Review

ANNALS OF MEDICINE & SURGERY

OPEN

Research progress on molecular mechanism of pyroptosis caused by *Helicobacter pylori* in gastric cancer

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Abstract

Gastric cancer (GC) is a prevalent malignancy worldwide. *Helicobacter pylori* (*H. pylori*), a Gram-negative spiral bacterium, has the ability to colonize and persist in the human gastric mucosa. Persistent *H. pylori* infection has been identified as a major risk factor for ~80% of GC cases. The interplay between *H. pylori* pathogenicity, genetic background, and environmental factors collectively contribute to GC transformation. Eradicating *H. pylori* infection is beneficial in reducing the recurrence of gastric cancer and residual cancer. However, the underlying molecular mechanisms involved in GC remain incompletely understood. Additionally, *H. pylori* reshapes the immune microenvironment within the stomach which may compromise immunotherapy efficacy in infected individuals. Clinical eradication of *H. pylori* infection still faces numerous challenges. In this review, the authors summarize recent research progress on elucidating the molecular mechanisms underlying *H. pylori* infection in GC development. Notably, CagA protein—a carcinogenic virulence factor predominantly expressed by Asian strains of *H. pylori*—induces inflammation and excessive ROS production within gastric mucosa cells. Dysregulation of multiple pyroptosis signalling pathways can lead to malignant transformation of these cells. MiRNA-1290 plays a crucial role in GC initiation and progression while serving as an indicator for disease progression dynamics. Pyroptosis exhibits dual roles both promoting carcinogenesis and inhibiting tumour growth; thus it holds potential clinical applications for drug-resistant GC treatment strategies . Furthermore , pyroptosis may play a regulatory role within the immune system during gastric cancer development . Lastly, the authors provide an overview on current concepts regarding pyroptosis as well as insights into miRNA-1290's pathogenicity and clinical value within immune mechanisms associated with GC , aiming to serve as reference material for researchers.

Keywords: gastric cancer, Helicobacter pylori, miRNA-1290, pyroptosis

Introduction

Gastric cancer (GC) caused by *Helicobacter pylori(H. pylori)* infection is more prevalent in eastern Asia[1]. In addition to dietary factors, the high prevalence of infection with highly pathogenic toxin strains may be the primary causative factor. Numerous studies have demonstrated that early detection and eradication of pathogenic *H. pylori* infection are beneficial for GC prevention and control. The carcinogenesis of *H. pylori* infection follows the Correa carcinoma mode while there is a certain risk of recurrence in residual gastric cancer[2]. Molecular mechanism studies have revealed that CagA, the main virulence factor of *H. pylori*, primarily induces inflammation in gastric mucosal epithelial cells and alters cell pyroptosis signalling, leading to stomach lesions[3]. The regulatory mechanism involving miRNA-1290 may play a crucial role in this process and thus holds diagnostic value as a potential tumour marker[4]. This review analyzed the dual action pattern of pyroptosis, which might also play distinct roles in other cancers beyond GC while exhibiting signalling pathways specific to each type of cancer. MiRNA-1290 exhibits high expression levels across most cancers and influences target gene expression diversity[5]. During the

HIGHLIGHTS

- This article mainly reviews the research progress of gastric cancer caused by *Helicobacter pylori* in recent years.
- The mechanism of *Helicobacter pylori* inducing cell pyroptosis in the occurrence and development of gastric cancer was described in details.
- The role and significance of miRNAs markers (miRNA-1290) in *Helicobacter pylori* 's carcinogenesis in cell pyroptosis and gastric cancer was briefly introduced.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:2016–2022

Received 7 November 2023; Accepted 29 January 2024

Published online 15 February 2024

http://dx.doi.org/10.1097/MS9.0000000000001802

occurrence and development of GC, it acts on complex and diverse targets involved in multiple critical pathways through signal factors' expression modulation[6]. Further investigation will help elucidate the mechanisms underlying GC induced by *H. pylori* infection and provide novel insights for clinical prevention, diagnosis, and treatment.

