Gastrin, somatostatin, G and D cells of gastric ulcer in rats

Feng-Peng Sun, Yu-Gang Song, Wei Cheng, Tong Zhao, Yong-Li Yao

AIM: To investigate the relationship among gastrin, somatostatin, G and D cells in gastric ulcer and in its healing process in rats.

METHODOLOGY: Forty-nine male Wistar rats weighing from 200g to 260g were obtained from the Experimental Animal Center of Sun Yat-Sen University of Medical Sciences. The rats were divided into seven experiment groups: 4, 7, 10, 14, 21, 28d groups, and a control group. The rats of six experimental groups were anesthetized with 30g·kg⁻¹ sodium pentobarbital intraperitoneally at a dose of 30mg·kg⁻¹. The abdomen was opened and its stomach was found, 0.05mL acetic acid was injected into rat’s antral tissues. Omentum majus and antral tissue of the injection site were stitched. The peritoneum, parietal abdomen and ventral muscle, and skin were stitched continually. After operation, the rats were raised separately, and fasted overnight with free access to water one day before sacrifice. No treatment was given to normal control group.

Plasma sampling
The rats’ abdomen and chest chambers were opened and 4mL blood was directly withdrawn from the heart ventricle. Forty µL(500u) aprotinin (Livzon Libao Biochemical & Pharmaceutical Co. Ltd) and 60µL of 100g·L⁻¹ EDTA was added to each blood sample. The samples were centrifuged at 3500r.min⁻¹ for 15min to obtain plasma. The plasma samples were then stored at -70°C until assay.

Gastric juice
After the rats’ abdomen was opened, a plastic catheter was inserted into the stomach through pylorus and another catheter was inserted through oral cavitas and esophagus into stomach. Two mL saline(pH7.0, 35°C) was infused into the stomach at a flow velocity of 12mL/h. The gastric fluid was collected and 40µL(500u) aprotinin was added. The samples were centrifuged at 3500r.min⁻¹ for 15min to obtain gastric fluid. The gastric fluid samples were then stored at -70°C until assay.

Antral mucosa
The rats’ stomach was separated and was split from the greater curvature of stomach. The antral tissues in the ulcer area and non-ulcer area were separately taken with ophthalmic scissors. The tissue was quickly weighed by an electric analytical balance and was boiled in a microwave stove. The boiled tissue was homogenized into homogenate in a homogenizer with 1mL of 1mol.L⁻¹ acetic acid. Then 1mL of 1mol.L⁻¹ NaOH was added to neutralize it. The homogenate was centrifuged at 3500r.min⁻¹ for 15 minutes and the supernatant was collected. The samples were then stored at -70°C until assay. The stomach was separated and was split from the greater curvature of stomach. About 1.0×0.5cm antral tissues in the ulcer area and non-ulcer area was separately taken with ophthalmic scissors. The specimen was fixed in 100mL·L⁻¹ neutrally buffered formalin. It was embedded with paraffin 24h later and was serially sectioned at 4µm. The sections were mounted onto histostick-coated slides. Adjacent ribbons were collected for immunohistochemical staining.

INTRODUCTION
Gastrin is secreted in G cells, while somatostatin is secreted in D cells. Gastrin, somatostatin and other gastrointestinal hormones regulate the function of gastrointestinal tract such as secretion, movement, absorption, circulation and nutrition of cells[1-12]. The nerve system and the endocrine system participate in the healing process of gastric ulcer and regulate the absorption of inflammatory filtrate, hyperplasia of granulation tissues, and regeneration of epithelial tissues. Obvious regular change takes place in many endocrine tissues[13-24]. In order to investigate the relationship between gastrin, somatostatin, G and D cells in the period of gastric ulcer and its healing process in rats, the gastrin and somatostatin in plasma, gastric juice and antral tissue were tested in rats. At the same time, the number of G and D cells was measured in the antral mucosa.

