MUC1 in Carcinomas

Olivia Caruso, Abhishek Kona, Allison Lu, Zara Saberi, Tara Shabazaz, Varun Vijay
Teacher: Tina Link, Ph.D., Science Department, Walton High School, Marietta, GA
Mentor: Daniel Carson, Ph.D.

Abstract
MUC-1 is a large transmembrane mucin glycoprotein, which was originally isolated from the human milk fat globule membrane (MMG). This source of MUC-1 was used as an immunoassay to raise a series of monoclonal antibodies. All of these first-generation MUC1-specific antibodies react against the large extracellular domain. This domain consists of a long series (20-50) of tandem repeat amino acid sequences that are heavily glycosylated. These MUC1-specific antibodies were used to determine that MUC1 is ubiquitously expressed in normal simple epithelia and overexpressed in a non-malignant, polyvalent fashion in a variety of epithelial cancers, including breast cancer. MUC1 overexpression and its high glycosylation often confers chemoresistance to cancer patients, and stem cell system of targeting the tumor and preventing tumor killing. One aspect of MUC1 that contributes to these properties is its heavy glycosylation, which largely contributes to the great difficulty in degrading and removing MUC1 from the cell surface. The carbohydrate decorations in MUC1 usually contain sialic acid as a terminal sugar. In some cases, this creates binding sites for factors that are needed for chemotherapeutic drug uptake of chemotherapeutic agents typically used to treat cancer. Because of this, the MUC1 gene family is currently being explored as a target for a variety of therapeutic approaches. The orientation and location of various cancers and is being explored as a target for certain therapeutic approaches. The Merlin SMART team has designed a 3D model of MUC1 to investigate the relationship between structure and function.

Structure and Function

MUC1 is a large transmembrane mucin glycoprotein expressed at the apical surface of epithelial cells including those of the mammary gland, female reproductive tract, lung, kidney, stomach, gallbladder, and pancreas. It is responsible for lubrication of cell surfaces through the expansion of its carbohydrate heavy structure as well as protecting cells from microorganisms by acting as a physical barrier and preventing proteolysis. The proline knot domains are also present in the tumor microenvironment. One advantage of using MUC1 is its ability to expand from 120-250 KDa, making it the physically largest molecules on epithelial cell surfaces. The high density of proline residues and heavy glycosylation contribute to the highly extended structures typical of mucins. Coupled with the large size, the protein provides an effective barrier that protects and hydrates cell surfaces. Mucins are often upregulated during inflammation and many cancers. Consequently, mucins also serve as serum cancer markers including CA 19-9 and CA 125, common tests for breast and ovarian cancer. Mucin expression helps protect cancer cells from attack by the host immune system and reduces uptake of chemotherapeutic agents typically used to treat cancer. Because of this, these patients have been known as MUC1-positive breast cancer patients.

MUC1 is a member of the mucin gene family. This family includes 21 members (MUC1 - MUC21). Mucins are characteristically tandem repeat regions that serve as sites for O-glycosylation. The family is broadly separated into two groups: secreted mucins and transmembrane mucins. Secreted mucins, like MUC2 or MUC6, in addition to their tandem repeat, heavily glycosylated domains typically also contain Von Willebrand Factor (VWF) and cysteine-knot domains. The VWF domains play roles in hemostasis. All mucins contribute to making viscous physical barriers at cell surfaces.

In cancer treatment, the MUC1 protein serves as a target for drug therapy, particularly with respect to breast cancer. Overexpressed MUC1, present in over 90% of breast cancer tissues, features exposed core protein sites at each tandem repeat in its extracellular domain. These O-glycosylation sites, exposed specific Trp-rich sequences and unique epitopes recognized by specific antibodies, serve as potential target for cancer therapies. The overexpression of MUC1 may be associated with an increased risk of metastasis and recurrence of disease.

The extra large, muscular mass of enzymes and antibodies provide an effective barrier that protects and hydrates cell surfaces. Mucins are often upregulated during inflammation and many cancers. Consequently, mucins also serve as serum cancer markers including CA 19-9 and CA 125, common tests for breast and ovarian cancer. Mucin expression helps protect cancer cells from attack by the host immune system and reduces uptake of chemotherapeutic agents typically used to treat cancer. Because of this, these patients have been known as MUC1-positive breast cancer patients.

MUC1 is a member of the mucin gene family. This family includes 21 members (MUC1 - MUC21). Mucins are characteristically tandem repeat regions that serve as sites for O-glycosylation. The family is broadly separated into two groups: secreted mucins and transmembrane mucins. Secreted mucins, like MUC2 or MUC6, in addition to their tandem repeat, heavily glycosylated domains typically also contain Von Willebrand Factor (VWF) and cysteine-knot domains. The VWF domains play roles in hemostasis. All mucins contribute to making viscous physical barriers at cell surfaces.

In cancer treatment, the MUC1 protein serves as a target for drug therapy, particularly with respect to breast cancer. Overexpressed MUC1, present in over 90% of breast cancer tissues, features exposed core protein sites at each tandem repeat in its extracellular domain. These O-glycosylation sites, exposed specific Trp-rich sequences and unique epitopes recognized by specific antibodies, serve as potential target for cancer therapies. The overexpression of MUC1 may be associated with an increased risk of metastasis and recurrence of disease.
Overall, the poster looks pretty good, but Dr. Link wants the posters to be less wordy and more figures. I recommend making maybe like a family tree for the family portion or for structure, labelling the structures on a diagram. Overall, try to add more pictures/diagrams.