Title: Analysis of colorectal cancer microenvironment in the FinCRC cohort

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Abstract

Colorectal cancer (CRC) is the third most common and the second most lethal cancer in the world. Despite curative-intent surgery of localized stage I-III cancer, 5-33% of CRCs get a local recurrence or distant metastases. Prognostic and predictive biomarkers are urgently needed to guide adjuvant treatment decisions.

Tumor microenvironment (TME) contains different cell types and structures, and describes their relationships and interactions. TME affects the behavior of CRC, and previous data show differences according to tumor and lymph node status (T- and N-stage), mismatch repair (MMR), and tumor location (right-sided colon, left-sided colon or rectum, respectively). In this project, we study how TME is associated with T-stage, N-stage, primary tumor location, MMR status, and local or distant recurrence in the Finnish CRC study (FinCRC).

We stained 531 tissue microarray (TMA) cores with multiplex immunohistochemistry. The cores were adenocarcinoma tissues from 81 curatively resected patients (2 punches from primary tumor core and 2 from invasive margin), and from metachronous metastases of 6 relapses (1-4 punches from distant metastases). The resulting images were computationally aligned, allowing us to measure 14 different protein markers from each tissue section. Staining

data was used to identify cancer cells and 11 different non-malignant cell types using a machine learning-based cell classifier.

Results demonstrate that the tumor immune microenvironment clearly differs between the primaries, and differences were also observed between the tumor core and invasive margin of the same tumor. Cellular neighborhood and association analyses are ongoing to discover new prognostic and predictive tools for clinical practice.