H. pylori infection caused gastric cancer

In 1983, Barry Warren and Robin Marshall first isolated *Helicobacter pylori* (*H. pylori*), establishing its pathogenic role in gastritis and gastric ulcers[7]. As a Gram-negative bacterium of the Helicobacter genus, H. pylori infects nearly half of the global population, with ~30% exhibiting clinical symptoms, while the majority of infected individuals remain asymptomatic. Colonization of gastric mucosal epithelial cells by *H. pylori* leads to infiltration of granulocytes and mucosal oedema, resulting in chronic gastritis, atrophic gastritis, and potentially GC[8]. The WHO has identified H. pylori infection as the main causative factor for 70% of gastritis cases and an increased incidence of GC in regions with high infection rates. Eradicating *H. pylori* can effectively reduce the risk of gastric precancerous lesions. Consequently, inhibiting *H. pylori* infection is widely recognized as a controllable factor for preventing GC, with antibacterial therapy being listed as a primary preventive measure.

Gastric cancer followed the Correa carcinaoma mode and prevalent in eastern Asia

China has a high prevalence of *H. pylori* infection, ranging from 40 to 60%, with an increasing incidence among young individuals in recent years. As an infectious disease, chronic active gastritis caused by *H. pylori* adheres to Koch's postulates[9]. The primary mode of transmission is through foodborne routes. Progression to peptic ulcer and even GC represents the severe clinical manifestations of this chronic infectious disease. Intestinal GC accounts for the majority of *H. pylori*-related cancers and follows the recognized Correa carcinoma mode[2]. In 1988, Correa proposed a model describing the transformation process from *H. pylori* infection to GC, which involves the development of chronic gastritis following early infection and long-term inflammatory stimulation leading to atrophic gastritis in later stages. Subsequent intestinal metaplasia can further progress into an adenomatous state, ultimately resulting in gastric cancer if not intervened upon. Throughout this entire process, coexistence with *H. pylori* infection occurs; therefore, eradicating *H. pylori* is crucial for preventing and controlling GC progression. This model has undergone continuous refinement and now specifies the following sequence: normal gastric mucosa → superficial gastritis → atrophic gastritis → intestinal metaplasia → atypical hyperplasia → GC. Approximately 17% of individuals infected with *H. pylori* may develop GC; however, its incidence varies across different countries or regions[1,10].

Most researchers currently believe that eradicating *H. pylori* infection can effectively inhibit the occurrence of GC. Gastric polyps are one of the precancerous lesions of GC, some of which are closely related to *H. pylori* infection. Bile reflux is also one of the risk factors for the occurrence of gastric polyps. However, there is no correlation between *H. pylori* and bile reflux[11]. As a common pathogenic factor, the relationship between the pathogenic types and pathological characteristics of gastric polyps is still unclear. *H. pylori* infection is one of the causes of precancerous lesions in GC, but it is not the only reason. The eradication of *H. pylori* may only reduce associated GC being related to its infection.

Pathogenicity of H. pylori in gastric stump cancer

According to statistical data in 2014, GC ranked as the second leading cause of cancer-related deaths in Asia and the fourth globally among malignant tumours. Gastric stump cancer (GSC), also known as metachronous GC, has shown an increasing incidence rate in recent years, particularly 10 years after early GC surgery. The main causes of GSC include *H. pylori* infection, acid reflux, and dysfunction of the gastric mucosal barrier. Research has indicated that the infection rate of *H. pylori* in residual GC is significantly lower (23–28%) compared to primary GC (54–71%)[12]. This discrepancy suggests that *H. pylori* infection alone is not an independent risk factor for GSC. It may interact with other factors such as bile reflux, leading to further atrophy of the gastric mucosa, intestinal metaplasia, and ultimately transformation into cancer cells[12]. Gastrointestinal ulcers, GC, and residual GC are more prevalent among males. Oestrogen plays a role in preventing the occurrence of GC to some extent[13]. It is generally believed that duodenogastric reflux fluid can inhibit *H. pylori* growth which results in a decreased infection rate among patients with residual GC. Therefore, it is likely that changes in the gastric environment such as damage caused by bile acids during reflux, reduced gastric acid secretion resulting in elevated pH levels post-surgery vagal nerve disconnection contribute more significantly to the progression of GSC than *H. pylori* infection itself[14]. In clinical practice studies have found that successful eradication of certain cases with *H. pylori* resulted in a low incidence rate (0.24%) for developing new cases of GC while metachronous GC had an incidence range between 2.3 and 9.8%[15].

