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Helicobacter pylori-Induced IL-8 Production by Gastric Epithelial Cells Up-Regulates CD74 Expression

Ellen J. Beswick,* Soumita Das,* Irina V. Pinchuk,**† Patrick Adegboyega,‡ Giovanni Suarez,* Yoshio Yamaoka,¶ and Victor E. Reyes*¶¶

CD74, or the class II MHC-associated invariant chain, is best known for the regulation of Ag presentation. However, recent studies have suggested other important roles for this protein in inflammation and cancer studies. We have shown that CD74 is expressed on the surface of gastric cells, and Helicobacter pylori can use this receptor as a point of attachment to gastric epithelial cells, which lead to IL-8 production. This study investigates the ability of H. pylori to up-regulate one of its receptors in vivo and with a variety of gastric epithelial cell lines during infection with H. pylori. CD74 expression was increased dramatically on gastric biopsies from H. pylori-positive patients and gastric cell lines exposed to the bacteria. Gastric cells exposed to H. pylori-conditioned medium revealed that the host cell response was responsible for the up-regulation of CD74. IL-8 was found to up-regulate CD74 cell surface expression because blocking IL-8Rs or neutralizing IL-8 with Abs counteracted the increased expression of CD74 observed during infection with H. pylori. These studies demonstrate how H. pylori up-regulates one of its own receptors via an autocrine mechanism involving one of the products induced from host cells. The Journal of Immunology, 2005, 175: 171–176.

Helicobacter pylori is a common human pathogen associated with chronic gastritis, duodenal ulcers, and at least 80% of gastric ulcers worldwide (1, 2). There is also considerable evidence linking this pathogen to gastric cancer (3, 4), which led to H. pylori becoming classified as a class I carcinogen by the World Health Organization. Pathogenesis of infection often includes inflammation, mucosal damage, or gastric atrophy. During infection, H. pylori maintain close association with gastric epithelium (5, 6). Clearly bacterial adhesion and colonization of the gastric mucosa are key events in pathogenesis (7). Although multiple bacterial adhesins and host cell receptors have been implicated in the attachment of the bacterium to the gastric epithelium (8–11), the interactions that lead to host cell responses associated with inflammation are not well understood. We have shown recently that CD74 is a receptor used by H. pylori, and engagement of this receptor leads to the production of IL-8 (12).

CD74 is also known as the class II MHC-associated invariant chain. The development of immune responses is influenced by CD74 because it regulates the intracellular transport and functions of class II MHC in APCs (13, 14). Recently, we and others (12, 15, 16) have found that CD74 is expressed on the surface of a variety of cell types, including gastric epithelial cells. CD74 has a long cytoplasmic tail that has been implicated in signaling events. A variety of studies involving signaling leading to NF-κB activation (17) and B cell maturation have been shown to be dependent on CD74 (18). Macrophage migration inhibitory factor (MIF), an important inflammatory cytokine, has been shown to bind to CD74 expressed on cell surfaces and initiate the MAPK activation (19). We recently showed that H. pylori binding to CD74 stimulates the NF-κB-signaling cascade that leads to IL-8 production (12).

Given the importance of CD74 in H. pylori attachment and signaling leading to a proinflammatory response, this study examines the mechanism leading to increased expression of this receptor by gastric cells in vivo and with a variety of gastric cell lines during infection with H. pylori. We observed that surface expression of CD74 on epithelial cells is increased in biopsies from H. pylori-infected individuals. Gastric cell lines infected with H. pylori also had increased CD74 expression as determined by flow cytometry and quantitative real-time RT-PCR. Interestingly, IL-8, which is among the earliest cytokines produced by the epithelium in response to H. pylori infection (20, 21), was found to induce CD74 up-regulation. The IL-8Rs CXCR-1 and CXCR-2 were also up-regulated during infection. CD74 up-regulation was decreased upon blocking these receptors with mAbs or by the addition of IL-8-neutralizing Abs to cell cultures before H. pylori exposure. These studies offer insights into H. pylori interaction with the gastric epithelium leading to inflammation and how the bacterium up-regulates one of its receptors through an autocrine mechanism involving one of the products induced from host cells.

