# HIGHLIGHTS

## 2011 - 2012

**NATIONAL INSTITUTE OF PATHOLOGY (ICMR)**
PO Box 4909, Safdarjang Hospital Campus, New Delhi 110 029
Email : info@instpath.gov.in • Website : www.instpath.gov.in

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# THRUST AREAS OF RESEARCH

## TUMOR BIOLOGY

The focus of research in Tumor Biology Division is on identification of diagnostic, predictive and prognostic biomarkers, new drug targets and gene-environmental links mainly in breast, prostate, urinary bladder and brain cancers, lymphomas and leukemia and cancers in northeast region of India.

## BREAST CANCER

### 1. STUDY ON GENE EXPRESSION AND HYPERMETHYLATION PROFILES IN EARLY ONSET BREAST CANCER

The present study was proposed to examine the gene expression and methylation profiles of early onset breast cancer patients by using microarray analysis with the aim to identify biological markers of clinical significance associated with risk and prognosis. Gene expression profiling of 20 early and 20 late onset cancers has led us to identify several genes families that are differentially expressed viz.: SLC, TMEM, Cadherins, FOX, and some of genes involved in chromatin modification and replication in early onset or late onset cancers. Validation of these genes at RNA and protein level in clinical samples is undergoing.

### 2. STUDY ON EFFECTS OF ANTI-CANCER DRUGS ON BREAST CANCER STEM CELLS

The identification of potential breast cancer stem cells is of importance as the characteristics of stem cells suggest that they are resistant to conventional forms of therapy. Several techniques have been proposed to isolate or enrich for tumorigenic breast cancer stem cells, including culture of cells in non-adherent non-differentiating conditions to form mammospheres and sorting of the cells by their

surface phenotype (expression of CD24 and CD44 or ALDH). This study elaborates phenotypic characteristics of breast cancer stem cells and their response to various chemotherapeutic agents.

Breast cancer cell line MCF7 was grown as an adherent culture. The cells were then stained with ALDH antibody using *Aldeflor* kit as per the manufacturer's instructions and sorted out using FACS ARIA II (Fig.1). The sorted ALDH+ cells were then cultured in non-adherent, non-serum conditions at 37°C in 5% $CO_2$ to form mammospheres (Fig.2). Primary mammospheres were dissociated with trypsin to obtain single cells. These sphere forming single cells, enriched for breast stem and early progenitor cells were used for serial passage (secondary and tertiary sphere formation) to test the functional definition of stem cells for self renewal. Dissociated cells from these mammospheres were again analyzed for the presence of $ALDH^{+/bright}$ cells and were sorted using FACS.

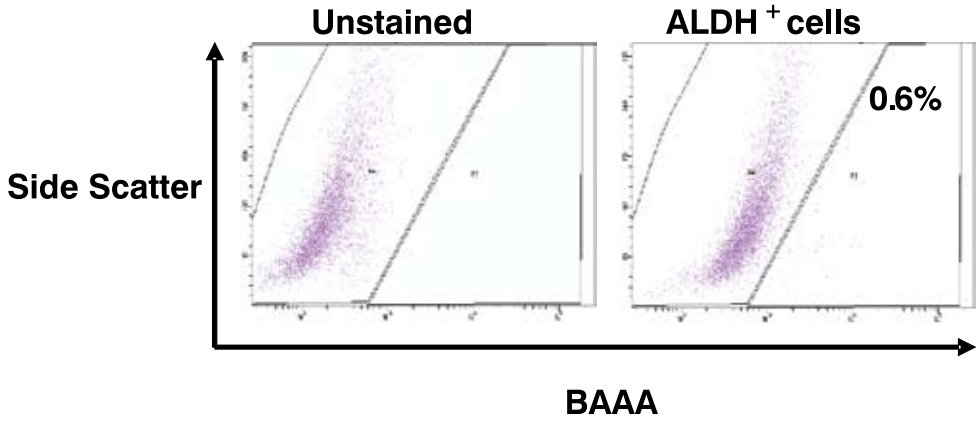



**Fig.1: Representative picture depicting the expression of ALDH+ marker by FACS**

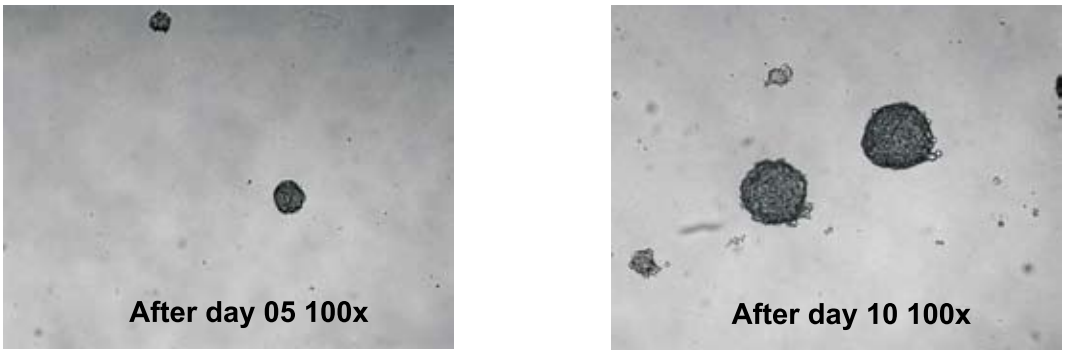


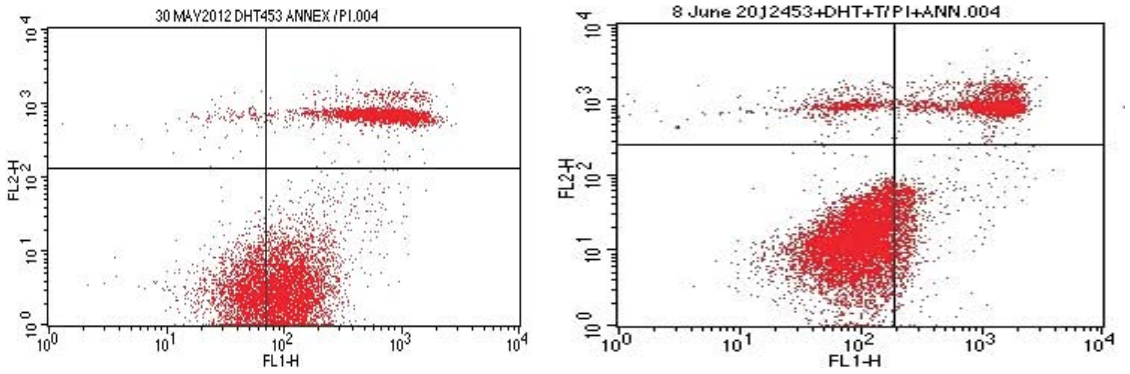

**Fig.2: Representative pictures of MCF7 mammospheres**

## 3. TO STUDY THE EFFECT OF SIRNA MEDIATED ANDROGEN RECEPTOR GENE SILENCING ON ANDROGEN SIGNALING PATHWAY IN BREAST CARCINOMA

The present study was proposed to assess AR-mediated transcription and cell growth in both AR (+) and AR (-) breast cancer cells through the knockdown of AR expression and to analyze the expression of a panel of genes associated with important biological pathway like TGF-beta.

Breast cancer cell lines MDAMB 453 (AR+) with or without 10nM DHT exposure and MDA MB 231(AR-) were subjected to Annexin-V binding assay using the Annexin-V kit (*BD Pharmingen*). Briefly, after 16 hrs, with or without DHT exposure, MDAMB 453 cells were transfected with AR siRNA and fourty eight hours (48 h) post-transfection, adherent breast cancer cells were detached with trypsin, washed twice with cold PBS and re-suspended in 1x binding buffer at a conc. of $1x10^5$ prior to incubating with Annexin V for 15 min at room temperature. Samples were analyzed by fluorescence activated cell sorting (FACS) within one hour of staining. At least 10,000 target cells from each sample were analyzed by FACS.

