Multicolor fluorescence in situ hybridization and comparative genomic hybridization reveals molecular events in lung adenocarcinomas and squamous cell lung carcinomas

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We have used the molecular cytogenetic techniques of multicolor fluorescence in situ hybridization (M-FISH) and comparative genomic hybridization (CGH) to analyze two established lung cell lines (A549, H520), 80 primary lung adenocarcinoma samples and 80 squamous cell lung carcinoma samples in order to identify common chromosomal aberrations. M-FISH revealed numerous complex chromosomal rearrangements. Chromosomes 5, 6, 11, 12, 17 were most frequently involved in interchromosomal translocations. CGH revealed regions on 1q, 2p, 3q, 5p, 5q, 7p, 8q, 11q, 12q, 14q, 16p, 17q, 19q, 20q, 21q and 22q to be commonly overrepresented and regions on 2q, 3p, 4p, 5q, 7q, 8p, 9p, 13q, 14q, 17p to be underrepresented. In lung adenocarcinomas the most common gains were found in 16p13 (50%); while in squamous cell lung carcinomas the most common gains were found in 17p15 (45%) and these alterations were observed to be associated with relative poor differentiation and late stage. In conclusion, the present study contributes to the molecular biological characterization in lung adenocarcinomas and squamous cell lung carcinomas and through evaluation of molecular events to the recently emergent focus on novel markers for lung cancer treatment.

Analyzing the methylation status and expression of adenomatous polyposis coli (APC) gene in lung cancer cell line

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Background & Objective: RAS association domain family protein 1A (RASSF1A) gene has been determined one of the most hypermethylated tumor suppressor genes in carcinoma. The present study aimed to analyze the CpG methylation status of RASSF1A gene promoter region in plasma DNA from CT-detected early stage lung carcinoma patients.

Methods: Blood samples were collected from 92 CT-detected thoracic solid tumor patients and 23 healthy volunteers. Plasma DNA was purified with magnetic beads, then treated with sodium bisulfite, and promoter hypermethylation of RASSF1A gene was detected by methylation-specific real-time PCR.

Results: Fifty-eight patients were diagnosed with early stage lung cancer, 31 had benign lung disease, and 3 showed miscellaneous other conditions. RASSF1A hypermethylation was found in 32.8% (19/58) and 6.4% (2/31) of plasma collected from patients diagnosed with early stage lung cancer and benign lung disease, respectively. It was also detected in one of the three unconfirmed cases. No hypermethylation was detected in healthy volunteers. The RASSF1A gene promoter methylation frequency between early stage lung cancer and benign lung disease as well as healthy volunteers was significantly different. But there was no significant difference between benign lung disease and health.

Conclusion: Our data suggest that promoter hypermethylation of RASSF1A gene in plasma DNA is a promising molecular biomarker for the early diagnosis of lung carcinoma.

Molecular basis of the effect of midkine on tumor growth in human gastric cancer cell BGC823

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Background: Midkine (MK), a heparin-binding growth factor, is expressed at higher levels in various malignant tumors, e.g., digestive cancer, lung cancer, hepatic cancer, breast cancer, neuroblastoma, and Wilms’ tumor. Our previous study also showed that MK highly expressed in gastric cancer tissue from Chinese patients and the expressions of MK mRNA and protein are both associated with the clinical stage and distant metastasis of gastric cancer in the Chinese patients. Over-expressed MK can promote BGC823 cells (gastric gland carcinoma cell line) growth in vitro and in vivo, and siRNA targeting MK downregulates MK expression in BGC823 and SGC7901, and inhibits cells growth and induces apoptosis. This study pursued to describe the differences between the MK-over-expressed human gastric cancer cell BGC823 and normal BGC823 at a molecular level, which would be essential in the study of the effect of MK on tumor growth.

Methods: Human MK highly expressed plasmids were constructed and the plasmids were transfected into BGC823 cells. Then genome-wide ologonucleotide microarrays were used. The expression rations of > 2 or < 0.5 genes chosen from microarray data were validated by real time RT-PCR.

Results: There are 550 differentially expressed genes, 407 upregulated genes, 143 downregulated genes. 20 genes were examed, pathways of ‘focal adhesion’ (with gene components of FN1, ITGAV, ITGA3, ITGA2, ITGA5, PXN, VASP, MP2K1, COL4A6, VEGF, EGFR), ‘MAPK signaling pathway’ (EGFR, NTF5, TP53, IL1B, ATF4, DUSP5, DDIT3), ‘ECM-receptor interaction’ (FN1, ITGAV, ITGA3, ITGA5, COL4A6, CD44) and two matrix metalloproteinases (MMP1, PLAU) represent some of the main differences between MK-over-expressed human gastric cancer cell BGC823 and normal BGC823.

PI3K/AKT Signaling in Tumorigenesis and Angiogenesis

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The phosphatidyl inositol 3-kinase (PI3K) is activated by a variety of extracellular signals and is involved in a number of cellular processes including cell proliferation, survival, protein synthesis, and tumor growth. Phosphatase and tensin homolog deleted on chromosome 10 (PTEN) is an antagonist of PI3K. The alterations of PI3K pathway such as activation of oncogenes, gene amplification, and inactivation of tumor suppressors, commonly occurred in many human cancers.