Materials and Methods

Gastric biopsy staining

Gastric antrum biopsy tissues were obtained from consenting donors undergoing gastro-esophageal-duodenoscopy at the University of Texas Medical Branch. The biopsies were obtained from grossly inflamed areas of the antrum, as well as from regions that appeared uninvolved. The tissue was received for prior approval of the Institutional Review Board. The immunohistochemical expression of CD74 was evaluated in 45 consecutive endoscopy gastric biopsy specimens previously determined to be H. pylori positive or negative; however, the specimens were obtained from our institutional gastro-intestinal endoscopy suites, so there was no bias as to the diagnosis or the

3 Abbreviations used in this paper: MIF, macrophage migration inhibitory factor; PAI, pathogenicity island; CM, conditioned medium.
clinical status of the patients. The tissue samples were fixed in 10% neutral buffered solution and then embedded in paraffin for immunohistochemistry. Four-micrometer thick sections of the paraffin-embedded tissue blocks were mounted on plus (coated) glass slides and deparaffinized in xylene followed by rehydration in ethanol. Endogenous peroxidase was blocked by incubation in 3% methanol peroxide for 10 min. For CD74 immuno-histochemical staining, Ag retrieval was done by pretreating the sections with citrate buffer (0.01 M citric acid at pH 6.0) for 20 min at 99°C in a microwave oven and then allowed to cool for 20 min at room tempera-
ture. Nonspecific endogenous proteins were blocked using the avidin-biotin blocking kit (Vector Laboratories), followed by 30 min of incubation at room temperature with biotinylated, mouse, and anti-human CD74 Ab clone LN-2 (DakoCytomation) at 1/200 dilution. The sections were stained with a streptavidin-biotin peroxidase detection kit (DakoCytomation), incubated with 3,3’ diaminobenzidine, and counterstained with hematoxylin followed by coverslipping. The immunostaining reactions were examined by light microscopy.

**Cell lines**

N87 human gastric carcinoma epithelial cells and Hs738.st/int (CRL-7869) normal human fetal gastric/intestinal cells were obtained from the Amer-
can Type Tissue Culture. Cells were maintained in RPMI 1640 medium supplemented with 10% FBS, 2 mM l-glutamine, and antibiotics. Antibiotics were removed from the medium before infection of the cells with *H. pylori*.

**Bacterial cultures**

*H. pylori* clinical isolate LC11 was described previously (22). The 26695 lab strain and its cag pathogenicity island (PAI) totally deleted mutants (cag PAI mutants) were also constructed. For constructing a cag mutant, regions upstream (hp0518-hp0519; 545,254-547,164 bp: hp number and location from *H. pylori* strain 26695: GenBank accession no. AE000511) and downstream (hp0549-hp0550; 584,570-586,563 bp) of the cag PAI were amplified from the *H. pylori* strain 26695 chromosome to delete the entire cag PAI from the *H. pylori* chromosome. These fragments, separated by a homologous flanking resistance cassette (cat) (a gift from Dr. D. E. Taylor, University of Alberta, Edmonton, Canada), were cloned into the T7Blue vector (Novagen), resulting in the deletion mutant’s plasmid Δcag PAI.:cat. The plasmids (1–2 µg) were used for inactivation of chromoso-
mal genes by natural transformation as described previously (23). Inactiv-
tation of the genes was confirmed by PCR amplification followed by Southern blot hybridization.

**Abs and reagents**

The anti-CD74 mAb MB-741 was obtained from BD Biosciences along with isotype controls. Anti-CXCR-1 and anti-CXCR-2 mAbs were ob-
tained from Sigma-Aldrich. For samples treated with human rIL-8 (Sigma-Aldrich), 100 pg/ml for N87 or 1000 pg/ml for HS-738 were added for 24 h. The IL-8 concentration that we typically see in each gastric cell line was obtained from Sigma-Aldrich and was used at a working concentration of 1 µg/ml.

**CD74, CXCR1, and CXCR2 staining for flow cytometry**

Gastric epithelial cells (2 × 10^6) were grown in medium alone or supple-
mented, when indicated, with IFN-γ (100 U/ml) for 48 h. Cells were incu-
bated with anti-CD74 MB-74 mAb (1 µg) or anti-CXCR1 and anti-
CXCR-2 mixture (1 µg each) in PBS buffer for 1 h on ice. The cells were washed with PBS and then incubated with PE-conjugated goat anti-mouse IgG (1 µg) for an additional 30 min on ice. Following incubation, the cells were washed and stained with 1% paraformaldehyde in PBS. The 1000 events/sample were collected for additional analysis. The flow cytometry analysis was done on a FACScan cytometer (BD Biosciences), and the data analysis was done using CellQuest software.