Most studies support the trend of gastric early cancer morphology towards normal gastric mucosal morphology after *H. pylori* eradication, which means that the range of gastric early cancer is reduced and the boundary with the surrounding mucosa is blurred[16]. After eradicating *H. pylori*, there exist still other high-risk factors for GC, which are different from the occurrence of primary GC. Considering the expansion of consensus for the treatment of *H. pylori*, some scholars suggest that endoscopy should be divided into three categories: the *H. pylori* negative group, the *H. pylori* current infection group, and the *H. pylori* previous infection group (after eradicating *H. pylori* infection)[17]. Distinguishing the morphology of gastric mucosa in endoscopic examination under different groups can help further diagnose the progression of GC and provide personalized treatment measures for clinical treatment. *H. pylori* infection not only causes gastric mucosal ulcers, chronic atrophic gastritis, and GC, but also causes other parts of the digestive tract, such as colon polyps and even colorectal cancer. Although the WHO International Agency for Cancer Research has listed *H. pylori* as a Class I carcinogen factor, it is not the unique pathogenic condition for GC. Clinically, *H. pylori* negative high-grade intragastric tumours can be seen, and pathological analysis shows that most of them are intestinal mixed immunophenotypes, which may be related to long-term bile reflux and chemical stimulation leading to chemical gastritis[18].

The mechanism of carcinogenesis caused by H. pylori infection

CagA and VacA proteins are the main virulence factors of *H. pylori*. The infection of both CagA and VacA positive strains causes severe gastric mucosal inflammation symptoms, which increases the risk of carcinogenesis. 87.5% of GC patients are infected with *H. pylori* type I virulence strains (both CagA and VacA are positive), and more than 75% of *H. pylori* infection in gastrointestinal ulcers and atrophic gastritis are also type I virulence strains. Studies have shown that artificial transgenic expression of CagA protein can also lead to GC in animal models[19]. People from Eastern Asian countries carry the same type of *H. pylori* strain, which contains stronger virulence factors than Western countries. Research shows that the positive rate of virulent strains infected in China is higher, and so it is suggested that eradication treatment should be taken to effectively inhibit the high incidence rate and mortality of GC in China[20]. In primary GC, *H. pylori* can promote GC lesions through the CagA protein, which serves as a growth factor for gastric mucosal cells. CagA, the main virulence factor encoded by *H. pylori* gene expression, activates the expression of NF-kB factor in the nucleus of gastric mucosa, and secretes the precursor of inflammatory factor IL-8. Neutrophil aggregation induces the production of reactive oxygen species (ROS). Excessive ROS recruitment, assembling and activating of NLRP series inflammasomes, and splicing of cytokine IL-1 β Precursor release[21].

There are multiple studies supporting that *H. pylori* infection can promote gastric epithelial mesenchymal transition and upregulate the expression of stem cell markers CD44 and Lgr5 in gastric epithelial tissue[22]. These factors in turn promoted the formation and continuous migration of GC stem cells. This process is induced by the main virulence factor CagA of *H. pylori*, which induces inflammation, but the specific mechanism of its internal signalling remains to be elucidated. *H. pylori* infection can also cause colorectal cancer by upregulating cyclooxygenase 2 (COX-2) and gastrin levels[23]. *H. pylori* infection can upregulate the expression of numerous gene proteins in mucosal cells, jointly promoting cell proliferation and carcinogenesis. Dietary habits, physical and chemical factors, regulation of gut microbiota, environmental pollution, and radiation may also be important reasons for the occurrence and development of GC, but there is no unified and standardized research indicating the pathogenic factors of these factors. Currently, it is still believed that *H. pylori* infection is the main single identified pathogenic factor for GC. Procadherin 10 (PCDH10) is widely involved in physiological functions such as intracellular signal transduction and intercellular adhesion. Most studies have shown that PCDH10 and its family members play a role as tumour suppressor genes in various tumour diseases. In GC[24], *H. pylori* infection is significantly associated with PCDH10. They may cause abnormal signal transduction and genetic changes in gastric mucosal cells by affecting the expression of its tumour suppressor genes, leading to proliferation and carcinogenesis[25]. *H. pylori* can cause a series of physiological and chemical changes in gastric mucosal epithelial cells, and abnormal expression of related signalling molecules.

