Unique insight into microenvironmental changes in colorectal cancer: Ex vivo assessment of matrix metalloprotease-mediated molecular changes in human colorectal tumor tissue and corresponding non-neoplastic adjacent tissue

Matrix metalloprotease (MMP)-mediated tissue remodeling is one of the malignant changes driving colorectal cancer. Measurement of altered MMP expression/activity is not sufficient to fully understand the effect of MMP-mediated tissue remodeling. Biomarkers are required that specifically reflect the dynamic processes of the MMP-mediated degradation of signature proteins from colorectal tissue. The aim of the present study was to profile and characterize the release of MMP-degraded type III collagen (C3M) and citrullinated and MMP-degraded vimentin (VICM) from tumor tissue and corresponding non-neoplastic adjacent tissue (NAT) in a human colorectal cancer ex vivo model. Colorectal tumor tissue and NAT biopsies from tissue removed during resection of colorectal cancer patients (n=13) were cut into pieces of 2 mm² and cultured for 24 h in growth medium. C3M and VICM were evaluated by ELISA. As part of the characterization, C3M was determined subsequent to the tumor tissue being cleaved with recombinant MMP-2/−9 and trypsin. C3M was generated by MMP-2/−9, but not by trypsin. In addition, the level of C3M was significantly elevated in the conditioned medium from tumor tissues (3.7 ng/ml) compared with that observed in the conditioned medium from the NATs (2.2 ng/ml) and in the growth medium alone (1.9 ng/ml). The level of VICM was significantly elevated in the tumor tissues (0.51 ng/ml) and NATs (0.52 ng/ml) compared with that in the growth medium alone (0.03 ng/ml). No differences were detected between the tumor tissues and NATs. No correlation was observed between biomarker levels from the tumor tissue and corresponding NAT, and the biomarker levels did not correlate with tumor stage. In conclusion, the present study provided support of the concept that C3M and VICM are applicable as tools to investigate dynamic tissue changes of colorectal tumor tissue and corresponding NAT. By the assessment of these specific MMP-mediated molecular changes, the present study provides novel and relevant insight into the dynamic changes of colorectal tumor tissue and corresponding NAT.

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