendix cancer (Shibahara et al., 2014).

2.3.1.3. MUC4

MUC4, also known as the Sialomucin complex or SMC, is more weakly expressed in tissues such as the respiratory tract, colon, cornea, female genital tract, and breast. It is rich in serine and threonine (Dharmaraj et al., 2014; Bansil and Turner, 2018). MUC4 begins to be synthesized in the digestive tract at 6.5 weeks of pregnancy, and its release increases with the increase of progesterone. It is found only in the trachea between 8-12 weeks of pregnancy. However, after the 12th week of pregnancy, it gradually increases in the small bronchi and bronchioles. It has been observed that it exists in the epithelial cell of the jejunum on the colon axis and the epithelial cells of the esophagus. It has been reported that there is an association between MUC4 and the differentiation to the squamous cell carcinoma stage. It has also been observed that MUC4 is not present in the liver, bile ducts, gallbladder, and pancreas during pregnancy. In adults, it is released in large quantities in

secretions of body parts such as the respiratory system, endolymph, and breast milk (Koscinski et al., 2006; Chaturvedi et al., 2008).

2.3.1.4. MUC11

MUC11 is a type of mucin produced from tandem repeats of 28 amino acids formed by the combination of serine, threonine, and proline. MUC11, which is one of the membrane-bound mucins, has been detected in the middle ear, thymus, lung, colon, pancreas, prostate, and uterus (Williams et al., 2001). The epithelial surface has various functions, including protection from pathogens that may cause infection, communication through intracellular signaling, cell differentiation, and cell proliferation (Hijikata et al., 2011). It is also thought to play a role in cystic fibrosis disease in lung tissue. It has been shown to prevent the adhesion of epithelial cells to each other in malignant tumors (Fowler et al., 2001; Hernandez-Jimenez et al., 2008).

2.3.1.5. MUC12

It is a type of mucin rich in proline, which is in the form of successive repetition of degenerate amino acids and has 28 amino acids in its structure. It is a methionine consisting of serine protein that contains epidermal growth factor and similar domains rich in extracellular cysteine. MUC12 is responsible for epithelial cell protection, adhesion modulation, and signal transduction (Önder, 2012; Alcântara et al., 2022).

2.3.1.6. MUC13

It is a membrane glycoprotein with high molecular weight. It has been reported that it is at a moderate level in the large intestine, trachea, and kidney, with the highest level in the small intestine. Also, it is crossover in stomach and mouse tissues and is found at an intermediate level in intestinal epithelial and lymphoid cells in situ hybridization (Pelaseyed et al., 2014; Pang et al., 2022).

MUC13 protein has been expressed in the GIS system and in the trachea's apical membrane of prismatic and goblet cells. The MUC13 protein is broken down into monomers in the GIS system and divided into two subgroups. The cytoplasmic tail of the protein containing the ß subunit, one of the monomer subgroups of the MUC13 protein, regulates gene expression in the nucleus by stimulating the protein kinase C signaling pathway (Williams et al., 2001; Corfield, 2017; Kumar et al., 2022).

2.3.1.7. MUC15

MUC15, a member of the mucin family, is a glycosylated substance found in lymphoid organs (thymus, spleen, bone marrow, etc.), placenta, testis, ovary, small intestine, colon, etc. has been identified as a transmembrane protein (Zhang et al.,2020).

2.3.1.8. MUC16

It is membrane-bound mucin and is also called CA125, which is a heavily O-glycosylated transmembrane protein (Giamougiannis et al., 2021). MUC16 is used to detect cystic fibrosis and various types of cancer. MUC16 has been found on the epithelial surface of the cornea, conjunctiva, respiratory tract, reproductive tract of the female, and on the epithelium of the tracheal surface as a component of the ocular surface (Aithal et al., 2018; Argüeso, 2022).

MUC16, together with MUC1 and MUC4, is involved in intercellular communication and intercellular signaling. MUC4 takes advantage of MUC16 to ensure that the cell surface glycocalyx of the ocular layer in the eye acquires hydrophilic properties. It protects the eye from foreign particles and infectious diseases. In addition, it helps to open and close the eyelid by ensuring the wetness of this area. In this way, it prevents dry eye disease (Menon et al., 2015; Lakshminarayanan et al., 2016; Li et al., 2018; Martens et al., 2018; Matte et al., 2019).

