BMC Research Notes

RESEARCH NOTE Open Access

Fusobacterium nucleatum confirmed in gastric biopsies of patients without *Helicobacter pylori*

Negin Kamali[1], Amin Talebi Bezmin Abadi[1*], Farid Rahimi[2] and Mojgan Forootan[3]

Abstract

Objective Putative associations between certain bacteria and gastric cancer have been described previously; however, the mechanisms underlying such associations are not thoroughly understood. We aimed to confirm the presence of *Fusobacterium nucleatum* in the biopsy samples of patients with gastroduodenal diseases, including gastric cancer, with concomitant or without *Helicobacter pylori* infection.

Results Three hundred patients with gastroduodenal disorders, including gastritis, duodenal ulcer, or gastric cancer, were included. One hundred and eighty (60%) patients were negative and 120 (40%) positive for *H. pylori*. Associations between the presence of *H. pylori* and age, gender, or other demographics were statistically insignificant ($p > 0.05$). The prevalence of *F. nucleatum* infection was determined for the two patient categories: 215 patients (72%) were positive for *F. nucleatum*; of these cases, 95 showed evidence of, and 120 lacked, concomitant *H. pylori* infection. Gastric biopsies obtained from patients with gastric cancer but negative for *H. pylori* revealed a significant prevalence of *F. nucleatum* infection.

Keywords Biopsy, DNA, *F. nucleatum*, Gastric cancer, Gastroduodenal diseases, *H. pylori*, PCR

Introduction

The human mucosal and epidermal microbiomes include microbial and fungal communities [1]. The gastric microbial community is a critical subset that warrants further study of its roles in human health and disease [2]. Cumulative evidence suggests that colonization by certain pathogens of the digestive system is associated with the progression of gastroduodenal disorders, including gastric cancer [3, 4]. Gastric cancer is influenced also by hosts' genetic polymorphisms and environmental factors. Among the microorganisms colonizing the human stomach [5], *Helicobacter pylori* crucially contributes to gastric cancer [6–8], and antibiotic therapy regresses cancerous tissues over time, but in some cases [9, 10]. Other bacterial species also may contribute to the pathogenesis, and been associated with an increased risk, of gastric cancer [11]; these include *Fusobacterium nucleatum*, *Propionibacterium acnes*, *Prevotella copri*, *Leptotrichia wadei*, *Prevotella melaninogenica*, and *Streptococcus anginosus*. Notably, *F. nucleatum* has been detected in gastric biopsies of patients with gastric cancer [12, 13]. This Gram-negative, rod-shaped, obligatory anaerobe normally colonizes the oral cavity and gastrointestinal tract [14]. Additionally, *F. nucleatum* is implicated in poor prognosis of colorectal cancer [15]. Discovery of gastric *F. nucleatum* in patients with gastric cancer challenges the conventional understanding of its roles and suggests a

*Correspondence:
Amin Talebi Bezmin Abadi
amin.talebi@modares.ac.ir
[1]Department of Bacteriology, Faculty of Medical Sciences, Tarbiat Modares University, Room 107, First floor, Tehran, Iran
[2]Research School of Biology, The Australian National University, Ngunnawal and Ngambri Country, Canberra, ACT, Australia
[3]Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

putative involvement in the pathogenesis of gastric cancer [16, 17]. Finding *F. nucleatum* at statistically significant levels among patients with gastric cancer without *H. pylori* infection thus warrants considering *F. nucleatum* as a therapeutic target, particularly for high-risk individuals, possibly to enhance the clinical management of the cancer.

Our research underscores the importance of gastroenterology in advancing our understanding of bacterial involvements in the pathogenesis of gastric cancer. Considering the present evidence, we conducted a cross-sectional study investigating the prevalence of *F. nucleatum* among Iranian patients with gastroduodenal disorders but without active *H. pylori* infection.

