

Serum TNF- α and IL-8 as predictors of gastric mucosal cancerization in *Helicobacter pylori*-positive gastritis

Zhuoyu Peng^{1#}, Xuelian Yang^{2#}, Min Li¹, Di Wan³, Juju Liu^{4*}

1. Department of Gastroenterology, The First Affiliated Hospital of Guangxi University of Chinese Medicine, Nanning, China
2. Department of Gastroenterology, Tai'an Central Hospital, Tai'an, China
3. Graduate School of Guangxi University of Chinese Medicine, Nanning, China
4. Clinical Medical College of Hubei College of Chinese Medicine, Jingzhou, China

ABSTRACT

Background: *Helicobacter pylori* (HP) infection is a well-established risk factor for gastric carcinogenesis, primarily through the induction and maintenance of chronic gastric mucosal inflammation. In this study, we aimed to explore the correlations of tumor necrosis factor- α (TNF- α) and interleukin-8 (IL-8) levels with the risk of gastric mucosal cancerization in patients with HP-positive gastritis.

Methods: Subjects (200 in total) in this retrospective study were enrolled from patients with HP-positive gastritis treated from January 2022 to December 2024. A non-cancer group (n=80, patients with chronic superficial gastritis and atrophic gastritis) and a cancer group (n=120, patients with gastric cancer) were set based on the condition of mucosal lesions. Measurement of serum TNF- α and IL-8 levels was completed through enzyme-linked immunosorbent assay. The ¹⁴C-urea breath test was conducted to determine the status of HP infection. Multivariate regression analysis was employed to identify the influencing factors of gastric mucosal cancerization risk. Receiver operating characteristic (ROC) curve analysis was also conducted.

Results: The serum TNF- α and IL-8 levels were significantly higher in the cancer group than in the non-cancer group ($p<0.05$). Both TNF- α and IL-8 levels displayed significantly positive correlations with the risk of gastric mucosal cancerization ($r=0.785$, $r=0.812$, $p<0.05$). Elevated TNF- α and IL-8 levels, high severity of HP infection and presence of virulence factor cytotoxin-associated gene A were independent risk factors for gastric mucosal cancerization ($p<0.05$). The areas under the ROC curves of serum TNF- α and IL-8 levels were 0.798 and 0.698, respectively ($p<0.01$).

Conclusions: This study reveals a close positive correlation between serum TNF- α and IL-8 levels and the risk of gastric mucosal cancerization in patients with HP-positive gastritis.

Keywords: correlation, gastritis, *Helicobacter pylori*, interleukin-8, tumor necrosis factor

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INTRODUCTION

Defined as gastric mucosal inflammation owing to various factors, gastritis is one of the most common diseases of the digestive system, in which the gastric mucosa experiences a series of inflammatory changes like congestion, edema, erosion, and bleeding, and epithelial damage plus inflammatory cell infiltration in the membrane propria may occur concurrently. The abovementioned variations will affect the normal physiological function of the stomach and lead to various uncomfortable symptoms [1,2]. *Helicobacter pylori* (HP), one of the usual contributing factors to gastritis, can easily penetrate the gastric mucosa by virtue of its spiral structure, and the

resulting urease is able to decompose urea, generating ammonia to neutralize gastric acid. Accordingly, a microenvironment conducive to HP survival is created. In the meantime, HP secretes various toxins and enzymes, damaging the gastric mucosal barrier and triggering an inflammatory response [3].