**Real-time PCR**

Real-time RT-PCR assays were used to determine gene expression using TaqMan technology on an Applied Biosystems 7000 sequence detection system. Applied Biosystems Assays-By-Design containing a 20X mix of primers and predeveloped 18S rRNA (VIC dye-labeled probe) Taq-
Man assay reagent (PE 4319413E) for internal control were used for real-
time PCR measurements. These assays were designed using primers that span exon-exon junctions so as not to detect genomic DNA. All primer and probe sequences were searched against the Celera database to confirm specificity. Target gene *CD74* primers were designed using accession no. NM_004355 (GenBank) and probe sequence 5’-CCTCGAGACGAACTG GCAGCGCCGGA-3’ (Applied Biosystems). HLA-DR target gene primers were designed using accession no. NM_019111 (GenBank) and probe sequence 5’-TGTAGGCACATGAGGTGTTAGT-3’ (Applied Bio-
systems). The efficiency of target amplification was validated using a refer-
ence amplification reaction. Absolute values of the slope of log input RNA amount vs ΔCT were <0.1 in all experiments. One-step RT-PCR reactions were performed on 20 ng of input RNA for both target genes and endogenous controls using the TaqMan one-step RT-PCR master mix re-
agent kit (Applied Biosystems). The cycling parameters were as follows: reverse transcription, 48°C for 30 min; AmpliTaq activation, 95°C for 10 
min; denaturation, 95°C for 15 s; and annealing/extension, 60°C for 1 min for 40 cycles. Duplicate cycle threshold values were analyzed in Micro soft Excel using the comparative CT(ΔΔCT) method as described by the man-
ufacturer (Applied Biosystems). The amount of target (2^-ΔΔCT) was ob-
tained by normalizing to an endogenous reference (18S mRNA) and rela-
tive to a calibrator.

**Attachment assays**

Cells were treated with 100 U/ml IFN-γ (Roche) or 100 or 1000 pg/ml IL-8 (Sigma-Aldrich) for 48 h to up-regulate CD74 expression. Media were replaced with IFN-γ-free medium for 24 h. *H. pylori* was stained with the red fluorochrome PKH26 (Sigma-Aldrich), according to the manufactur-
er’s instructions, washed three times with RPMI 1640 medium, and resus-
pended in RPMI 1640 medium. Bacteria were added to pelleted cells that were treated with medium, IFN-γ, or IL-8 in a ratio of 30:1 bacteria to cells and incubated for 4 h at 37°C. Cells were washed and resuspended in 2% paraformaldehyde and analyzed by flow cytometry. Negative control samples consisted of cells treated with the wash from stained *H. pylori* to assess background staining of cells.

**Statistical analysis**

Results are expressed as mean ± SEM. In vivo CD74 expression among groups were compared using a Fisher’s exact test and *H. pylori* binding, and IL-8 production results were compared using an ANOVA analysis of the variance and considered significant if p was <0.05.

**Results**

CD74 expression is increased on gastric epithelial cell biopsy samples during *H. pylori* infection

Because we have shown previously that cell surface CD74 plays a pivotal role in *H. pylori* attachment leading to the inflammatory response (12), we sought to determine the effect of *H. pylori* in-
fection on CD74 expression. Gastric antrum biopsy tissues were obtained from consenting donors undergoing gastro-esophageal-duodenoscopy. Staining was done using anti-CD74 clone LN-2. As seen in Fig. 1, there is a marked increase in CD74 staining of epithelial cells during *H. pylori* infection. In this study, 45 patient biopsies were examined for CD74 expression. Of the 45 patients, 13 were positive for *H. pylori* infection (Table I), as determined by staining, and of the 13 biopsies, 11 (85%) were found to have high CD74 expression. High expression was considered >30% of epithelial cells staining positive for CD74. CD74 expression also correlated with an influx of inflammatory cells. There were nine patients from samples that did not have *H. pylori* infection or gastritis, and only two (22%) of those had high CD74 expression (p < 0.01 compared samples from patients with *H. pylori*-positive gastritis). These results indicate a correlation between *H. pylori* in-
fection and CD74 expression. Of the 23 samples from patients with gastritis but no infection, 14 (61%) had high CD74 expression,
suggesting there is also a link between inflammation, which is a hallmark response to *H. pylori* infection, and CD74 expression.

