239 POSTER

Single nucleotide polymorphisms of cancer related genes involved in signal-transduction pathways in Korea lung cancer patients

Y.H. Kim[1,2], H. Choi[1,2], J. Sung[1,2], K. Park[1,2], I. Choi[1,2], J. Seo[1,2], S. Shin[1,2], J. Kim[1,2]. [1]*Korea University Anam Hospital, Medical Oncology, Seoul, Korea;* [2]*Lung, Breast/Ovary Cancer Genome Research Center, Seoul, Korea*

Background: Lung cancer is a leading cause of cancer death in Korea. Single nucleotide polymorphisms (SNPs) represent an important class of genetic variation and susceptibility of individual. To search Korean specific SNPs for lung cancer, we explored SNPs of genes involved in diverse cancer related signal transduction pathways.
Methods: We analyzed 11 SNP points from 3 genes (ERBB2, ATM, CDK5) by SNaPshot assay and Restriction Fragment Length Polymorphism (RFLP) using genomic serum DNA from 291 Korean lung cancer patients and 281 healthy controls. Written informed consent was obtained from all patient study subjects, and the study protocol was approved by the institutional review board. The allele frequencies of each SNP between cases and control were estimated by the chi square test and odds ratios (OR) with 95% confidence interval (95% CI).
Result:

			p-value
CDK5 (rs1549760, −904)	G:A = 0.654:0.346 (LP)	0.711:0.289 (N)	**0.041**
CDK5 (rs2069442, −270)	C:G = 0.657:0.343 (LP)	0.659:0.341 (N)	0.947
CDK5 (rs2069443, −238)	A:C = 0.659:0.341 (LP)	0.665:0.335 (N)	0.849
ATM (rs228589, −5144)	A:T = 0.531:0.469 (LP)	0.518:0.482 (N)	0.709
ATM (rs189037, −4519)	G:A = 0.570:0.430 (LP)	0.542:0.458 (N)	0.417
ATM (rs664677, IVS22)	C:T = 0.603:0.397 (LP)	0.604:0.396 (N)	0.976
ATM (rs609429, IVS48)	G:C = 0.558:0.442 (LP)	0.540:0.460 (N)	0.543
ERBB2 (rs2643194, −3444)	C:T = 0.603:0.397 (LP)	0.631:0.369 (N)	0.392
ERBB2 (rs2934971, −1985)	G:T = 0.603:0.397 (LP)	0.619:0.381 (N)	0.567
ERBB2 (rs189200, I655V)	A:G = 0.875:0.125 (LP)	0.888:0.112 (N)	0.534
ERBB2 (rs1058808, P1170A)	C:G = 0.610:0.390 (LP)	0.625:0.375 (N)	0.638

Conclusion: We identified differences in frequencies of 11 SNP points in Korean lung cancer. In result, A polymorphism in the promoter region of CDK5 (−904) gene was statistically significant but others not. Further study needed to explore the association between SNP points and histopathological factors of the lung cancer patients and to evaluate the role of each polymorphism in lung cancer.

240 POSTER

Comparison of gene expression profile between RER+ and RER− sporadic colorectal tumours

F. Rodríguez Jiménez[1], P. Iniesta[1], A. Diaz-López[1], C. García-Aranda[1], C. Frías[1], C. de Juan[1], A. Sánchez-Pernaute[2], A. Torres[2], E. Díaz-Rubio[2], M. Benito[1]. [1]*Facultad de Farmacia, Bioquímica y Biología Molecular, Madrid, Spain;* [2]*Hospital Clínico San Carlos, Servicios de Cirugía y de Oncología Médica, Madrid, Spain*

Background: Replication error positive (RER+) and negative (RER−) sporadic colorectal tumors display distinctive pathological features and prognosis. To elucidate their gene expression profile may contribute to understand their different molecular pathogenesis and their corresponding clinical evolution.
Material and methods: Seventy sporadic colorectal tumours were classified according to their RER status. Total RNA extracted from normal tissues as well as from RER+ and RER− tumours was reverse transcribed. The labelled cDNA was used to hybridize a commercially available cDNA array corresponding to 96 human extracellular matrix and adhesion molecule genes. The candidate genes were selected by computational analysis (using Gearray analyzer software). Verification of the cDNA array results was performed by Real Time Quantitative PCR using TaqMan probes. The resulting expression of tumor tissues was normalized using GAPDH as housekeeping gene and referred to the expression of normal tissues.
Results: We observed common events occurring in RER+ and RER− tumours. Thus, the matricellular glycoprotein osteopontin (SPP1) was expressed at high levels in both kinds of tumors in comparison to normal tissue. However, the expression profile of this gene defined two subgroups of RER− tumours. On the other hand, significant overexpression of MMP11 in RER− in comparison to RER+ tumors was observed as a differential event. Interestingly, RER− tumors subgroup which showed higher expression level for SPP1 also expressed more MMP11 mRNA transcripts, both gene profile contributing to better define both RER− subgroups. The first RER− subgroup expressed MMP11 mRNA at significant higher level (P = 0.021) in comparison with RER+ tumours. In contrast, the second RER− subgroup did not display this tendency (P = 0.252)
Conclusion: RER− tumours show a more heterogeneous expression profile than RER+ tumours. Our knowledge of the differential molecular events between RER+ and RER− sporadic colorectal tumours may allow us to a better understanding of their different clinicopathological outcome.

