豆包结果：

Yes, the gut microbiome (also termed gut microbiota) has been extensively investigated in hepatocellular carcinoma (HCC) across multiple research dimensions, including tumor pathogenesis, diagnostic/prognostic biomarkers, prediction of immunotherapy efficacy, and microbiota-targeted therapeutic strategies. These studies are grounded in the well-established *gut-liver axis*—a bidirectional signaling network that links intestinal microbial composition, microbial metabolites, and hepatic immune and metabolic pathways.

1. Role in HCC Pathogenesis

Substantial evidence confirms that gut microbial dysbiosis drives the development and progression of HCC, particularly in the setting of chronic liver diseases (e.g., cirrhosis, chronic viral hepatitis, nonalcoholic/alcoholic fatty liver disease) which are the main precursors of HCC.

因果表述过强：现有人体研究多为关联性证据，“drives”不能由这些研究直接推出

- At the mechanistic level, compromised intestinal barrier function ("leaky gut") enables translocation of viable bacteria and microbial [illegible] lipopolysaccharide, LPS) into the portal venous syst[illegible] hepatic inflammation, hepatic stellate cell activation malignant transformation [10] [11].
- Microbial metabolites—including secondary bile acids, short-chain fatty acids, and choline-derived metabolites—also act as key signaling molecules that regulate hepatocyte proliferation, inflammation, and genotoxicity during hepatocarcinogenesis [3].
- For etiology-specific HCC subtypes, studies have identified distinct gut microbial signatures in HBV-related HCC, where dysbiosis is closely correlated with an immunosuppressive tumor microenvironment and impaired liver function [6].

2. Gut Microbiome as Diagnostic and Prognostic Biomarkers

Alterations in gut microbial composition and diversity have shown potential as non-invasive biomarkers for HCC detection and risk stratification:

- A cohort study of elderly HCC patients (aged 60–80) demonstrated significant differences in both α-diversity and β-diversity of gut microbiota compared with healthy controls. A random forest model based on key differential genera (*Eggerthella*, *Anaerostipes*, *Lachnospiraceae_ND3007_group*) achieved favorable diagnostic performance, with AUC values ranging from 0.730 to 0.791 [4].

- Multiple systematic reviews have concluded that gut microbiota profiles represent promising early diagnostic markers for HCC, especially in patients with underlying chronic liver disease [8]

该证据来源为会议摘要（JCO Global Oncology supplement abstract），并非完整同行评议原始研究论文

3. Prediction of Immune Checkpoint

Given the limited objective response rate of ICIs in unselected HCC patients, the gut microbiome has emerged as a promising predictive biomarker for ICI efficacy:

- A clinical study enrolling 66 advanced HCC patients found that long-term responders to anti-PD-1/anti-CTLA-4 therapy had significantly higher gut microbial diversity than non-responders. The abundance of *Clostridium butyricum* and fatty acid biogenesis pathways were markedly enriched in long-term responders, suggesting their potential as predictive markers for durable ICI benefit [2]
- Multiple comprehensive reviews have synthesized evidence that gut microbiome composition modulates ICI efficacy by shaping systemic and hepatic immune activation, and can be used to stratify patients who are more likely to benefit from immunotherapy [1 5 9].

4. Microbiota-Targeted Therapeutic Strategies

Preclinical and clinical studies have explored various microbiota-modulating interventions for HCC management, including probiotics, prebiotics, fecal microbiota transplantation (FMT), and selective antibiotics. These strategies aim to restore gut eubiosis, reduce bacterial translocation, and enhance anti-tumor immunity, representing promising adjunctive approaches for HCC treatment [1 5 11].

