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Citation	The 6th Medical Research Conference, Hong Kong, China, 13-14 January 2001, v. 23 n. 2 Supp, p. 46
Issued Date	2001
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S-GH-3

Overexpression of Protein Kinase C-Beta 1 Isoenzyme Suppresses SC-236-Induced Apoptosis in Gastric Epithelial Cells

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Background and Aims: It has previously been shown that a specific COX-2 inhibitor suppressed tumor growth in nude mice bearing gastric cancer xenografts. Our group has found that the specific COX-2 inhibitor SC-236 could induce apoptosis in gastric cancer cells. The present study investigated the role of protein kinase C isoforms in the regulation of SC-236-induced apoptosis in gastric cancer cells.

Methods: Apoptosis in the gastric cancer cell line AGS was determined by acridine orange staining and flow cytometry. The mRNA and protein levels of 12 PKC isoforms and apoptosis-related genes including p53, p21waf1/cip1, p27 kip1 , bcl-2, bax and c-myc were detected by RT-PCR and Western blotting. The effect of PKC-beta 1 overexpression by transfection with its complementary DNA (cDNA) on SC-236-induced apoptosis and apoptosis-related genes was further investigated.

Results: SC-236 induced apoptosis in AGS cells dose-dependently. Treatment with SC-236 decreased the protein expression of PKC-beta 1, increased the expression of PKCdelta and PKCbeta, but did not alter the expression of the other PKC isoforms in AGS cells. Overexpression of PKC-beta 1 attenuated the apoptotic response of AGS cells to SC-236, associated with overexpression of both p21waf1/cip1 mRNA and protein. Inhibition of PKCbeta 1-mediated overexpression of p21waf1/cip1 partially reduced the antiapoptotic effect of PKCbeta 1.

Conclusions: SC-236-induced apoptosis in gastric cancer cells is partly mediated by differential regulation of PKC isoform expression. Enhanced expression of exogenous PKC-beta 1 protects against SC-236-induced apoptosis through upregulation of p21waf1/cip1.

S-GH-4

Expression of Ki-67 and Bcl-2 in Gastric Epithelial Cells: Role of Antralization in Gastric Carcinogenesis

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Background: We reported that *H. pylori*-induced "antralization" of the gastric incisura was associated with precancerous lesions such as gastric atrophy and intestinal metaplasia. This study aimed to determine epithelial expression of Ki-67 and Bcl-2 at different gastric sites, and their associations with *H. pylori* infection, antralization, and precancerous lesions.

Patients: 105 patients (M/F 49/56, age: mean ± SD 60.4 ± 13.5 years) were included. Eight gastric biopsies taken from gastric antrum, incisura, body and fundus were used for the histological assessments of gastric mucosa and *H. pylori* infection after H&E staining, and the detection of Ki-67 and Bcl-2 expression in gastric epithelial cells by immunohistochemistry.

Results: Proliferation indices (PIs, % of Ki-67 positive cells over total cells) were 46, 41, 37 and 36, respectively, in the antrum, incisura, body and fundus. The PIs were greater in the presence than in the absence of *H. pylori* infection at all gastric sites (all $P<0.001$). In the gastric incisura, the PI was greater in patients with antralization than those without (47 vs 32, $P<0.001$). However, there was no difference in the PI between patients with and those without precancerous lesions. Bcl-2 expression was detected in 29%, 31%, 35% and 44%, respectively, of the antral, incisura, body and fundus biopsies. No differences in Bcl-2 expression were observed between *H. pylori* infected and uninfected biopsies at all sites. However, Bcl-2 expression was significantly increased in the presence of antralization (39% vs 17%, $P<0.001$). Moreover, patients with precancerous lesions had a higher Bcl-2 expression than those with normal gastric mucosa.

Conclusions: Cell proliferation is associated with *H. pylori* infection and antralization at the gastric incisura. Expression of Bcl-2 was not associated with *H. pylori* infection, but significantly associated with antralization at the gastric incisura and gastric atrophy and intestinal metaplasia at all sites of the stomach. Antralization may be am important step in the process of gastric carcinogenesis.