

## Gene Section

### Review

# MUC17 (mucin 17, cell surface associated)

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## Identity

**Hugo:** MUC17

**Other names:** MUC3; mucin-17; mouse Muc3; small intestinal mucin MUC3; membrane mucin 17; secreted mucin 17; intestinal membrane mucin MUC17

**Location:** 7q22.1

**Note:** Mucin glycoproteins are a diverse family of high molecular mass, heavily glycosylated proteins differentially expressed in epithelial tissues of the gastrointestinal, reproductive and respiratory tracts. Membrane mucins such as MUC17 are expressed by epithelial cells to provide protection, maintain luminal structure, and provide signal transduction. Often these molecules are over- or aberrantly expressed in cancers of epithelial origin. Mucins confer anti-adhesive properties in cancer cells that lose their apical/basal polarization. They also provide adhesive properties towards endothelial cells favoring dissemination of mucin expressing cancer cells.

MUC17 is a recently fully characterized mucin that belongs to the membrane-bound subfamily of mucin (Moniaux et al., 2006). It is a cell surface glycoprotein that is found on epithelial cells in select tissues of the body (wade need to precise the know profile). Its structure consists of an extracellular domain that extends above the cell surface and an intracellular domain of 80 amino acid residues. New evidence suggests its de-regulation in pancreatic cancer (Moniaux et al., 2006; Moehle et al., 2006). The first partial length cDNA sequence, now known to correspond to MUC17, was identified by Van Klinken et al. (1997). At that time, van klinken isolated a chimeric cDNA clone overlapping MUC3 specific tandem repeat sequence and a new 59 aa sequence

repeated in tandem. This sequence was therefore believed to be part of MUC3 until Gum and collaborators identified the carboxy terminal sequence of the 59 aa tandem repeat and identified this sequence has part of a new mucin called MUC17. Indeed, in 2002, driven with the hypothesis that the 177 bp tandem repeated sequences were part of a new unidentified mucin, Gum et al. screened the public GenBank™ database and the proprietary Lifeseq Gold database (Incyte Genomics Inc., CA). By database searching and RT-PCR they extended the partial mucin sequence found during analysis of MUC3 and cloned a MUC17 fragment of 3,807 bp (accession number AF430017) (Gum et al., 2002). In 2006, Moniaux and Junker reported the complete coding sequence and organization of the MUC17 gene (Moniaux et al., 2006).

## DNA/RNA

**Note:** MUC17 was identified and localized to chromosome 7q22 by radiation hybridization mapping (Gum et al., 2002) where it resided in a gene cluster with mucins MUC3A, MUC3B, and MUC11/12 (Figure 1). These mucins reside next to each other and have function in intestinal epithelium integrity, but are expressed in other different tissues and likely have different functions as well. The mucin genes within the cluster are transcribed independent of one another. MUC17 shows a low degree of VNTR (variable number of tandem repeats) polymorphism with only three different genomic DNA sizes detected for the large tandemly repeated extracellular domain in 24 cancer lines (pancreas, colon, and breast) and in four healthy individuals control samples (Moniaux et al., 2006).