The long inflammatory process involves the activation and release of multiple cytokines. Among them, tumor necrosis factor- α (TNF- α) and interleukin-8 (IL-8) acting as core regulators of inflammatory responses are capable of causing fever and inflammatory responses, which have gradually become research focuses. As a crucial inflammatory mediator, TNF- α is mainly generated by acti-

* Corresponding author: Juju Liu, Clinical Medical College of Hubei College of Chinese Medicine, Jingzhou, China. E-mail: liujhccm@sdsch.cn
These authors contributed equally to this work and share first authorship

vated macrophages and monocytes, inducing fever and an inflammatory response [4]. IL-8, produced by various cells upon stimulation, is able to participate in the regulation of inflammatory responses, facilitate angiogenesis, and enhance vascular permeability, thus increasing the blood supply to inflammatory sites, which is conducive to the arrival of immune cells and mediators [5]. However, the specific mechanism by which TNF- α and IL-8 levels modulate the risk of gastric mucosal cancerization in patients with HP-positive gastritis has been rarely studied.

Therefore, we hypothesized that elevated serum levels of TNF- α and IL-8 are significantly associated with an increased risk of gastric mucosal cancerization in patients with HP-positive gastritis, reflecting systemic inflammatory activation linked to mucosal malignant transformation. The study aimed to clarify this relationship within a defined clinical population by integrating clinical characteristics with serum biomarker analysis.

METHODS

The study was approved by the research ethics committee of the The First Affiliated Hospital of Guangxi University of Chinese Medicine (approval No. 2023-KY-KZ-214-01).

Subjects

Subjects (n=200) were recruited from patients with HP-positive gastritis treated in our hospital from January 2022 to December 2024 and then assigned to two groups. All participants were patients who underwent gastroscopy in our hospital, either for upper gastrointestinal symptoms (such as epigastric discomfort, bloating, or reflux) or as part of routine health examination. Tissue specimens obtained during endoscopy were used for histopathological examination to confirm the presence of HP infection, but no additional molecular or immunohistochemical analyses were performed on the tissue samples. Namely, a non-cancer group and a cancer group according to the condition of gastric mucosal lesions. The non-cancer group consisted of 80 patients suffering from chronic superficial gastritis and chronic atrophic gastritis diagnosed based on gastroscopic and pathological examination results. The histopathological manifestations of the gastric mucosa suggested the presence of chronic infiltration of inflammatory cells (mainly lymphocytes and plasma cells) in the mucosal membrane propria, together with the absence of cancer cells. The cancer group was composed of 120 patients diagnosed with gastric cancer by gastroscopy pathological biopsy.

The implemented inclusion criteria were as follows: 1) patients with confirmed HP infection, determined by either a positive ^{14}C -urea breath test or histopathological detection of HP on gastric biopsy specimens, 2) those

with an age of >18 years old, 3) those with normal cognitive and communication function, and 4) those who and whose family members were informed of the present study and had signed the consent form.

The following exclusion criteria were adopted in the current study: 1) patients with congenital heart disease or other congenital cardiovascular diseases, 2) those complicated with multiple myeloma or other diseases of the immune or hematological system, 3) those administered with antibiotics, proton pump inhibitors or other drugs probably affecting HP test results in the past 4 weeks, or 4) those with other severe inflammatory diseases (such as rheumatoid arthritis and inflammatory bowel disease) and those who had recently used anti-inflammatory drugs.

^{14}C -urea breath test

The patient was instructed to orally take a capsule containing ^{14}C -labeled urea and drink 20-30 ml of warm water. After taking the capsule, the patient needed to sit or lie still for 30-60 minutes. During this period, the patient had to remain quiet and avoid strenuous exercise and eating. Then the patient exhaled into the gas collection bottle until the liquid in the bottle changed from pink to colorless, without blowing saliva to affect the test results. The collected breath sample was then examined for HP infection by detecting the level of ^{14}C -labeled carbon dioxide.

All participants underwent endoscopic gastric mucosal biopsies as part of routine care. The severity of HP infection was graded histologically according to the Updated Sydney System on antral and corpus specimens by two experienced pathologists blinded to clinical data (0-3: none, mild, moderate, severe) [6].

