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MUC13 is a novel molecular signature, for early detection and metastatic colorectal cancer

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Colorectal cancer (CRC) is a leading cause of cancer mortality. Biological markers for early detection and distant metastatic disease in patients with CRC are not well defined. We have identified transmembrane mucin MUC13, as early detection marker for distant metastatic disease. Underlying pathways and the signaling mechanisms involved in MUC13-CRC pathogenesis are not well known. Retrospective institutional tumor registry of archived FFPE tissues, reviewed by a pathologist was serially sectioned and IHC staining was performed using an in-house MAb for MUC13 and analyzed using a modified H-score. MUC13 was correlated with disease stage, aggressiveness and inflammatory markers, indicating poor prognosis in CRC patients. 196 tissues, of which 56.1% were female, 52% were white and the median age at resection was 70. 38 (19.4%) were stage I, 64 (32.7%) stage II, 84 (42.9%) stage III and 10 (5.1%) stage IV. 100% of colon adenocarcinoma tissues stained positively for MUC13, including definitive tumor epithelial staining, little-to-no background stromal staining, and mild staining of adjacent normal colon mucosa. Typical colon adenocarcinoma cells exhibited strong apical membranous staining with varying degrees of cytoplasmic staining. Advanced stage tumors had basolateral and/or circumferential membranous staining compared to early stage tumors, which more frequently displayed apical membrane staining alone. MUC13 was correlated with disease stage, aggressiveness and inflammatory markers, indicating poor prognosis in CRC patients. Two of the protein coding MUC13 variants showed differential expression in aggressive cell lines and patient tissues. Cyclic turnover between the short and long isoforms were observed during Anoikis resistance. SNPs have been associated with increased risk of cancer incidence or fatality. Relevant MUC13 SNPs have been identified through TCGA patient database. This is the first study to correlate MUC13 expression with disease outcome. Alternative transcripts and single nucleotide polymorphisms gave genetic insight of the role of MUC13 in CRC pathogenesis.

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