P2-016 BSTB: Cancer Genetics Posters, Tue, Sept 4

**Interactive effect of smoking and NQO1 for lung cancer risk**

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To evaluate the role of genetic polymorphisms of NAD(P)H:quinone oxidoreductase 1 (NQO1) related to the carcinogen metabolism and oxidative status, genotypes of two NQO1 polymorphisms IVS1-27C>G and Ex6+40C>T were determined in 616 lung cancer cases and 616 lung cancer-free controls. When the effect of each NQO1 allele and diplotype composed of two NQO1 SNP sites on lung cancer risk was evaluated, any NQO1 genotype or diplotype did not show the association with lung cancer risk. However, in the analyses of the combined effects of smoking and NQO1 diplotype, smokers with other than CT/CT diplotype showed significantly increased risk of lung cancer compared with nonsmoker with other than CT/CT diplotype (adjusted OR=2.2, 95% CI, 1.67-3.02) and smokers with CT/CT diplotype showed the highest OR of lung cancer (adjusted OR=2.7, 95% CI, 1.78-4.21). Trend test showed an additive interaction between smoking and NQO1 diplotype (Ptrend<0.01). In the subgroup analyses, the additive effect between smoking and NQO1 diplotype was found to be more apparent in squamous cell carcinoma although this effect was statistically significant in all lung cancer cell types (NSCLC, Ptrend<0.01; AC, Ptrend=0.02; SCC, Ptrend<0.01; other NSCLCs, Ptrend<0.01; and SCLC, Ptrend<0.01). This result suggests that haplotypes of NQO1 gene play an important role in the development of lung cancer by producing an additive interaction between smoking and NQO1 gene for lung cancer risk.

P2-017 BSTB: Cancer Genetics Posters, Tue, Sept 4

**DNA Methylation Changes in Developing Lung Adenocarcinoma**

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**Background:** Lung cancer is the leading cause of cancer death in the United States and Western Europe. Adenocarcinoma, the histological subtype most frequently seen in never smokers and former smokers, is now the most common type of lung cancer in men and women in the United States. The increasing incidence of lung adenocarcinoma and its lethal nature underline the importance of understanding the development and progression of this disease, and the need for the development of accurate tools for early diagnosis. Atypical adenomatous hyperplasia (AAH) and bronchioalveolar carcinoma (BAC), defined as non-invasive lesions, are thought to be sequential precursors along the path of progression to lung adenocarcinoma. Elucidation of the molecular changes underlying the development and progression of lung adenocarcinoma is of great importance for devising targeted drugs and methods of early detection. DNA hypermethylation at promoter CpG islands is now recognized as a key mechanism for tumor suppressor gene inactivation in cancer. Identification of abnormal methylation changes could provide important insights into the mechanism of cancer development, and in addition could yield powerful biomarkers for cancer.

**Methods:** Here we use MethyLight®, a sensitive, quantitatively accurate, automated DNA methylation analysis technique to examine DNA methylation levels at loci that we have previously shown to be highly significantly hypermethylated in lung adenocarcinoma compared to adjacent non-tumor tissue from the same patient. We examine the methylation levels in a unique collection of normal adjacent lung, pre-invasive lesions (AAH and BAC), mixed adenocarcinoma samples with a BAC component, and adenocarcinoma, representing adenocarcinoma in its different developmental stages.

**Results:** We observe differences in methylation levels for the different loci examined, with some loci (such as CDKN2A) showing hypermethylation already in adjacent non-tumor lung, others (such as SFRP1) showing no methylation in normal lung but methylation in AAH and BAC/adenocarcinoma, and yet others (such as SFRP5) showing only methylation in adenocarcinoma.

**Conclusions:** The occurrence of methylation of different loci in distinct subsets (normal lung, AAH, BAC, adenocarcinoma) suggests that individual loci might be methylated in a temporally distinct fashion during developing lung adenocarcinoma. The identification of sequential epigenetic alterations during progression to lung adenocarcinoma will broaden our molecular understanding of the disease, providing insights that may be applicable to the development of targeted drugs. Equally important, such DNA methylation changes will be powerful markers for early detection and patient classification.

P2-018 BSTB: Cancer Genetics Posters, Tue, Sept 4

**Numerical chromosomal aberrations of normal mucosal cells in smokers and non-smokers**

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**Background:** Small cell and non small cell lung carcinomas exhibit a series of chromosomal abnormalities. However, few reports exist concerning the chromosomal alterations of normal bronchial mucosa cells of smokers. In the current study, we examined the possible relationship of smoking and 3p and other numerical chromosome aberrations of normal mucosal cells.

**Methods:** Brush cytology samples of 25 patients were available for this study, where bronchoscopy was performed for clinical symptoms of haemoptysis, dyspnoea, pulmonary infiltration etc., but lung cancer was not found. Cytological smears were prepared and one H&E stained smear was used for cytological examination to rule out dysplasia, whereas dual color fluorescent in situ hybridization (FISH) was performed on the others. A mixture of chromosome 3 centromeric probe (red) and telomeric 3p probe (green) were used to detect the possible 3p deletion or other numerical chromosome alterations.

**Results:** 10 patients were non-smoker, 9 patients were smoker and 6 patients were ex-smoker. The ex-smokers had given up smoking 5-31 years (mean: 8,1 years) before our examination. 4 of 10 smoker patients and 3 of 6 ex-smoker patients had significantly higher 3p chromosome or other numerical aberrations (deletion, monosomy, trisomy) compared to the healthy control (non-smoker) patients. Average percentage of chromosomal alteration in non smoker patients was 2.7%.