Materials and methods

Sampling

We aimed to identify the *F. nucleatum* DNA in biopsy samples obtained from patients diagnosed with digestive disorders, including gastritis, duodenal ulcer, and gastric cancer (Fig. 1). Voluntary participants were enrolled in the Mehrad Hospital and Labafi-Nejad Hospital, Tehran, Iran. For each patient, two biopsy samples were collected by a gastroenterologist by endoscopy. One of the samples was fixed in 10% (w/v) buffered formalin and forwarded to the pathology department for histology. The second sample was placed in a sterile tube containing fresh phosphate-buffered saline and transported within 3 h of endoscopy for microbiological and molecular analyses. The inclusion criteria were a specified age range and availability of gastric biopsy specimens. Our exclusion criteria included antibiotics therapy six weeks before endoscopy, pregnancy, history of abdominal surgery in the last two years, patients younger than 19 or older than 65, hypertension, and inflammatory bowel disease. The study was approved by the Ethics Committee of Tarbiat Modares University, Tehran, Iran (IR.MODARES.REC.1399.158) and conformed with the principles of the Declaration of Helsinki [18]. All participants provided written informed consents after being briefed about the study's objectives. They were assured that they may withdraw at any time without affecting their medical treatment.

DNA extraction

Genomic DNA was extracted from the biopsy samples using a commercial DNA-extraction kit (QIAGEN, Germany) according to standard instructions. The concentration and purity of the DNA were assessed at $\lambda = 260$ nm using a spectrophotometer (WPA, Biochrom, UK). Samples with a 260/280 absorbance ratio between 1.8 and 2.0 were deemed to be highly pure. One hundred µL of sample was kept at − 20 °C to prevent degradation until subsequent analyses. To detect *F. nucleatum* and *H. pylori*, specific primers targeting the *fusA* and *glmM*, respectively, were used [19]. *glmM* is a housekeeping gene crucial for the growth of microorganisms and has been extensively used to confirm the *H. pylori* presence

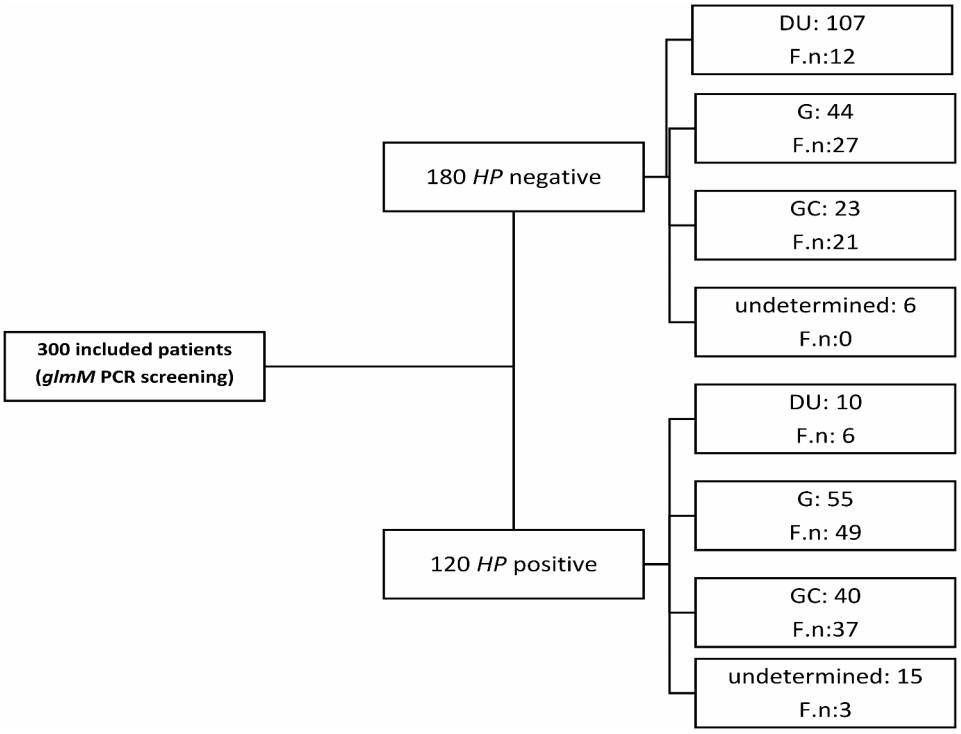

Fig. 1 Schematic of screening conducted in our survey including 300 patients

Table 1 Primer sequences and corresponding details for PCR amplification of *F. nucleatum* and *H. pylori fusA* and *glmM*, respectively