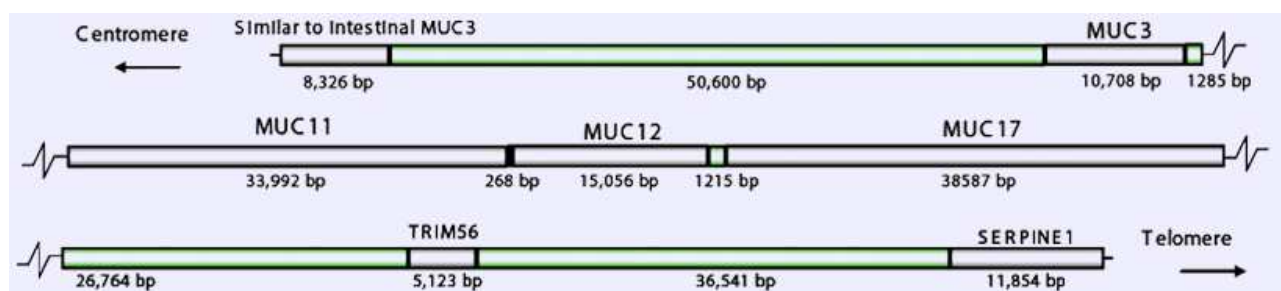


Figure 1

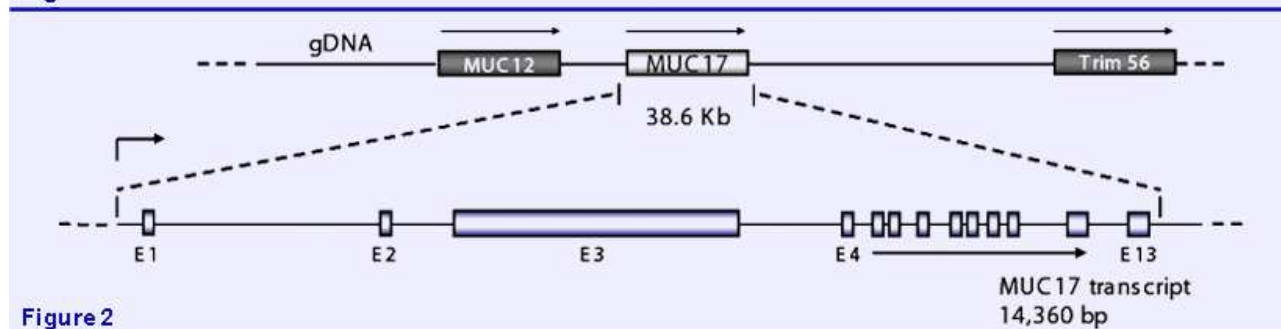


Figure 2

**Figure 1** - Chromosome location within the 7q22 mucin gene cluster.

MUC17 resides in a gene cluster with mucins MUC3A, MUC3B, and MUC11/12 on chromosome 7 in the region q22.1. Upstream of the gene cluster 50 Kb is a potential open reading frame that shares similarity to MUC3. Approximately 26.7 Kb downstream of MUC17 reside TRIM56 and SERPINE1. Less than 1.2 Kb of genomic distance separates the 3' end of MUC12 from the beginning of MUC17.

**Figure 2** - MUC17 genomic and transcript bp size.

The MUC17 gene encompasses (38,587 bp) 38.6 Kb of genomic sequence. The coding sequence contains 13 exons and is transcribed as a (14,360 bp) 14.4 Kb RNA that gives rise to full-length MUC17. The presence of an alternative splice site results in exclusion of exon 7, and produces a processed RNA that gives rise to a shorter MUC17/SEC.

## Description

Radiation hybridization mapping was performed using the GeneBridge4 radiation hybrid panel (Research Genetics, Huntsville, AL). Following hybridization, the MUC17 probe was detected in the panel of 93 independent human/hamster fusion clones with MUC17 specific primers, and data were analyzed using the GeneBridge4 server. This analysis indicated linkage to markers on chromosome 7q22 with an LOD score of 15. The presence or absence of MUC17 was concordant with STS (Sequence Tagged Site) marker D7S666 in 83 of 84 panel DNA samples that were unambiguous for both markers, thus positioning MUC17 near base 101,250,000 of chromosome 7 using the National Center for Biotechnology Information (NCBI) STS map. The NCBI electronic PCR server refined the interval to bases 98,871,000 and 99,054,000 of the STS map and positioned MUC17 approximately 2,000,000 bases telomeric of MUC3A on 7q22 (Gum et al., 2002).

The MUC17 sequence has now been extended toward its 5'-extremity to complete the sequence and localize the promoter and regulatory elements. Rapid amplification of cDNA ends (RACE) and sequences from the Human Genome databases were used. The MUC17 gene is located within a 39-kb DNA fragment between MUC12 and SERPINE1 on chromosome 7 in the region q22.1 (Moniaux et al., 2006).

