**Discussion:** Specific and non-random chromosome rearrangements in Burkitt's lymphoma cell lines have been reported previously. Our results demonstrated some well characterized chromosome abnormalities and also some variations in both the numerical and structural chromosomal abnormalities from those reported in other studies. Some of these chromosome abnormalities also have reported from Burkitt's lymphoma patents. Therefore characterizing these abnormalities might be of great importance in understanding the progression of the disease.

598 POSTER

## Identification of two loci of frequent allelic deletions on chromosome 6 involved in cervical cancer progression

I. Beliakov[1], F. Kisseljov[2], N. Mazurenko[1]. [1] *Institute of Carcinogenesis Blokhin Cancer Research, Lab Oncovirus Immunology, Moscow, Russian Federation;* [2] *Institute of Carcinogenesis Blokhin Cancer Research, Dep. of Tumor Transforming Genes, Moscow, Russian Federation*

Several regions of frequent allelic deletions on chromosome 6 were identified by loss of heterozygosity (LOH) analysis in 145 cervical carcinomas (CC) and cervical intraepithelial neoplasias (CIN) using 30 microsatellite markers. More than 50% of CC cases had allelic deletions at 6p21.3 within the region of major histocompatibility complex (MHC) and at 6q16-21. Some of these frequently deleted microsatellites are located in introns of recently described but not fully characterized genes and we analyzed the structure of two of them. Predicted exon-intron structure of these genes were characterized according to expressed sequences deposited in NCBI database and published data. The first gene is located at 6p21.3 in the region of MHC class III and is frequently deleted in CIN and early stages of CC, so can be designed as EDCC gene (early deleted in cervical carcinomas). The predicted size of this gene is about 10kb with at least 3 exons and its function is still unknown. The second gene, located at 6q16-21 was deleted mostly in invasive cervical cancer and was designed as LDCC gene (lately deleted in cervical carcinomas). The predicted gene spans across 700kb of genomic sequence with at least 15 exons. It contains two domains of enzyme belongs to lipid metabolism and associated with posttranslational protein modification. The data of expression of these genes in normal and cervical cancer RNA samples with and without allelic deletions will be presented.

599 POSTER

## Promoter hypermethylation of hMLH1 gene in liver fluke related cholangiocarcinoma

T. Limpaiboon[1], P. Khaenam[1], M. Soonklang[1], P. Jearanaikoon[1], B. Sripa[2], V. Bhuhisawasdi[3], C. Pairojkul[2]. [1] *Khon Kaen University, Clinical Chemistry, Khon Kaen, Thailand;* [2] *Khon Kaen University, Pathology, Khon Kaen, Thailand;* [3] *Khon Kaen University, Surgery, Khon Kaen, Thailand*

**Background:** Cholangiocarcinoma is a malignant tumor arising from bile duct epithelium. It is a leading cancer in Northeast Thailand where the liver fluke *Opisthorchis viverrini* is highly endemic. Many epidemiological and experimental studies suggest that liver fluke infection causes chronic inflammatory and enhances the susceptibility of bile duct epithelium to carcinogenic chemicals leading to genetic and epigenetic damages in the cells. Genetic aberration of DNA mismatch repair gene *hMLH1* has been described in liver fluke related cholangiocarcinoma. However, hypermethylation of the *hMLH1* gene promoter has never been reported in this cancer. This study aimed to elucidate an epigenetic mechanism underlies *hMLH1* gene inactivation in liver fluke related cholangiocarcinoma.

**Material and methods:** DNA methylation patterns in the *hMLH1* promoter were determined in 55 intrahepatic cholangiocarcinoma and matching normal liver tissues using methylation-specific PCR (MSP).

**Results:** Hypermethylation of the *hMLH1* promoter occurred in 25 of 55 cholangiocarcinoma patients (45.5%). Of 31 cases whose genetic alterations (LOH or MSI) of *hMLH1* gene (D3S1611) were previously determined, 7 cases showed positive for both methylation and D3S1611 alteration whereas 11 cases showed methylation positive without D3S1611 alteration (Table 1).

**Discussion:** This study suggests that genetic and epigenetic mechanism plays an important role in *hMLH1* gene inactivation in liver fluke related cholangiocarcinoma and *hMLH1* gene inactivation might be a pivotal cause of cholangiocarcinogenesis.

