

Dysregulation of secretory IgA underlies poor prognosis in *Fusobacterium*-infected colorectal cancer

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Fusobacterium nucleatum (Fn) is commonly enriched in colorectal cancer (CRC) and associated with poor outcomes, though its mechanisms remain unclear. Our study investigated how Fn affects the tumor microenvironment through single-cell transcriptomic analyses of 42 CRC patient tissues, comparing Fn-positive and Fn-negative tumors. We discovered that Fn impairs IgA plasma cell

development and secretory IgA (sIgA) production by disrupting communication with tumor-associated macrophages. Additional experiments in germ-free mice, together with our re-analysis of a publicly available single-cell RNA-seq data set from a CRC mouse model with an intact gut microbiome—both models having been orally gavaged with Fn—jointly validated the causal role of Fn in impairing sIgA induction. We identified a dysregulated IgA maturation (IGAM) module in Fn-positive patients, indicating compromised mucosal immunity and increased bacterial infiltration. This IGAM signature effectively stratified Fn-positive patients, suggesting potential for targeted therapeutic approaches. Our findings reveal that Fn disrupts sIgA production, increasing tumor microbial burden and worsening prognosis through chronic inflammation in Fn-positive CRC.