## Transcription

The MUC17 full-length coding sequence is transcribed as a (14,360 bp) 14.4 Kb mRNA encompassing 13 exons from a (38,587 bp) 38.6 kb genomic fragment (Figure 2). Alternate splicing generates two variants coding for a membrane-anchored and a secreted form of the protein (Moniaux et al., 2006) (Figure 3). The presence of an alternative splice event/site in the 3'-extremity of MUC17 was investigated by RT-PCR. RT-PCR was carried out on AsPC-1 cDNA. The generated amplification products were cloned into pCR® 2.1 and screened. Two distinct fragments were identified through sequencing. One of the fragments was 100% identical to the previous referenced sequence of MUC17 (accession number AJ606307). The second product revealed the occurrence of an alternative splice event that resulted in the skipping of exon 7. This alternative splice event generated a frame-shift which coded for the 21 (MUC17/SEC) specific amino acid residues and introduced a stop codon positioned 66 nucleotides after the junction. The resulting protein encodes a secreted form of MUC17 (accession number AJ606308), lacking the second EGF domain, the transmembrane domain and cytoplasmic tail (Figure 3). RT-PCR was carried out in four distinct cell lines, (pancreatic AsPC-1, and colonic LS174T, CaCo-2, and Ls180), representing different tissues, i.e. pancreas and colon (Moniaux et al., 2006). Two

amplification products were detected. Sequencing of the major amplification product identified it as the MUC17 sequence described by Gum et al. (accession number AF430017), while the other amplicon (minor) corresponded to an alternatively spliced variant (skipping of exon 7), the secreted form of MUC17, referred to as MUC17/SEC. The level of expression of MUC17/SEC seemed very low in the cell lines investigated; the intensity of the corresponding band was very faint as compared to the MUC17 fragment (Moniaux et al., 2006).

MUC17 is expressed in select cell lines including pancreatic AsPC-1 and HPAF-II; and colon cancer cell lines LS174T, Caco-2, NCI-H498, and HM3 (Gum et al., 2002; Moniaux et al., 2006). Tissue expression was first shown by RNA dot blot analysis (Clontech multiple tissue expression blot). MUC17 is expressed in intestinal tissues, with the highest levels found in the duodenum (highest level) and in the transverse colon (85% of the level detected in duodenum). The only non-intestinal tissues found to express MUC17 in this analysis were stomach and fetal kidney. Both tissues showed approximately 7% of the expression level detected in the duodenum (Gum et al., 2002). In-situ hybridization was conducted to determine the cell specificity of MUC17 expression in the small intestine. In-situ hybridization showed MUC17 expression predominantly in the apical region of villi absorptive cells. Barely detectable expression was found in immature cells of the crypts. No expression was detected in goblet cells (Gum et al., 2002). Therefore, MUC17 expression is localized to the mature, absorptive cells of intestinal villi epithelium and is expressed in pancreatic cancer tissue (Moniaux et al., 2006).

The MUC17 gene is located within a 39 kb DNA fragment between MUC12 and SERPINE1 on chromosome 7. Approximately 1.2 Kb of sequence lies between the 3' end of MUC12 and the 5' UTR of the MUC17 gene. Expression of MUC17 is regulated by this 1,146-bp fragment upstream of MUC17 which contains various VDR/RXR, GATA, NFkB, and Cdx-2 response elements. Like mouse *Muc3* (mMUC3), regulation of expression is controlled by both growth factors and cytokines (unpublished data, Junker and Batra, 2007). The mMuc3 promoter has consensus binding sites for AP1, CREB, SP1, NF kappa B, GATA binding protein, and Cdx. Reporter constructs demonstrate that IL-4, IL-6, EGF, and PMA increase mMuc3 promoter activity 35-58% of control levels. TNF-a and IFN-g showed a lesser degree of stimulation (Shekels et al., 2003). Regulation of mMuc3 by cytokines and growth factors suggests an active role of mouse *Muc3* and its human homologue, MUC17 in intestinal mucosal defense.

A recent study conducted by Moehle et al. (2006) concerned the aberrant expression and allelic variants of mucin genes associated with inflammatory bowel

disease (IBD). The aim of the study was to characterize changes in the expression profiles of genes related to intestinal epithelial function by comparing biopsy samples from patients with Ulcerative Colitis (UC) and Crohn's disease (CD), to controls; as the loss of intestinal mucosal integrity is an important factor in IBD.

