Opinion



# Helicobacter pylori infection suppresses anti-cancer immunotherapy

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Konovich EA
National Medical Research Center of Coloproctology, Russia

**Correspondence:** Konovich EA, Ryzhikh National Medical Research Center of Coloproctology, Moscow, Russian, Email evgkonovic@mail.ru

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## Opinion

Helicobacter pylori infection suppresses anti-cancer immunotherapy. Helicobacter pylori is ubiquitous. By suppressing the functions of the immune system, it promotes the development of chronic infection, ulcers, stomach cancer and reduces the effectiveness of anti-cancer immunotherapy. This issue is analyzed in a detailed review by P. Oster and colleagues at the University of Lausanne (Switzerland).[1]

In response to tumor development, the immune system generates various populations of cells, including CD8 T cells, which produce molecules (perforin, granzyme, tumor necrosis factor α, and others) that have a cytotoxic effect on cancer cells. In recent years, the attention of researchers has been focused on the study of surface immune checkpoint receptors (CTLA-4 and PD-1/PD-L1) of immune cells that regulate their activation and suppression. In tumors, the activity of these receptors limits the effectiveness of anticancer immunity.[2] With *H. pylori* infection, the expression of immune checkpoint receptors increases. Therefore, these receptors are considered important targets for anti-cancer therapy using their inhibitor-blocking monoclonal antibodies (ipilimumab, pembrolizumab, nivolumab/atezolizumab).[3] The gut microflora protects the body from pathogens and is involved in maintaining antitumor control.[4] A number of microorganisms (Bacteroides fragilis, Bifidobacterium and others) enhance the effectiveness of immune checkpoint inhibitors, while *H. pylori* suppresses them.[5] It has been established that lymphoid cells from the periphery migrate to the mucous membrane of the gastrointestinal tract and then settle back into the lymphoid organs. In the gastric tissue, there is a direct interaction between *H. pylori* antigens and stromal cells, such as lymphocytes, plasma cells, granulocytes, and others. *H. pylori* reduces the activity of immune system cells involved in antitumor immunity: Th1 and Th17 cells, dendritic cells, macrophages and natural killer T cells (NKT cells).[5–7] In infected mice, there was a significant decrease in the level of inflammatory cytokines, including INFγ, one of the main functions of which is to support antitumor immunity.[5]

In immunotherapy of mouse colon cancer with anti-CTLA antibodies, the number of tumors in uninfected mice was significantly lower than in those infected with H. pylori.[5] The number and activation of tumor-specific T cells decreased. Multiple *H. pylori* virulence factors limit adaptive immune responses by inhibiting T cell proliferation.[8] The ability of tumor-specific cytotoxic CD8 T cells to migrate to the tumor and draining lymph nodes is also reduced.[9] *H. pylori* infection inhibits the ability of dendritic cells to activate tumor-specific immune responses. The proliferation of tumor-specific T cells was reduced when they were co-cultivated with spleen dendritic cells from infected mice. H.pylori suppresses phagocytic killing of macrophages and promotes their apoptosis. Macrophages isolated from the gastric mucosa of infected mice exhibit an anti-inflammatory phenotype. Therefore, it is assumed that macrophages in infected tumor carriers, localized within the tumor and in draining lymphoid organs, do not adequately respond to anticancer immunotherapy.[10]

In general, these defects in infection may be key in reducing the effectiveness of cancer immunotherapy. In particular, this was confirmed in Canada during immunotherapy of patients with lung cancer with anti-PD-1 antibodies, while the survival of patients seropositive for *H. pylori* was 9.3months versus 21.7months in seronegative patients.[5]

An important factor is the age of infection. Studies with various microorganisms have shown that infection in the neonatal period leads to the development of immune tolerance, causing a decrease in T-cell and inflammatory responses to infection. As a result, the colonization of the microorganism reaches a high level.[11] Therefore, it is considered realistic that *H. pylori* infection in the neonatal period will lead to the development of local and systemic tolerance and subsequent immunosuppression in anticancer immunotherapy.[12] Investigation of the mechanisms of reduced response to immune checkpoint inhibitors caused by *H. pylori* infection will allow the development of new approaches to cancer immunotherapy.

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## Conflicts of interest

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## References

1. Oster P, Vaillant L, McMillian B, et al. The Efficacy of Cancer Immunotherapies Is Compromised by Helicobacter pylori Infection. *Front Immunol.* 2022;13:899161.
2. Ahmed MME. Innovative immune checkpoint inhibitors (ICIs) for cancer treatment: an overview. *Gastroenterol Hepatol Open Access*. 2023;14(1):1–5.

3. 3. Wei SC, Levine JH, Cogdill AP, et al. Distinct Cellular Mechanisms Underlie Anti-CTLA-4 and Anti-PD-1 Checkpoint Blockade. *Cell*. 2017;170(6):1120–1133.

4. Routy B, Le Chatelier E, Derosa L, et al. Gut Microbiome Influences Efficacy of PD-1-based Immunotherapy Against Epithelial Tumors. *Science*. 2018;359(6371):91–97.

5. Oster P, Vaillant L, Riva E, et al. Helicobacter Pylori Infection Has a Detrimental Impact on the Efficacy of Cancer Immunotherapies. *Gut*. 2022;71(3):457–466.

6. Bergman MP, Engering A, Smits HH, et al. Helicobacter Pylori Modulates the T Helper Cell 1/T Helper Cell 2 Balance Through Phase-Variable Interaction Between Lipopolysaccharide and DC-SIGN. *J Exp Med*. 2004;200(8):979–990.

7. Moyat M, Velin D. Immune Responses to Helicobacter Pylori Infection. *World J Gastroenterol WJG*. 2014;20(19):5583–5593.

8. Sundrud MS, Torres VJ, Unutmaz D, et al. Inhibition of Primary Human T Cell Proliferation by Helicobacter Pylori Vacuolating Toxin (VacA) is Independent of VacA Effects on IL-2 Secretion. *Proc Natl Acad Sci USA*. 2004;101(20):7727–7732.

9. Wu J, Zhu X, Guo X, et al. Helicobacter Urease Suppresses Cytotoxic CD8+ T-Cell Responses Through Activating Myh9- dependent Induction of PD-L1. *Int Immunol*. 2021;33(9):491-504.

10. Duan Z, Luo Y. Targeting Macrophages in Cancer Immunotherapy. *Signal Transduct Target Ther*. 2021;6(1):127.

11. Arnold IC, Lee JY, Amieva MR, et al. Tolerance Rather Than Immunity Protects From Helicobacter PyloriInduced Gastric Preneoplasia. *Gastroenterology*. 2011;140(1):199-209.

12. Shi Y, Zheng H, Wang M, et al. Influence of Helicobacter Pylori Infection on PD-1/PD-L1 Blockade Therapy Needs More Attention. *Helicobacter*. 2022;27(2):e12878.

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