P6-06

Genomic Mapping of 12p Amplifications in Gastric Cancer Reveal a 0.5-Mb Target Region Including KRAS Locus

Hiroaki Mita, Fumio Aoki, Hirofumi Akashi, Reo Maruyama, Yasushi Sasaki, Hiromu Suzuki, Masashi Idogawa, Lisa Kashima, Minoru Toyota, Kohzoh Imai, Yasuhisa Shinomura, Takashi Tokino

Aim: We report the development of a novel method known as digital genome scanning (DGS) to quantitate copy number variations by utilizing the tag-counting concept in order to characterize genomic alteration of gastric cancer.

Method: Genomic DNA of a gastric cancer cell line was digested with MboI restriction enzyme, and the short restriction fragments (termed tags) were mapped onto the human chromosome sequences. Tag densities were evaluated to detect abnormalities in DNA content. Copy-number alterations were validated by real-time PCR, FISH, and Immunoblot analysis.

Results: DGS analysis of the gastric cancer cell line revealed amplification of 0.5-Mb region on 12p12.1 containing the KRAS gene. Furthermore, amplification of KRAS locus was detected in 15% (3/20) of gastric cancer cell lines. Overexpression of KRAS protein directly correlated with the increase in copy number of KRAS. Knocking down of KRAS in gastric cancer cells with amplification of the KRAS locus resulted in the inhibition of cell growth and corresponding suppression of downstream p44/42 MAP kinase and AKT.

Conclusion: Our study highlights the utility of DGS for the identification of copy number alterations, and clarifies that KRAS overexpression is a contributor to the proliferation of gastric cancer cells with KRAS amplification.

P6-07

Can CEA be a Risk Factor for Recurrence in Stage II Colon Cancer?

Toshiyuki Suwa, Joe Sakurai, Takehito Ohtsubo

Gastroenterological and General Surgery, St. Marianna University School of Medicine

Purpose: To reveal the risk factors of recurrence for stage II colon cancer and consider the indications for postoperative adjunctive chemotherapy.

Subjects: Among the 1,659 cases of surgery for colon cancer treated before 2000, the subjects comprised 375 cases that were at stage II and who had not undergone postoperative adjunctive chemotherapy, and the risk factors for recurrence were examined.

Method: Comparisons were made between the 63 cases that had recurrence and the 312 cases in the non-recurrence group with regard to the respective items: age, gender, tumor growth type, region of occurrence, largest size of the tumor, histological type, histological invasion depth, lymphatic invasion, venous invasion, and the preoperative blood CEA value.

Results: In the comparisons between the recurrence group and the non-recurrence group, there were no differences in age, gender, growth type, tumor size, or histological type. For the histological invasion depth, it was commonly deeper than SE in the recurrence group (p<0.05), and there were significantly more cases therein with high CEA values (p<0.01). In addition, there were significantly more positive cases of lymphatic invasion in the recurrence group (p<0.01). There were also significantly more positive cases of venous invasion in the recurrence group (p<0.01). In a multivariate analysis, significant risk factors for recurrence included: 1. the rectum; 2. an invasion depth deeper than SE; 3. positive lymphatic invasion; 4. positive venous invasion; and 5. high preoperative blood CEA value. The cases that had two or less of these five positive items had an 8.8% rate of recurrence, and the cases that involved three or more items had a 36.1% rate of recurrence (p<0.01).

Conclusion: A high preoperative blood CEA value may therefore be a risk factor for recurrence in stage II colon cancer.