DNA-microarray analysis was applied and showed that mucin genes are differentially regulated in CD and UC. The loss of intestinal integrity is an important factor in the pathogenesis of inflammatory bowel disease. A coordinate down regulation of mucins was observed in a pool of biopsy RNAs (n=4) taken from affected and unaffected (control) regions of the terminal ileum and colon of CD and UC patients. No expression in the biopsy samples was detected for MUC6, MUC7, MUC8, MUC9, MUC11, MUC15, MUC16, and MUC18. Highest mucin expression values were displayed by MUC2, MUC13, and MUC17 in the ileum and the colon, while MUC12 was expressed in the colon. The relative expression levels for MUC1, MUC2, MUC4, MUC5B, MUC12, MUC13, MUC17, and MUC20 showed strong down regulation with decrease factors ranging from -1.3 to -48.5 fold. MUC17 showed a -4.3 and -2.6 fold decrease in Crohn's disease and Ulcerative Colitis respectively in the colon, but showed an apparent increase of 1.2 and 1.1 fold respectively in the same diseases in the ileum biopsy pooled RNAs.

Real-time RT-PCR TaqMan assays were conducted to obtain a specific overview of mucin expression in human tissues. An initial analysis of nine mucin genes in a panel of 26 different tissues was completed. The authors confirmed the relative expression values (average intensity) of DNA-microarray data (i.e., higher expression levels of MUC4, MUC5B, MUC12, and MUC20 were obtained in the colon compared to the ileum RNA; MUC17 was expressed higher in the ileum than in the colon). A meta-analysis of 11 genome-wide linkage studies for IBD revealed 38 significant IBD loci (Brant et al., 2004). Interestingly, all mucin family member loci reside within or directly beside these IBD candidate loci. Therefore, Moehle et al. performed allelic discrimination of one candidate exonic SNP within each mucin gene in UC (n=220), CD (n=181), and control (n=250) patient samples. Significant associations were detected for the MUC2, MUC4, and MUC13 mucin SNPs. The von Willebrand Factor (vWF) domain of MUC2 (11p15, A/G, V116M) is associated with CD, the vWF domain of MUC4 (3q29, G/T, A585S) with UC, and the cytoplasmic tail domain of MUC13 (3q13.1, A/C, R502S) with UC. Unassessed SNPs in the mucin genes may still be associated and remain unchecked.

The abundance of NFkB sites present in mucin promoters prompted the authors (Moehle et al., 2006) to explore regulation of mucin expression in the LS174T colon cell line model. The ligands TNF-a,

TGF $\beta$ , and LPS induced expression of MUC17 as assayed by quantitative real-time PCR. TNF- $\alpha$  was able to induce a time-dependent up-regulation of all the monitored mucin genes (MUC-1, -2, MUC-5AC, -5B, -12, -13, -17, -20). All monitored mucin genes showed increased expression with TGF $\beta$  treatment. Cooperation of NF $\kappa$ B with TGF $\beta$  signaling has been reported (Jono et al., 2002). Co-incubations of TGF $\beta$  with NF $\kappa$ B pathway inhibitors (CAPE and MG132) resulted in a decrease of mucin expression, thus demonstrating a link between these two pathways with regards to mucin gene regulation.

Treatment of the Ls174T colon cancer cell line with sodium butyrate had little or no effect on induction of MUC17 expression level but did induce expression of MUC3 which is not highly expressed in the cell line (Gum et al., 2002). Similarly, incubation of MUC17 non-expressing cell line, MiaPaCa, with HDAC inhibitor 5-aza-cytosine had little effect if any on MUC17 expression.