2.3.1.9. MUC17

In addition to gel-forming mucin, it is found on microvilli in the GIS system (small and large intestine), which are among the transmembrane mucins and have a brushy appearance. Microvilli here ensure the capture of foreign substances. It has been reported that it helps to protect against harmful toxins in the GIS system and to provide intracellular vesicle localization in epithelial cells. The carboxy-extremity of MUC17 in the GIS system contains a hydrophobic domain. This feature allows the cells to stick to each other on the apical surface of the tissue (Sakurai et al., 2007; Önder, 2012).

2.3.1.10. MUC18

MUC18 is also known as CD146. MUC18 is a transmembrane glycoprotein with a length of 113-kDa. MUC18, first found in malignant cells in humans, has also been detected in smooth muscle and endothelial cells in the airway wall of lung tissue in subsequent studies. It is noted that it defends the body against foreign microorganisms by activating T lymphocytes in the lung. It has been

determined that it protects the body against pathogens by creating an inflammatory response to pathogens in patients with COPD (Chronic obstructive pulmonary disease) and asthma (Simon et al., 2011; Sun et al., 2016).

2.3.1.11. MUC20

It has been revealed that it is responsible for the protection of epithelial cells on mucosal surfaces. It has a unique localization in the cell layers between multilayered epithelium cell types and throughout the epithelial cells of the human cornea and conjunctiva. During MUC20 differentiation, it is thought to be secreted from the ocular surface and to play an important role in keeping the wetness of this place in balance and maintaining this balance (Bafna et al., 2010). In epithelium ovarian cancer (EOC) cells, it activates integrin ß1 and provides signal transduction. In this way, it provides a new perspective on the role of signaling by resisting pathogens (Woodward and Argüeso. 2014; Chen et al., 2016).

2.3.2. Secretory Mucins

It has been reported that they can be divided into gel-forming and non-gel-forming mucins (Cha et al. 2015).

2.3.2.1. Gel-Forming Mucins

It has been stated that it has an viscoelastic feature, which has a supporting role in mucosal defense (Oh et al. 2015).

2.3.2.1.1. MUC2

It contains serine, proline, and threonine in its structure. It is intestinal-type secretory mucin mainly synthesized in goblet cells. It is considered to be biochemical insoluble mucin that causes high viscosity in the region where it is synthesized (Büyük, 2014; Birchenough et al. 2015 Liu et al., 2020).

It has been reported that MUC2 release in the lung is observed especially in mucinous adenocarcinomas (colon cancer) and its release increases in tumors related to the GIS system (Wang and El Bahrawy, 2015; Astashchanka et al., 2019; Liu et al., 2020). It is a marker that can be used in the diagnosis of ovarian tumors. It is secreted in mucinous tumors of the appendix and abdominal region. It has also been noted that it is the most secreted mucin in breast cancer (O'Connell et al., 2002; Lau, et al., 2004; Astashchanka et al., 2019).

2.3.2.1.2. MUC5AC

MUC5AC forms an internal mucus layer in organs such as the colon, pancreas, and stomach for the regulation of body fluids. It has been determined that it plays a role in protecting organs by increasing hydrochloric acid. It is gel-secreted mucin released from goblet cells in the lungs, eyes, and stomach, and was first reported to be detected in the middle ear (Büyük, 2014; Val et al., 2015; Bonser at al., 2017; Ratan et al., 2021).

MUC5AC has been reported to increase in endocervical cancers and has also been observed in other adenocarcinomas, endometrium, and lung adenomas (Lau et al., 2004; Bonser and Erle et al., 2017; Okuda et al., 2019).

2.3.2.1.3. MUC5B

It is one of the macromolecular proteins containing polymers, monomers, and glycopeptides in its structure. It has been reported that this mucin is secreted in saliva, normal lung mucus, and the cervical region, making a significant contribution to the viscoelastic property of the structures here (Val et al., 2015; Joshi et al., 2018; Ratan et al., 2021).

MUC5B mucin has been detected in regulated chronic rhinosinusitis (CRS), chronic obstructive pulmonary disease (COPD), a gastric disease associated with *Helicobacter Pylori,* and sinus mucosa diseases and has been reported to play a role in the pathogenesis of these diseases (Wang and El-Bahrawy, 2015; Evans and et al., 2016; Hughes et al., 2019).

2.3.2.1.4. MUC6

It occurs in Brunner's glands and pancreatic ducts during 18-19 weeks of pregnancy. Its presence was determined also in the gastric glands during the 20th week of pregnancy. It has been reported to be present in the stomach mucosa, the gallbladder, seminal vesicles, pancreatic centroacinar cells, and the periductal area of the bile duct. It may have the function of preserving epithelial tissues (Wang and El-Bahrawy, 2015).