Enzyme-linked immunosorbent assay

The presence of the virulence factor cytotoxin-associated gene A (CagA) was determined by enzyme-linked immunosorbent assay (ELISA) using a commercial CagA IgG detection kit (Shanghai Enzyme-linked Biotechnology Co., Ltd., China), according to the manufacturer's instructions. Serum samples were collected from all participants after overnight fasting and prior to endoscopic examination. The concentrations of TNF- α and IL-8 were determined from serum using ELISA kits from the same manufacturer, following the provided protocols. No cytokine measurements were performed on gastric tissue specimens.

Venous blood (3-5 mL from each subject) was collected into a vacuum blood collection tube containing anti-coagulant, which was then inverted 5-8 times to mix the blood and the anticoagulant, let stand at room temperature for 15-30 min, and centrifuged at 2,000-3,000 rpm for 10-15 min. Next, the upper plasma was harvested

into a clean EP tube. The gastric mucosal tissue samples were subjected to homogenization and centrifugation, and the resulting supernatant was collected. The reagents in the kit were equilibrated at room temperature for 30-60 min. The standard was diluted to 6-8 concentration gradients through doubling dilution according to the instructions. Afterwards, the plasma or supernatant was added into wells of the plate at 50-100 μ L/well and incubated for 30-60 min. Thereafter, the liquid was removed, and the plate was washed 3-5 times. Subsequently, 50-100 μ L of enzyme-labeled antibodies were added to each well, followed by 30-60 min of incubation and then plate washing. Afterwards, substrates A and B were added for 15-30 min of color development in the dark. Finally, the stop buffer was added at 50 μ L/well, and reading was accomplished within 15-30 min.

Collection of clinical data

The detailed clinical data were collected from patients, covering age, gender, smoking history (smoking 1 or more cigarettes per day for ≥ 1 year), drinking history (drinking alcohol ≥ 2 times per week for ≥ 1 year), history of gastric diseases (gastric ulcer, duodenal ulcer, and gastric polyps, for example), and family history of gastric cancer.

Statistical analysis

Statistical analysis was completed with SPSS 26.0 and MedCalc (V 20.0.3) software. Measurement data with normal distribution were expressed as ($\bar{x} \pm s$) and compared using the independent-samples t test, while count data were presented as [n (%)] and analyzed by the chi-square test. Prior to correlation analysis, the normality of continuous variables was tested using the Shapiro-Wilk test. As TNF- α and IL-8 levels followed an approximately normal distribution, Pearson correlation analysis was applied to assess their relationships with

the risk of gastric mucosal cancerization. Multicollinearity among independent variables was examined using variance inflation factor (VIF) values (<5 indicating acceptable levels). Multivariate logistic regression analysis was conducted on factors with $p < 0.05$ in univariate analysis, with the regression coefficient β , standard error (SE), odds ratio (OR) and 95% confidence interval (95% CI) of each factor recorded. Model fitness was evaluated using the Hosmer–Lemeshow goodness-of-fit test ($p > 0.05$ indicating adequate fit). Receiver operating characteristic (ROC) curves were plotted to determine the optimal cut-off values of significant factors, and the area under the ROC curve (AUC), Youden index (YI), and 95% CI were calculated. P value < 0.05 was considered statistically significant.

RESULTS

General data

No differences of statistical significance were found in the age, gender, smoking history, and drinking history between the non-cancer group and the cancer group ($p > 0.05$), but statistically significant differences were observed in the history of gastric diseases and family history of gastric cancer between the two groups ($p < 0.05$) (Table 1).

TNF-alpha and IL-8 levels

The serum TNF- α levels were higher in the cancer group than in the non-cancer group (1.44 ± 0.30 ng/mL vs 1.07 ± 0.28 ng/L, with statistically significant differences ($p < 0.01$). Similar findings were recorded for IL-8 (5.89 ± 1.42 vs 4.55 ± 1.22 mmol/L, $p < 0.01$).

Moreover, significant positive correlations were found between TNF- α and IL-8 levels, and mucosal cancerization: $r = 0.785$ and $r = 0.812$, respectively ($p < 0.01$ for both).