**66.25%**
**32.20%**




before transfection　　after transfection

**Fig. 1: MDA MB 453 cells exposed to 10 nM DHT labeled with Annexin $V^{FITC}$**

DHT promotes apoptosis in MDAMB 453 cells and the effect got reduced after AR gene silencing. The MDAMB 231 cells didn't respond to DHT. The impact of AR silencing on drug sensitivity (CAF) will be assessed and expression of a focused panel of genes targeting TGF-β signaling pathway will be analyzed next.

# URINARY BLADDER CANCER

## 1. CHARACTERISATION OF HOST IMMUNE PROFILE ASSOCIATED WITH PROGRESSION OF SUPERFICIAL TCC OF BLADDER BY MICROARRAY ANALYSIS

Gene expression was studied by Real-Time PCR (SYBR-Green) for 84 genes of the cytokine network and 84 genes of the NFκB pathway. Cytokine gene expression in tumour tissue revealed dysregulation of 7 (5 upregulated and 2 downregulated) genes in urothelial cancer. The upregulated genes included IL-17A, Th2 cytokines (IL-4 and IL-9), INH and Stat1. SOCS1 and IL-6R were found to be downregulated. In high grade tumours, 6 genes were found significantly upregulated and included IL-17A, IL-4, IL-9, INHA, CD28 and Stat1. Three genes were found dysregulated (>2-fold change) in low-grade urothelial cancer. Low grade cancers were found associated with upregulation of GATA3, a good prognostic marker. High grade cancers showed a Th2 dominant state.

In Non-Muscle Invasive Urothelial Cancer (*NMIUC),* 8 genes were dysregulated and included IL-4 and GATA3 (Th2), IL-17A, and STAT1. Chemokine receptor CCR3 was found downregulated. SOCS1 (Suppressor of cytokine signaling 1) was found markedly downregulated indicating the loss of regulatory control on cytokine secretion. Th2 cytokine polarization was observed in *NMIUC.* In Muscle Invasive Urothelial Cancer *(MIUC),* the Th1/Th2 balance showed polarization towards Th1.

Gene expression of 84 genes of NFκB pathway showed dysregulation of 7 genes in urothelial cancer. Of these, 2 were found upregulated (EDARADD and Stat 1) and others were downregulated. EDARADD and HTR2B were found dysregulated in both *NMIUC* and *MIUC*. Akt1 was found downregulated in *MIUC* and TBK1 was found upregulated in *NMIUC* indicating the activation of the non-canonical NFκB pathway.

Serum and urinary cytokine analysis by xMAP technology has been performed in 34 patients and 10 controls. A subset of nine patients included samples collected at 2 time-points – at the time of initial presentation and at the time of recurrence. Urine samples from patients showed significant increase in concentration of IL-1b and IL-9 and decrease in concentration of Eotaxin (CCL11) and IL-2 in patients. Other cytokines which appeared to

be increased included VEGF, IL-8, IP-10, RANTES and IL-6. Serum of patients of urothelial cancer showed significant decrease in concentration of IL-1b, IL-9, Eotaxin (CCL11) and IL-2 in patients. IP-10 was found to be significantly increased in patients' serum.

## 2. TO STUDY THE ROLE OF CYCLOOXYGENASES IN CYTOKINES DYSFUNCTION OF INVASIVE AND NON-INVASIVE TCC OF HUMAN BLADDER

The cyclooxygenases cause the release of prostaglandins which ultimately are responsible for inflammation, angiogenesis and tumour progression. However the reason of Cox-2 overexpression in cancer is not fully understood. In cell culture experiments, it has been observed that Cox-2 is induced by inflammatory cytokines like IL-6 and IL-1 beta indicating an association between Cox-2 expression and expression of few proinflammatory cytokines like IL-1 beta, IL-2, IL-6, TNF, TGF-beta and CD4. This study has been undertaken to analyze Cox-2 expression in invasive and non-invasive transitional cell carcinoma (TCC) of urinary bladder with correlation to production of proinflammatory cytokines.

The flow cytometric analysis for expression of Cox-2 and proinflammatory cytokines: IL-1beta, IL-2, IL-6, TNF, TGF-beta and CD74 were done in PBMC from 86 patients of TCC (70 non-invasive and 16 invasive) and 28 normal healthy individuals. Among 86 samples, 10, 47 and 29 samples were in grade I, II and III respectively. Cox-2 expression was found increased in cancer patients in comparison to normal healthy individuals. Significant variation in IL-1B ($p>0.003$) and IL-6 ($p>0.01$) level was observed in patients in comparison to normal group. The expression of CD74 was more in cancerous patients ($p>0.001$) compared to normal group.

To study the local response, the expression of Cox-2 was studied by IHC on biopsy samples from TCC. While no expression of Cox-2 was observed in normal urothelium, low grade cases showed expression Cox-2 in 49.1% cases and high grade tumours in 86.2% cases indicating its possible role in the progression of disease and invasion. Significant higher expression of IL-6 and IL-1 beta and its significant correlation with cox-2 expression might have a role to induce Cox-2 in cancerous condition and in turn leading to invasion.

# CANCERS IN NORTH-EAST INDIA

## 1. EFFECT OF TOBACCO & PESTICIDE ON CANCERS IN NORTH-EAST INDIA

### A. Oral Cancer

Oral cancer is a multi-factorial disease and influenced by both aetiological factors and ethnicity; as a result, molecular profiles of oral cancer vary throughout the world. Altered gene expression profiling may be attributed to several types of genetic alterations such as base changes, insertions, deletions, chromosomal translocations, inversions, loss of heterozygosity and copy number variations. In the current study, targeted re-sequencing of 169 functionally relevant and potentially important genes was done to analyze mutational changes. In our study, 4837 exon regions of interest were analyzed with average read depth of 47.14. A large number of mutational changes were observed including 96 SNPs (50 novel and 46 known SNPs) and 46 InDels (29 novel and 17 known InDels). Most of the known SNPs with high read depths (>50) were located in tumor suppressor genes in addition to some SNPs in non-coding regions. GO analysis is being done to understand various biological functions of these genes that may have possible relevance in the carcinogenic mechanism of oral cancer.

### B. Lung Cancer

Complex disease such as cancer results from interactions of multiple genetic and environmental factors. Studying these factors singularly cannot explain the underlying pathogenetic mechanism of the disease. Multi-analytical approach, including Logistic Regression (LR), Classification And Regression Tree (CART) and Multifactor Dimensionality Reduction (MDR), was applied in 188 lung cancer cases and 290 controls to explore high order interactions among xenobiotic metabolizing genes and environmental risk factors. Smoking was identified as the predominant risk factor by all three analytical approaches. Individually, CYP1A1*2A polymorphism was significantly associated with increased lung cancer risk (OR = 1.69;95%CI =

1.11–2.59,p = 0.01), whereas EPHX1 Tyr113His and SULT1A1 Arg213His conferred reduced risk (OR = 0.40; 95%CI = 0.25–0.65, p,0.001 and OR = 0.51; 95%CI = 0.33–0.78, p = 0.002 respectively). In smokers, EPHX1 Tyr113His and SULT1A1 Arg213His polymorphisms reduced the risk of lung cancer, whereas CYP1A1*2A, CYP1A1*2C and GSTP1Ile105Val imparted increased risk in non-smokers only. While exploring non-linear interactions through CART analysis, smokers carrying the combination of EPHX1 113TC (Tyr/His), SULT1A1 213GG (Arg/Arg) or AA (His/His) and GSTM1 null genotypes showed the highest risk for lung cancer (OR = 3.73;95%CI = 1.33–10.55,p = 0.006), whereas combined effect of CYP1A1*2A 6235CC or TC, SULT1A1 213GG (Arg/Arg) and betel quid chewing showed maximum risk in non-smokers (OR = 2.93;95%CI = 1.15–7.51,p = 0.01). MDR analysis identified two distinct predictor models for the risk of lung cancer in smokers (tobacco chewing, EPHX1 Tyr113His, and SULT1A1 Arg213His) and non-smokers (CYP1A1*2A, GSTP1 Ile105Val and SULT1A1 Arg213His) with testing balance accuracy (TBA) of 0.6436 and 0.6677 respectively. Interaction entropy interpretations of MDR results showed non-additive interactions of tobacco chewing with SULT1A1 Arg213His and EPHX1Tyr113His in smokers and SULT1A1 Arg213His with GSTP1 Ile105Val and CYP1A1*2C in non-smokers. These results identified distinct gene-gene and gene environment interactions in smokers and non-smokers, which confirms the importance of multifactorial interaction in risk assessment of lung cancer.