**CD74 expression is increased by gastric cell lines during *H. pylori* infection**

Multiple gastric epithelial cell lines have been shown to express CD74 on the cell surface, and this expression is important in the attachment of *H. pylori* and the resulting proinflammatory immune response (12). To examine the mechanism responsible for the up-regulation of CD74 during *H. pylori* infection, N87 carcinoma cells and untransformed fetal gastric cells, HS738, were analyzed for CD74 expression by flow cytometry. Untreated cells, IFN-γ treated cells, and cells treated with *H. pylori* LC11 and 26695 strains for 24 h were stained with mAbs specific for CD74. As seen in Fig. 2, A and B, both cell lines express surface CD74, and expression is markedly increased by *H. pylori* exposure between 40 and 50% above basal level expression with both strains. HS-738 cells express overall more CD74 than N87, although the fold increase in expression is similar for both cell lines. To determine whether the increased expression resulted from de novo transcription of CD74 message, real-time PCR was used. Results were normalized to 18S mRNA and calculated relative to untreated cells. Similar to CD74 surface expression, CD74 mRNA levels were also increased in response to *H. pylori* strains. N87 cells showed a 6-fold increase upon LC11 exposure and a 4-fold increase with 26695, whereas HS-738 cells showed 7- and 5-fold increases (Fig. 2C).

**CD74 up-regulation depends upon gastric cell responses to *H. pylori***

To investigate the specific factors involved in the up-regulation of CD74, gastric cells were exposed to 0.02-μm filtered culture supernatants of previous cells treated with *H. pylori* (*H. pylori*-conditioned medium (CM)) for 24 h. Although the bacteria were removed during filtration, cell response factors and bacterial factors were present and tested for the ability to up-regulate CD74. Under these conditions, cell surface expression was increased 30–40% above basal expression (Figs. 3, A and B). Similar to CD74 surface expression, treatment with *H. pylori* CM led to increases in mRNA. The increase in mRNA expression of treated cells compared with that of untreated cells was increased 3- and 4-fold with

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**FIGURE 1.** CD74 expression by gastric epithelial cells in biopsies is increased in *H. pylori*-positive samples. Staining of two representative biopsy samples for CD74 shows increased expression by epithelial cells in samples positive for *H. pylori* compared with similar biopsies from non-infected biopsies. Arrows point to representative epithelial cells stained with the Ab. L, lumen; LP, lamina propria.

**FIGURE 2.** CD74 expression by gastric epithelial cell lines exposed to *H. pylori* is increased. Flow cytometric analysis of N87 and HS-738 cells stained for CD74 after exposure to *H. pylori* strains LC11 or 26695 shows increased expression in (A) a representative histogram for HS-738 cells exposed to LC11 where the solid peak is the isotype control, and (B) percent-positive cells above background staining with isotype control Ab for N87 and HS-738 are shown. C, CD74 RNA levels normalized to 18S RNA and relative to untreated controls after exposure to *H. pylori* strains LC11 or 26695. The means are shown as the results of duplicates in four experiments, *n* = 8.
CD74 expression is increased on gastric cells by IL-8

Because we have shown that CD74 is up-regulated in inflammatory conditions in biopsy samples by *H. pylori* CM, and this response is limited in the absence of *cag* PAI, the role of IL-8 in CD74 up-regulation was investigated. Recombinant IL-8 was added to cells based on average amounts produced by each of the cell lines in response to *H. pylori* infection (12). Thus, 100 and 1000 pg/ml IL-8 were added to N87 cells and HS-738 cells, respectively. Flow cytometric analysis revealed that IL-8 treatment led to increased surface expression of CD74 by 40% over basal expression with both cell lines at 24 h treatment time (Fig. 5A). Upon adding IL-8-neutralizing Ab to cell medium or blocking the IL-8Rs CXCR-1 and CXCR-2 with mAbs before *H. pylori* exposure, CD74 up-regulation was much reduced compared with *H. pylori* treatment alone or rIL-8 treatment of cells. A mixture of anti-CXCR-1 and anti-CXCR-2 was used because some reduction of CD74 expression was seen when blocking with both Abs individually (data not shown), with an additive effect upon using the mixture (Fig. 5A).