Table 1. General data of the cancer and non-cancer groups

		Cancer group (n=120)	Non-cancer group (n=80)	t/ χ^2	p value
Sex, n (%)	Male	75 (62.50)	48 (60.00)	0.127	0.722
	Female	45 (37.50)	32 (40.00)		
Age (years)		54.32 ± 4.89	54.85 ± 4.56	0.771	0.441
Disease course (months)		4.52 ± 0.31	4.58 ± 0.30	1.358	0.176
Smoking history, n (%)	Yes	47 (39.17)	25 (31.25)	1.306	0.253
	No	73 (60.83)	55 (68.75)		
Drinking history, n (%)	Yes	38 (31.67)	19 (23.75)	1.476	0.224
	No	82 (68.33)	61 (76.25)		
History of gastric diseases, n (%)	Yes	83 (69.17)	41 (51.25)	6.540	0.011
	No	37 (30.83)	39 (48.75)		
Family history of gastric cancer, n (%)	Yes	85 (70.83)	37 (46.25)	12.194	< 0.01
	No	35 (29.17)	43 (53.75)		
Severity of HP infection*		8.54 ± 0.21	4.11 ± 0.12	170.907	< 0.01
CagA-positive, n (%)	Yes	89 (74.17)	38 (47.80)	14.727	< 0.01
	No	31 (25.83)	42 (52.50)		

* Severity of HP infection was graded histologically according to the Updated Sydney System on antral and corpus specimens by two experienced pathologists blinded to clinical data (0-3: none, mild, moderate, severe). Abbreviations: CagA – cytotoxin-associated gene A, HP – *Helicobacter pylori*.

Results of multivariate regression analysis

Variables of statistical significance identified from the analysis of general data and serum TNF- α and IL-8 levels were incorporated into a multivariate regression model for analysis, which included: serum TNF- α , serum IL-8, severity of HP infection, CagA (yes=0, no=1), history of gastric diseases (yes=0, no=1), and family history of gastric cancer (yes=0, no=1). The results revealed that highly expressed TNF- α and IL-8, high severity of HP infection, presence of virulence factor CagA, history of gastric diseases and family history of gastric cancer were independent risk factors for gastric mucosal cancerization (Table 2).

Results of ROC curve analysis on TNF-alpha and IL-8 levels in patients with HP-positive gastritis

For the ROC analysis, the risk of cancerization in patients with HP-positive gastritis was set as the positive outcome. The statistical analysis revealed that the AUCs of serum TNF- α and IL-8 levels were 0.798 [0.731-0.848] and 0.698 [0.629-0.761], respectively ($p < 0.01$ for both). The curves are plotted in Figure 1.

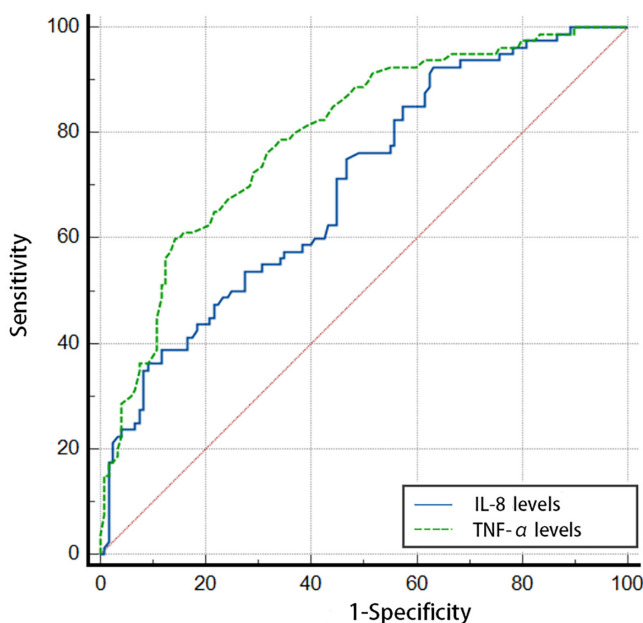


Figure 1. ROC curves for the risk of cancerization in patients with *Helicobacter pylori*-positive gastritis.