Primer	Oligonucleotide sequence (5′–3′)	Temperature (°C)	Product (bp)	References
fusA	CAACCATTACTTTAACTCTACCATGTTCA TACTGAGGGAGATTATGTAAAAATC	59	105	This study
glmM	AAGCTTTTAGGGGTGTTAGGGGTTT AAGCTTACTTTCTAACACTAACGC	58	294	[21]

Table 2 Observed prevalence of *F. nucleatum* in the samples and their predicted values by logistic regression model

Disease	H. pylori negative		H. pylori positive	
	Observed	Predicted	Observed	Predicted
Duodenal ulcer	0.113	0.119	0.444	0.380
Gastritis	0.600	0.615	0.891	0.879
Gastric cancer	0.913	0.848	0.925	0.962
Undetermined cases	0.000	0.043	0.188	0.171

in epidemiological studies. In our previous study, we used *fusA* for specifically identifying *F. nucleatum* in the biopsy specimens collected from patients admitted to our clinic [20]. Details of the primers, including their sequences, annealing temperatures, and product sizes, are presented in Table 1.

Polymerase chain reaction (PCR)

The target genes were amplified using PCR in 15 µL mixture that included 5 µL distilled water, 0.5 µL of each primer (10 pmol/µL), 8 µL of 2× master mix (Ampliqon, Copenhagen, Denmark), and 1 µL of extracted DNA. The master mix contained $MgCl_2$ (1.5 mM), dinucleotide triphosphates (0.2 mM each), and Taq polymerase (0.5 units). PCR was performed in a T100 Thermal Cycler (Bio-Rad, Berkeley, California) under the following conditions: initial denaturation at 95 °C (5 min) followed by 35 cycles of denaturation at 95 °C (30 s), annealing at 58–59 °C (30 s), extension at 72 °C (1 min), and a final extension at 72 °C (10 min). PCR products were confirmed by electrophoresis on a 1% (w/v) agarose gel (Sina Clon, Tehran, Iran) and stained with ethidium bromide. The gel was visualized under ultraviolet light using an transilluminator (Biometra, Germany), and the expected amplicon sizes were verified by comparison with a DNA ladder. All data were analyzed using SPSS version 20. To compare the presence of *F. nucleatum* and *H. pylori* among enrolled patients and the control group, Fisher's exact test and χ^2 test were used. $P<0.05$ was deemed statistically significant.

Results

Three hundred patients were enrolled in the study, with 180 (60%) who tested negative and 120 (40%) positive for *H. pylori*. Associations between the presence of *H. pylori* and age, gender, or other demographic variables were not statistically significant ($p>0.05$). The prevalence of *F. nucleatum* was analyzed in both groups. In this study, 215 patients (71%) were positive for *F. nucleatum*; of these, 95 showed evidence of concomitant *H. pylori* infection, whereas 120 were negative. For screening, observed rates of infection were determined across different disease categories. The results, modeled using logistic regression, are presented in Table 2. The highest prevalence of *F. nucleatum* occurred in patients diagnosed with gastric cancer, particularly among those negative for *H. pylori*. In contrast, the prevalence was significantly lower in patients with duodenal ulcers and those with undetermined conditions. Logistic regression analysis (Table 2) confirmed that *F. nucleatum* infection is more strongly associated with gastric cancer than with other gastric diseases, regardless of *H. pylori* status. Table 2 presents the prevalence of *F. nucleatum* in different disease groups, stratified by *H. pylori* status. For patients without *H. pylori* (*H. pylori* negative), the observed prevalence of *F. nucleatum* was the highest for gastric cancer (0.913), followed by gastritis (0.6), duodenal ulcer (0.113), and undetermined cases (0). The predicted rates were similar, with gastric cancer showing the highest chance (0.848); gastritis (0.615), duodenal ulcer (0.119), and undetermined cases (0.043) followed a similarly decreasing trend. In patients with *H. pylori*, observed rates were also the highest for gastric cancer (0.925), followed by gastritis (0.891), duodenal ulcer (0.444), and undetermined cases (0.188). The predicted prevalence mirrored the observed values closely, with gastric cancer showing the highest predicted chance at 0.962, gastritis at 0.879, duodenal ulcer at 0.380, and undetermined cases at 0.171. Thus, the logistic regression model closely predicted the presence of *F. nucleatum* in various conditions, with gastric cancer consistently showing the highest chance, especially in the presence of *H. pylori*.