## C. Gastric Cancer

In our earlier study on gene expression profiling, we found genes responsible for apoptosis, inflammatory response, immune response, angiogenesis, cell migration and cell proliferation to be significantly deregulated and genes, *viz.: LDHB*, *PXN*, *RYK*, *RET*, *ANG*, *BMP7*, *RAD51L3* and *CXCL10* involved in these biological processes were analyzed by Real Time PCR. Further genomic alteration in gastric cancer is being analyzed by NGS on Solexa plateform.

The total number of SNPs observed were 178 in cases whereas those of indels were 23 (12 insertion and 11 deletion). Most of the observed SNPs were known SNPs,

however, a few novel SNPs were also found in the intronic regions of genes that may have functional relevance in the pathogenesis of gastric cancer. This study is continuing and data is being analyzed.

## 2. IMMUNOGENETIC PROFILE OF NASOPHARYNGEAL CANCER IN A HIGH-PREVALENCE REGION OF NORTH-EAST INDIA

Nasopharyngeal carcinoma (NPC) is one the most confusing, commonly misdiagnosed, and poorly understood disease. NPC has a remarkable racial and geographical distribution affecting southern China and south-east Asia and some regions in NE India. The etiological factors of NPC include a complex interaction of genetic, viral, environmental and dietary factors. Antigenic presentation of EBV-derived peptides is suspected to be involved in the pathogenesis of EBV-associated diseases. In addition, polymorphisms in the HLA region, particularly in the class I region, might affect the proper presentation of EBV antigens to cytotoxic T-lymphocytes. The goal of the study is to find out if Epstein Barr viral sequences in the tumor tissue can modulate host immunity or if some host imunogenetic factors can explain the high prevalence of nasopharyngeal carcinoma in different ethnic groups of northeastern states.

During the year, 91 blood samples from newly diagnosed cases of NPC and 80 controls were collected. Of these, 37 are from B. Barooah Cancer Institute, Guwahati, Assam and 54 from Regional Institute of Medical Science, Imphal, Manipur. 35 tissue samples from these 91 cases have also been collected. Genomic DNA has so far been isolated from 55 whole blood samples obtained from patients with nasopharyngeal cancer and 55 controls.

Of the 33 markers that will be analyzed in this study, standardization of PCR conditions for 31 microsatellite markers was done during this year by using FAM labeled forward primer and unlabelled reverse primer at gradient temperatures. Following the confirmation of amplification, samples were prepared for fragment length analysis in a DNA sequencer using a master-mix containing PCR product, GeneScan -500 LIZ Size Standard and Hi-Di formamide. The capillary electrophoresis was performed using the Applied Biosystems ABI PRISM 3130*x*/ Genetic Analyzer with Data Collection Solfware

Version 2.0. Analysis of preliminary results was done using Gene Mapper software which showed many allelic variants for all micosatellite markers.

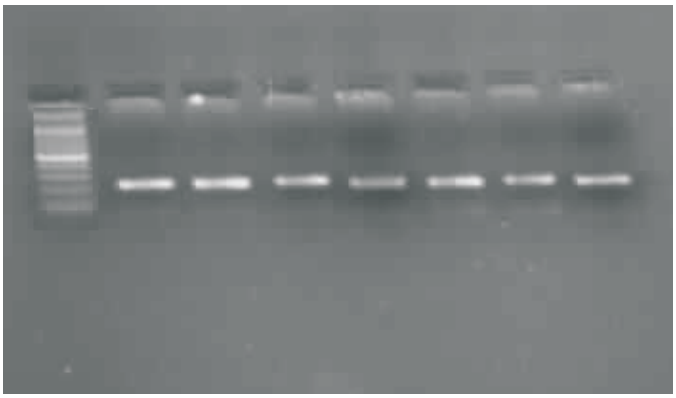
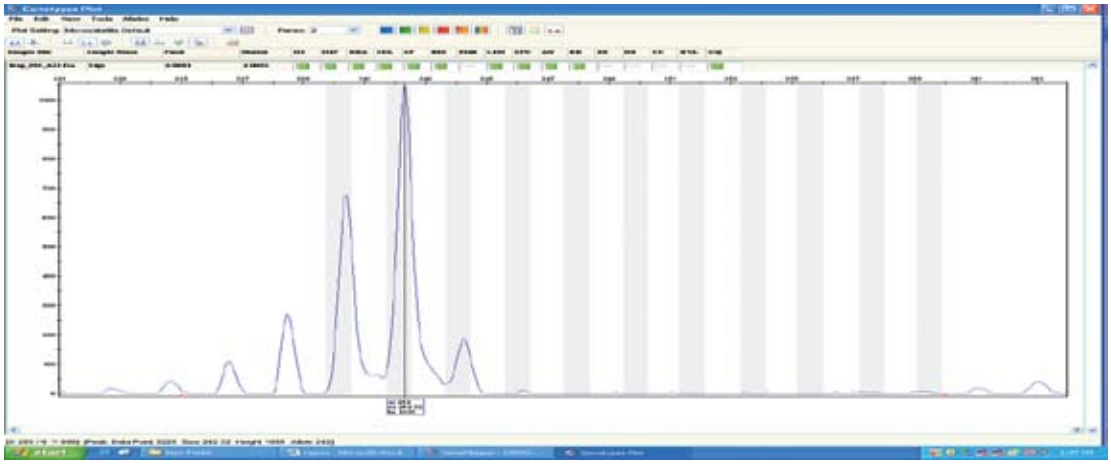


**Fig. 1: Agarose gel showing PCR amplification of microsatellite marker RING 3CA in 7 different samples of northeast India. The size of the band was expected around 210-220 bp.**



Genotyping for 6SI001 analyzed by Gene mapper software: sample shows homozygous allele of 242 sizes.

**Fig. 2: Optimum temperature for PCR standardization of EBNA2 (Annealing Temperature: 60ºC and MgCl2 Concentration: 1.8mM)**

## Detection of EBV

Molecular methods are being used to detect EBV in tissue/ blood samples using PCR. During the year, to standardize the PCR conditions for EBV-presence, EBV-positive cell line B95.8 (marmoset blood leukocytes EBV transformed cell line that releases high titers of transforming EBV) was obtained from ATCC. Conventional PCR

method was applied in both cases and control samples to standardize the optimum PCR conditions for detection of EBV. In addition, another cell line which is also EBV-positive (Raji cell line) was also obtained and processed for standardization of PCR to detect EBV. For PCR standardization, the primers were synthesized from *M/s Biolink (India)* and were standardized with various concentrations of $MgCl_2$ (1.5mM, 1.8mM, 2.0mM 2.5mM, 3mM and 3.5mM) at gradient temperatures.

## 3. GENOME-WIDE ANALYSIS OF GENETIC ALTERATIONS IN PATIENTS WITH ESOPHAGEAL CANCER FROM NORTH-EAST INDIA USING SINGLE NUCLEOTIDE POLYMORPHISM ARRAYS

Esophageal cancer is sixth leading cause of death from cancer and more than 3.9 lakhs (2.6 male and 1.3 female) deaths each year in world. Highest incidence of this cancer in India has been reported from north-east region where it is the second leading cancer in man and the third leading cancer in women. It has been reported earlier that chewing of fermented areca nut with or without tobacco is independently associated with development of cancer in this population.