DISCUSSION

Summary of main findings

In the present study, serum TNF- α and IL-8 levels were found to be significantly higher in patients with gastric mucosal cancerization compared with those without cancerization, and both cytokines were independently associated with the risk of malignant transformation in HP-positive gastritis. These results highlight the potential value of TNF- α and IL-8 as inflammatory mediators linking chronic HP infection to gastric carcinogenesis.

Our findings demonstrate that elevated TNF- α and IL-8 levels are not merely byproducts of inflammation but play active roles in promoting mucosal damage and tumorigenic transformation. TNF- α contributes to inflammation-induced cellular injury through activation of immune cells, regulation of the inflammatory cascade, and promotion of angiogenesis and cell proliferation, whereas IL-8 enhances neutrophil chemotaxis and angiogenic signaling, amplifying the inflammatory micro-environment. Collectively, these results support the concept that persistent inflammatory activation mediated by TNF- α and IL-8 constitutes a key mechanism driving the progression from HP-positive gastritis to gastric mucosal cancerization.

Comparison with previous studies

The findings of this study are generally consistent with previous research investigating the relationship between inflammatory cytokines and HP-related gastric mucosal lesions. In the present analysis, serum TNF- α and IL-8 levels were significantly elevated in the cancer group compared with the non-cancer group, which agrees with earlier reports that chronic HP infection induces persistent inflammatory activation leading to tissue injury and carcinogenic progression [7].

Previous studies have shown that, within the inflammatory microenvironment caused by HP infection, activated macrophages, monocytes, and other immune cells secrete TNF- α , which stimulates the expression of adhesion molecules in vascular endothelial cells and promotes leukocyte adhesion and infiltration at inflammatory sites, thereby aggravating local inflammation [8].

Table 2. Multivariate regression analysis on risk of gastric mucosal cancerization in patients with HP-positive gastritis

Influencing factor	Regression coefficient	SE	p value	OR	95% CI for OR
High expression level of serum TNF- α	0.421	0.118	< 0.001	1.52	1.21 – 1.92
High expression level of serum IL-8	0.387	0.134	0.004	1.47	1.13 – 1.91
High severity of HP infection	0.296	0.102	0.004	1.34	1.10 – 1.63
Presence of virulence factor CagA	0.512	0.181	0.005	1.67	1.17 – 2.38
History of gastric diseases	0.463	0.192	0.016	1.59	1.09 – 2.33
Family history of gastric cancer	0.538	0.210	0.010	1.71	1.13 – 2.58

Abbreviations: CagA – cytotoxin-associated gene A, CI – confidence interval, HP – *Helicobacter pylori*, IL-8 – interleukin-8, OR – odds ratio, SE – standard error, TNF- α – tumor necrosis factor-alpha.

In addition, TNF- α can trigger the NF- κ B signaling pathway to upregulate pro-inflammatory mediators such as IL-1 β and IL-6, forming a self-perpetuating inflammatory network that disrupts gastric mucosal integrity [9].

Similarly, IL-8 has been reported to mediate chemotaxis of neutrophils and lymphocytes and to induce DNA damage in gastric epithelial cells, while its activation of the MAPK signaling cascade promotes cellular proliferation and angiogenesis, further contributing to malignant transformation [10,11]. Consistent with these observations, our study confirmed that elevated serum TNF- α and IL-8 levels correlate with the severity of gastric mucosal lesions, reinforcing their carcinogenic roles in HP-related gastric disease progression.