Discussion

H. pylori has long been recognized as a risk factor for gastric cancer [22]. Over the past decade, besides *H. pylori*, infection with *F. nucleatum* has been discussed contextually to cancer progression in the human gastroduodenal tract [23, 24]. Consequently, our study was designed to investigate the presence of this potentially carcinogenic bacterium in this context. Accordingly, new findings highlight the complex interplay between colonization by different pathogenic bacteria and gastric cancer pathogenesis, suggesting mechanisms surpassing *H. pylori* [25]. Notably, detection of *F. nucleatum* in patients with

gastric cancer lacking *H. pylori* infection underscores the potential roles of alternative microbial entities in gastric carcinogenesis [26]. This hypothesis challenges the conventional perspective that *H. pylori* is the sole bacterial contributor to this malignancy and emphasizes the need to consider the broader gastric microbiome. By exploring the role of *F. nucleatum* and other microbial species, we can better understand the multifactorial nature of gastric cancer and uncover novel targets for prevention and treatment. *F. nucleatum* is commonly found in the oral cavity and the gut and has been linked to colorectal cancer because it can promote inflammation, immune evasion, and carcinogenesis [27]. We surmise that *F. nucleatum* may similarly contribute to gastric cancer by colonizing the gastric environment, particularly without *H. pylori*. The pathogenic mechanisms by *F. nucleatum* (e.g., immunosuppressive tumor microenvironment) align with those observed in other gastrointestinal malignancies [28, 29]. We hypothesize that the presence of *F. nucleatum* in patients with gastric cancer, but lacking *H. pylori*, may reflect the former's ability to exploit ecological niches left by the absence of *H. pylori*, highlighting its adaptability and pathogenic potential. Other bacterial species, such as *Streptococcus anginosus*, *Prevotella* spp., and *Propionibacterium acnes*, were detected in gastric biopsies from patients lacking *H. pylori* infection, suggesting that the influential gastric microbiota may constitute a broader network [30]. These bacteria may act synergistically or competitively (e.g., by using peptides and amino acids [31]), altering the homeostasis of gastric epithelial cells and contributing to the pathogenesis of gastric diseases [32, 33]. Interestingly, the absence of *H. pylori* may generate a favorable environment for opportunistic pathogens like *F. nucleatum*.

H. pylori infection was shown to influence the diversity of the gastric microbiota, often by limiting the colonization of other bacteria [34]. In its absence, other microbes may fill the ecological gaps, leading to an altered microbial profile that could contribute to gastric carcinogenesis. This hypothesis is supported by our finding of distinct microbial profiles in patients negative for *H. pylori* compared with their positive counterparts. The observed and predicted prevalences of *F. nucleatum* in our study further illustrate its potential role in gastric diseases. In patients colonized with *H. pylori*, *F. nucleatum* was most strongly associated with gastric cancer, followed by gastritis and duodenal ulcer. The relatively high prevalence of *F. nucleatum* in gastritis and gastric cancer suggests that it may play a key role by promoting chronic inflammation to malignancy. The low but notable observed prevalence of *F. nucleatum* in duodenal ulcers indicates a potential involvement in other conditions of the upper gastrointestinal tract. These findings support the hypothesis that *F. nucleatum* may contribute to the full spectrum of gastroduodenal diseases, from inflammatory conditions to malignancies.