The current study aims to investigate a link between genetic variations including chromosomal changes, LOH and copy number alterations associated with ethnic variation in NE populaton of India with history of wide spread tobacco conusumption and familial aggregation through Affymetrix GeneChip Human Mapping 6.0.

Endoscopic biopsy specimens from 28 tumor and adjacent normal tissue distant to the tumor were collected in RNA later from patients during diagnostic endoscopy at Dr. Bhubaneshwar Borooah Cancer Institute (BBCI), Guwahati, Assam and stored at −70º C until processed. In addition, 5 ml of peripheral blood was collected in EDTA vials from the 28 patients and frozen.

In the preliminary study, 5 tumor tissues and blood samples (germ line DNA) from the same patients, have been processed, including 3 moderately differentiated and 2 poorly differentiated carcinomas. All patients had betel quid chewing and smoking habits but one patient had in addition alcohol habit. Further the Genome wide analysis;

the genomic DNA plate was processed using Affymetrix GeneChip Human Mapping 6.0 set by following major stages. Stage 1: Sty Restriction Enzyme Digestion, Stage 2: Sty Ligation, Stage 3: Sty PCR, Stage 4: Nsp Restriction Enzyme Digestion, Stage 5: Nsp Ligation, Stage 6: Nsp PCR, Stage 7: PCR Product Pooling and Purification, Stage 8: Quantitation, Stage 9: Fragmentation, Stage 10: Labeling Stage 11: Target Hybridization. Study is being continued for analysing more number of cases.

# HEMATOPOIETIC-LYMPHOID MALIGNANCIES

## 1. GENETIC AND EPIGENETIC PROFILE OF ACUTE MYELOID LEUKEMIA

Recent evidence suggests that AML is also associated with epigenetic changes in hematopoietic progenitor cells that alter normal mechanisms of cell growth, proliferation and differentiation. Understanding the contribution of epigenetic molecular mechanisms and biological pathways involved in AML or subtype may help in developing epigenetic biomarkers. The current study has been designed with the objective to characterize the epigenetic modifications associated with AML and if there is any correlation between epigenetic modifications and cytogenetic abnormalities.

This study is being conducted on patients with a confirmed diagnosis of Acute Leukemia (AL) who are admitted to the Department of Hematology, Safdarjung hospital, New Delhi for induction chemotherapy.

Flow cytometric immunophenotyping has been done in all 52 samples collected to diagnose Acute Leukemia (AL) as Acute Lymphocytic Leukemia (ALL) and Acute Myeloid Leukemia (AML). Of these, 14 samples of B-ALL, 11 samples of T-ALL and 27 samples of AML have been diagnosed. Mononuclear cells (Blasts) were isolated from bone marrow and peripheral blood samples of pediatric and adult AML patients. These cells were cultured for short term with RPMI 1640 and with or without foetal bovine serum for upto 72 hrs. Cells were harvested and stored in liquid nitrogen. These cells will be used to understand methylation patterns in leukemia cells.

## 2. REDOX REGULATION OF LYMPHOCYTE SIGNALING IN BCLL

Chronic Lymphocytic Leukemia (CLL) is a clonal B-cell malignancy characterized by several defects in both cellular and humoral immunity. In Chronic Lymphocytic Leukemia (CLL), an abnormal neoplastic proliferation of B-cells originates in the bone marrow and develops in the lymph nodes. Intracellular redox environment depends on the relative production and removal of Reactive Oxygen Species (ROS). Small changes in ROS or the intracellular redox environment modulate physiologic and pathologic processes. ROS such as superoxide and hydrogen peroxide can act as signaling molecules directly; alternatively, a change in redox environment can affect signaling cascades and redox sensitive transcription factors involved in proliferation, survival and hormonal response. It has been hypothesized that ROS production in cell leads the B-cell activation which enhances the clonal proliferation of B-cell leading to B-cell accumulation. Analysis of B cells in BCLL patients for its proliferation and activation was done using flow cytometry in 20 blood samples from the patients and 20 age and sex-matched controls. To study the effect of ROS on B-cell activation, healthy human PBMC and CLL PBMC were analysed using CD80 (B7-1) as an activation marker for B-cell activation. Cells were cultured in different conditions including poke weed mitogen as contol to study the role of redox.

There was significant increase in activation of CLL B cells as compared to age and sex matched control samples.

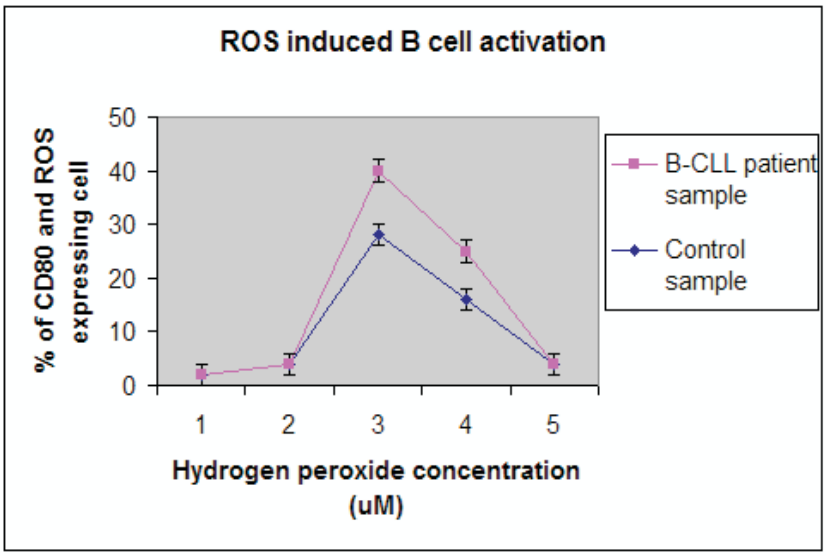



**Fig. 1 Represents B-cell activation in response of exogenous ROS.**

The figure shows that percentage of cells expressing CD80 (B-cell activation marker) and ROS increased with increasing concentration of $H_2O_2$ in leukemia cells in comparison to control cell. It further declined with increased concentration due to saturation in activation status.

# BRAIN TUMORS

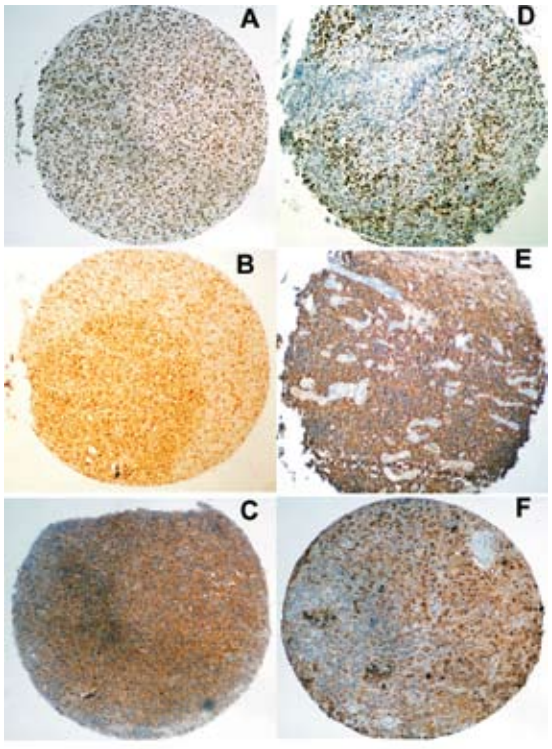
## 1. IMMUNOHISTOCHEMICAL EXPRESSION OF IDH1 IN GLIOMAS: A TISSUE MICROARRAY BASED APPROACH

Mutations in the gene encoding isocitrate dehydrogenase (IDH1) have been reported in acute leukemias and gliomas. The objective of this study is to compare immunohistochemical expression of IDH1 in low-grade and high-grade gliomas. With this objective, we analysed a series of 195 glioma cases to assess the frequency of R132H point mutations in formalin fixed, paraffin embedded tissue samples using a tissue microarray-based approach.

