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Spatial profiling reveals molecular and immunological hallmarks of colorectal cancer tumourigenesis

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Abstract

To enhance effective early detection, diagnosis, and treatment of colorectal cancer (CRC), it is crucial to understand the molecular and immunological changes that occur during the disease's development and progression. In our study, we utilized GeoMx-digital spatial profiling to investigate biological alterations during tumorigenesis in early-stage (pT1) CRC samples. We analyzed gene expression in the epithelial and stromal segments across different stages of disease progression, including normal mucosa, low-grade and high-grade dysplasia, and cancer. In addition, we used imaging mass cytometry to reveal immune cell populations associated with malignant transformation. Furthermore, publicly available single-cell RNA-sequencing data was analyzed to determine the cellular origin of relevant transcripts.
Our findings demonstrate that there is differential gene expression in the epithelium and stromal segments across distinct histologies in the pT1 CRC samples. We identified an early onset of inflammatory responses during malignant transformation, characterized by upregulation of gene signatures related to innate immune sensing. We also detected increased infiltration of myeloid cells and observed a shift in macrophage populations from pro-inflammatory to immune-suppressive subsets as the disease progressed. These changes were accompanied by the upregulation of the CD47/SIRPα "don't eat me signal". Our study identified biomarkers associated with disease progression and targetable immune processes that could be exploited in a clinical setting. Overall, our findings provide insights into the stepwise progression of CRC that are instrumental for the development of effective strategies for early detection, diagnosis, and treatment of the disease.