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Modifying the Gut Microbiome to Make Cancer Immunotherapy Effective

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Abstract:

Background: A complex and diverse ecosystem residing at all epithelial barriers of host body constitutes the mammalian microbiome. When the gut microbiome is disrupted it is associated with a variety of inflammatory disorders and malignancies.

Microbiota-host interactions may affect the host response to immunotherapies by modulating innate and adaptive immunity.

Conclusion: Our goal should be development of precision immunotherapies by identification of specific causative bacteria and modulation of cancer progression.

Keywords: microbiome, immunotherapy, dysbiosis

I. BACKGROUND

A healthy individual possesses a good microbial ecosystem. In humans the microbiome comprises bacteria, fungi, archaea, protozoa and virus that reside on body's epithelial barrier(1). The gut microbiome contains approximately 3×10^{13} bacteria, most of which are symbiotic with the host(2,3). For maintaining the intestinal epithelial homeostasis the gut microbiome, immune cells and mucosal barrier act together. The gut microbiome plays a key regulatory role. They regulate barrier function, maintain mucosal immune homeostasis and host-microbial symbiosis, prevent pathogen infection, control overgrowth of pathological organisms, and regulate metabolism, including vitamin synthesis and metabolism of indigestible dietary fiber (4–8).

Among the human microbiome certain bacteria have been known to play an important role in the development of cancer(9). These days immune checkpoint inhibitors (ICIs) are used in cancer immunotherapy.(10) However in certain patients resistance to immunotherapy is developed. Recent studies have shown the role of gut microbiome in improving the efficacy of ICIs against cancer(11-15). In this article we will be analyzing the role of gut microbiome in increasing the efficiency of cancer immunotherapy and the challenges faced by them with possible solutions.

II. ROLE OF GUT MICROBIOME IN CANCER IMMUNOTHERAPY

Immune checkpoint inhibitors play a major role in cancer immunotherapy. They inhibit the interactions between immune checkpoint molecules and inhibitory T cell receptors and stimulate T cell-mediated antitumor immunity. A wide range of metastatic malignancies have been effectively treated using PD-1 blockade as immunotherapy. Varied responses are shown by patients and some have become resistant to it(16-18).

Antibiotic-related dysbiosis was associated with a lower response to PD-1 blockade which means that disruption of microbial networks and loss of specific bacterial species can affect the efficacy of immunotherapy(19). One of the important bacterial species found in fecal microbiota of the patients was *A. muciniphila*. Oral supplementation with *A. muciniphila* or fecal microbiota transplantation (FMT) from responders restored the efficacy of PD-1 blockade in murine models. Cytokines induced by microbiota-host interactions increase the efficacy of PD-1 blockade. But this is not applicable universally in all human races and the response varies from individual to individual(20).

III. CONCLUSION

Thus our goal should be the development of precision immunotherapies. The identification of specific causative bacteria may allow modulation of cancer progression, raising the possibility of precision immunotherapies.



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