# Mucins

Mucins are large, highly glycosylated proteins containing tandem repeats of amino acids that are rich in serine and threonine.

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# MUCINS

J.A. Voynow, B.M. Fischer, in Encyclopedia of Respiratory Medicine, 2006

Mucins are the major macromolecular components of mucus. Each mucin has a unique and characteristic sequence of tandemly repeating amino acids rich in serine and/or threonine. The tandem repeat domain is the primary region for *O*-linked glycosylation of the molecule. There are at least 20 different mucin genes (*MUC*) classified into two families: secreted and membrane-associated. At least 12 *MUC* genes are expressed in the respiratory tract and at least six MUC glycoproteins have been detected in lung tissue. A variety of stimuli including bacteria, cytokines, proteases, and pollutants regulate *MUC* gene expression; this regulation occurs at both the transcriptional and posttranscriptional level and is mediated by several intracellular signaling cascades. The functions of mucins in the healthy lung are currently being elucidated. Secreted mucins act as a shield protecting the airway epithelia. Owing to their structure and charge, mucins may influence hydration at the cell surface. Their complex oligosaccharide structures may function as ligands for cellular lectins; mucin binding permits mucociliary clearance of pathogens and prevents access to the cell membrane. Membrane-associated mucins may interact via epidermal growth factor-like domains or cytoplasmic tails with receptor tyrosine kinases, activating intracellular signaling, and regulating gene expression. In chronic inflammatory airway diseases, overproduction and hypersecretion of mucin glycoproteins contribute to airway obstruction. In several cancers, aberrant expression and

glycosylation of mucins contribute to tumor survival and proliferation. Thus, mucin structures play a critical role in determining their functions in health and disease.

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# Mucins

Brendan Dolan, Gunnar C. Hansson, in Reference Module in Life Sciences, 2021

## *O*-Glycans

All mucins are highly glycosylated, often comprising more than 80% of their mass. This means that outer surface of mucins and especially the mucin domains will appear as large glycan assemblies. Although mucins have, as other secreted proteins, some *N*-linked glycans, the vast majority of glycans are of the *O*-glycan type. The first glycan added is the GalNAc to the hydroxyl group of the amino acids Ser and Thr by the peptidyl-GalNAc transferases (ppGalNAcTs) (Bennett *et al.*, 2012). Once this first monosaccharide has been attached, this acts as an anchor for other glycosyltransferases adding Gal or GlcNAc to the C-3 or C-6 hydroxyl group of the GalNAc. These are the substrates for further addition of monosaccharides and sulfate groups to build short or long, more or less complex oligosaccharides.

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# PATHOPHYSIOLOGY OF GASTROINTESTINAL MUCINS

Adel Gad, in Gastrointestinal Defence Mechanisms, 1981

## SUMMARY

Mucins of the human gastrointestinal tract can no longer be thought of merely as a mechanical lubricant or an innert protective barrier. The increasing interest in mucins shared by molecular biologists, oncologists and experimental pathologists led during the last few years to the accumulation of vast knowledge about the biological significance of these secretions. Mucins reflect in their composition changes in the functional state of the mucosa in health and disease.

After an introduction, a brief account dealing with the nomenclature, structure, biosynthesis and degradation of mucins is given. This is followed by an outline

of the histochemical and biochemical characteristics of gastrointestinal mucins of man and mouse under normal conditions and in some disease states. Against this background, the function of the different types of gastrointestinal mucin is reviewed and some areas for future research are suggested.

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# Ocular Mucosal Immunity

Nancy L. O'Sullivan, Paul C. Montgomery, in Mucosal Immunology (Fourth Edition), 2015

## The Glycocalyx

Mucins can be divided into two subfamilies—the secreted gel-forming mucins and the membrane-tethered mucins. The three major membrane-tethered mucins produced by corneal and conjunctival epithelial cells are MUC1, MUC4, and MUC16 (Govindarajan and Gipson, 2010). The extracellular domains of MUC4 are constitutively shed into the tear film; thus, they are a component in the mucous/aqueous layer. The membrane-tethered mucins of the corneal and conjunctival glycocalyx are multifunctional proteins that (1) facilitate tear film spreading and ocular surface wetting; (2) act as an antiadhesive that prevents adherence of foreign debris, cells, or pathogens; (3) act as a selective barrier to the penetration of molecules; and (4) signal through their epidermal growth factor (EGF) domains or their cytoplasmic tails (Govindarajan and Gipson, 2010).