MUC6-related diseases: pancreatic ductal carcinomas and bile papillomatosis (Matte et al., 2019).

2.3.2.1.5. MUC19

It is among the most recently discovered gel-forming mucins. It is present in the submucosal glands and within the secretion in the middle ear (Kerschner et al., 2009; Kumar et al., 2022).

It is a type of mucin that acts as an exocrine in the sublingual mucus and salivary glands in mice. MUC19 plays a role in maintaining the wetness of the respiratory tract and against irritations caused by nutrients (Das et al., 2010).

2.3.2.2. Non-Gel-Forming Mucins

It has been stated that it is divided into two as MUC7 and MUC8 (Dhanisha et al., 2018).

2.3.2.2.1. MUC7

The increase of MUC7 in the glycosylation mechanism leads to mucins settling in an abnormal order, increasing the potential for tumor invasion and metastasis (Büyük, 2014). It is secreted from the mucous cells of the submandibular and sublingual salivary glands and is thought to give the saliva a viscous property (Önder, 2012). The presence of MUC7 has been detected in respiratory secretions in asthmatic patients and pediatric patients. Thus, it prevents foreign bodies from entering the body in the respiratory system (Ratan et al., 2021).

2.3.2.2.2 MUC8

It was first detected in 1994 thanks to a successive series of repeating cDNA tandems (Shankar and et al., 1994). It contains many cysteines and consecutive serine and threonine in its structure. It has been reported that it helps to secrete mucus for healing respiratory diseases by stimulating an adipocytokine synthesized by white adipose tissue in the epithelial cells of the respiratory tract. It has also been found that MUC8 increases in the lungs of cystic fibrosis patients (Finkbeiner et al., 2011; Cha et al., 2015).

2.3.2.7. MUC9

MUC9, also known as Oviductin, is secreted in large quantities in the female's oviducts by the influence of the estrogen hormone. It is responsible for the protection of the oviducts of the female and the developing embryo. It is also considered to play an important role in the development of the embryo. It has also been reported to be a marker for the diagnosis of ovarian cancer (Hendrix et al., 2001; Laheri et al., 2017). MUC9 is thought to have positive effects on sperm capacity, motility, and viable cell in sperm in mammals. It has also effects on sperm-egg fusion and ovum penetration (Zhao et al., 2022).

2.4. Histochemical Classification of Mucins

They are divided into two, including acidic mucins and neutral mucins (Yakan, 1990; Ali et al., 2012).

A. Acidic mucins

Sulfate Mucins (Sulfomucin)

- Strongly sulfated acidic
- Strongly sulfated epithelial mucin
- Atypical sulfated mucins

Carboxylated mucins (sialomucins)

- Carboxylated mucins
- Sulfated sialomucins
- Hyaluronic acid

B. Neutral mucins

2.4.1. Acidic Mucins

Acidic mucins are classified into two parts among themselves. It has been stated that acidic mucins play a protective role by preventing the passage of microorganisms, such as bacteria-originating viruses and fungi. In addition, it has been reported that they help leukocytes to be transported to the target organ in growth factors, cell development, and signal transmission (Saruhan et al., 2016).

2.4.1.1. Sulfate Mucins (Sulfomucin)

- **Strongly sulfated acidic** mucins are found in connective and supporting tissue and stain negatively with Periodic acid-Schiff (PAS) and positively with Alcian blue (Ph 2.5).
- **Strongly sulfated epithelial mucin** appears in the serous bronchial glands and is positively stained with PAS.
- **Atypical sulfated mucins** are located in the bronchial glands in the trachea and stained with Alcian blue (Ph 2.5) (Yakan, 1990; Anđelković et. al., 2009).

2.4.1.2. Carboxylated (Sialomucin)

- **Carboxylated mucins** are present in the salivary gland and small intestine and are negatively stained with PAS.
- **Sulfated sialomucins** are found in prostate cancer.
- **Hyaluronic acid** is present in goblet cells in connective tissue (Yakan, 1990; Anđelković et. al., 2009).

2.4.2. Neutral Mucins

It has been stated that neutral mucins, which are composed of various hexosamines combined with free hexose groups, contain mannose, galactose, and monosaccharides in their structure. It is of the epithelial type and is most commonly found in the Brunner glands, in the mucus secreted by the epithelial cells lining the stomach, and it is stained with alkaline dyes. It was also reported that they

did not react with alcian blue but gave a positive reaction with PAS (Suvarna et al., 2013; Ghiurce et al., 2021)

2.5. The Relationship of Mucins with diseases

2.5.1. The Relationship of Mucins with Cancer

The carbohydrate sequencing of mucins in the tissues of a healthy individual is happening linearly. But the carbohydrate sequencing of mucins in tissues that encounter cancer manifests itself in the form of intermittent disconnections. Because of these properties, it causes cancer cells to spread directly out of the tissue where the mucins are located or to other areas through blood and lymph vessels (Haugstad et al., 2015).