241 POSTER

Detection of CEA mRNA expressing cells in peripheral blood 7 days after surgery influences relapse in colorectal cancer

Y. Maeda[1], S. Sadahiro[1], T. Suzuki[1], A. Kamijo[1], H. Makuuchi[1], C. Murayama[2]. [1]*Tokai University, Surgery, Isehara, Kanagawa, Japan;* [2]*Tokai University, Radiology, Isehara, Kanagawa, Japan*

Background: No consensus has been reached on whether cancer cells detected in blood during surgery in patients (pts) with colorectal cancer(CRC) may correlate with prognosis. Cancer cells could not be detected when blood was taken 7days after intravenous injection in experiment (Fidler, 1970). The aim of this study was to examine the detection of cancer cells in blood at more than 7 days after curative resection may serve as a prognostic indicator.
Methods: Two hundred and one pts with CRC who underwent curative surgery were the subjects. Peripheral blood was collected between 7 and 10 days after resection. Cancer cells were detected using RT-PCT targeting CEAmRNA. The median follow-up period was 42 months (range 22−59 months).
Results: Recurrence has been confirmed in 51 pts (25%). Recurrence was noted in liver in 16 pts, locoregional in 13 pts, lung in 10 pts, peritoneum in 6 pts, lymph node in 3 pts. Cancer cells were detected in blood in 45 pts (22%). Recurrence was observed in 18 out of 45 pts positive for CEAmRNA (40%) and in 33 out of 156 pts negative for CEAmRNA (21%) (p = 0.02). There were statistical differences in disease-free survival and recurrence-free survival between pts with positive CEAmRNA and pts with negative CEAmRNA, respectively (p = 0.04, P = 0.03). However, difference did not reach the significance in overall survival (P = 0.28). There was no correlation between recurrence site and positivity of CEAmRNA. There was no significant correlation between pathological stage and PCR status.
Conclusion: Detection of cancer cells in blood taken 7 days after curative resection was an independent prognostic indicator in CRC.

242 POSTER

Interaction of biological variables in tumour cells and stroma, and their clinicopathological significance in colorectal cancers

X. Sun. *Colorectal cancer research Group, Institute of Biomedicine and Surgery, Department of Oncology, Linköping, Sweden*

Background: Disruption of stromal-epithelial interactions and cell adhesion alters cellular signalling, which influences proliferation, angiogenesis, differentiation, motility, death, genomic integrity and other phenotype in the tissues. We examined the relationships of the factors expressed in tumour cells or/and stroma including legumain, Nup88, MAC30, PINCH (particularly interesting new cysteine-histidine rich protein) and ST3 (stromelysin-3) as well as their clinicopathological significance in colorectal cancers.
Material and methods: The study included the matched distant normal mucosa, adjacent normal mucosa, primary tumour and metastasis in the lymph nods from 212 patients with colorectal cancer. Methods included immunohistochemistry, Western blotting and immunofluorescence.
Results: Legumain, Nup88 and MAC30 mainly in tumour cells, while PINCH and ST3 were expressed in stroma mainly in the fibroblasts, myofibroblasts and a proportion of endothelial cells of the tumor vasculature. The expression of the five proteins had positive relationships. Legumain expression was increased from normal mucosa to primary tumour, MAC30 was increased from primary tumour to metastasis. Nup88 and PINCH expression was increased from normal mucosa to primary tumour and to metastasis. Legumain, Nup88 and PINCH expression were more intense at the invasive margin of tumour than their expression in intratumour/intrastroma. Legumain expression was positively related to poorer differentiation/mucinous carcinoma and higher degree of necrosis. Nup88 expression was positively related to distal tumour location and infiltrative growth pattern. ST3 expression was positively related to infiltrative growth pattern. Strong expression of legumain, Nup88 and PINCH predicted unfavourable survival, independent of clinicopathological factors.
Conclusions: Legumain (as an early event), MAC30 (as a later event), Nup88, PINCH and ST3 had a positive interaction in the development and