MATERIALS AND METHODS
Animal
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REFERENCES
13. GC, FC, TC, YL, FS, YS, WS, ZT, YY. Gastrin and somatostatin in plasma, gastric juice and antral tissue of rats with gastric ulcer. World J Gastroenterol. 2002;8(2):375-378.

www.wjgnet.com
Measurement of gastrin and somatostatin

Gastrin and somatostatin were detected by using RIA method. The gastrin kits were purchased from Tianjin Qianye Biotech Co. Ltd, and the somatostatin kits were bought from the Department of Neurobiology of the Second Military Medical University. Measurement procedures were performed according to the instruction attached to the kits. The unit of result of plasma and gastric fluid was transformed to ng·L⁻¹, while the unit of result of antral mucosa tissue to ng·g⁻¹.

Immunohistochemical staining for G and D cells

The anti-gastrin antibody(Sigma Co. USA) and anti-somatostatin antibody(GYMED Co. USA) were used and immunohistochemical staining for G and D cells was performed with the strept-avidin-biotin-peroxidase complex(SABC)(Wuhan Boster Biological Technology Co. Ltd), negative control sections were normal serum blocking and PBS instead of the primary antibody. Images of 5 views randomly selected under microscope(10×40) from each anti-gastrin immunohistochemical staining section were input into the Quaintm 500 image analysis system(Leica Co, Germany). The number and area of G cells were calculated by the computer. The mean number and area of G cells in 5 views of the section served as the number and area of G cells of a section. That of D cells was calculated in the same way as the G cells. The ratio of G/D number and G/D area was acquired by separately dividing the number of G cells and the area of G cells by the number of D cells and the area of D cells in adjacent sections.

Statistical analysis

The result of quantitative data was expressed as mean±SE. Data was analyzed using the variance analysis(ANOVA). Post hoc analysis between factors was performed using least significant difference test. Unpaired data was compared using the Wilcoxon ranksum test and correlated using Pearson’s correlation.

RESULTS

The concentration of gastrin and somatostatin in the plasma, gastric juice, antral mucosa is shown in Tables 1 and 2. The number and area of G and D cells in the rat antral mucosa, and the ratio of G/D number and G/D area is shown in Table 3. The relationship between rat G and D cells, and the relationship between G or D cells with gastrin or somatostatin are shown in Table 4.

Table 1 Gastrin concentration in rat plasma, gastric juice, and antral mucosa (Tas, n=7)

| Group   | Plasma(ng·L⁻¹) | Gastric juice(ng·L⁻¹) | Ulcer mucosa(ng·g⁻¹) | Non-ulcer mucosa(ng·g⁻¹) |
|---------|----------------|-----------------------|----------------------|--------------------------|
| Control | 147±41         | 44±15                 | -                    | 3.7±1.1                  |
| 4d      | 397±130        | 56±16                 | 2.0±0.7              | 6.7±2.3                  |
| 7d      | 364±91         | 114±34                | 1.3±0.4              | 6.1±1.8                  |
| 10d     | 255±87         | 60±20                 | 2.3±0.8              | 1.9±0.7                  |
| 14d     | 238±88         | 45±21                 | 1.9±0.7              | 1.1±0.4                  |
| 21d     | 211±65         | 44±17                 | 1.3±0.4              | 1.1±0.7                  |
| 28d     | 216±95         | 60±18                 | 1.5±0.5              | 1.5±0.3                  |

Table 2 Somatostatin concentration in rat plasma, gastric juice, and antral mucosa (Tas, n=7)

| Group   | Plasma(ng·L⁻¹) | Gastric juice(ng·L⁻¹) | Ulcer mucosa(ng·g⁻¹) | Non-ulcer mucosa(ng·g⁻¹) |
|---------|----------------|-----------------------|----------------------|--------------------------|
| Control | 45±12          | 64±16                 | -                    | 1.4±0.4                  |
| 4d      | 13±5           | 46±15                 | 0.3±0.1              | 0.4±0.1                  |
| 7d      | 22±8           | 42±15                 | 0.3±0.1              | 0.4±0.2                  |
| 10d     | 41±9           | 54±17                 | 0.2±0.1              | 0.8±0.2                  |
| 14d     | 33±8           | 54±12                 | 0.9±0.4              | 1.3±0.4                  |
| 21d     | 32±9           | 49±12                 | 1.1±0.2              | 1.1±0.4                  |
| 28d     | 35±10          | 51±20                 | 1.1±0.3              | 1.1±0.3                  |