Our study highlights the need to further investigate the microbial interactions that occur in patients with gastric cancer without *H. pylori*. Understanding the role of *F. nucleatum* in the gastric environment, as well as its interactions with other microorganisms (for example [31]), could provide new insights into the mechanisms of gastric carcinogenesis. Future studies should focus on the competitive and cooperative dynamics between microbial species (especially dysbiosis), the potential for interspecies interactions, the impact of these interactions on hosts' inflammatory and immune responses, and epithelial homeostasis. Investigating how *F. nucleatum* and other opportunistic pathogens adapt to the gastric mucosa could inform therapeutic strategies aimed at modulating the microbiome to prevent or treat gastric cancer. *F. nucleatum* infection reportedly correlates with increased accumulation of mutations such as in *ERBB2* and *ERBB3* and progression of gastric cancer [23, 35]. Our study may serve as a pilot study for future large-scale investigations of the microbial communities that inhabit the human stomach particularly without *H. pylori*. *F. nucleatum* reportedly promotes the development of host immune responses that favor the progression of colorectal cancer. The distinct cell surface proteins Fap2 and FadA produced by *F. nucleatum* reportedly enhance the production of inflammatory factors, which support tumor growth within the human gut microenvironment [36]. Additionally, several virulence factors of *F. nucleatum* can inhibit activity of the T cells and may accelerate the carcinogenic processes [37]. Given the biological cascade initiated by infection with *F. nucleatum*, considering it as a potential contributor to the pathogenesis of other types of cancer in the human stomach is reasonable providing that all favorable conditions are present.

In conclusion, the colonization of bacteria like *F. nucleatum* in patients without *H. pylori* opens new avenues for understanding gastric carcinogenesis [23]. Our findings suggest that microbial communities, irrespective of *H. pylori*, play a significant role in determining gastric health and disease [38]. While we do not propose *F. nucleatum* as a definitive cancer-inducing microbial signature, we recommend further investigation into its role in patients without *H. pylori* infection, mainly diagnosed with gastric cancer. Such research could lead to the development of targeted microbiome-based therapies for gastric cancer and improve our understanding of the complex relationships between microorganisms and gastric malignancies.

Limitations

- We used solely a DNA-based approach to confirm the presence of the studied bacteria. For better insight into the proposed hypothesis, further molecular, and genomic analyses, and interactomics may provide encompassing data on the composition of microbial communities and their potential interactions.
- A larger sample size may help strengthen the conclusions. Ethical considerations limited our intention to procure a large sample size.
- We intended to obtain biopsies from the gastric corpus and antrum, but ethical and operational considerations hampered the biopsy process. We suggest designing a project to compare the gastric antrum and corpus samples.
- Our study coincided with the resurgence of the SARS-CoV-2 Omicron variant that may have affected the patient populations presenting to the hospital.

Author contributions
All authors contributed equally to writing, conception, and data curation, and they all agreed to submit this paper to BMC. All authors approved the presented version of the paper for publication.

Funding
The study was financially supported by the grant 99023373 by the Iran National Science Foundation.

Data availability
The datasets used and/or analysed in the study are available from the corresponding author on reasonable request.

Declarations

Human ethics and consent to participate
We obtained ethical approval from the Tarbiat Modares University, Tehran, Iran (IR.MODARES.REC.1399.158). Informed consent was obtained from all participants involved in the research. Each participant was provided with detailed information regarding the study's purpose, procedures, potential risks, and benefits, ensuring that they understood their rights to withdraw at any time without penalty. None of the study participants were under 19 years; thus, consents by legal guardians or parents were not required.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 23 December 2024 / Accepted: 24 February 2025
Published online: 11 March 2025