CD74 mRNA levels in response to IL-8 treatment were also measured by real-time PCR. As shown in Fig. 5B, IL-8 treatment for 16 h resulted in 9-fold increases in CD74 mRNA levels compared with untreated cells for HS-738 and 4-fold for N87 cells. Upon adding anti-IL-8-neutralizing Abs to the medium or blocking IL-8Rs before *H. pylori* LC11 treatment, mRNA levels were decreased to approximately one-third of that seen with *H. pylori* treatment. Very similar results were seen with *H. pylori* 26695 but not shown here. These results indicate that IL-8 up-regulates CD74 expression. The *H. pylori*-induced up-regulation is decreased by neutralizing IL-8 or blocking IL-8Rs.

CXCR-1 and CXCR-2 are up-regulated by *H. pylori*

The role of CXCR-1 and CXCR-2 (IL-8R) was further investigated by measuring their expression on gastric cell surfaces by flow cytometry. As seen in Fig. 6, A and B, LC11 and 26695

FIGURE 3. CD74 expression by gastric epithelial cell lines exposed to *H. pylori* CM is increased. Flow cytometric analysis of N87 and HS-738 cells stained for CD74 after exposure to *H. pylori* strains LC11 CM or 26695 CM shows increased expression in (A) a representative histogram for HS-738 cells exposed to LC11 CM where the solid peak is the isotype control, and (B) percent-positive cells above background staining with isotype control Ab for N87 and HS-738 are shown. C, CD74 RNA levels normalized to 18S RNA and relative to untreated controls after exposure to *H. pylori* strains LC11 CM or 26695 CM. The means are shown as the results of duplicates in four experiments, n = 8.

26695 and LC11, respectively, when cells were treated with CM. These results suggest that not only does exposure of *H. pylori* to gastric cells result in CD74 up-regulation but the products released by cells in response to infection can enhance CD74 as well, but the induction is not as vigorous as that observed with the bacteria.

Because the *cag* PAI has been shown to be responsible for a variety of gastric epithelial cell responses to *H. pylori* (2), we used a *cag* PAI mutant of strain 26695 to examine CD74 expression in the absence of this major virulence factor that requires attachment of the bacteria to be injected by a type IV secretion system. We have shown previously that there is very little difference in attachment between this wild-type and *cag* PAI-deficient strain, but there was a >40% decrease in IL-8 production (12). As seen in Fig. 4A, flow cytometric analysis revealed that the *cag* PAI mutant led to lower increases in CD74 expression, ~20% increase over basal levels, whereas wild-type bacteria led to 50% increases in expression for both cell lines. Similar results were seen with RNA levels in real-time PCR where 2- to 3-fold increases were seen with the *cag* PAI mutant, whereas 4- to 5-fold increases were seen with the wild type (Fig. 4B). These results suggest that the up-regulation of CD74 with gastric cells in response to *H. pylori* is both a *cag* PAI-dependent and a *cag* PAI-independent process.

FIGURE 4. CD74 expression by gastric epithelial cell lines exposed to *H. pylori* cag PAI mutant is increased minimally. Flow cytometric analysis of N87 and HS-738 cells stained for CD74 after exposure to *H. pylori* strains 26695 and cag PAI mutant shows expression with (A) percent-positive cells above background staining with isotype control Ab for N87 and HS-738. B, CD74 RNA levels normalized to 18S RNA and relative to untreated controls after exposure to *H. pylori* strain 26695 and cag PAI mutant. The means are shown as the results of duplicates in four experiments, n = 8.
treatment of cells yielded 2.5- to 3-fold increases in IL-8R surface expression with both examined. Treatment with *H. pylori* CM led to increases in IL-8R expression but to a lesser extent than with *H. pylori* treatment. Recombinant IL-8 also induced small increases in IL-8R expression, and the remaining response must be due to another bacterial or cell response factor. The IL-8Rs were found to be likewise up-regulated by *H. pylori*, which is needed for IL-8-induced CD74 expression.