Table 3 Number and area of G and D cells, and the ratio of G/D number and G/D area (Tas, n=7)

| Group | No.(G cells) | Area of G cells (x10⁻⁶m²) | No.(D cells) | Area of D cells (x10⁻⁶m²) | Number ratio of G/D | Area ratio of G/D |
|-------|--------------|----------------------------|--------------|---------------------------|---------------------|------------------|
| Control | 33±6         | 99±7                      | 15±2         | 70±11                     | 2.3±0.1             | 1.4±0.1          |
| 4d     | 50±7         | 87±7                      | 10±2         | 56±8                      | 4.9±0.3             | 1.6±0.1          |
| 7d     | 69±8         | 91±7                      | 9±2          | 60±9                      | 7.6±0.5             | 1.5±0.2          |
| 10d    | 73±13        | 94±7                      | 10±1         | 63±7                      | 7.4±0.4             | 1.5±0.1          |
| 14d    | 62±11        | 95±9                      | 11±2         | 66±11                     | 5.8±0.5             | 1.5±0.1          |
| 21d    | 46±8         | 95±8                      | 14±2         | 68±11                     | 3.4±0.2             | 1.4±0.1          |
| 28d    | 43±6         | 95±7                      | 14±2         | 66±8                      | 3.1±0.3             | 1.4±0.1          |

Table 4 Relationship between rat G and D cells, and between G or D cells and gastrin or somatostatin

| Group | No. of G cells | No. of D cells | Area of G cells | No. of G cells | Area of G cells | Area of D cells | Area of D cells |
|-------|----------------|---------------|----------------|----------------|----------------|----------------|----------------|
| Control | 0.97          | 0.95          | 0.95          | 0.93          | 0.94          | 0.94          | 0.93          |
| 4d     | 0.92          | 0.93          | 0.93          | 0.90          | 0.98          | 0.98          | 0.86          |
| 7d     | 0.97          | 0.95          | 0.92          | 0.98          | 0.93          | 0.93          | 0.94          |
| 10d    | 0.97         | 0.96          | 0.93          | 0.88          | 0.93          | 0.93          | 0.95          |
| 14d    | 0.91          | 0.99          | 0.87          | 0.89          | 0.78          | 0.78          | 0.99          |
| 21d    | 0.97          | 0.88          | 0.90          | 0.68          | 0.98          | 0.98          | 0.99          |
| 28d    | 0.99          | 0.94          | 0.95          | 0.89          | 0.92          | 0.92          | 0.96          |
Both gastrin and somatostatin are gastrointestinal hormones closely related to the function of gastrointestinal system. Gastrin is mainly secreted in G cells in antral and upper small intestines. It has several kinds of molecules and distributes in plasma, tissues, gastric juice, and intestinal juice. Somatostatin is a 14 amino peptide. It also has several kinds of molecules and distributes vastly in the body. The somatostatin in gastrointestinal system is secreted in D cells. It is mainly in intestinal nerve plexus, stomach and pancreas, and it is also in gastric and intestinal fluid. In the antrum there are many G and D cells, most of which belong to the open type endocrine cells that can directly secrete gastrin or somatostatin into gastric fluid. Elevated gastrin level can increase the secretion of basal and peak gastric acid, pepsin and inhibit the invoking function of gastrin to the function of gastrointestinal system. Gastrin is mainly secreted in G cells, Caruana P, Bordi C, Delle Fave G. Relationship between fundic G, antral G and D cells. The association between antral G and D cells and mucosal inflammation, the ratio and function of G/D cells were imbalance.