## Protein

**Note:** 4493 aa; 425.5 kDa (note: without modification such as glycosylation)

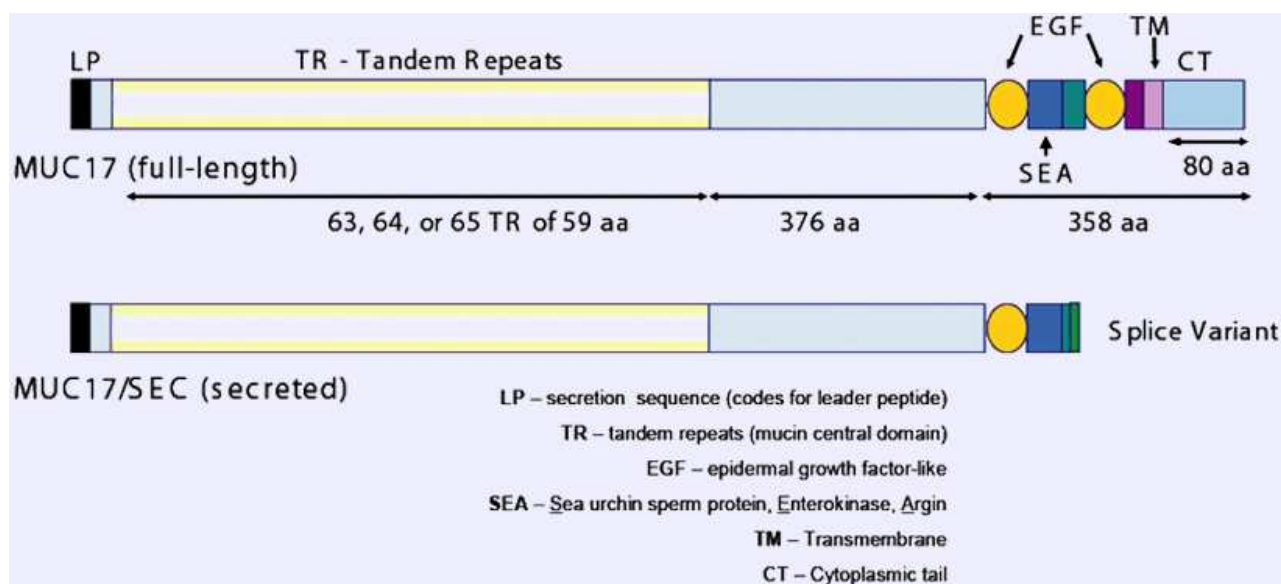
### Description

MUC17 is classified as a membrane-bound mucin glycoprotein. The protein may serve as a cellular receptor. The deduced full-length membrane-bound amino acid sequence (4493 aa) shows the presence of various mucin domains (Figure 3). A signal sequence

targets the protein to the plasma membrane. The majority of the molecule encodes the mucin central domain that is modified extensively by glycosylation and is displayed on the extracellular face of the cell. The central domain of MUC17 contains 63 repeats of 59 amino acid sequence (177 bp) that are repeated in tandem. This tandem repeat 'central domain' is followed by a region of unique degenerate tandem repeats and mucin-like sequences (i.e. that are repetitive, G/C rich, and contain a high content of threonine, serine, and proline amino acids). Two EGF-like domains flank both sides of a SEA module and precede the transmembrane domain. Putative N-glycosylation sites occur near the carboxyl terminus. The 80 amino acid C-terminal cytoplasmic domain has potential serine and tyrosine phosphorylation sites.

### Expression

RNA blot analysis and RT-PCR suggests MUC17 is expressed in the digestive tract, primarily in the duodenum (highest level) and the transverse colon (85% of the level detected in duodenum) (Gum et al., 2002). Expression is also reported in the terminal ileum (Moehle et al., 2006) with MUC17 expressed higher in the ileum than in the colon (quantitative RT-PCR, microarray analysis). Many colon and pancreatic cancer cell lines do express varied levels of MUC17 (Gum et al., 2002; Moniaux et al., 2006). An over-expression of MUC17 by Western blot and immunohistochemical analyses in pancreatic tumor cell lines and tumor tissues compared to normal pancreas samples is seen (Moniaux et al., 2006).



**Figure 3** - full length MUC17 and secreted MUC17/SEC.

Full-length MUC17 contains a 25 amino acid leader peptide (secretion, membrane targeting signal), a central domain with tandemly repeated sequence, two EGF-like domains, a SEA domain, transmembrane domain, and an 80 amino acid cytoplasmic tail domain. Usage of an alternative splice site excludes exon 7 and introduces a frame shift that creates a premature stop codon 66 nucleotides after the splice junction, within the SEA domain coding sequence. This shorter transcript results in a secreted form of the protein, MUC17/SEC, which has 21 unique C-terminal amino acids, and lacks the second EGF domain, transmembrane domain, and C-terminal cytoplasmic tail.