References
1. Dzutsev A, Goldszmid RS, Viaud S, Zitvogel L, Trinchieri G. The role of the microbiota in inflammation, carcinogenesis, and cancer therapy. Eur J Immunol. 2015;45(1):17–31.
2. Bravo D, Hoare A, Soto C, Valenzuela MA, Quest AF. *Helicobacter pylori* in human health and disease: mechanisms for local gastric and systemic effects. World J Gastroenterol. 2018;24(28):3071–89.
3. Hsieh Y-Y, Tung S-Y, Pan H-Y, Chang T-S, Wei K-L, Chen W-M et al. *Fusobacterium nucleatum* promotes gastric cancer aggressiveness through upregulation of cell mobility and interferon genes. Res Sq. 2020.
4. Lin CS, Chang CJ, Lu CC, Martel J, Ojcius DM, Ko YF, et al. Impact of the gut microbiota, prebiotics, and probiotics on human health and disease. Biomed J. 2014;37(5):259–68.
5. Wong SH, Kwong TNY, Wu CY, Yu J. Clinical applications of gut microbiota in cancer biology. Semin Cancer Biol. 2019;55:28–36.
6. Thrift AP, El-Serag HB. Burden of gastric cancer. Clin Gastroenterol Hepatol. 2020;18(3):534–42.
7. Wroblewski LE, Peek RM Jr., Wilson KT. *Helicobacter pylori* and gastric cancer: factors that modulate disease risk. Clin Microbiol Rev. 2010;23(4):713–39.
8. Hussein RA, Al-Ouqaili MTS, Majeed YH. Association between alcohol consumption, cigarette smoking, and *Helicobacter pylori* infection in Iraqi patients submitted to gastrointestinal endoscopy. J Emerg Med Trauma Acute Care. 2022;2022:6.
9. Fiocca R. Epidemiology and interventiaonl studies. *Helicobacter pylori* and gastric cancer: progression/regression of histopathological lesions. Eur J Gastroenterol Hepatol. 2000;12(9):1044–9.
10. Nam SY, Park BJ, Ryu KH, Nam JH. Effect of *Helicobacter pylori* eradication on the regression of gastric polyps in National Cancer screening program. Korean J Intern Med. 2018;33(3):506–11.
11. de Leeuw MA, Duval MX. The presence of periodontal pathogens in gastric cancer. Explor Res Hypothesis Med. 2020;000(000):1–10.
12. Boehm ET, Thon C, Kupcinskas J, Steponaitiene R, Skieceviciene J, Canbay A, et al. *Fusobacterium nucleatum* is associated with worse prognosis in Lauren's diffuse type gastric cancer patients. Sci Rep. 2020;10(1):16240.
13. Hsieh YY, Tung SY, Pan HY, Yen CW, Xu HW, Lin YJ, et al. Increased abundance of Clostridium and Fusobacterium in gastric microbiota of patients with gastric cancer in Taiwan. Sci Rep. 2018;8(1):158.
14. Abed J, Maalouf N, Manson AL, Earl AM, Parhi L, Emgard JEM, et al. Colon cancer-associated *Fusobacterium nucleatum* may originate from the oral cavity and reach colon tumors via the circulatory system. Front Cell Infect Microbiol. 2020;10:400.
15. Yamamura K, Baba Y, Miyake K, Nakamura K, Shigaki H, Mima K, et al. *Fusobacterium nucleatum* in gastroenterological cancer: evaluation of measurement methods using quantitative polymerase chain reaction and a literature review. Oncol Lett. 2017;14(6):6373–8.
16. Janati AI, Karp I, Laprise C, Sabri H, Emami E. Detection of *Fusobaterium nucleatum* in feces and colorectal mucosa as a risk factor for colorectal cancer: A systematic review and meta-analysis. Syst Rev. 2020;9(1):276.
17. Loke YL, Chew MT, Ngeow YF, Lim WWD, Peh SC. Colon carcinogenesis: the interplay between diet and gut microbiota. Front Cell Infect Microbiol. 2020;10:603086.
18. World Medical Association. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.
19. Espinoza MG, Vazquez RG, Mendez IM, Vargas CR, Cerezo SG. Detection of the *GlmM* gene in *Helicobacter pylori* isolates with a novel primer by PCR. J Clin Microbiol. 2011;49(4):1650–2.
20. Kashani N, Bezmin Abadi AT, Rahimi F, Forootan M. *FadA*-positive *Fusobacterium nucleatum* is prevalent in biopsy specimens of Iranian patients with colorectal cancer. New Microbes New Infect. 2020;34:100651.
21. Lu JJ, Perng CL, Shyu RY, Chen CH, Lou Q, Chong SK, et al. Comparison of five PCR methods for detection of *Helicobacter pylori* DNA in gastric tissues. J Clin Microbiol. 1999;37(3):772–4.
22. Reyes VE. *Helicobacter pylori* and its role in gastric cancer. Microorganisms. 2023;11(5):1312.
23. Hsieh YY, Kuo WL, Hsu WT, Tung SY, Li C. *Fusobacterium nucleatum*-induced tumor mutation burden predicts poor survival of gastric cancer patients. Cancers (Basel). 2022;15(1).
24. Wen J, Lau HC, Peppelenbosch M, Yu J. Gastric microbiota beyond *H. pylori*: an emerging critical character in gastric carcinogenesis. Biomedicines. 2021;9(11).
25. Zhang C, Chen Y, Long Y, Zheng H, Jing J, Pan W. *Helicobacter pylori* and gastrointestinal cancers: recent advances and controversies. Clin Med Insights Oncol. 2024;18:11795549241234637.
26. Hatakeyama M. Impact of the *Helicobacter pylori* oncoprotein CagA in gastric carcinogenesis. Curr Top Microbiol Immunol. 2023;444:239–57.
27. Petkevicius V, Lehr K, Kupcinskas J, Link A. *Fusobacterium nucleatum*: unraveling its potential role in gastric carcinogenesis. World J Gastroenterol. 2024;30(35):3972–84.