具体干预结论仅对应综述性文献，未直接给出支撑各类干预的原始研究

References

1. Chen PJ, Devkota S, Shiao S, Hendifar A, Yang JD. Gut microbiome, a novel precision medicine biomarker for hepatocellular carcinoma. *Frontiers in Immunology*. PMC12719415. https://pmc.ncbi.nlm.nih.gov/articles/PMC12719415/
2. Zhao C, Chen W, Li S, Xu W, Liang Z, Kong FMS. Gut microbiome to predict durable response to immunotherapy in patients with hepatocellular carcinoma. *JCO Global Oncology*. https://discovery.researcher.life/article/gut-microbiome-to-predict-durable-response-to-immunotherapy-in-patients-with-hepatocellular-carcinoma/f49ca2218c1e329fa9e01f992980f026
3. Pallozzi M, De Gaetano V, Di Tommaso N, et al. Role of Gut Microbial Metabolites in the Pathogenesis of Primary Liver Cancers. *Nutrients*.

https://pdfs.semanticscholar.org/7ea7/0f5423a4e08ea7d33
d.pdf

4. Zhang W, Xu X, Cai L, Cai X. Dysbiosis of the gut microbiome in elderly patients with hepatocellular carcinoma. *Scientific Reports*. 2023;13:14877. https://www.nature.com/articles/s41598-023-34765-w
5. Du J, Guan Y, Zhang E. Regulatory role of gut microbiota in immunotherapy of hepatocellular carcinoma. *Hepatology International*. https://www.semanticscholar.org/paper/Regulatory-role-of-gut-microbiota-in-immunotherapy-Du-Guan/fddeeb575d5a80915f3f48557f8973f464b72472
6. Yan F, Zhang Q, Shi K, et al. Gut microbiota dysbiosis with hepatitis B virus liver disease and association with immune response. *Frontiers in Cellular and Infection Microbiology*. 2023;13:1152987. https://www.frontiersin.org/articles/10.3389/fcimb.2023.1152987
7. Tripathi A, Debelius J, Brenner DA, et al. The gut-liver axis and the intersection with the microbiome. *Nature Reviews Gastroenterology & Hepatology*. 2018;15(7):397-411. https://www.researchgate.net/profile/Anupriya-Tripathi/publication/325062224_The_gut-liver_axis_and_the_intersection_with_the_microbiome/links/5b240491458515270fd0f10b/The-gut-liver-axis-and-the-intersection-with-the-microbiome.pdf
8. Kang Y, Cai Y, Yang Y. The Gut Microbiome and Hepatocellular Carcinoma: Implications for Early Diagnostic Biomarkers and Novel Therapies. *Liver Cancer*. 2022;11(2):113-126. Karger Publishers. http://prod.karger.com/lic/article-pdf/11/2/113/3726842/000521358.pdf
9. Scarpellini E, Scarlata GGM, Santori V, et al. Gut Microbiota, Deranged Immunity, and Hepatocellular Carcinoma. *Biomedicines*. 2023;12(9):1797. MDPI. https://mdpi-res.com/d_attachment/biomedicines/biomedicines-12-01797/article_deploy/biomedicines-12-01797.pdf?version=1723041261
10. Zhou A, Tang L, Zeng S, et al. Gut microbiota: a new piece in understanding hepatocarcinogenesis. *Cancer Letters*. 2020;478:124-133. ScienceDirect. https://www.sciencedire 300021
11. Luo W, Guo S, Zhou Y, e Gut Microbiota Contributes to Pathogenesis, Diagnosis, and Therapy. *Frontiers in Microbiology*. 2022;13:873160. https://www.frontiersin.org/articles/10.3389/fmicb.2022.873160
12. Rattan P, Minacapelli CD, Rustgi V. The Microbiome and Hepatocellular Carcinoma. *Liver Transplantation*. 2020;26(S1):S27-S35. AASLD Journals. https://aasldpubs.onlinelibrary.wiley.com/doi/pdf/10.1002/lt.25828

书目信息错误：该论文实际为Scientific Reports 2023;13:7797，并非13:14877

书目信息错误：实际为Biomedicines 2024;12(8):1797

Reference[1][3][5][7]：入口及格式不统一，且未直接列出DOI；混用PMC、Semantic Scholar、ResearchGate等页面

以上结果来自豆包 2.1 Turbo

原始研究与Review大量混合：12篇References中，[3][5][7][8][9][10][11][12]为Review/综述性文章，并非直接产生HCC患者或实验数据的原始研究。