## Localisation

Surface localization of the smaller subunit of MUC17 is reported to be dependent on its N-glycosylation status (Ho et al., 2003). MUC17 contains a SEA domain, a transmembrane domain, and putative N-glycosylation sites in the carboxyl terminus. Mucins that possess a SEA domain usually undergo an auto-proteolytic cleavage event within the domain (Macao et al., 2006) to yield two subunits, the smaller of which is associated with the surface membrane. Ho and colleagues reported that the ASPC-1 pancreatic cancer cell line shows three main bands (38, 45, and 49 kDa) of immunoreactivity with an antibody directed against a site downstream of the postulated SEA cleavage site (Ho et al., 2003). Treatment with N-glycan specific hydrolases showed the 38 kDa band contained high mannose glycans, whereas the 45 and 49 kDa bands contained complex-type glycans. Surface biotinylation studies revealed that only forms possessing complex-type N-glycans were localized to the cell surface. Both tunicamycin (N-glycosylation inhibitor) and brefeldin A (an inhibitor of protein transport) reduced surface localization. Surface localization of the smaller subunit of MUC17 therefore appears to be dependent on its N-glycosylation status in ASPC-1 pancreatic cancer cells. Immunohistochemical analysis of mouse Muc3 (the homologue of MUC17) revealed strong staining in goblet cells and patchy staining of surface columnar cells in the duodenum, small intestine, caecum, colon and rectum (Shekels et al., 1998). Northern blot analysis indicates that the mRNA is approximately 13.5 kb. Highest expression was detected in the caecum with lesser amounts detected in the colon and small intestine. No message was found in mouse stomach, trachea, lung, kidney, esophagus or pancreas (Shekels et al., 1998). In-situ hybridization studies show expression at the tips of villi, in the upper crypts, and in surface cells of the caecum and colon (Shekels et al., 1998).

Rodent (mouse) mMuc3 and (rat) rMuc3 are assumed to represent secretory mucins expressed in columnar and goblet cells of the intestine. In-situ hybridization with a 3'-probe localized (rat) rMuc3 expression generally to columnar cells. Two antibodies specific for the C-termini of rat rMuc3 localized the protein to apical membranes and cytoplasm of columnar cells. An antibody to the tandem repeat sequence, however, localized the protein to both columnar and goblet cells. Cesium chloride ultracentrifugation was used to isolate both light- and heavy-density fractions. A full-length membrane-associated form (light density) was found in columnar cells, whereas, the carboxyl-truncated soluble form of rat Muc3 (heavy density) was present in goblet cells (Wang et al., 2002). A similar localization of human MUC17 may exist as the splice variant, MUC17SEC, encodes a truncated protein that is missing the second EGF-like domain, the

transmembrane domain, and the cytoplasmic tail. The MUC17/SEC protein is believed to be a soluble protein as the absence of the transmembrane domain would result in its secretion from the cell. In a mouse model of human cystic fibrosis, both soluble Muc3 and goblet cell Muc2 are increased and hyper-secreted contributing to the excess intestinal mucus of cystic fibrosis mice (Khatiri et al., 2001).

## Function

MUC17 is a membrane-bound glycoprotein that may serve as a cellular receptor through its extended, repetitive extracellular glycosylation domain. The extracellular domain may serve a lubricant functionality and provide a signal transduction capability. Membrane mucins, such as MUC17, function in epithelial cells to provide cytoprotection, maintain luminal structure, provide signal transduction, and confer anti-adhesive properties to cancer cells which lose their apical/basal polarization. Outside-in signaling may be transduced by the protein's interaction with extracellular matrix constituents including growth factors and cytokines and/or potentially binding of Ca<sup>2+</sup> or EGF ligands to extracellular displayed EGF-like domains. The 80 amino acid cytoplasmic domain has potential serine and tyrosine phosphorylation sites to convey extracellular signals.

Analysis of mouse Muc3 showed that a definitive proteolytic cleavage occurs during processing in the endoplasmic reticulum. Recombinant products consisted of a V5-tagged 30 kDa extracellular glycopeptide and a Myc-tagged 49 kDa membrane-associated glycopeptide. Throughout their cellular transport to the plasma membrane, the two fragments remained associated by non-covalent SDS-sensitive interactions. Site-specific mutagenesis showed requirement for glycine and serine residues in the cleavage sequence Leu-Ser-Lys-Gly-Ser-Ile-Val-Val, which is found in the SEA domain between the two EGF-like motifs of the mucin. A similar cleavage sequence has been reported in human MUC1 and analogous sites are present in human MUC3, MUC12, MUC16 and MUC17. Proteolytic cleavage may be a conserved characteristic of the membrane-bound mucins, and possibly precedes the release of their large extracellular domains at cell surfaces (Wang et al., 2002).