Potential mechanisms

In the present study, correlation and multivariate regression analyses demonstrated that serum TNF- α and IL-8 levels were strongly associated with the risk of gastric mucosal cancerization in patients with HP-positive gastritis, suggesting that these inflammatory cytokines may actively participate in the malignant transformation process. The results revealed a significantly positive relation between the level of TNF- α and the risk of gastric mucosal cancerization, signifying that TNF- α may promote gastric mucosal cancerization through multiple biological pathways. Mechanistically, high TNF- α expression can activate intracellular signaling cascades such as the NF- κ B pathway, inducing resistance to apoptosis and enhancing the survival of damaged cells. As a result, survival of injured cells together with accumulation of genetic damage is observed, increasing the risk of cancerization [12].

IL-8 appears to exert a similarly crucial role but through distinct mechanisms. The results of the present study showed that IL-8 displayed an even stronger correlation with the risk of gastric mucosal cancerization. Mainly secreted by inflammatory and epithelial cells, IL-8 mediates chemotaxis of neutrophils, T lymphocytes, and other immune cells to inflammatory sites, sustaining chronic inflammation and tissue injury [13]. In addition, IL-8 activates downstream pathways such as MAPK, promoting cell proliferation, angiogenesis, and inhibition of apoptosis, thereby facilitating malignant transformation of gastric epithelial cells [14].

Beyond cytokine-mediated mechanisms, HP infection itself serves as the initiating driver of this pathogenic cascade. The higher the severity of infection, the more extensive the mucosal injury and the greater the cancerization risk. HP strains carrying the virulence factor CagA are particularly pathogenic, as CagA interferes with intracellular signaling, disrupts cell polarity, and induces abnormal epithelial proliferation, thereby facilitating tumorigenesis [15].

Host-related factors further amplify these molecular effects. The history of gastric diseases, including gastric ulcer

and atrophic gastritis, places the gastric mucosa in a state of repeated injury and repair, predisposing it to genetic mutations and abnormal cell proliferation, thus increasing the likelihood of cancerization. Likewise, a family history of gastric cancer underscores the role of inherited susceptibility, potentially involving genetic variations of oncogenes and tumor suppressor genes, which collectively enhance the individual's predisposition to malignant transformation.

Clinical implications

The clinical findings of this study provide important implications for early detection and prevention of gastric mucosal cancerization in HP-positive patients. Multivariate regression analysis confirmed that elevated serum TNF- α and IL-8 levels, greater severity of HP infection, presence of the virulence factor CagA, a history of gastric diseases, and a family history of gastric cancer served as independent risk factors for gastric mucosal cancerization. The AUCs of serum TNF- α and IL-8 levels were 0.798 and 0.698, respectively, indicating their potential diagnostic and predictive value.

From a clinical perspective, TNF- α and IL-8 may serve as accessible and noninvasive biomarkers reflecting the degree of inflammatory activation and malignant transformation risk in HP-related gastric lesions [16,17]. TNF- α , a key inflammatory mediator, is a crucial player in HP-induced gastric mucosal inflammation, and its persistently elevated levels can significantly increase the risk of mucosal cancerization. This aligns with previous studies demonstrating the proinflammatory and tumor-promoting effects of TNF- α in gastric carcinogenesis, further confirming its pivotal role in the progression from HP-positive gastritis to gastric cancer [18,19]. IL-8, which regulates inflammation and angiogenesis, may facilitate tumor growth, metastasis, and immune evasion when overexpressed, thereby aggravating mucosal malignant transformation [20].

From a preventive perspective, the present findings suggest that serum TNF- α and IL-8 levels may serve as accessible biomarkers for identifying HP-positive gastritis patients at higher risk of gastric mucosal malignant transformation. Early detection of elevated inflammatory cytokines could help stratify patients who would benefit from closer endoscopic surveillance or timely eradication therapy of HP infection. Incorporating these markers into preventive screening strategies may therefore contribute to reducing the incidence of gastric cancer through early risk identification and intervention.