**REFERENCES**

1. Schmitz F, Schrader H, Otte J, Schmitz H, Stuber E, Herzig K, Schmidt WE. Identification of CCK-B/gastrin receptor splice variants in human peripheral blood mononuclear cells. *J Exp Biol* 2001; 101:25-33
2. Caplin M, Khan K, Grimes S, Michaeli D, Savage K, Pounder R, Dhillon A. Effect of gastrin and anti-gastrin antibodies on proliferation of hepatocyte cell lines. *Dig Dis Sci* 2001; 46:1356-1366
3. Janecka A, Zubrycka M, Janecki T. Somatostatin analogs. *J Pept Res* 2001; 58:91-107
4. Klisovic DD, O’Dorriso MS, Katz SE, Sall JW, Balster D, O’Dorriso TM, Craig E, Lubow M. Somatostatin Receptor Gene Expression in Human Ocular Tissues: RT-PCR and Immunohistochemical Study. *Invest Ophthalmol Vis Sci* 2003; 43:2193-2201
5. Hoeker M, Cramer T, O’Connor DT, Rosewicz S, Wiedenmann B, Wang TC. Neuroendocrine-specific and gastrin-dependent expression of a chromogranin A-luciferase fusion gene in transgenic mice. *Gastroenterology* 2001; 121:43-55
6. Monstein HJ, Obilsson B, Axelsson J. Differential expression of gastrin, cholecystokinin-A and cholecystokinin-B receptor mRNA in human pancreatic cancer cell lines. *Scand J Gastroenterol* 2001; 36:738-743
7. McWilliams DF, Grimes S, Watson SA. Antibodies raised against the extracellular tail of the CCKB/gastrin receptor inhibit gastrin-stimulated signalling. *Regul Pept* 2001; 99:157-161
8. Yamamoto S, Kaneko H, Konagaya T, Mori S, Koteria H, Hayakawa T, Yamaguchi C, Uruma M, Kusugami K, Mitsuura T. Interactions among gastric somatostatin, interleukin-8 and mucosal inflammation in Helicobacter pylori-positive peptic ulcer patients. *Helicobacter* 2001; 6:136-145
9. Morisset J, Wong H, Walsh JL, Jaine J, Bourassa J. Pancreatic CCK(B) receptors: their potential roles in somatostatin release and delta-cell proliferation. *Am J Physiol Gastrointest Liver Physiol* 2000; 279:G148-G156
10. Cui RT, Cai G, Yin ZB, Cheng Y, Yang QH, Tian T. Transretinoic acid inhibits rats gastric epithelial dysplasia induced by N-methyl-N-nitro-N-nitrosoguanidine: influences on cell apoptosis and expression of its regulatory genes. *World J Gastroenterol* 2001; 7:394-398
11. Takeuchi K, Kawauchi S, Araki H, Ueki S, Furukawa O. Stimulation of nitridiazidine, a histamine H2-receptor antagonist, of duodenal HCO3- secretion in rats: relation to anti cholinesterase activity. *World J Gastroenterol* 2000; 6:651-658
12. Li W, Zheng TZ, Qu SY. Effect of cholecystokinin and secretin on contractile activity of isolated gastric muscle strips in guinea pigs. *World J Gastroenterol* 2000; 6:939-955
13. Kermorgant S, Lehy T. Glycine-extended gastrin promotes the invasiveness of human colon cancer cells. *Biochem Biophys Res Commun* 2001; 285:136-141
14. Berger AC, Gibril F, Venzon DJ, Doppman JL, Norton JA, Bartlett DL, Libutti SK, Jensen RT, Alexander HR. Prognostic value of initial fasting serum gastrin levels in patients with Zollinger-Ellison syndrome. *J Clin Oncol* 1999; 17:3051-3057