**Enhanced CD74 expression increased *H. pylori* attachment**

Because we have shown previously that *H. pylori* use CD74 as a point of attachment to gastric epithelial cells, we sought to determine the effect of CD74 up-regulation on *H. pylori* attachment. Attachment of PKH26-labeled bacteria to untreated cells, IFN-γ-treated cells, IL-8-treated cells, and both IFN-γ and IL-8-treated cells was measured by flow cytometry. Fig. 7 demonstrates that attachment to both cell lines was increased independently by either IFN-γ or IL-8 treatments and enhanced further with both treatments. Overall attachment was increased from ~40% with untreated N87 cells to ~60% with IFN-γ or IL-8 treatment and to 80% when both treatments were used. Similar results were observed with HS-738 cells where 55% attachment to untreated cells increased to 75% with one treatment and 90% with both treatments. Upon treating cells with anti-CD74 blocking Abs, attachment was decreased to levels similar to untreated cells. This additive effect of increased CD74 expression and *H. pylori* attachment along with the decreases in attachment seen when blocking CD74 with mAbs demonstrates an important role for CD74 during infection, which is increased in proinflammatory conditions induced during the infection.

**Discussion**

CD74 has been thought traditionally to only play a role intracellularly in regulating the transport and functions of class II MHC molecules (13, 14). Reports have shown that CD74 is present on a variety of cell surfaces (16), whereas we have shown it is present on gastric epithelial cell surfaces (12). We have also shown that it plays an important role in mucosal immunology (24). A variety of roles have been suggested recently for CD74 independent of its function in the regulation of Ag presentation. CD74 has been shown to be a receptor for MIF, which is an important regulator of innate and acquired immune responses (19). MIF binding to CD74 has been shown to lead to signaling events such as ERK activation, cell proliferation, and PGE2 production (25). Other studies have indicated that CD74 is required for the signaling that induces B cell maturation (17, 18). One study indicated that the cytoplasmic domain of CD74 activates a pathway leading to up-regulation of...
several transcription factors that allow B cells to differentiate into mature cells capable of participating in immune responses.

We have previously shown that CD74 is among the receptors H. pylori uses to attach to gastric epithelial cells (12). Upon attachment to CD74, NF-κB is activated, and the inflammatory response is initiated. This study demonstrating that signaling through the attachment to CD74 was the first to demonstrate a H. pylori receptor directly initiating signaling. This study illustrates that H. pylori up-regulates one of its receptors on gastric cells through an autocrine response system. Increased expression of CD74 in the presence of H. pylori was demonstrated on the biopys of infected patients. This observation was confirmed in vitro by increased CD74 mRNA levels and surface protein expression on two different gastric cell lines. Additional investigation using the H. pylori CM of previously exposed gastric cells, filtered to remove bacteria, or a cag PAI mutant revealed that a gastric cell product or a bacterial product could be responsible for the up-regulation of CD74. The recent discovery of the presence of IL-8Rs on gastric epithelial cells (26), along with IL-8 being an important early response after H. pylori attachment to gastric epithelial cells and being induced from cross-linking CD74 (12), led us to consider IL-8 as a candidate responsible for the up-regulation of CD74 expression by gastric cells. Concentrations of rIL-8, equivalent to those produced by the cells in response to H. pylori, were found to up-regulate CD74 surface expression. The addition of anti-IL-8-neutralizing Abs or blocking IL-8Rs on cultures of gastric cells exposed to H. pylori prevented the up-regulation of CD74. Although a previous study showed that CD74 is an essential receptor for H. pylori attachment to gastric epithelial cells and being induced by binding to CD74, NF-κB, we found that blocking either receptor reduced the level of CD74 induction by H. pylori or IL-8; however, the effect of blocking CD74 was slightly more pronounced and perhaps reflecting the level of that receptor that is induced by H. pylori (data not shown). To confirm the role of IL-8 in the noted increase of CD74 expression by gastric epithelial cells, we blocked both receptors with the corresponding Abs.

These results suggest that IL-8 induced by H. pylori or by general inflammatory conditions when IL-8 is induced is a mechanism for up-regulation of CD74 surface expression.

Adherence to the gastric epithelium is undoubtedly a primordial event in bacterial colonization of the gastric mucosa (7). We have shown that CD74 is an essential receptor for H. pylori on gastric epithelial cells, and this bacterium is capable of up-regulating one of its receptors. When CD74 is up-regulated on the surface of gastric cells, more receptors are present for increased bacterial attachment, leading to enhanced attachment. These results uncover relevant information pertaining to lengthy infections and chronic gastritis often seen with H. pylori infection. IL-8 is a central player in this system, and the up-regulation of CD74 by IL-8 is an important immunological finding that extends beyond H. pylori studies and should be further studied for its role in the inflammatory response in gastritis unrelated to H. pylori infection.

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Disclosures

The authors have no financial conflict of interest.

References


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