Limitations and future directions

Several limitations should be acknowledged in this study. First, the retrospective single-center design may introduce selection bias and limit the generalizability of the findings. Second, although multivariate regression

analysis was conducted to identify independent risk factors, other potential confounding variables-such as dietary habits, medication use, and coexisting metabolic conditions-were not included due to incomplete clinical data. Third, the assessment of HP infection severity was based on ^{14}C -urea breath test values, which, although widely used, may not fully reflect the bacterial load in the gastric mucosa. Finally, the relatively limited sample size warrants validation in larger, multicenter prospective studies. In future research, longitudinal and multicenter cohort studies should be conducted to dynamically monitor changes in TNF- α and IL-8 levels during the progression from HP-positive gastritis to gastric mucosal cancerization. Moreover, integrating cytokine measurements with other biomarkers may enable the development of more accurate and individualized predictive models.

CONCLUSIONS

In conclusion, the present study reveals the close correlations of TNF- α and IL-8 levels with the risk of gastric mucosal cancerization in patients with HP-positive gastritis, offering valuable information for the assessment and prevention of gastric mucosal cancerization in clinical practice. Nevertheless, further in-depth research should also be conducted to perfect the understanding of the mechanism of gastric mucosal cancerization and enhance the levels of early diagnosis and prevention of gastric cancer.

ABBREVIATIONS

AUC – area under the curve

CagA – cytotoxin-associated gene A

HP – *Helicobacter pylori*

IL-8 – interleukin-8

OR – odds ratio

ROC – receiver operating characteristic

TNF- α – tumor necrosis factor- α

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AUTHORS' CONTRIBUTION

ZP: conceptualization, methodology, investigation, validation.

XY: data curation, formal analysis, software, supervision.

ML: investigation, data curation, supervision.

DW: software, validation.

JL: conceptualization, supervision, writing – original draft preparation, review and editing

All authors have read and approved the final version of the manuscript.

CONFLICT OF INTEREST

None to declare.

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REFERENCES

1. Elghannam MT, Hassanien MH, Ameen YA, Turkey EA, ELattar GM, ELRay AA, et al. Helicobacter pylori and oral-gut microbiome: clinical implications. *Infection*. 2024;52(2):289-300. DOI: 10.1007/s15010-023-02115-7
2. Koch MRA, Gong R, Friedrich V, Engelsberger V, Kretschmer L, Wanisch A, et al. CagA-specific Gastric CD8+ Tissue-Resident T Cells Control Helicobacter pylori During the Early Infection Phase. *Gastroenterology*. 2023;164(4):550-66. DOI: 10.1053/j.gastro.2022.12.016
3. Xia T, Zhang Z, Xie J, Yuan H, Ren Y, Xu Y, et al. Gastric mucosal CD8+TRM cells are recruited through CXCR5-CXCL13 axis in Helicobacter pylori infected subjects. *Cytokine*. 2025;190:156904. DOI: 10.1016/j.cyto.2025.156904
4. Jang DI, Lee AH, Shin HY, Song HR, Park JH, Kang TB, et al. The Role of Tumor Necrosis Factor Alpha (TNF- α) in Autoimmune Disease and Current TNF- α Inhibitors in Therapeutics. *Int J Mol Sci*. 2021;22(5):2719. DOI: 10.3390/ijms22052719
5. Liu H, Zhao Q, Tan L, Wu X, Huang R, Zuo Y, et al. Neutralizing IL-8 potentiates immune checkpoint blockade efficacy for glioma. *Cancer Cell*. 2023;41(4):693-710.e8. DOI: 10.1016/j.ccell.2023.03.004
6. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol*. 1996;20(10):1161-81. DOI: 10.1097/00000478-199610000-00001
7. Yu B, Xiang L, Peppelenbosch MP, Fuhler GM. Overlapping cytokines in H. pylori infection and gastric cancer: A tandem meta-analysis. *Front Immunol*. 2023;14:1125658. DOI: 10.3389/fimmu.2023.1125658
8. Wang H, Zhao M, Shi F, Zheng S, Xiong L, Zheng L. A review of signal pathway induced by virulent protein CagA of Helicobacter pylori. *Front Cell Infect Microbiol*. 2023;13:1062803. DOI: 10.3389/fcimb.2023.1062803
9. Dolcetti E, Bruno A, Azzolini F, Gilio L, Pavone L, Iezzi E, et al. Genetic regulation of IL-8 influences disease presentation of multiple sclerosis. *Mult Scler*. 2023;29(4-5):512-20. DOI: 10.1177/13524585231155049
10. Domínguez-Martínez DA, Fontes-Lemus JL, García-Regalado A, Juárez-Flores Á, Fuentes-Pananá EM. IL-8 Secreted by Gastric Epithelial Cells Infected with Helicobacter pylori CagA Positive Strains Is a Chemoattractant for Epstein-Barr Virus Infected B Lymphocytes. *Viruses*. 2023;15(3):651. DOI: 10.3390/v15030651