A total of 195 gliomas (30 pilocytic astrocytoma (PA), 45 diffuse astrocytoma (DA), 75 glioblastoma multiforme (GBM), 25 oligodendroglioma (OLIG) and 20 ependymoma (EPEN) was studied. A TMA of core size 1.0 mm was constructed using a semi-automatic tissue arrayer. Immunohistochemical staining for IDH1, p53 and EGFR proteins was performed by LSAB method. The results of immunohistochemial evaluation showed that none of the PA or EPEN showed any immunostaining with IDH1protein. However, 17/40 (42.5%) DA showed positive labeling with IDH1 and 27/40 (67.5%) showed mutant p53. This IDH1 expression was positively correlated with p53 expression ($p=0.018$). OLIG also showed positive immunoexpression of IDH1 in 22.5% of cases but mutant p53 in only 41% cases ($p=0.07$). Among primary GBM, only 1/65 showed IDH1 immunopositivity whereas 6/7(85%) of sec-GBM showed expression of this protein. Prim-GBM showed p53 and EGFR positivity in 64.5% and 60% respectively. In the 6/7 sec-GBM that showed mutant IDH1 expression, 5/7 also showed mutant p53 but in GBM co-expression of IDH1 and EGFR was rarely seen. Also sec-GBM, which showed IDH1 mutations more frequently in comparison to prim-

GBM, occurred in younger patients (mean age : 42.5 years) as compared to prim-GBM (mean age : 47.2 years).

Study showed that monoclonal antibody to IDH1 (R132) is a useful and less labor-intensive method to detect mutations of IDH1 gene in gliomas. IDH1 is a useful immunohistochemical marker to differentiate reactive gliosis from low-grade astrocytoma, has potential as an independent prognostic marker and also helps in distinguishing primary from secondary glioblastoma.




**Photomicrograph of TMA cores showing IDH1 expression in DA(A), GBM (B),OLIG (C), p53 in GBM(D), EGFR in GBM (E) and p53 in DA, (x100)**

# PATHOLOGY OF INFECTIOUS DISEASES

## *Leishmaniasis*

### 1. DRUG SUSCEPTIBILITY IN LEISHMANIA ISOLATES FOLLOWING MILTEFOSINE TREATMENT IN CASES OF VISCERAL LEISHMANIASIS AND POST KALA-AZAR DERMAL LEISHMANIASIS

Miltefosine is an oral drug with a long half-life, has been introduced as first line treatment in the Indian subcontinent and it is feared that resistance may emerge rapidly, threatening control efforts under the VL elimination program. We measured *in vitro* susceptibility towards miltefosine and paromomycin in *L. donovani* isolated from VL and PKDL, pre- and post-treatment cases, using an amastigote-macrophage model. Miltefosine susceptibility of post-treatment isolates from cured VL cases was comparable ($p>0.05$) whereas that from relapses was significantly higher ($p=0.04$) to that of the pre-treatment group. In PKDL, post-treatment isolates exhibited significantly lower susceptibility ($p=0.03$) than pre-treatment isolates. Overall, PKDL isolates exhibited significantly higher tolerance ($p<0.0001$) to miltefosine than VL isolates (Fig. 1). Point mutations in the miltefosine transporter (LdMT) and its beta subunit LdRos3 genes previously reported in parasites with experimentally induced MIL resistance were not present in the clinical isolates. Further, the mRNA expression profiles of these genes were comparable in the pre- and post-treatment isolates of VL and PKDL.

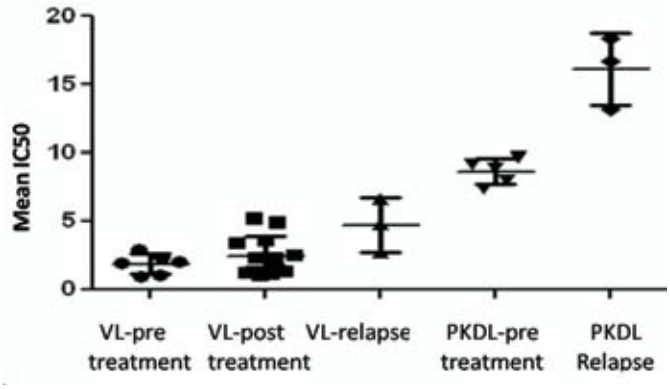



**Fig. 1: In vitro miltefosine susceptibility of VL and PKDL isolates before and after Mil treatment. Sensitivity of VL and PKDL isolates at intracellular amastigote stage were determined by infection in murine macrophage cell line J774A.1. Each individual value represents mean IC50±SD of the results from two separate assays.**

## 2. NON-INVASIVE PKDL DIAGNOSIS AND DETERMINATION OF PARASITE LOAD

At NIP, efforts have been made to develop non-invasive, simpler and rapid diagnostic method and slit aspirate sample were introduced for both immunological and molecular based PKDL diagnosis. Q-PCR determined parasite load in slit aspirate and tissue biopsy were comparable with a significantly high correlation ($r=0.927$). LD body positivity in tissue sections and slit smear was 31.58% and 53.66% respectively. At 1 month post-treatment, the parasite load was undetectable in slit aspirate in a majority of the cases examined. Slit aspirate Q-PCR assay provides a least-invasive, simple, rapid and reliable assay for diagnosis of PKDL, subsequent to initial screening with slit aspirate rk39 strip test, with potential for field application and assessment of cure.

## 3. FOXP3 AND IL-10 EXPRESSION CORRELATES WITH PARASITE BURDEN IN LESIONAL TISSUES OF POST KALA-AZAR DERMAL LEISHMANIASIS (PKDL) PATIENTS

The precise immunological cause of PKDL outcome remains obscure, although, overlapping counte- regulatory responses with elevated IFN-g and IL-10 are reported. We investigated ex-vivo mRNA and protein analysis of natural regulatory T-cells (nTreg) markers (Foxp3, CD25 and CTLA-4) and IL-10 levels in lesion tissues of PKDL patients at pre and post-treatment stages. mRNA levels of nTreg markers and IL-10 were found significantly elevated in pre-treatment PKDL cases compared to controls, and were restored after treatment. The accumulation of nTreg cells was evident as Foxp3 positive cells in lesion tissues of PKDL patients (Fig. 2). Analysis of nTreg cell markers and IL-10 in different clinical manifestations of disease revealed elevated levels in nodular lesions compared to macules/papules. Further, Foxp3, CD25 and IL-10 mRNA levels directly correlated with parasite load in lesions tissues. Data demonstrated accumulation of nTreg cells in infected tissue and a correlation of both IL-10 and nTreg levels with parasite burden suggesting their role in disease severity in PKDL.

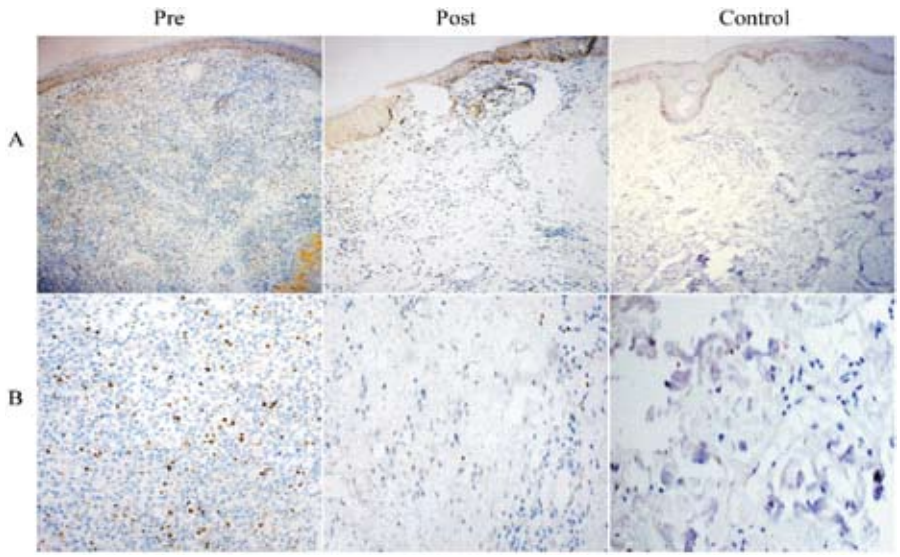



**Fig. 2: Immunohistochemical analysis of Foxp3 in lesions of PKDL patients. Distribution of Foxp3 cells following DAB staining in dermal lesion tissue sections at pre treatment, post treatment stages and normal skin of healthy individuals. Panel A (10X), Panel B (40X) magnification.**

## 4. MILTEFOSINE FOR TREATMENT OF PKDL PATIENTS

In a study conducted at NIP, oral miltefosine (50 mg thrice daily for 60 days or twice daily for 90 days) has been shown to have a beneficial effect in PKDL in a larger series of patients.

