

Normal and abnormal mucus – what do the mucins in colorectal cancer tell us?

Free compartments of all of the secretory epithelia are covered by mucus, working as a physical barrier, as well as first line of defence from harmful factors, such as bacteria, viruses and toxins. It is a “trap” for most of the microorganisms, protecting cells from e.g. inflammation. As a dynamic structure, it can vary in thickness and create 1-2 layers. The surface portion of the mucus, loose, easily removable by washing or suction but also quickly regenerating, attains maximum thickness in the large intestine. The deeper layer is more stable and strongly adheres to the epithelium. The mucus is colourless, tensile, and sticky. To better visualise mucus-producing cells under microscope, various histological staining is used (Fig. 1).

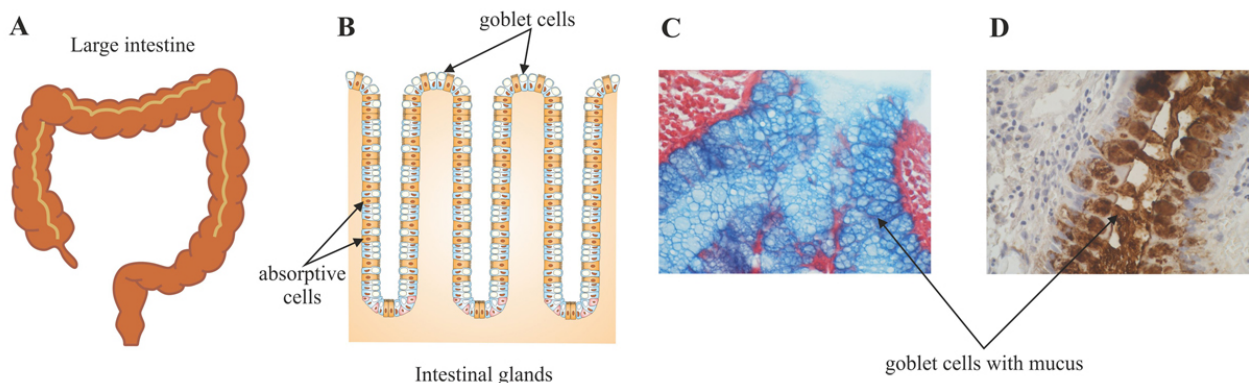


Fig. 1. Mucus produced in the human large intestine. A. Anatomy of the large intestine. B. The goblet cells present in columnar epithelium that forms many tubular glands. C. Mucin-associated carbohydrates stained with alcian blue. D. An apomucin stained by immunohistochemistry.

The most important constituents of mucus, apart from water (over 98%), are glycoproteins of large molecular mass called mucins (0,5-5%). The outer layer of mucus contains so called gel- or polymer-forming mucins, while transmembrane mucins, mixed with glycocalyx structures, are present in the inner portion.

The protein portion of mucins (apomucin) constitutes to about 20% of their dry mass. Saccharides (mainly O-glycan family) make over 50% of the molecular mass, densely packed along the polypeptide chain, which results in a characteristic filament-like appearance of mucins.

The first of the described transmembrane mucins localized on the surface of epithelial cells was mucin 1 (MUC1), present in the biggest abundance in the stomach mucus. Meanwhile, MUC2 was the first characterised secretory mucin. Its production mostly occurs in the large intestine, in which

the thickest layer of mucus can be observed. MUC2 is insoluble, packed in secretory granules, serving as a perfect protective filter for colonic epithelial cells due to its spatial structure (dense polymers).

In chronic inflammatory diseases and cancers of the large intestine, disturbances of glandular epithelium structure and function are often observed. The colorectal cancer (CRC), as the third most prevalent cancer in males and second most prevalent in females, still poses a major challenge for science and clinical medicine. During its course, quantitative and qualitative changes in mucins occur, with the presence of tumor-associated epitopes, which are both a diagnostic-prognostic factor and can be a target of treatment.

Our lab recently published a paper that examined the tissue expression (transcripts, proteins) of MUC1 and MUC2 in patients with CRC and control samples using real-time quantitative PCR and immunohistochemical (IHC) techniques. A novel quantitative digital software type was used for evaluation of mucin IHC reactivity.

We confirmed higher expression of the MUC1 mRNA, lower levels of MUC2 protein, and higher MUC1/MUC2 expression ratio in CRC compared to the control (Fig. 2). Moreover, MUC2 protein expression characterized higher histological stage of tumors and was negatively correlated with cellular proliferation and mutated p53 protein expression. In addition, MUC2 tissue expression allowed to differentiate mucinous and non-mucinous CRC subtypes.

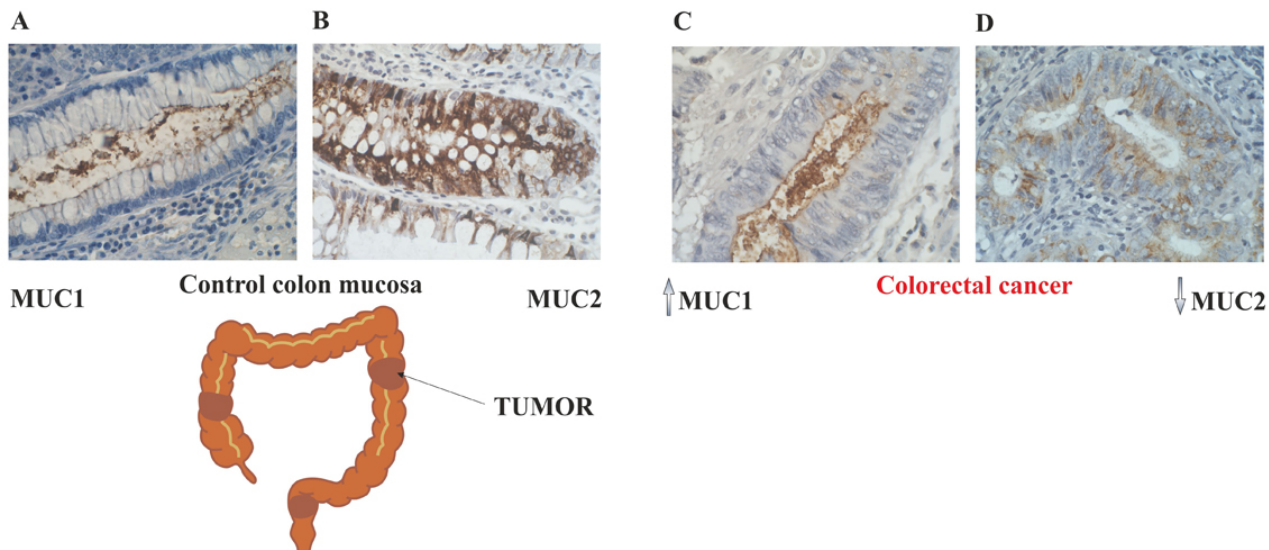


Fig. 2. The qualitative and quantitative immunohistochemical differences in MUC1 and MUC2 expression in a normal colon (A, B) and colorectal cancerous tissue (C, D).

Summarizing, a combination of tissue overexpression of MUC1, reduced MUC2 expression, and high ratio of MUC1/MUC2 may be a useful factor of poor prognosis in CRC patients. We hope that providing immunocytochemical characterization of normal and cancerous tissue through MUC1 and MUC2 expression pattern in correlation with clinicopathological data, will help in the introduction of targeted CRC therapies.

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Publication

[Differential Expression of Mucin 1 and Mucin 2 in Colorectal Cancer](#)

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