H. pylori affected immune cell inflammation through miRNA-1290

H. pylori can induce downregulation of miRNA-1290 expression, losing control of its downstream target genes, and affecting the normal differentiation of epithelial cells[3]. It is speculated that the impact of *H. pylori* on miRNA-1290 may be indirect. The anti-inflammatory response between *H. pylori* and innate immune cells in the body's immune system can release various pro-inflammatory cytokines such as IL-1 β, IL-18, TNF - α, etc[26]. The products released by the inflammatory response of immune cells play an important pathogenic role in the process of GC lesions. The IL-8 released by innate immune cell inflammation caused by *H. pylori* infection has been identified as an important carcinogen, which can promote inflammation, oxidative damage, and promote angiogenesis, leading to continuous proliferation and proliferation of epithelial cells until carcinogenesis[27]. Further research and elucidation of the inflammatory response between *H. pylori* and immune system cells on the pathological changes of gastric mucosal epithelial cells can help to understand the pathogenic mechanism of *H. pylori* in GC and contribute to the prevention and treatment of GC in clinical practice.

Cell pyroptosis and GC

Pyrotosis is one of the controllable programmed cell death modes, which is mainly activated by caspase-cascade-enzyme cleavage reaction to activate multiple signalling protein molecules. Ultimately, members of the GSDM protein family cause cell membrane poring, cell swelling, and then the cell will release a series of cytokines which enhancing local inflammatory response[28]. As early as 2001, Cookson and Brennan proposed and described the phenomenon of programmed cell death "pyroptosis" triggered by macrophages infected with Salmonella in mice[29]. Later, more and more studies have proved that pyroptosis is closely related to a variety of clinical diseases, such as infectious diseases, autoimmune diseases, cardiovascular diseases and most tumours[6]. Cell pyroptosis is a unique way of programmed cell death, which involves a cascade of inflammatory reactions caused by cell swelling, membrane rupture, and release of internal substances. Pyroptosis, as a stress mechanism that resists external infection stimulation signals, plays a combustion driving role in tumour occurrence, carcinogenesis, and malignant metastasis. In the later stage of tumour treatment, it is closely related to tumour cell resistance and the outcome of patients. According to the different activation molecules of caspase, it can be divided into caspase-1 regulating the classical pathway, caspase-4/5/11 regulating the non-classical pathway, caspase-3/8 regulating pathway, and caspase-independent regulating pathway[30]. The specific pathway of cell pyroptosis mainly involves the assembly of external or internal danger signal molecules (mainly NLRP series protein receptors, AIM2 proteins, etc.) with intracellular junction proteins (such as ASC) and cysteine aspartate protease (caspase) precursors to form inflammasome splicing and caspase series proteases forming with hydrolase activity. Caspase reactivates its downstream GSDM family protein molecules. As the executing protein of pyroptosis, GSDM series enzymes can form non-selective channels on the cell membrane, causing cell swelling, lysis, and even death due to imbalance of intracellular and extracellular factors. After cell's death, a large amount of released intracellular substances can form dangerous signalling factors in the surrounding microenvironment causing a cascading amplification of pyroptosis reaction and increasing tissue inflammatory response[31,32]. The