Post-kala-azar dermal leishmaniasis (PKDL) constitutes a parasite reservoir important in the transmission of visceral leishmaniasis (VL). Unacceptable treatment regimens and increasing drug resistance blight control programmes. The success of oral miltefosine in VL prompted a clinical, histopathological and parasitological study of this drug in PKDL. Twenty-six patients confirmed by slit-skin smear, histopathology and molecular tests were enrolled in the study. They received miltefosine capsules 50 mg thrice daily after food. Treatment was for 60 days with a provision to increase by 30 days if a responder had not attained a cure. Cure was ascertained by clinical and histopathological examination, and measuring parasite burden using real-time polymerase chain reaction. Twenty-four patients with a wide range of parasite burden completed the study. Twenty-three achieved a cure giving an initial cure rate of 96% (95% confidence interval 79–

99%). Sixteen patients were cured with 50 mg thrice daily,13 in 60 days and three within 90 days (Fig. 3). In seven cases, miltefosine had to be reduced, because of gastrointestinal intolerance, to 50 mg twice daily to a total of 180 capsules. Lesional parasites were undetectable at 1 month post-treatment. Treatment was safe with no relapses at 1-year follow-up. Thus, oral miltefosine, 50 mg thrice daily for 60 days or twice daily for 90 days, could be an effective treatment for PKDL.

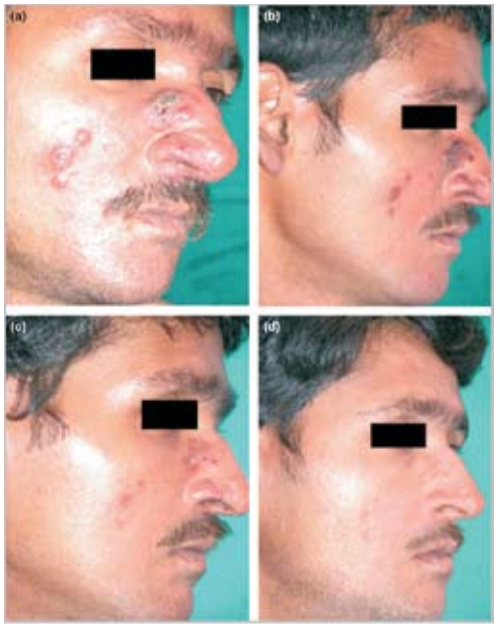


**Fig. 3: Images of a patient's face showing**
- **Papulonodules and plaque at start of therapy,**
- **Regression at mid-therapy,**
- **Improvement at the end of therapy (2 months), and**
- **Appearance at 1-year follow-up.**

## *Chlamydiasis*

### 1. ROLE OF OXIDATIVE STRESS IN CHLAMYDIA TRACHOMATIS INFECTED FIRST TRIMESTER SPONTANEOUS ABORTERS

Oxidative attack by reactive oxygen species as a result of disturbed oxidant-antioxidant system balance is recognized in the pathogenesis of placental deficiency syndromes such as preeclampsia and fetal growth restriction. It is speculated that early pregnancy failure might also be associated with oxidative stress throughout the

placenta. Our earlier reverse transcription-PCR and biochemical studies, performed on various biomarkers of oxidative stress including lipid peroxide/nitric oxide/superoxide dismutase/glutathione reductase, suggested role of superoxide dismutase in *C. trachomatis*-positive women undergoing spontaneous abortion in the first trimester. During the reporting period, the *in situ* expression of Cu, Zn-SOD and Mn-SOD was studied by immunohistochemistry in the endometrium of women throughout the menstrual cycle, and in the endometrial curettage tissue during early pregnancy and in *C. trachomatis* infected spontaneous aborters. The epithelial cells showed a positive immunostaining for Cu, Zn-SOD and Mn-SOD in the endometrium throughout the menstrual cycle and in early pregnancy. In the stroma, weak immunostaining for Cu, Zn-SOD and moderate immunostaining for Mn-SOD were observed in the pre-decidual cells in the late secretory phase, but no immunostaining was observed in the stromal cells from early proliferative phase to mid-secretory phase. Decidual cells in early pregnancy showed strong immunostaining for Cu, Zn-SOD and Mn-SOD. In curettage tissue from spontaneous aborters diagnosed as *C. trachomatis* positive, moderate immunostaining for Cu, Zn-SOD was observed in the cytotrophoblast while endothelial cells exhibited occasional staining.

## 2. IMMUNOMOLECULAR EXPRESSION OF CYCLOOXYGENASES AND PROSTAGLANDIN RECEPTORS IN ENDOMETRIAL CURETTAGE TISSUE OF CHLAMYDIA TRACHOMATIS INFECTED WOMEN DURING SPONTANEOUS ABORTION

It is well known that cyclooxygenase-2 signaling pathway is important for maintenance of early pregnancy. However, the exact role of cox-2 in recurrent aborters is not clear yet. Our previous study revealed that the expression of cox-2 was increased in the *C. trachomatis* infected spontaneous aborter group during 8–12 weeks of pregnancy (early pregnancy loss), by reverse-transcription PCR and immunohistochemistry. During the year under report, the expression of cox-2 gene was validated by real-time PCR assay. For this, endometrial curettage tissue was further collected from two sets of patient's groups, *viz.: C. trachomatis*-positive recurrent spontaneous aborters and *C. trachomatis*-negative women undergoing medical termination of pregnancy. None

of the patients had prior history of genitourinary infection/ VDRL/ HIV. Results showed that mRNA expression of cox-2 gene was upregulated (2.0-fold) in *C. trachomatis* infected women undergoing recurrent spontaneous abortion in comparison with women undergoing MTP and were *C. trachomatis*-negative (1.5-fold). The study is continuing to quantitate the chlamydial load by real-time PCR in spontaneous aborters with increased cox-2 expression and to compare the prostaglandin E receptor genes expression pattern in infected recurrent spontaneous aborters and uninfected women undergoing surgical abortion.

## 3. IMMUNOPATHOGENESIS OF REACTIVE ARTHRITIS/ AXIAL SPONDYLOARTHROPATHY INDUCED BY CHLAMYDIA TRACHOMATIS

Reactive arthritis (ReA) is an inflammatory joint condition triggered by an extra-articular bacterial infection. *C. trachomatis* is the most common cause of ReA in the course of a urogenital tract infection. In order to identify *Chlamydia* as the triggering organism and to establish the diagnosis of *Chlamydia*-induced reactive arthritis (CiReA), the utilization of PCR for detection of bacterial DNA in the inflamed synovial compartment has increasingly gained importance over the last few years. The present study is aimed to determine the frequency of *C. trachomatis* in synovial samples from patients diagnosed with ReA and Axial Spondyloarthropathy (AS) by utilizing a nested PCR.

