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Short-Chain Fatty Acids from Gut Microbiota in Modulating Immune Response and Therapeutic Outcomes in Colorectal Cancer

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ABSTRACT

The short-chain fatty acids (SCFAs), especially acetate, propionate, and butyrate, are produced by the gut microbiota as byproducts during the fermentation process of dietary fiber. Data from several recent studies emphasizes the role of SCFAs in colorectal cancer (CRC). These compounds are known to alter immune response and impact the treatment outcomes. SCFAs promote anti-inflammatory phenotypes in innate immune cells, such as macrophages, dendritic cells, and neutrophils, and enhance cytotoxic T cell function, thereby modulating the CRC tumor microenvironment. Through epigenetic processes and receptor-mediated signaling SCFAs fortify the gut wall and prevent tumor-promoting inflammation. Preclinical and early clinical investigations demonstrate better responses to chemotherapy and immunotherapy owing to these effects. Increasing the production of SCFAs by dietary therapies and prebiotic supplements can assist in the treatment of CRC patients due to their potential in modulating metabolic activity and composition of gut microbiota. However, the success of consistent treatment is attributable to the variability of the gut microbiota and host factors. CRC management can be tailored through monitoring the SCFA levels and microbial fingerprints due to their potential to serve as biomarkers in predicting therapeutic response. Enhancement of microbiome-targeting methods, validation of biomarkers in larger cohorts, and comprehending the intricate connections among SCFAs should be the main goals of future studies in this specialty. Integrating SCFA regulation into precision medicine frameworks may improve the efficacy and durability of CRC therapy. This review summarizes current understanding of SCFAs' role in CRC immune regulation and therapeutic results, as well as the translational prospects and constraints of using microbiome-derived metabolites to improve patient care.

KEYWORDS: Short-Chain Fatty Acids, Colorectal Cancer, Immune Regulation, Gut Microbiota, Tumor microenvironment

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