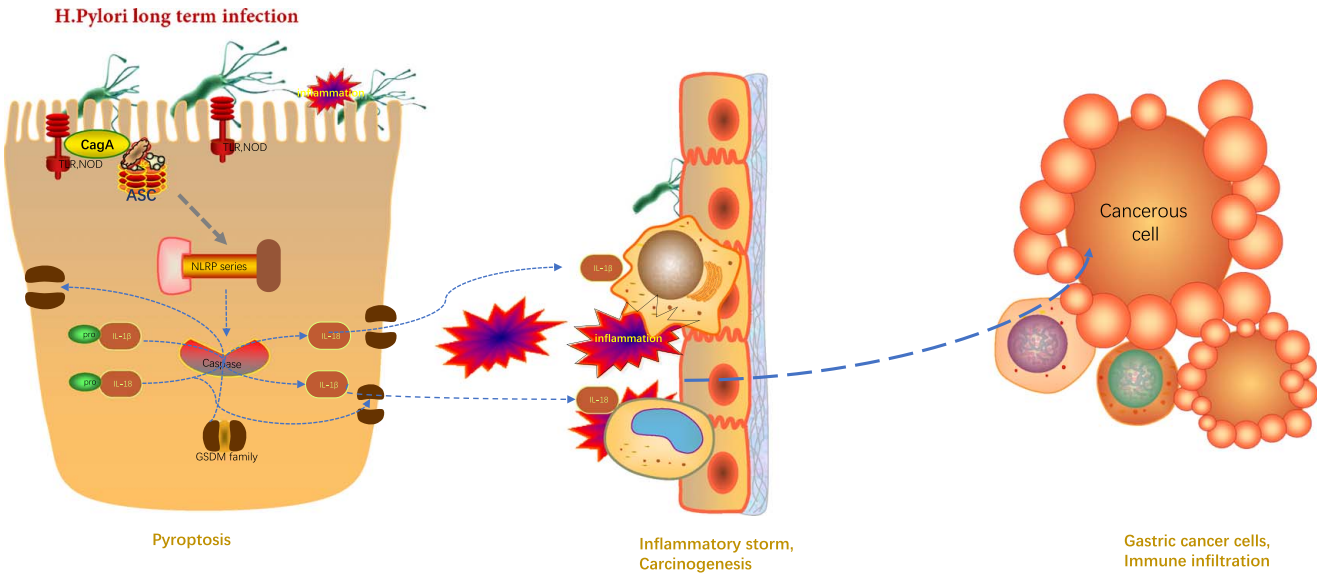

Figure 1. *H. pylori* promoting pyroptosis and carcinogenesis of gastric mucosal cells. (*H. pylori* infects gastric mucosal cells, and the virulence factor CagA binds to NOD-like receptors, which are transferred by ASC protein to activate the NLR series of inflammasomes. NLRP activates caspase hydrolase activity, promotes the conversion of cytokines from precursors to mature factors, and activates the N terminus of GSDMD. GSDMD forms holes in the cell membrane and activated cytokines are released. The cytokine storm further damages the gastric mucosa. Under the effect of persistent pyloric infection, mucosal cells undergo carcinogenesis, and immune cells infiltrate into the cancer tissue).

process of *H. pylori infection*, pyroptosis inflammation of gastric mucosal cells and immune cell infiltration is shown in Figure 1.

Long-term inflammation and cell death ultimately breed diseases related to multiple tissues including tumour progression. The relationship between pyroptosis and cancer varies in different stages of the same organization[33]. It is generally believed that cell pyroptosis is caused by increased inflammatory response in normal tissue cells and immune cells in the surrounding microenvironment in the early stage, and sustained inflammatory response stimulates the process of cellular pathology. At this point, the pyroptosis of cancerous cells inhibits the occurrence and development of tumours to a certain extent. On the other hand, when cancer cells continue to develop and fail to be cleared in a timely manner to form malignant tumours, their internal microenvironment still requires inflammatory factors, etc. At this time, the cascade of inflammatory reactions caused by cell death will promote the faster growth of cancer cells. A small number of cancer cells undergo pyroptosis to form an inflammatory microenvironment, which is beneficial for tumour growth.

