role of genetic factor is a perspective direction of oncogynecology. The clinical-genealogical analysis of thousands of genealogies of patients with cancer of female reproductive organs, allowed H.Linch et al to unify the clinical-genealogical criteria which allow to distinguish between inherited and sporadic tumors. The study goal was establishment of features and patterns of distribution of tumors in families of patients with ovarian and endometrial cancer. The clinical-genealogical analysis of 520 patients with ovarian cancer and 482 patients with endometrial cancer in Chernivtsi region was conducted. The analysis revealed that the most common malignancies in families of these patients were tumors of female reproductive organs (ovarian, endometrial and breast cancer), gut (stomach, colon), lungs, prostate etc. Among 520 genealogies of patients with ovarian cancer and 482 genealogies of patients with endometrial cancer we selected 103 genealogies in which malignant tumors of female reproductive sphere were twice more common, which is a clinical-genealogical criterion of family cancer of female reproductive sphere. We analyzed the spectrum of family aggregation of cancer of different anatomic localizations in these 103 genealogies. The features of spectrum of aggregation of cancer in these families were a base of classification of family cancer of female reproductive organs. The analysis revealed 6 typical family situations. 2 of 6 syndromes are organ-specific (they show up as a cancer of the same localization, and 4 syndromes are variants of "general family cancer syndrome" and are characterized with wide spectrum of tumors mainly of the female reproductive organs.

Classification of variants of accumulation of cancer in Chernivtsi region:

1. Family ovarian cancer
2. Family endometrial cancer
3. Family ovarian and breast cancer
4. Family ovarian/endometrial and breast cancer
5. Family ovarian/endometrial/breast/colon cancer (Lynch II)
6. Family endometrial/gut cancer.

Conclusions: The results of the study could be a base for development and planning of early diagnostics and prevention of tumors in families of patients, such as the use of tumor markers, determination of genes of disposition, which is effective from the economic and social point of view.

P6

Generation of Coronavirus-based multigene RNA vectors

D. Makia, K.K. Eriksson, L. Cervantes, V. Thiel, B. Ludewig.
LFA, Research Department, St. Gallen, Switzerland

Coronavirus-based vectors are currently considered a promising means to genetically deliver multiple heterologous genes to specific target cells. They are positive-stranded RNA viruses replicating in the cytoplasm without a DNA intermediary, making insertion of viral derived sequences into the host cell genome unlikely. Coronaviruses have the largest known RNA genome, therefore a cloning capacity of more than 6 kb is expected. They posses a unique transcription strategy resulting in the synthesis of 6-8 subgenomic mRNAs encoding mainly structural genes encoded at the 3' third of the genome, these genes can be replaced by multiple heterologous genes such as tumor antigens and cytokines. These vectors are attenuated since 2-3 structural genes are replaced resulting in replication competent but propagation deficient vectors. An important consideration for viral vaccine vectors is the potential for efficient delivery of their genetic material to specific target cells. Targeting of viral vaccine vectors to dendritic cells (DCs) is highly desirable in order to optimise vaccine efficacy. The mouse hepatitis virus (MHV) and the human coronavirus (HcoV) 229E have their receptors (CEACAM-1 and hAPN or CD13, respectively) expressed on DCs and macrophages. This indicates that MHV and HCoV 229E based vectors could be used to deliver genetic cargo efficiently to DCs via receptor-mediated transduction. Since MHV is able to infect DCs, recombinant MHV vectors in the context of a murine model can serve as a paradigm for the development and evaluation of coronavirus vaccine vectors suitable for in vitro and in vivo transduction of human DCs.The anticipated results in the murine animal model will guide the development of coronavirus-based vaccines in general and will pave the way for the generation of HCoV 229E-based vaccines in humans.

P7

Immune surveillance-related genes are significantly over expressed in the breast epithelium of postmenopausal parous women

G.A. Balogh[1], I.H. Russo[1], C. Spittle[2], R.C. Heulings[1], D.A. Mailo[1], J. Russo[1]. [1]*Fox Chase Cancer Center, Breast Cancer Research Laboratory, Philadephia, United States of America;* [2]*Fox Chase Cancer Center, Biomarker and Genotyping Facility, Philadelphia, United States of America*

Endocrine and reproductive influences significantly affect play major roles in the lifetime risk steadily increasing incidence of breast cancer development in women. Nulliparity is one of the most firmly established risk factors for breast cancer, whereas early full term pregnancy and parity confer a significant protection. In order to elucidate the molecular pathways through which pregnancy exerts a protective effect, we have analyzed the genomic profile of lobules type 1 (Lob 1) present in reduction mammoplasty specimens obtained from 5 parous and 2 nulliparous postmenopausal women. Total RNA was obtained from epithelial cells of Lob 1 that were dissected using laser capture microdisection. RNAs were individually amplified employing oligo-DT T7 primer and in vitro transcription reaction. We hybridize cDNA microarrays containing 40,000 genes and after normalization of the data using Lowess method, we performed the confidence analysis of 99% level using GeneSight software. We found an interesting cluster of genes up-modulated (>2.0 log, $p<0.01$) that were related to the immune system. In the present work we performed real time RT-PCR using a microfluidic card platform. The TaqMan® Low Density Immune Profiling Array contained 90 genes related to the immune system, and 18S rRNA as an internal control (Applied Biosystems 7900HT TaqMan® Low Density Array Upgrade, ABI). Epithelial cells from parous women significantly over-expressed 20 genes related to immune surveillance when compared with the RNA from nulliparous women. Those genes included: BCL2-associated X protein (BAX), complement component 3 (C3), chemokine (C-C motif), receptor 4 (CXCR4), CD34 antigen, Collagen IV (COL4A5), glucuronidase beta (GUSB), interleukin 1 b (IL-1b), interleukin 6 (IL6), major histocompatibility complex class II, DR alpha (HLA-DRA),

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.

This work was supported by NIH-NCI grant RO1-CA093599 from the National Cancer Institute.

P8

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

S. Sen[1], B. Ateeq[1], H. Sharma[1], P. Datta[1], S. Bal[2], A. Kumar[2], N. Singh[1]. [1]*All India Institute of Medical Sciences, Deptt. of Biochemistry, New Delhi, India;* [2]*All India Institute of Medical Sciences, Deptt. of Surgery, New Delhi, India*

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

C.P. Li[1], R. Chen[2], W. Wu[3], J. Liu[4], L.X. Qian[5], Q.Z. Liu[6], Z.D. Zhang[7], Q.Y. Wei[8], J.W. Zhou[9]. [1]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [2]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [3]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [4]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [5]*the First Affiliate Hospital of Nanjing Medical University, Department of Urology, Nanjing, China;* [6]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [7]*School of Public Health, Nanjing Medical University, Dept. of Molecular Cell Biology and Toxicology, Nanjing, China;* [8]*The University of Texas M.D. Anderson Cancer Center, Department of Epidemiology, Houston, USA*

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.