During the year under report, 53 patients (16 with ReA, 22 with AS, 9 with RA, 6 with OA) were included in the study. Among these, 38 ReA/ AS patients (age range=18-48 years) with mono and oligoarthritis and fulfilling ESSG criteria comprised the study group. The male: female ratio was 23: 15 in these patients while the mean disease duration was 16.2 months. Most patients had an oligoarthritis of the lower limbs with at least one swollen joint, *i.e.* knee synovitis. 15 RA/ OA were enrolled as inflammatory/ non-inflammatory controls (age range=19-50 years; male:female ratio=9:6). 2 patients in the control group were found to be *C. trachomatis*-positive and were excluded.

8/38 (21.05%) ReA/ AS patients were positive for *C. trachomatis* MOMP/ plasmid genes by conventional PCR. Nested PCR for *C. trachomatis* plasmid gene showed

4/38 (10.5%) patients to be positive for this microorganism. *C. trachomatis*-specific IgA antibodies were found in the synovial fluid of 12/38 (31.5%) patients while 6/38 (15.7%) patients were positive for serum anti-*C. trachomatis* IgA antibodies. Positive nested PCR patients were compared with the presence of *C. trachomatis*-specific IgA antibodies. Among 4/38 (10.5%) nested PCR *C. trachomatis* positive ReA/ AS patients, all four patients (two with ReA, two with AS) were IgA-positive. The study is continuing. More number of patients is being enrolled to study the prevalence pattern in our population.

## *Leprosy*

### 1. CLINICOPATHOLOGICAL DETERMINANTS IN LEPROSY T1R

120 patients of clinically diagnosed leprosy T1R were included in this study. The relevant clinical parameters like clinical diagnosis according to Ridley-Jopling classification, presence or absence of nerve tenderness and neuritis, clinically detectable edema in the lesion, and whether new lesion appeared and additional features like scaling and treatment were noted. If more than one reactional lesions were present, the one showing the most active clinical presentation was biopsied. In addition to the suspected T1R patients, 50 cases from non-reactional leprosy were also recorded. The slides of all cases were coded by labeling the slides as numbers from 1-120 thereby hiding the identity of the clinical diagnosis. Their observations were recorded as P1 for (pathologist 1), P2 (pathologist 2) and P3 (pathologist 3). The presence or absence of predefined histopathological parameters like dermal edema, intragranuloma edema, intragranuloma lymphocytes, epidermal erosion by the granulomatous infiltrate, abnormal size and number of multinucleate giant cells, granuloma fraction and bacillary index were tabulated.

The primary antibodies to i-NOS, cxcl10/IP10 and NF-kappa B were standardized for immunohistochemical study. Sixty skin biopsies were selected with consensus among all three pathologists after seeing the hematoxylin-eosin stained slides. These were 15 BT Hansens, 15 BT Hansens in type 1 reaction, 10 BB Hansens disease, 10 BB

Hansens in type 1 reaction, 5 BL Hansens disease and 5 BL Hansens in type 1 reaction. The envision detection system of immunostaining was used and diaminobenzidine was the chromogen used for detection of a reaction. All three pathologists observed that epidermal erosion and dermal edema and intragranuloma edema were the most common parameters seen in a T1R. Another most consistent finding seen by all three pathologists was higher than expected lymphocyte accumulation within the granulomas. For studying immunohistochemical expression of i-NOS, NFkB, CXCL10 and CXCR3 in confirmed T1R biopsies versus non-reaction leprosy, biopsies were divided into 3 groups. Group 1 included BT and BT-T1R, group 2 included BB and BB-T1R while group 3 included BL and BL-T1R. The immunohistochemical scores were then analyzed by determining the Odds ratio and 95% confidence interval (CI) for each of the marker so as to find any statistically significant correlation that can differentiate a reaction from non-reaction. The results are being evaluated further and immunolocalization of these markers will be studied by immunofluorescence.

# ADULT STEM CELL BIOLOGY

## 1. A NOVEL ARITHMETIC APPROACH FOR FOOL-PROOF PRODUCTION OF GROWTH ARREST IN 3T3 CELLS SUITABLE FOR HUMAN EPIDERMAL CULTURE

Effective *in vitro* propagation of stem cell is routinely achieved using feeder cells that are growth arrested either by Gamma irradiation or exposure to Mitomycin C (MMC), although choice of these methods is highly disputed. We have so far demonstrated that the actual effectiveness of MMC approach is dependant on the calculated availability of the drug to the cells present at the time of exposure in a 'numerical' dose-dependant manner using a co-culture model comprising of NIH 3T3 fibroblasts as feeders and human epidermal keratinocytes as target stem cells (Yerneni & Kumar. A culture system for the growth of stem cells. Indian Patent filed, 2086/DEL/2009, publication date 13/8/2010, 33/2010, pp 24092). Subsequently, we initiated similar approach but using Swiss 3T3 cells as feeders which were originally well worked out as feeders. The research has been aimed at standardizing the complex protocol to generate human Cultured Epidermal Autograft (CEA) towards clinical application in burns patients. Until now, it has been shown that the effective growth arrest of Swiss 3T3 cells by MMC was dependant on exposure cell density of Swiss 3T3, as determined by the post exposure cellular extinction rate which was proportional to the arithmetically derived doses of MMC per cell. Thereafter, it was proposed to verify the differential attenuation potential of these arithmetic doses within each of the actual concentration of MMC resulting in appropriate volumetric titrations, followed by co-culture with epidermal keratinocytes.

Out of a myriad of arithmetically derived doses tested, four doses under each of two intermediate concentrations yielded maximal dose dependant significant differences in cell extinction rates within each of these concentrations as compared to the lower and higher concentrations. The regression analysis on extinction rates induced by all the 4 doses of mitomycin C under intermediate concentrations, respectively, over

12- day period showed highly significant fall in cell number proportionate to the increase in dose. Concomitant to the arithmetically calculated dose dependant cellular extinction of Swiss 3T3 cells, the human epidermal keratinocytes plated along with these feeders showed similar dose dependent cell proliferation but in a negatively correlated fashion.

It is thus summarized that the mitomycin C induced growth arrest is not only concentration-dependent, but also on the arithmetically derived doses employed, more particularly, in the range of effective but not too toxic doses and this could perhaps be the reason behind a number of contradictory on the efficacy of this method compared to $\gamma$-irradiation.

## 2. STUDIES ON EPITHELIAL-MESENCHYMAL INTERACTIONS USING HUMAN EPIDERMAL KERATINOCYTE STEM CELLS AND INNOVATIVELY GROWTH-ARRESTED FIBROBLAST FEEDERS IN 3-D COLLAGEN MODEL

It is hypothesized that the demonstrated varied extent of attenuation of 3T3 fibroblasts through manipulation of arithmetically derived numerical doses of Mitomycin C (MMC) resulting in differential stimulation of epidermal keratinocyte proliferation could be the consequence of altered fibroblast-keratinocyte interactions that probably bring about qualitative and quantitative differences in morphogenesis of epidermis *in vitro*. This project has been aimed at understanding the crucial mechanisms of differential growth stimulation of keratinocytes achieved by modulating the feeder cell growth arrest employing mitomycin C (MMC) with an innovative dosimetric protocol.

Swiss 3T3 cells were differentially growth arrested employing our novel MMC protocol (Yerneni & Kumar 2009, Indian Patent No.2086/DEL/2009) and their cell extinction rates in DE and routine 2-D culture, were estimated. In brief, the 3T3 fibroblasts were exposed to a 2-hour pulse of MMC at four concentrations. The intermediate concentrations were further subdivided into 2 arithmetically derived doses which expressed maximal extinction differential in 2-D culture. The fibroblasts exposed to MMC vehicle served as control. The cells were subsequently seeded into DE at a

density of 3.3 x $10^5$ cells per $cm^3$. The results indicated varied cell extinction patterns in a concentration as well as dose-dependant manner similar to the 2-D experiments.