Cancer cells often experience drug resistance during drug therapy. Cancer cells continue to proliferate and adaptively readjust the intracellular signalling pathway mechanism to avoid the killing effect of external drugs. To cope with the emergence of drug resistance in cancer cells, updated drugs or new combinations of drugs can only be continuously introduced. Alternatively, it could alter the previous way in which drugs alone induced cancer cell apoptosis, stimulating the immunogenicity of cancer cells to activate the immune system and kill cancer cells. Cell pyroptosis, an inflammatory and controllable programmed death mode, can generate immune antigen properties from cell itself, which can mobilize immune cells to fight cancer proliferation and provide a new therapeutic approach against cancer cell resistance.

Pyroptosis can effectively alter the microenvironment of tumour cells. It can activate potential T cells to produce anticancer activity, inhibit cancer cell proliferation, and induce cancer cell sensitivity to chemotherapy drugs. As an inflammatory death, pyroptosis also provides a suitable inflammatory environment for cancer cell growth. The Correa pattern of the occurrence and development of GC is a complex and multifactorial process leading to cancer progression[34]. In GC associated with *H. pylori* infection, cell pyroptosis is present in a large number of inflammatory reactions caused by infection. Therefore, the occurrence of GC is closely related to cell pyroptosis, and the complex mechanisms involved have been partially elucidated in recent years[35]. The relationship between cell pyroptosis and GC is complex and variable, and there may be different or even completely opposite effects at different stages. During the inflammatory period, pyroptosis promotes the transition from chronic gastritis to GC. *H. pylori* can induce the activation of caspase series (caspase-1,3,8,9,11) enzymes by various members of the NLR family (NLRP1,3,6,7,12; NLRC4) which finally catalyzing GSDM family perforation activity, and releasing more cytokines (mainly IL-1) β/ IL-18)[36]. Pro-inflammatory factors continue to recruit immune cells to form a local immune network, inducing an aggravation of cellular inflammatory response. This long-term inflammation ultimately leads to inflammatory transformation into cancerous degeneration. Tumour necrosis factor alpha (TNF-α) can also induce excessive accumulation of ROS in pre-malignant cells. When DNA damage touches oncogenes or tumour suppressor genes, it will lead to a series of cancerous effects[37]. GSDMB may serve as an oncogene in GC, which is not expressed in normal tissues, but is moderately expressed in precancerous lesions and GC tissues. Research has found that GSDMB in gastrointestinal epithelial tumours can be activated by granular enzyme A secreted by cytotoxic T lymphocytes, which can induce cancer cell pyroptosis[38]. GSDMA, GSDMC, and GSDMD may have the same effect in GC cells, with low or no expression. But after overexpression, it can inhibit the

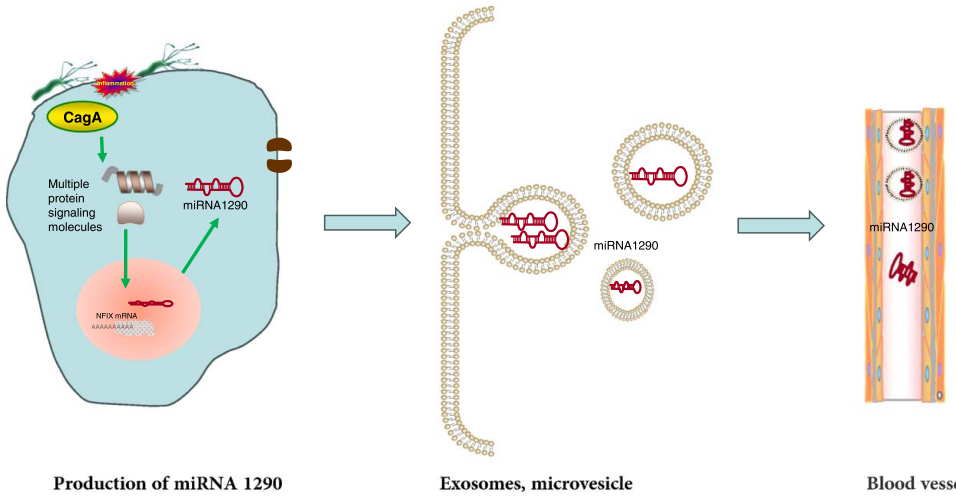

Figure 2. Production and releasing of miRNA-1290 in GC (CagA induces the abnormally high expression of miRNA-1290 in the inflammatory response of *H. pylori* infection. miRNA-1290 in GC cells forms microvesicles through the cell membrane. The exosomes are released to the extracellular space into the tissue fluid, and then into the peripheral blood circulation system).

