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Dysfunction of secretory IgA contributes to poor outcomes in Fusobacterium-infected colorectal cancer.

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Fusobacterium nucleatum (Fn) is commonly enriched in human colorectal cancer (CRC) and is associated with poor prognosis. To uncover the cellular and molecular mechanisms behind this Fn-associated prognostic effect, we conducted single-cell transcriptomic analyses of 42 colon tissues from newly diagnosed colon cancer patients. Through single-cell transcriptome analysis corroborated by spatial transcriptome analysis, we found that the development of IgA plasma cells producing functional secretory IgA was impaired due to disrupted communications between IgA plasma cells and tumor-associated macrophages involved in IgA induction in Fn-positive CRC. Additionally, we identified a dysregulated IgA maturation (IGAM) module in Fn-positive patients, indicating compromised IgA-mediated mucosal immunity. This finding was further supported by an increase in bacterial infiltration within tumors of Fn-positive patients. Remarkably, Fn-positive patients were stratified based on IGAM activity, potentially leading to the development of novel treatment strategies for Fn-positive CRC patients. Our findings collectively suggest that an increased tumor microbial burden, due to impaired secretory IgA, leads to worse prognosis through chronic inflammation in Fn-positive CRC. Additionally, identifying a novel gene expression biomarker for stratifying Fn-positive patients offers the potential for a more tailored approach to patient care.