15. Waldum LH, Aase S, Kvetnoi I, Brenna E, Sandvik AK, Syversen U, Johnsen G, Vatten L, Polak JM. Neuroendocrine differentiation in human gastric carcinoma. *Cancer* 1998; 83:435-444
16. Sun FP, Song YG, Zhu XS, Tang SN, Du J, Qiu QL, Zhao T. The establishment of acetic acid-induced rat’s gastric ulcer model and the observation of ulcer antral mucosa microscope through and electromicroscope. *Shijie Huaren Xiaohua Zazhi* 2001; 9:135-138
17. Annibale B, Aprile MR, Ferraro G, Marignani M, Angeletti S, D’Ambra G, Caruana P, Bordi C, Delle Fave G. Relationship between fundic endocrine cells and gastrin and acid secretion in hypersecretory duodenal ulcer patients. *Aliment Pharmacol Ther* 1998; 12:779-788
18. Wright NA. Aspects of the biology of regeneration and repair in the human gastrointestinal tract. *Phil Trans R Soc Lond B Biol Sci* 1998; 353:925-933
19. Solcia E, Rindi G, Buffa R, Fiocca R, Capella C. Gastric endocrine cells: types, function and growth. *Eur J Pept Sci* 2000; 93:31-35
20. Ling YL, Meng AH, Zhao XY, Shan BE, Zhang JL, Zhang XP. Effect of cholecystokinin on cytokines during endotoxic shock in rats. *World J Gastroenterol* 2001; 7:667-671
21. Zhang LH, Yao CB, Li HQ. Effects of extract F of red-rooted Salvia on mucosal lesions of gastric corpus and antrum induced by hemorrhagic shock-reperfusion in rats. *World J Gastroenterol* 2001; 7:672-677
22. Zhang H, Jiang SL, Yao XX. Study of T-lymphocyte subsets, nitric oxide, hexosamine and Helicobacter pylori infection in patients with chronic gastric diseases. *World J Gastroenterol* 2000; 6:601-604
23. Zhu L, Yang ZC, Li A, Cheng DC. Reduced gastric acid production in burn shock period and its significance in the prevention and treatment of acute gastric mucosal lesions. *World J Gastroenterol* 2000; 6:854-88
24. Huang Y, Li SJ, Dong JX, Li F. The new proof of neuro-endocrine-immune network-expression of islet amyloid polypeptide in plasma cells in gastric mucosa of peptic ulcer patients. *World J Gastroenterol* 2000; 6:417-418
25. Zavros Y, Fleming WR, Hardy KJ, Shulkes A. Regulation of fundic acid secretion in rats: relation to anti cholinesterase activity. *World J Gastroenterol* 2000; 6:417-418
26. Ray JM, Squires PE, Meloche RM, Nelson DW, Snutch TP, Buchan AM. L-type calcium channels regulate gastric release from human antral G cells. *Am J Physiol* 1997; 273:C281-C288
27. Kamada T, Haruma K, Kawaguchi H, Yoshihara M, Sumii K, Kajiyama T, Yamada T, Kusugami K, Mitsuma T. Interactions among gastric somatostatin, interleukin-8 and mucosal inflammation in Helicobacter pylori-positive peptic ulcer patients. *Helicobacter* 2001; 6:136-145
atrophy, and Helicobacter pylori infection in subjects with normal mucosa, chronic gastritis, and duodenal ulcer. *Am J Gastroenterol* 1998; 93:748-752