proliferation function of GC cells, so it is considered to belong to the same inhibitory gene[39]. GSDMD is low expressed in most GC tissues, such as in common GC cell lines MKN-45, SGC-7901, AGS, and BGC823, where its expression is significantly reduced. In vitro experiments have also shown that knocking down GSDMD in GC cells can promote cancer cell proliferation, while upregulating its expression level can have an inhibitory effect on cancer cell[39].

MiRNA-1290-related signalling pathways in GC

MiR-1290 was discovered for the first time in human embryonic stem cells, and under typical physiological situations, plays an essential role in differentiation and stem cell proliferation. Its coding sequence is located at the 1p36.13 regions in the first intron of the aldehyde dehydrogenase 4 gene member A1. miR-1290 is out of control in many cancers such as breast cancer, colorectal cancer, oesophageal squamous cell carcinoma, gastric cancer, lung cancer, pancreatic cancer, and plays a vital role in their development. Therefore, it is suggested that miR-1290 can be considered as a potential diagnostic and therapeutic target in many cancers[4].

RNA is a large class of molecules of signal expression and regulation mechanism in organism cells. Among them, miRNAs (microRNAs) play an important regulatory role in physiological function and disease development. As micro endogenous non-coding RNAs, miRNAs regulate gene expression after transcription. MiRNA-1290 can participate in multiple tumour mechanisms and play an important role in tumour related gene regulation. There are a large number of miRNAs with abnormal expression in GC cells, including the phenomenon of increased expression of miRNA-1290[40]. Production and releasing of miRNA-1290 in GC was simply showed in Figure 2. *H. pylori* virulence factor CagA can lead to intestinal metaplasia of gastric mucosal cells, activation of the NF-κB pathway, increased expression of miRNA-1290, and proliferation and migration of cancer cells. Inhibiting the expression of miRNA-1290 in vitro can inhibit the proliferation activity of GC cell lines[41]. There is a high expression of miRNA-1290 in the tissues and serum of patients with colorectal cancer. After surgical treatment, the expression level of miRNA-1290 significantly decreased in patients[5]. The highly expressed miRNA-1290 in solid tumour tissue is released into the serum or produced by circulating cancer cells in the peripheral blood, which can reflect the status of colorectal tumours. MiRNA-1290 is highly expressed in GC tissue, and inhibiting GC cell line SGC-7901 in vitro can significantly inhibit the proliferation and migration ability of GC cells[42].

The relatively stable expression level of miRNA-1290 in plasma can provide real-time feedback on the activity of GC tumours. Monitoring shows that miRNA-1290 has certain diagnostic biomarker application value. In oesophageal squamous cell carcinoma, miRNA-1290 can bind to nuclear factor I/X (NFIX) mRNA, leading to its degradation. The loss of negative regulatory effect of NFIX suppressor genes promotes the proliferation and invasion ability of oesophageal squamous cell carcinoma cells[43]. In the plasma of GC patients, miRNA-1290 showed out certain detection and diagnostic efficacy, but its specific molecular mechanism of action in GC cell lines has not been elucidated. The relative expression levels of miRNA-1290 in tumour tissues and peripheral blood serum of patients with liver cancer, lung cancer, cervical cancer, and GC were significantly increased, and there was a positive correlation with tumour pathological staging, malignancy, invasion, and distant metastasis[44]. Clinically, miRNA-1290 can serve as a marker for early diagnosis and prognosis of cancer. Studies have shown that it had considerably high sensitivity and specificity in GC[45]. MiR-1290 was highly expressed in GC samples, which was correlated with clinical stages, depth of invasion and lymph node metastasis by targeting FOXA1 gene. MiRNA-1290 is directly related to the malignant degree and clinical stage of GC because FOXA1 directly affects the proliferation and differentiation of tumour stem cells as a transcription factor[41]. MiRNA-1290 can inhibit cell apoptosis, promote the proliferation, invasion, and metastasis of GC cells, but it is worth further exploring which genes and targets are involved.