Table 1. Correlation between D3S1611 alteration and *hMLH1* promoter hypermethylation

| D3S1611 alteration | Methylation positive | Methylation negative | Total |
|---|---|---|---|
| Positive | 7 (22.6%) | 1 (3.2%) | 8 (25.8%) |
| Negative | 11 (35.5%) | 12 (38.7%) | 23 (74.2%) |
| Total | 18 (58.1%) | 13 (41.9%) | 31 |

600 POSTER

## The expression of the transcript isoforms oh human Arg gene is differently regulated in different cell types

M. Corizzato, C. D'Orlando, C. Bianchi, P. Mocarelli, R.A. Perego. *Milano-Bicocca University, Experimental Medicine, Monza, Italy*

**Background:** The products of the Arg and Abl genes belong to the Abelson family of non receptor tyrosine protein kinases and both have high similarity. Arg has alternatively spliced amino terminal chains and the protein isoforms are defined IA and IB, the IB forms have a myristoilation site (Proc. Natl. Acad. Sci. 1990, 87, 5802). In the C-terminal domain Arg has two actin binding sequences. Arg is ubiquitously expressed with a higher expression in nervous tissue and Arg protein has a cytoplasmic localization. Arg expression increments during granulocytic and macrophage-like differentiation of HL-60 cells and in the maturation of B lymphoid cells. Altered Arg expression has been described in colon, pancreas and bladder carcinoma. Arg gene rearrangement has been reported in acute leukemias (Blood 1999, 94, 4370). To gain insight into the biological function of Arg we determined the relative abundance of the different forms of Arg transcripts.

**Materials and methods:** With Real-time PCR we analyzed different cell lines and primary cell cultures. The Arg mRNA expression in cells was measured as $2^{-\Delta CT}$, a quantitative value representing the amount of Arg transcripts.

**Results:** All tested cells contained the different forms of Arg mRNA, but their relative abundance varied. Based on the abundance of the different forms of Arg mRNA the cells can be grouped in different categories. In hematopoietic cell lines AllP0, Raji, LP-1 (B cells), Jurkatt, Molt-4 (T cells), HL-60, GFD8, K562, U937 (myeloid cells), and in donor lymphocytes, granulocytes and monocytes the IB isoforms are about 20 fold higher than IA forms. In epithelial cell lines and in primary cultures of renal cortex and renal carcinomas (clear cells) that derives from kidney cortex the IA forms are higher than IB forms. Also in fibroblastic cell line HEL-299 the Arg IA mRNA is higher than IB mRNA. In A172 glioblastoma cell line and, of note, in HL-60 cells differentiated to macrophage-like cells with TPA, the IA forms are 2-3 fold higher than the IB forms.

**Conclusions:** These observations show that the expression of the type-specific Arg mRNA is differently regulated in tissues with a pattern that can be typical. This expression pattern can be used to characterize the cells deriving from different tissues. The role of the IA and IB forms during cell differentiation needs to be investigated further.

601 POSTER

## p53 codon 72 polymorphism in basal cell carcinoma of skin

A. Pezeshki[1], F. Sari-Aslani[2], A. Ghaderi[1,3], M. Doroudchi[1,3]. [1] *Shiraz University of Medical Sciences, Shiraz Institute for Cancer Research, Shiraz, Iran;* [2] *Shiraz University of Medical Sciences, Department of Pathology, Shiraz, Iran;* [3] *Shiraz University of Medical Sciences, Department of Immunology, Shiraz, Iran*

**Background:** A common polymorphism at codon 72 of exon 4 of p53 tumor suppressor gene has been reported to be associated with increased heritable susceptibility to several cancers.

**Subjects and Methods:** In this study we investigated the frequency of p53 codon 72 polymorphism in 91 patients with Basal Cell Carcinoma (BCC) of skin compared to 205 healthy normal individuals. DNA extracted from peripheral blood lymphocytes was examined by an allele-specific polymerase chain reaction.

**Results:** 34(37.4%) BCC patients and 75(36.6%) normal individuals had *Arg/Arg* genotype while 10(11%) BCC patients and 40(19.5%) normal individuals had *Pro/Pro* genotype. The frequency of heterozygotes in BCC and healthy individuals were 51.6% and 43.9%, respectively. In total, there was no significant difference in the p53 genotypes in patients and controls. However, there was an apparent increase in *Arg/Arg* genotype among those BCC patients who had a history of occupational sun-exposure compared to non-exposed patients (46.3% vs. 23.1%, P = 0.11). The increase in *Arg* allele among sun-exposed patients was marginally significant (69.4% vs. 53.8%, P = 0.07). Comparison of the genotype frequencies between sun-exposed patients and normal controls confirmed the accumulation of *Arg/Arg* genotype in these patients (46.3% vs. 36.6%, P = 0.09). In addition, the frequency of *Arg* allele was significantly higher in sun-exposed patients compared to controls (69.4% vs. 58.5%, P=0.05) **Conclusion:** Our results