## Homology

The similarity of human MUC17 to rodent Muc3 (mouse and rat) was first reported by JR Gum Jr and colleagues. This similarity was represented by a cladogram calculated using sequences initiating at the start of the second EGF-like domain and continuing through to the carboxy-termini of the proteins. The analysis suggests that MUC17 diverged from human MUC3 earlier in evolution than the divergence of primates and rodents, and suggests that MUC17 is the

true structural homolog of rodent Muc3 (Gum et al., 2002). Whether MUC17 is the functional homolog of rodent Muc3 is still unclear, however, and needs to be experimentally proven. Chromosome computer analysis assigns mouse Muc3 to mouse chromosome 5, a region of synteny to human chromosome 7, the location of the human MUC3, MUC12, and MUC17 mucin genes. NCBI HomoloGene reports MUC17 is conserved in Coelomata or in organisms higher than coelenterates and certain primitive worms.

Expression of the mouse Muc3 mucin has been characterized in terms of regulation of its promoter by cytokines and growth factors. Mouse Muc3 is now believed to be the true structural homologue of human MUC17 due to higher sequence similarity to MUC17

than human MUC3 (Moniaux et al., 2006). The N-terminal domain for MUC17 is coded by two exons, whereas for MUC3, it is coded by a single exon. Gum and colleagues (2002) showed that the degree of sequence homology between the carboxy-extremity of MUC17 and mMuc3 was higher than that between MUC3 and mMUC3. An alignment of the amino-extremities of MUC17, MUC3, and mMuc3 is shown. No similarity is shown by MUC3 and mMuc3, but a high degree of identity exists between MUC17 and mMUC3. Their similar structural organization and high degree of identity show that MUC17 is the human homologue of mMuc3.

A search of the National Center for Bioinformatics HomoloGene and UniGene databases returned the following suggested sequences for comparison.

## HomoloGene:88635. Gene conserved in Coelomata

Human	H. sapiens	MUC17	mucin 17, cell surface associated, chromosome 7q22.1, GeneID: 140453
Chimpanzee (West African)	P. troglodytes	MUC17	mucin 17, chromosome 7, GeneID: 740201
Mouse	M. musculus	Muc3	mucin 3, intestinal
Rhesus monkey	Macaca mulatta		chromosome 3
Human	Homo sapiens	CAE54435	membrane mucin MUC17 (Homo sapiens) gi/51869309/emb/CAE54435.1/(51869309)
Human	Homo sapiens	CAE54436	secreted mucin MUC17 (Homo sapiens) gi/51869311/emb/CAE54436.1/(51869311)
Human	Homo sapiens	AAL89737	intestinal membrane mucin MUC17 (Homo sapiens) gi/19526645/gb/AAL89737.1/AF430017_1(19526645)
Human	Homo sapiens	AAI26316	MUC17 protein (Homo sapiens) gi/118835615/gb/AAI26316.1/(118835615)
Human	Homo sapiens	NP_001035194	mucin 17 (Homo sapiens) gi/91982772/ref/NP_001035194.1/(91982772)
Chimpanzee (West African)	Pan troglodytes	XP_001142083	PREDICTED: mucin 17 (Pan troglodytes) gi/114615083/ref/XP_001142083.1/(114615083)
Opossum (gray short-tailed)	Monodelphis domestica	XP_001375221	PREDICTED: similar to membrane mucin MUC17 (Monodelphis domestica) gi/126323716/ref/XP_001375221.1/(126323716)
Opossum (gray short-tailed)	Monodelphis domestica	XP_001371346	PREDICTED: similar to MUC17 protein (Monodelphis domestica) gi/126309309/ref/XP_001371346.1/(126309309)
Chicken	Gallus gallus	XP_001233667	PREDICTED: similar to intestinal membrane mucin MUC17, partial (Gallus gallus) gi/118121828/ref/XP_001233667.1/(118121828)
Mosquito	Aedes aegypti	EAT36316	secreted mucin MUC17, putative (Aedes aegypti), gi/108872091/gb/EAT36316.1/(108872091)
Opossum (gray short-tailed)	Monodelphis domestica	LOC100017948	similar to MUC17 protein (Monodelphis domestica) , Chromosome: 2, GeneID: 100017948
Chicken	Gallus gallus	LOC770330	similar to intestinal membrane mucin MUC17 (Gallus gallus), Chromosome: Un, GeneID: 770330
Opossum (gray short-tailed)	Monodelphis domestica	LOC100023779	similar to membrane mucin MUC17 (Monodelphis domestica), Chromosome: 3, GeneID: 100023779
Chimpanzee (West African)	Pan troglodytes	LOC463614	similar to membrane mucin MUC17 (Pan troglodytes), Chromosome: 7, GeneID: 463614
Rat (Brown Norway)	Rattus norvegicus	Muc17_predicted	Muc17_predicted and Name: mucin 17 (predicted) (Rattus norvegicus), Chromosome: 7, GeneID: 295035
Fruit Fly	D. melanogaster	Sgs1	Salivary gland secretion 1, 25B2-3 puff, salivary glands, third instar