Exosomes rich in RNAs and proteins are regarded as vital mediators of intercellular communication. Numerous studies

have shown that miRNA-1290 can affect the physiological function of tissue cells through exosomes[46]. A large number of exosomes were secreted in the peripheral blood of patients with GC and the culture medium of GC cells. MiR-1290 is over-expressed in these exosomes which increased the proliferation and invasiveness of cancer cells. Studies on the interaction of targeted molecules showed that miRNA-1290 directly acted on NKD1 gene which interact with β-catenin in the cytoplasm negatively regulating the progression of GC[46]. The intracellular signalling network is complex and intertwined, and miR-1290 can serve as a target molecule for circular RNAs Circ-0026344. The high expression of miR-1290 reduced the anticancer effect of Circ-0026344 and upregulated the expression of FBP2 gene. FBP2 is also one of the directly targeted regulatory genes of R-1290[47]. FBPR2, as a positive regulator of glycolytic enzymes involved in mitochondrial generation, plays an important role in promoting the development of GC. The expression level of FBP2 is generally inhibited in GC. Its main regulatory mechanism may be the role of miR-1290[47,48]. MiRNA-1290 in exosomes or microcapsules participates in the immune escape mechanism of GC cells through the signal axis Grhl2/ZEB1/PD-L1[49]. MiRNA-1290 may also have important regulatory mechanisms in tumour immune regulation.

Conclusion

Long-term infection of *H. pylori* expressing virulence factors can result in characteristic changes in gastric mucosal cells, particularly alterations in the inflammatory cell death—pyroptosis signalling pathway, which can lead to precancerous lesions in gastric tissues. Without clinical intervention over an extended period, Correa mode will progress to GC. *H. pylori* infection may also be one of the contributing factors for recurrence of residual gastric cancer, although it is not the sole factor. The major oncogenic protein factor involved in carcinogenesis is CagA, a virulence factor of Helicobacter pylori. CagA's action on gastric cells leads to high expression of inflammasomes in mucosal cells, excessive oxidative reactions and production of ROS, and resulting in inflammatory effects and release of various cytokines. In this process, pyroptosis signalling molecules such as caspase and GSDMD play crucial roles. Pyroptosis may have different functions during early and late stages of GC development. Further research is needed to elucidate its mechanism in clinical practice. Current studies have demonstrated that pyroptosis causes dysfunction of key transcriptional regulators including CD44, LGR5, COX-2 and PCDH10, resulting in cell proliferation and malignant lesions. As a regulatory non-coding microRNA, miRNA-1290 plays a significant role in numerous signal regulation mechanisms. The substantial changes observed in its expression during *H. pylori*-induced gastric lesions indicate its potential application as a tumour marker. Studies have revealed that miRNA-1290 mainly targets FOXA1, NKD1, and FBP2 genes in regulating GC development. *H. pylori* CagA induces high expression of miRNA-1290 which affects the expression of tumour suppressor genes and results in cell cycle malignant lesions. Clinical studies have shown that early eradication of *H. pylori* could be beneficial for preventing and controlling the incidence of GC.

Ethical approval

There was no need for ethical approval for this article.

Consent

There is no need to provide informed consent form for this submission as it does not involve clinical patient information.

Source of funding

This project was supported by a grant from Changshu science and technology project (CS202018,CSWZD202043, CSWS202106).

Author contribution

C.W.: data collection and writing the paper; Y.X.: data analysis and writing. P.W.: data collection and study concept. Y.Z.: data collection. Y.G.: manuscript review and funding.

Conflicts of interest disclosure

The author declares that there is no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

This is a review. No experiments, it doesn't need registration.

Guarantor

Yulan Gu and Chuandan Wan.

Data availability statement

There is no data sharing that is applicable to this article.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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