FadA-Secreting Fusobacterium nucleatum Promotes Inflammatory and Immunomodulatory Response in Colorectal Cancer (Year 2)

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The pandemic-induced decline in colonoscopies and the continuing rise of colorectal cancer (CRC) rates in younger populations makes the need for early CRC indicators higher than ever. The role of the diverse gut microbiota has become a major focus in CRC development. Fusobacterium nucleatum, a commensal oral bacteria, was shown in an earlier study to promote colorectal carcinogenesis by inducing epithelial-mesenchymal transition through its virulence factor, FadA adhesin. The current project investigated the interplay of F. nucleatum with tumor-promoting inflammation and immune response. Immunofluorescence staining of formalin-fixed paraffin embedded colorectal tissue was used to elucidate spatial profiling of the tumor microenvironment. Immune response was studied through the presence of B lymphocytes and macrophages with CD20 and CD68 staining, respectively. COX-2, an enzyme mediator for inflammatory pathways, was used as a marker for inflammation. B lymphocytes had a surprisingly positive association with F. nucleatum in pre-cancerous and cancerous samples, while macrophages had a negative association with F. nucleatum, indicating immune suppression. COX-2 was also shown to have a positive association with F. nucleatum, suggesting inflammatory response. To supplement this study, 1) a meta-analysis of F. nucleatum occurrence in fecal and tissue samples was conducted through literature review, and 2) a metagenomic analysis of whole genome sequencing data using CosmosID was used to determine F. nucleatum presence in CRC specimens. The findings suggest F. nucleatum is a reliable, noninvasive target for CRC risk screenings, and may serve as an immunomodulatory and anti-inflammatory target to enhance effectiveness of chemotherapeutic agents in cold tumors.

Awards Won:
Fourth Award of $500