Mucoepidermoid carcinoma (MEC) is the most common tumor in the salivary gland. Shemirani et al. studied salivary gland tumors and analyzed MUC12, MUC13, MUC17, MUC18, and MUC19 genes in twenty-three patients using PCR and RT-PCR techniques. It was reported that MUC19 was 26% in normal tissue. Still, when encountered with tumor cells, the rate of MUC19 in the tissue increased by 65%, the distribution of MUC18 in tumor and normal tissues was equal, MUC12 and MUC17 mucin were not seen at all in MEC, MUC13 is at the rate of 0% in normal tissue without disease and increased by 13% when the disease was encountered, MUC1 and MUC4, on the other hand, increased 21 folds more in the case of illness compared to the normal tissues (Shankar et al., 1994, Shemirani et al.,2011).

2.5.2. The Relationship of Mucins Pancreatic Cancer

Pancreatic cancer is one of the most important diseases that ranks fourth in mortality in the world. It has been reported that the uncontrolled increase of MUC1MUC4, MUC5AC and MUC16, which are transmembrane and secretory mucins, in pancreatic tissue causes pancreatic cancer (Kaur et al., 2013).

2.5.3. The Relationship of Mucins Covid-19

Covid-19 disease was reported in 2019 as a highly contagious respiratory disease. It has been stated that mucins play an important role in the diagnosis of covid-19 disease. It was stated that especially the MUC5AC, MUC5B and MUC1 mucins were found to be excessively increased in sputum content in the trachea region of Covid -19 patients (Bose et al., 2020; Lu et al., 2021).

2.5.4. The Relationship of Mucins Asthma

It has been stated that asthma is one of the lung diseases characterized by the obstruction in the airways caused by the combination of many factors, including mucus-producing cells, lipids, and proteins (Mirershadi et al. 2020). It has been stated that MUC5AC and MUC5B in the respiratory tract play an important role. It has been reported that MUC5AC increase and MUC5B decrease cause acute asthma by creating airway obstructions (Welsh et al., 2017).

2.5.5. The Relationship of Mucins Ulcerative Colitis

It is an Inflammatory Bowel Disease characterized by persistent inflammation of the large intestine. It has been reported that MUC2 mucin is expressed in the colon in healthy individuals and individuals with ulcerative colitis. It has been stated that goblet cells in the large intestine play a role in MUC2 expression and excretion. It has been stated that goblet cells are decreased as a result of mucosal damage in ulcerative colitis disease, resulting in a decrease in mucin production. It has been suggested that microbes infiltrate the mucosa excessively, increase inflammation and cause disruption of the integrity of the mucosal barrier. It is stated that it may play a role in the occurrence of ulcerative colitis as a result of the lack of mucin production (Van et al., 2019; Bankole et al., 2021).

2.5.6. The Relationship of Mucins Dry Eye Diseases

Surface epithelial cells have been reported to secrete glycosylated membrane-associated mucins, such as the glycocalyx, MUC1, MUC4, and MUC16, which form a hydrophilic barrier for eye protection, lubrication, and homeostasis. It has been stated that galectin-3 interacts from the anterior surfaces of the conjunctiva and cornea thanks to these mucins glycosylation, preventing the entry of pathogens into the eye, reducing friction during clipping, and keeping the eye wet. It has been stated that it is associated with the emergence of dry eye disease as a result of defects in the production of mucins (Baudouin et al., 2019; Jin et al., 2022).

2.5.7. The Relationship of Mucins Dental Caries Diseases

It has been reported that MUC5B and MUC7 play a role in salivary mucins. It has been indicated that mucins bind to bacteria in the mouth and play a role in removing the bacteria from the mouth. For this reason, it has been pointed out that the decrease in

mucins in the mouth causes infections and inflammations, which plays a role in the thinning of the intraoral epithelial barriers, bleeding of the gums, and the emergence of dental caries (Linden et.al. 2009; Rusthen et. al., 2019).

CONCLUSION

Mucins must be investigated in more detail regarding providing moisturization of epithelial cell surfaces, epithelial cell renewal, and differentiation, intracellular signal transduction, cell adhesion, protection of body tissues against infections and injuries, as well as usability as a marker in the detection of cancer cells in some cancerous tissues.

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