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TNF-a and IL-1b induce IL-8 response in human gastric epithelial cells and the signal pathway is mediated by protein tyrosine kinase and dexamethasone.

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Background: Tumor necrosis factor (TNF)-α and interleukin (IL)-1β have been shown to induce IL-8 response in gastric epithelial cells, while the signal transduction pathways that mediated such a response have not been fully understood. We aimed to study the IL-8 expression in gastric epithelial cell line MKN-28 after TNF-α and IL-1β stimulation and to study their signal pathways. *Methods:* MKN-28 cell was cultured in 10% FCS RPMI-1640 media and stimulated with different doses of TNF-α and IL-1β, protein kinase stimulators or inhibitors. Cell culture supernatant IL-8 level was determined by ELISA. Cell viability was tested by routine MTT methods. *Results:* TNF-α and IL-1β induced a time- and dose-dependent IL-8 increase in MKN-28 cells. The protein tyrosine kinase (PTK) inhibitor genistein, at the doses of 1, 10, 50 and 100 μM dose-dependently reduced TNF-α and IL-1β induced IL-8 expression by 7.5%, 19.06%, 32.52%, 48.83% and 11.08%, 18.31%, 42.9%, 57.94% respectively. Dexamethasone and another PTK inhibitor herbimycin A mimiced this effect by reducing TNF-α and IL-1β induced IL-8 expression in a dose related manner. Recombinant human IL-10 and protein kinase A (PKA), and C (PKC) inhibitors and stimulators had no effect on TNF-α and iL-1β induced IL-8 production. *Conclusion:* The present results indicated that TNF-α and IL-1β induced IL-8 expression on gastric epithelial cell line MKN-28 and this was mediated by PTK activation and dexamethasone-sensitive mechanism, but not by PKA and PKC activation.

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AGE IS A PREDICTING FACTOR FOR THE ASSOCIATION BETWEEN *CagA* POSITIVE *HELICOBACTER PYLORI (Hp)* INFECTION AND SERUM PEPSINOGEN I:II RATIO IN A HIGH GASTRIC CANCER RISK REGION IN CHINA.

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Background: We have shown previously that in this cohort of subjects in Changle, China, a low serum pepsinogen I:II ratio is a marker of atrophic gastritis. Recently *CagA* strains of *Hp* infection has also been shown to increase atrophic gastritis. We evaluate the effect of age and *CagA* status on serum pepcinogen I:II ratio.

Methods: 2434 volunteers in Changle (1388 males, mean age 45.2 yrs and 1046 females, mean age 40.6 yrs) were endoscoped after blood taking during a gastric cancer screening program. Sera from subjects with normal endoscopy were tested for anti-*Hp* antibody using ELISA kit (Bio-rad GAP IgG). *CagA* bearing strains were detected by anti-*cagA* antibody assay using a recombinant *CagA* fragment fusion protein (Am J Gastro 1996:91:949). Serum pepcinogen I and II levels were measured using RIA method.

Results:

Mean Pepcinogen I:II Ratio	Age 25-45		Age 46-65	
	n	mean	n	mean
Hp-	119	5.51	98	5.13
Hp+CagA -	46	4.89	37	5.18
Hp+CagA +	203	4.89	140	4.01

The pepcinogen I:II ratio was significantly lower in *Hp* positive *CagA* positive subjects compared with *Hp+CagA-ve* subjects at age 46-65 (p=0.021) but showed no significant difference for those at age 25-45. The pepcinogen I:II ratio showed no significant difference between the *Hp+CagA-ve* and *Hp-ve* subjects.

Conclusion: Subjects infected with *CagA* strains of *H. pylori* showed a significant reduction in the pepcinogen I:II ratio, but only at the group with age above 45. This implies that *CagA* is associated with atrophic gastritis and age is a predicting factor for the development of atrophic gastritis in *CagA* carriers.