Summary of 'Therapeutic Opportunities in Inflammatory Bowel Disease: Mechanistic Dissection of Host-Microbiome Relationships'

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The current and most advanced research in Inflammatory Bowel Disease (IBD) is revealing an increasingly complicated relationship between host genetics, immunologic pathways, and microbiome dysbiosis that drives the underlying pathophysiology of the disease. The genetic and molecular pathways implicated in the characteristic mucosal inflammation have become targets for therapeutic interventions, however the inherent complexity of host and microbial interactions poses significant challenges to developing next-generation therapies. In a newly published paper in *Cell,* researchers provide direction on how we can approach our current research of molecular pathways to guide the development of future treatment strategies.

Treatment regimens for IBD have historically been fraught with challenges. The heterogeneous nature of the disease and phenotypic variation from patient to patient translates to variable, and often ineffective, response to crude therapeutic interventions. These limitations have called for a rigorous approach to understanding the microbial and immune mechanisms that drive disease. In this paper, the authors outline several areas that are promising avenues for the development of future therapies.

While genetic sequencing has successfully identified risk variants that predispose patients to IBD, we still have yet to fully understand how the microbiome interacts with host genetics to lead to pathologic inflammation. The authors explain how new advancements in computational and metabolomic analysis will help to uncover the functional connections between genetic variables and microbiome traits, thus exposing opportunities for more targeted treatment interventions. This will also require rigorous investigations of the host immune pathways that underpin the mucosal inflammation responsible for disease phenotypes. A detailed understanding of both microbial and host pathways will provide opportunities for more directed hypothesis-driven approaches to manipulating microbial species, metabolites, and inflammatory responses for therapeutic effect. The authors elucidate the future potential of several different treatment modalities, including microbial-derived bioactive compounds, direct fecal microbial transplantation (FMT), probiotics and specifically engineered microbial consortia, strategies for targeted removal of deleterious microbial strains, and finally specific dietary changes that promote re-establishment of healthy microbiomes. These future directives hold promise for more elegant, effective, and targeted treatment of this complicated disease.