11. Yuan W, Shi Y, Dai S, Deng M, Zhu K, Xu Y, et al. The role of MAPK pathway in gastric cancer: unveiling molecular crosstalk and therapeutic prospects. *J Transl Med.* 2024;22(1):1142. DOI: 10.1186/s12967-024-05998-8
12. Wu X, Meng W, Duan C, Cao J, Wei Y, Cui X, et al. AFG1-induced TNF- α -mediated inflammation enhances gastric epithelial cell injury via CYP2E1. *Food Chem Toxicol.* 2023;176:113756. DOI: 10.1016/j.fct.2023.113756
13. Zhang S, Shen Y, Liu H, Zhu D, Fang J, Pan H, et al. Inflammatory microenvironment in gastric premalignant lesions: implication and application. *Front Immunol.* 2023;14:1297101. DOI: 10.3389/fimmu.2023.1297101
14. Ma Y, Fu Y, Fan X, Ji Q, Duan X, Wang Y, et al. FAK/IL-8 axis promotes the proliferation and migration of gastric cancer cells. *Gastric Cancer.* 2023;26(4):528-41. DOI: 10.1007/s10120-023-01384-3
15. Takahashi-Kanemitsu A, Lu M, Knight CT, Yamamoto T, Hayashi T, Mii Y, et al. The *Helicobacter pylori* CagA oncoprotein disrupts Wnt/PCP signaling and promotes hyperproliferation of pyloric gland base cells. *Sci Signal.* 2023;16(794):eabp9020. DOI: 10.1126/scisignal.abp9020
16. Hou Y, Li X, Yang Y, Shi H, Wang S, Gao M. Serum cytokines and neutrophil-to-lymphocyte ratio as predictive biomarkers of benefit from PD-1 inhibitors in gastric cancer. *Front Immunol.* 2023;14:1274431. DOI: 10.3389/fimmu.2023.1274431
17. Rosu MC, Tarta C, Moldovan S, Neamtu AA, Ardelean A, Capitanio M, et al. Integrating TNF- α with Established Tumor Markers to Enhance Prognostic Accuracy in Gastric Cancer: A Prospective Observational Study. *Biomedicines.* 2025;13(4):928. DOI: 10.3390/biomedicines13040928
18. Reyes ME, Pulgar V, Vivallo C, Ili CG, Mora-Lagos B, Brebi P. Epigenetic modulation of cytokine expression in gastric cancer: influence on angiogenesis, metastasis and chemoresistance. *Front Immunol.* 2024;15:1347530. DOI: 10.3389/fimmu.2024.1347530
19. Matsuoka T, Yashiro M. Molecular Mechanism for Malignant Progression of Gastric Cancer Within the Tumor Microenvironment. *Int J Mol Sci.* 2024;25(21):11735. DOI: 10.3390/ijms252111735
20. Li X, Peng J, Su X. Expression of immune regulatory factors, chemokines and growth factors in differentiated gastric cancer cells treated with an anticancer bioactive peptide combined with oxaliplatin. *Mol Clin Oncol.* 2023;20(1):9. DOI: 10.3892/mco.2023.2707