Nagano T, Itoh H, Takeyama M. Effect of Dai-kenchu-to on levels of 3 brain-gut peptides (motilin, gastrin and somatostatin) in human plasma. *Biomed Pharmacother* 1999; 53(Suppl 1):S113-S116

Naito T, Itoh H, Yasunaga F, Takeyama M. Rikkunshito raises levels of somatostatin and gastrin in human plasma. *Bio Pharm Bull* 2001; 24:841-843

Johansson B, Uvnas-Moberg K, Knight CH, Svennersten-Sjaunja K. The influence of Helicobacter pylori infection on antral gastrin and somatostatin cells and in serum gastrin concentrations. *Korean J Intern Med* 1999; 14:15-20

Fung LC, Greenberg GR. Somatostatin-14 modulates acid-dependent inhibition of meal-stimulated gastrin via muscarinic pathways in dogs. *Regul Pept* 1998; 74:159-166

Hiraoka S, Miyazaki Y, Kitamura S, Toyota M, Kiyohara T, Shinomura Y, Mukaida N, Matsuzawa Y. Gastrin induces CXC chemokine expression in gastric epithelial cells through activation of NF-kappaB. *Am J Physiol Gastrointest Liver Physiol* 2001; 281:G735-G742

Vantus T, Keri G, Krivickiene Z, Valius M, Stetak A, Keppens S, Csermely P, Bauer PI, Bokonyi G, Declercq W, Vandenabeele P, Merlevede W, Vandenheede JR. The somatostatin analogue TT-232 induces apoptosis in A431 cells. Sustained activation of stress-activated kinases and inhibition of signalling to extracellular signal-regulated kinases. *Cell Signal* 2001; 13:733-725

Zavros Y, Paterson A, Lambert J, Shulkes A. Expression of progastrin-derived peptides and somatostatin in fundus and antrum of nonulcer dyspepsia subjects with and without *Helicobacter pylori* infection. *Dig Dis Sci* 2000; 45:2058-2064

Gromada J, Hoyer M, Buschard K, Salehi A, Rorsman P. Somatostatin inhibits exocytosis in rat pancreatic alpha-cells by G(i2)-dependent activated kinases and inhibition of signalling to extracellular signal-regulated kinases. *Eur J Gastroenterol Hepatol* 1999; 11:361-365

Yamamoto M, Yano M, Shimizu T, Imada A, Kusugami K, Mitsuma T. Effect of intragastric administration of gastrin to dogs. *Am J Physiol Gastrointest Liver Physiol* 2001; 276:G227-G237

Camouard P, Walter P, Wittersheim C, Meunier O, Demuynck P, Meunier O, Merlevede W, Vandenheede JR. The somatostatin analogue TT-232 induces apoptosis in A431 cells. Sustained activation of stress-activated kinases and inhibition of signalling to extracellular signal-regulated kinases. *Cell Signal* 2001; 13:733-725

Zavros Y, Paterson A, Lambert J, Shulkes A. Expression of progastrin-derived peptides and somatostatin in fundus and antrum of nonulcer dyspepsia subjects with and without *Helicobacter pylori* infection. *Dig Dis Sci* 2000; 45:2058-2064

Gromada J, Hoyer M, Buschard K, Salehi A, Rorsman P. Somatostatin inhibits exocytosis in rat pancreatic alpha-cells by G(i2)-dependent activation of calcineurin and depriving of secretory granules. *J Physiol* 2001; 535:519-532

Feng X, Feng JB, Yan H, Zhao Y, Wang SL. Distribution of nitric oxide synthase in stomach myenteric plexus of rats. *World J Gastroenterol* 2001; 7:852-854

Tuo BG, Yan YH, Ge ZL, Ou CW, Zhao K. Ascorbic acid secretion in the human stomach and the effect of gastrin. *World J Gastroenterol* 2000; 6:704-708

Pesc C, Rossi R, Lenti E, Tanzi R. G-cell density in the antral mucosa: a feasibility study. *Histopathology* 1997; 30:315-318

Sun FP, Song YG, Zhu XS, Tan SG, Du J, Qiu QL, Liang QM, Zhao T. Establishment of acetic-acid-induced rat’s gastric ulcer model and the histological observation of ulcer antral mucosa in healing stage. *Digi Juxu Daxue Xuebao* 2001; 21:578-581

Larsson LJ. Developmental biology of gastrin and somatostatin cells in the antrophic mucosa of the stomach. *Microsc Res Tech* 2000;48:272-281

Mihaljevic S, Katicic M, Karner I, Vuksic-Mihaljevic Z, Dmitrovic B, Ivancic A. The influence of Helicobacter pylori infection on gastrin and somatostatin values present in serum. *Hepatogastroenterology* 2000; 47:1482-1484

