signal transducer and activator of transcription 3 (STAT3) and CD34 antigen (CD34), among others. The observed activation of immune surveillance genes in the breast epithelial cells of postmenopausal parous women leads us to postulate that changes induced by an early pregnancy has permanently have changed its the genomic signature, of the cells making them more easily recognized by the immune surveillance system if they are exposed to able to be protected from toxic carcinogenic or agents, by eliciting and early immune surveillance of the transformed cells.

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P8

Differential gene expression in human Lung Squamous Cell Carcinoma in Asian Indians may help to identify genetic predisposition

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Background: Early metastasis and a poor five-year survival make lung cancer (LC) the leading cause of cancer related deaths worldwide. The clinical profile of lung cancer patients in India differs from the West as they present almost 15-20 years earlier, squamous cell carcinoma (SCC) being the commonest histological type. To identify the genes involved in lung carcinogenesis in Asian Indians, we compared gene expression profiles in lung squamous cell carcinoma (LSCC) and matched normal lung tissues.

Methods: Using suppression subtractive hybridization (SSH), two subtracted cDNA libraries containing up- and down-regulated genes in the tumors were constructed. The differential expression of these genes was confirmed by reverse Northern blot analysis. DNA of confirmed clones was sequenced and subjected to GenBank Blast searches. RNA expression levels were then individually analyzed by semiquantitative RT-PCR and Northern blotting.

Results: By this technique, 16 differentially expressed gene cDNA fragments of LSCC were obtained. The differentially expressed genes included those associated with cellular metabolism, cell cycle, cell structure, cell adhesion, transcription, proliferation, apoptosis and signal transduction. RT-PCR analysis and Northern blotting of lung tumor and matched normal lung tissues provided the first evidence that KIAA0767, a Death Inducing Protein, a novel p53 independent target of E2F1 and Geminin, an inhibitor of DNA replication are down-regulated in LSCC.

Conclusions: This is the first study in Asian Indians where identification of genes responsible for early onset of this disease will be invaluable for early diagnosis and secondary prevention. Identification of these differentially expressed genes in lung cancer adds to the repertoire of genes associated with lung carcinogenesis and they may thus serve as potential novel molecular targets for early diagnosis and therapy. Further characterization of known and unknown differentially expressed cDNAs identified in this study may provide significant clues for understanding the molecular mechanisms underlying lung tumorigenesis.

P9

Identification and Functional Relevance of Novel Variants of the JWA Gene and Risk of Bladder Cancer in a Southern Chinese Population

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JWA is a novel cell differentiation-associated gene and up-regulated in response to DNA damage and repair induced by environmental stressors, such as hydrogen peroxide and heat shock. To date, there is no reported study of genetic variants of JWA and their association with disease phenotypes such as cancer. We first screened for sequence variation in seven fragments of JWA by the polymerase chain reaction-single-strand conformation polymorphism method, followed by confirmation by direct DNA sequencing and functional evaluation of the variants in the promoter by transient expression study with a reporter gene vector. By treating the host NIH-3T3 cells with H2O2, we further evaluated the response of the variants in terms of the promoter transcription activity. Finally, we further evaluated the functional relevance of the newly identified genetic variants by conducting an association study in 207 bladder cancer patients and 253 cancer-free controls. We identified two novel single nucleotide polymorphisms: 723T>G in exon 3 and -76G>C in the 5'-flanking region. We found that the -76C variant allele had a more than 4-fold loss of baseline and 12-fold loss of H2O2 induced transcript activities compared with the -76G allele and the -76C variant genotypes was associated with significantly increased risk of bladder cancer (OR = 2.40 and 95% CI = 1.64-3.51 for 723TG+GG and OR = 2.48 and 95% CI = 1.34-4.57 for -76GC) (Ptrend < 0.001). Furthermore, there were suggestive interactions between these two polymorphisms and smoking/drinking status. Larger studies with diverse ethnic groups are needed to verify our findings.