## Selected Protein Similarities

Comparison of sequences in UniGene with proteins supported by a complete genome. The alignments can suggest function of a gene.

C. elegans	32.92 % / 636 aa	ref:NP_505150.1 - reverse transcriptase (Caenorhabditis elegans)
S. cerevisiae	30.55 % / 644 aa	pir:S48478 - S48478 glucan 1,4-alpha-glucosidase
R. norvegicus	27.24 % / 647 aa	pir:A53577 - A53577 ascites sialoglycoprotein 1 - rat
M. musculus	24.77 % / 633 aa	ref:NP_035871.1 - zonadhesin (Mus musculus)
A. thaliana	23.94 % / 531 aa	ref:NP_564694.1 - expressed protein (Arabidopsis thaliana)
D. melanogaster	22.31 % / 637 aa	sp:Q02910 - CPN_DROME CALPHOTIN
E. coli	18.05 % / 563 aa	ref:NP_287395.1 - putative membrane protein of prophage CP-933X (Escherichia coli O157:H7 EDL933)

## Implicated in

### Pancreatic adenocarcinoma

#### Disease

Worldwide, pancreatic cancer is the eleventh most common cancer. In the United States of America, pancreatic cancer is the fourth leading cause of cancer related death. Pancreatic cancer presents a 5-year survival rate of just 5%. The incidence and age-adjusted mortality rate (approximately 95%) are almost equal, underscoring the aggressive nature of the disease.

#### Prognosis

Currently, no approved diagnostic biomarker for pancreatic cancer is licensed in the United States. The CA19-9 mucin epitope is used for the diagnosis of ovarian cancer and other mucins are being developed for the detection of breast cancer (MUC1) and pancreatic cancer (MUC1, MUC4, MUC3, MUC17). The DUPAN-2 antibody recognizes a tumor-associated antigen carried by the MUC4 protein and is used as a clinical diagnostic for pancreatic adenocarcinoma in Japan. MUC4 is aberrantly expressed in 80% of pancreatic adenocarcinomas and is not expressed in the normal pancreas or benign pancreatitis. In addition MUC4 is expressed early in the onset of pancreatic cancer (detected in pancreatic intraepithelial neoplasia (PanIN) stage I disease). Similarly, MUC17 is aberrantly expressed in pancreatic adenocarcinomas as compared to no expression in the normal pancreas or benign pancreatitis. MUC17 is expressed early in the progression of pancreatic cancer with localization to well defined pancreatic ductal structures undergoing malignant transformation (Moniaux et al., 2006).

#### Oncogenesis

In an in vivo model, subcutaneous injection of MUC17 AsPC-1 knock-down cells show slight increase in tumorigenicity in relation to parental control cells; although no significant difference was detected due to large variation in tumor weights. A xenograph model with knock-down cell lines injected orthotopically into the pancreas head showed an increased potential to metastasize to the peritoneal cavity and increased

tumor mass (weight) in relation to mice injected with the parental cell line (control group) transfected with a scrambled RNAi sequence (unpublished data, Junker and Batra, 2007).

## To be noted

**Note:** Conserved in Coelomata. From (HomoloGene: 88635. Gene conserved in Coelomata).

Coelome: the cavity within the body of all animals higher than the coelenterates and certain primitive worms, formed by the splitting of the embryonic mesoderm into two layers. In mammals, the coelome forms the peritoneal, pleural, and pericardial cavities.

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