28. Sun J, Feng S, Ding T, Wang T, Du L, Kang W, et al. *Fusobacterium nucleatum* dysregulates inflammatory cytokines and NLRP3 inflammasomes in oral cells. Oral Dis. 2024;30(7):4767–81.
29. Wang N, Fang JY. *Fusobacterium nucleatum*, a key pathogenic factor and microbial biomarker for colorectal cancer. Trends Microbiol. 2023;31(2):159–72.
30. Sgamato C, Rocco A, Compare D, Priadko K, Romano M, Nardone G. Exploring the link between *Helicobacter pylori*, gastric microbiota and gastric cancer. Antibiot (Basel). 2024;13(6):484.
31. Tang-Larsen J, Claesson R, Edlund MB, Carlsson J. Competition for peptides and amino acids among periodontal bacteria. J Periodontal Res. 1995;30(6):390–5.
32. Sohn SH, Kim N, Jo HJ, Kim J, Park JH, Nam RH, et al. Analysis of gastric body microbiota by pyrosequencing: possible role of bacteria other than *Helicobacter pylori* in the gastric carcinogenesis. J Cancer Prev. 2017;22(2):115–25.
33. Gomez-Ramirez U, Valencia-Mayoral P, Mendoza-Elizalde S, Murillo-Eliosa JR, Solorzano Santos F, Contreras-Rodriguez A, et al. Role of *Helicobacter pylori* and other environmental factors in the development of gastric dysbiosis. Pathogens. 2021;10(9):1203.
34. Kim N, Jo HJ. The effect of *H. pylori* infection on the gastric microbiota. In: Kim N, editor. Helicobacter pylori. Singapore: Springer Nature Singapore; 2023. pp. 701–23.
35. Gholizadeh P, Eslami H, Kafil HS. Carcinogenesis mechanisms of *Fusobacterium nucleatum*. Biomed Pharmacother. 2017;89:918–25.
36. Wu J, Li Q, Fu X. *Fusobacterium nucleatum* contributes to the carcinogenesis of colorectal cancer by inducing inflammation and suppressing host immunity. Transl Oncol. 2019;12(6):846–51.
37. Zhang N, Liu Y, Yang H, Liang M, Wang X, Wang M, et al. Clinical significance of *Fusobacterium nucleatum* infection and regulatory T cell enrichment in esophageal squamous cell carcinoma. Pathol Oncol Res. 2021;27:1609846.
38. Slade DJ. New roles for *Fusobacterium nucleatum* in cancer: target the bacteria, host, or both? Trends Cancer. 2021;7(3):185–7.

Publisher's note