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# Protein Modifications | Mucin Family of Glycoproteins☆

R.B. Brown, ... Jason E. Schaffer, in Encyclopedia of Biological Chemistry (Third Edition), 2021

## Abstract

Mucins are large glycoproteins expressed by epithelial membranes and as components of the mucus secretions that cover epithelia in harsh environments – the air–water interface of the respiratory system, the acidic environment of the stomach, the complex environment of the intestinal tract, and secretory epithelial surfaces

of specialized organs such as liver, pancreas, kidneys, gall bladder, salivary glands, lacrimal glands, and eye. Mucins are critical in maintaining homeostasis in environments that fluctuate in molecular composition – including pH, ionic concentration, oxygenation, and hydration. The molecular composition and higher-order structures of mucins offer specialized functions in the external environment, while relaying information about the environment to the cell via signal transduction through membrane-associated mucins.

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# Tear Film Overview

M. Uchino, K. Tsubota, in Encyclopedia of the Eye, 2010

## The Structure and Function of Mucous Layer of the Tear Film

Ocular mucins provide lubrication to the ocular surface, allowing the eyelid margins and the palpebral conjunctiva to slide smoothly over one another with minimal friction during blinking and ocular rotational movements. Another important function is protection of the epithelial surfaces by covering foreign bodies with a slippery coating, thus protecting the cornea and conjunctiva.

The last 10 years have seen remarkable progress in understanding the structure and character of mucins which are heavily glycosylated glycoproteins with 50–80% of their mass comprised of carbohydrates. Molecular cloning and sequencing of genes encoding mucin apoproteins have extended the definition of glycoproteins from, "mucins are large molecules that have as their major mass carbohydrate" to include the fact that they have tandem repeats of amino acids rich in serine and threonine in their protein backbone that serve as sites for *O*-glycosylation.

Mucins have been given number designation in order of their molecular characterization. To date, although 20 numbers have been assigned, cloning has shown that several mucins are in fact the result of different gene products. For example, MUC3 and MUC5 have now been redesignated to include MUC3A, MUC3B and MUC5AC, and MUC5B.

Mucins can be either secreted or associated with the cell surface. The membrane-associated mucins form the scaffold for the mucous layer. The secreted mucins can either be small soluble mucins or large gel-forming mucins. They are stored in secretory granules in the condensed form and secreted with the appropriate stimulus. Soluble mucins are smaller in molecular weight than the gel-forming mucins, but are stored and secreted similarly to them.

Multiple mucins have been identified in tears and localized to corneal or conjunctival epithelial cells. The gel-forming mucin MUC5AC is secreted solely by the goblet cells. The membrane-bound mucins MUC1, MUC4, and MUC16 are produced in the stratified squamous cells of both the cornea and conjunctiva. In addition, the cornea and conjunctival epithelia also produce MUC2 and MUC7, and other membrane-bound mucins.

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# Mucin Family of Glycoproteins

Juan Perez-Vilar, Robert L. Hill, in Encyclopedia of Biological Chemistry, 2004

## Definitions

Mucins are structurally diverse but share similar structural features. One region of the polypeptide backbone of mucins has an amino acid sequence rich in threonine and/or serine residues that is repeated several times. O-linked oligosaccharide chains are covalently bound to these residues, resulting in the formation of highly glycosylated domains, known as the tandem repeat domains, O-glycosylated domains, or just mucin domains. Because proline residues are commonly found in the mucin domains, they are also known as PTS domains. The term mucin domain is preferred because it is not in conflict with the existence of nonglycosylated repeated domains in many mucins, O-glycosylated regions in the polypeptide chains of many glycoproteins, and mucins (e.g., MUC2) with either serine or threonine residues, but not both, in their mucin domains.

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