Zavros Y, Fleming WR, Shulkes A. Concurrent elevation of fundic somatostatin prevents gastrin stimulation by GRP. *Am J Physiol* 1999; 276:C211-C217

Witzbrock SL, McDowell GH, Hardy KJ, Shulkes A. Active immunization against somatostatin alters regulation of gastrin in response to gastric acid secretagogues. *Am J Physiol* 1998; 274:G751-G756

Ren J, Dunn ST, Tang Y, Wang Y, Gao J, Brewer K, Hardy RF. Effects of calcitomin gene-related peptide on somatostatin and gastrin gene expression in rat antrum. *Eur J Pept* 1998; 73:79-82

Weigert N, Schepp W, Haller A, Schusdziarra V. Regulation of gastrin, somatostatin and bombesin release from the isolated rat stomach by exogenous and endogenous gamma-amino但 nervous acid. *Digestion* 1999; 60:159-163

Squires PE, Meloche RM, Buchan AM. Bombesin-evoked gastrin release and calcium signaling in human antral G cells in culture. *Am J Physiol* 1999; 276:G227-G237

Cappelli E, Degan P, Thompson LH, Frosina G. Efficient repair of 8-oxo-7,8-dihydroxyguanosine in human and hamster xeroderma pigmentosum D cells. *Biochemistry* 2000; 39:10408-10412

Chen YQ, Guo WH, Chen ZM, Shi L, Chen YX. Effect of gastrectomy on G-cell density and functional activity in dogs. *World J Gastroenterol* 2000; 6:419-420

Chamouard P, Walter P, Wittersheim C, Demuyynnck P, Meunier O, Baumann R. Antral and fundic D-cell numbers in Helicobacter pylori infection. *Eur J Gastroenterol Hepatol* 1997; 9:361-365

Ito Y, Kaneko H, Konagaya T, Nishi S, Kotera H, Uruma M, Rhee N, Shimizu T, Imada M, Kusugami K, Mitsuma T. Effect of intragastric administration of gastrin-34, somatostatin-14 and somatostatin receptor subtype 2-positive cells in rat antral mucosa. *Life Sci* 1999; 64:2497-2504

Lloyd KC, Amirmoazzami S, Friedik F, Chew P, Walsh JH. Somatostatin inhibits gastrin release and acid secretion by activating sst2 in dogs. *Am J Physiol* 1997; 272:C1481-C1488

Kamada T, Haruma K, Kawaguchi H, Yoshihara M, Sumii K, Kiyajiya G. The association between antral G and D cells and muscular inflammation, atrophy, and Helicobacter pylori infection in subjects with normal mucosa, chronic gastritis, and duodenal ulcer. *Am J Gastroenterol* 1998; 93:746-752

Tzaneva M. Light and electron microscopic immunohistochemical investigation on G and D cells in antral mucosa in Helicobacter pylori-related gastritis. *Exp Toxicol Pathol* 2001; 52:523-528

Magert HJ, Reinecke M, David I, Raab HR, Adermann K, Zacht HD, Hill O, Hess R, Forsmann WG. Uroguanylin: gene structure, expression, processing as a peptide hormone, and co-storage with somatostatin in gastrointestinal D-cells. *Regul Pept* 1998; 73:165-176

Beales IL. Effect of platelet-activating factor on gastric release from cultured rabbit G-cells. *Dig Dis Sci* 2001; 46:301-306

Ford MG, Valle JD, Soroka CJ, Merchant JL. EGF receptor activation of Helicobacter pylori infection in canine G cells and in subjects with normal mucosa, chronic gastritis, and duodenal ulcer. *Am J Gastroenterol* 1998; 93:746-752

Yao YL, Xie B, Zhang WD, Song YG. Gastrin, somatostatin, and experimental disturbance of the gastrointestinal tract in rats. *World J Gastroenterol* 2001; 7:399-402

Edited by Ma JY