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Future prospect of “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients”

Kang YB *et al.* Future prospect of “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients”

Abstract

Recently, the article “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients” has been read with interest, and it is preliminary suggested that gut microbiota is closely related to therapeutic effect of nivolumab. Based on the meaningful results of this article, many valuable research directions are proposed to enhance the therapeutic effect of immune checkpoint inhibitors on advanced hepatocellular carcinoma.

Key Words: Gut microbiome; Immunotherapy; Immune checkpoint inhibitor resistance; Probiotics; Faecal microbiota transplantation; Hepatocellular carcinoma; Prognosis

Kang YB, Cai Y. Future prospect of “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients”. *World J Gastroenterol* 2022; In press

Core Tip: The article “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients” has been read with interest, and it is preliminary suggested that gut microbiota is closely related to therapeutic effect of nivolumab. Future research should pay attention to the relationship between gut microbiota and therapeutic effect of immune checkpoint inhibitors (ICIs) on advanced hepatocellular carcinoma and the way of regulating gut microbiota to improve the therapeutic effect of ICIs.

TO THE EDITOR

We read with interest the article “Gut microbiome composition can predict the response to nivolumab in advanced hepatocellular carcinoma patients”^[1], in which the authors analyzed and summarized the correlation between gut bacterial composition and the prognosis of nivolumab therapy in hepatocellular carcinoma (HCC) patients. The highlight of this article was that gut microbiota composition and diversity of responders

differed significantly from those of non-responders following nivolumab therapy. Several intestinal bacterial species such as *Citrobacter freundii*, *Azospirillum* sp., and *Enterococcus durans* were specific to the responders. Moreover, a higher *Prevotella/Bacteroides* ratio and the presence of *Akkermansia* species can serve as predictive markers of response. Altogether, the study not only demonstrates that the therapeutic effect of nivolumab has something to do with the composition of gut microbiota in advanced HCC patients, but also provides some inspiration for our future research direction.

In our opinion, it is of importance to underline that the relationship between the therapeutic effect of various immune checkpoint inhibitors (ICIs) such as pembrolizumab, nivolumab atezolizumab, durvalumab and avelumab on HCC and gut microbiota. At present, the response rates of ICIs are very low in advance HCC. To be specific, the response rate to ICI monotherapy is merely 15%-23%, which is increased to approximately 30% after combination treatment^[2]. How to improve the effectiveness of ICI treatment is essential and has been extensively investigated. While the human gut microbiota has been shown to be associated with clinical responses to ICIs in HCC^[3], the available data in this field remain limited and the relevant scientific work is recently only in the initial stage. Thus, more research is required in the future. Firstly, clinical studies with large sample sizes are needed to further clarify the relationship between gut microbiota and the therapeutic effect of various ICIs. At the same time, which types of gut microbiota are suitable for which ICIs should also be figured out. Furthermore, construction based on gut microbiota can function as a prognostic marker for the response to various ICI therapies. These results will provide clinicians a valuable reference for rational use of ICIs and personalized precision therapy. Secondly, the mechanism by which the gut microbiota promotes the therapeutic effect of various ICIs needs to be further studied, with the focus on key pathways such as intestinal mucosal barrier function, bacterial metabolites and microorganism-related molecular patterns, thus being conducive to discovering how to enhance the therapeutic effect of various ICIs by targeting gut microbiota. Thirdly, probiotics, prebiotics, synbiotics and

antibiotics may represent innovative, safe and low-cost strategies for promoting the therapeutic effect of various ICIs^[4]. In this respect, it is of necessity to determine which beneficial bacteria and harmful bacteria are bound up with the therapeutic effects of which ICIs. Meanwhile, it will also be significant to confirm how probiotics, prebiotics, synbiotics and antibiotics vary the composition of the gut microbiota and how relevant it is to the therapeutic effect of various ICIs. In other words, these results will contribute to the identification of probiotics, prebiotics, synbiotics and antibiotics that may increase the efficacy of ICIs when being used in combination. Last but not least, faecal microbiota transplantation (FMT) may be a direct and superior approach to enhancing the therapeutic effect of various ICIs through modulating the gut microbiota in human beings. Considering that, it is extremely valuable to explore the therapeutic method of FMT in combination with ICIs. Besides, the optimal gut microbiota composition for enhancing the therapeutic effect of various ICIs should be recognized. On this basis, it is of great importance to choose the right donors^[5].

In summary, based on the meaningful research results of this article, it is expected that readers can pay attention to the relationship between gut microbiota and therapeutic effect of ICIs on advanced HCC and the method of regulating gut microbiota to improve the therapeutic effect of ICIs.

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