Additionally, the basic methodology of preparing the organotypic co-culture skin model consisting of 3T3 fibroblasts in Type-I collagen gel as DE and an epithelialization of the same using human epidermal keratinocytes (Fig. 1) has been accomplished. This method is currently being fine tuned to make the epithelial tissue fully mature at air-liquid interface for evaluating the action of the experimentally produced various stocks of growth arrested 3T3 cells on epithelialization.

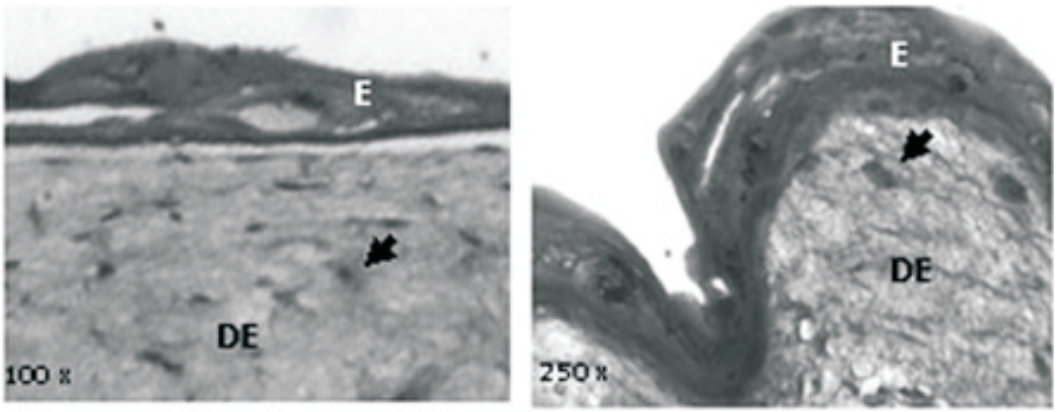



Figure 1. H&E stained paraffin sections of organotypic co-cultures. In vitro constructed organotypic skin model consisting of dermal equivalent (DE) prepared using Swiss 3T3 fibroblast cells (arrows) infused into Collagen gel followed by epithelialization (E) using human epidermal keratinocytes plated over DE.

The differentially growth arrested 3T3 cells have exhibited periodic cell extinction patterns similar to what was observed with 2-D culture technique.

# ENVIRONMENTAL TOXICOLOGY

## 1. HEALTH HAZARDS OF PHTHALATE VIS-À-VIS IDIOPATHIC MALE INFERTILITY

Phthalates are a class of multifunctional chemicals used in a variety of consumer and personal care products. High MW phthalates such as DEHP and BBzP are primarily used as plasticizers in the manufacture of flexible vinyl products while low MW phthalates are used in personal care products. Experimental studies in laboratory animals have shown that some phthalates are reproductive and developmental toxicants.

Phthalates are ubiquitous in environment and are able to reach the body of living organisms through a variety of routes but they do not accumulate, metabolize quickly, and are primarily excreted in urine. Urinary concentrations of phthalate metabolites have been used as a biomarker of exposure to the precursor phthalate diesters. However, the human evidence on the potential testicular toxicity of phthalates is very limited. In the year under report, attempts were made to estimate the levels of phthalate metabolites in the urine of both infertile and fertile males.

Phthalate metabolites were extracted from urine samples employing solid-phase extraction method and analyzed by HPLC using the protocol developed for detection of phthalate metabolites. Out of five metabolites screened, only two metabolites i.e. MEHP and MBP were found in urine samples. Although the concentration of MEHP and MBP varied widely, the average level of MEHP was observed to be 113.46$\mu$g/ml and that of MBP was 138.19 $\mu$g/ml.

## 2. ASSESSMENT OF PESTICIDE EXPOSURE IN TEA GARDEN WORKERS OF NORTH-EASTERN STATE OF INDIA (HEBM)

Pesticides are extensively being used in tea bushes of north-eastern region of India and tea garden workers are exposed to these pesticides. Pesticides were detected and quantified in a total of 167 samples of placenta and blood (maternal and cord)

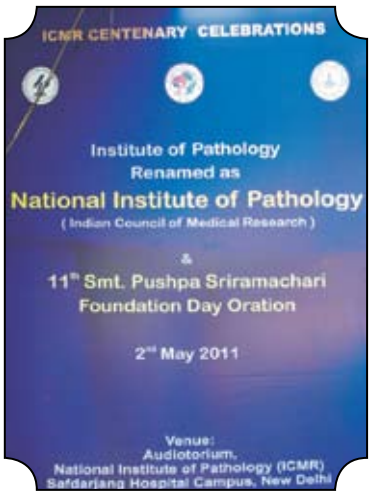
samples by GC and HPLC. Placental tissue as well as maternal and cord blood samples showed presence of predominantly organophosphorus pesticides such as acephate, parathion, malathion, ethion and phosalone in addition to organochlorine pesticides, *viz.:* heptachlor, DDT, chlordane, etc. The study further revealed correlation between presence of pesticides and different clinical manifestations such as headaches, dizziness, blurred vision, nausea and vomiting, stomach cramps, diarrhoea, excessive salivation and sweating, tightness of the chest, muscle twitching, etc.

## 3. ASSESSMENT OF CADMIUM AND LEAD LEVELS IN BLOOD AND PLACENTA IN INTRAUTERINE GROWTH RESTRICTION (IUGR) DELIVERIES

The present study was designed to assess the association between levels of cadmium & lead and IUGR. Samples of placenta, maternal blood and cord blood were collected from 126 cases of IUGR delivery and 88 AGA deliveries. Estimation of Cd & Pb in the placental digest, maternal & cord serum digest was done by ICP-MS. After excluding all the known factors responsible for IUGR except genetic, significantly high concentration of Cd & Pb was observed in all the three samples, *viz.:* placenta, maternal & cord blood serum, collected from the mother delivered IUGR foetus than samples collected from the mother delivered AGA foetus. Detection of moderate concentration Cd & Pd in cord blood serum justifies that placenta is not acting as a perfect barrier for toxic elements.

# Major Activities at National Institute of Pathology

1. Institute attained the status of '**National Institute of Pathology**' on the Foundation Day of Institute of Pathology on 2nd May 2011.

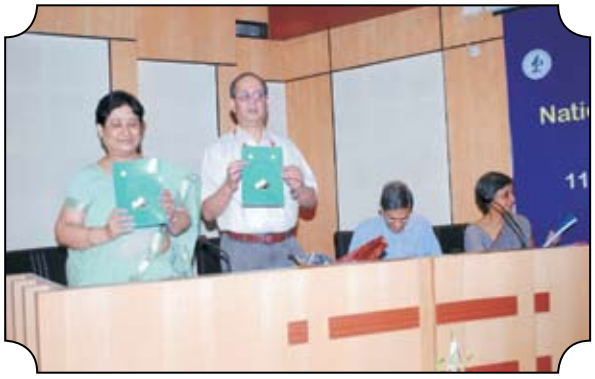



2. Annual meeting of **IAPM (Delhi Chapter)** was organized by National Institute of Pathology (ICMR) with Department of Pathology, Safdarjang hospital at Vallabhbhai Patel Chest Institute on 17th April 2011.

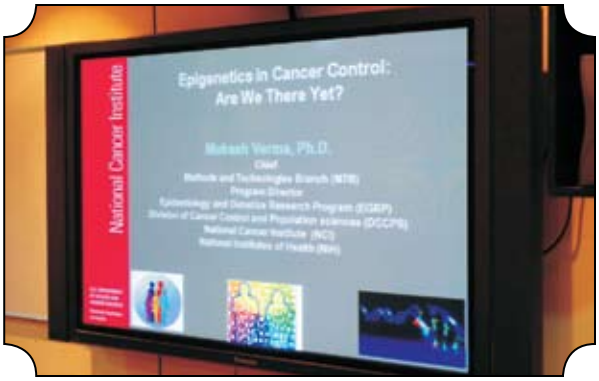

3. Organized **Director's Meeting of Indian Council of Medical Research** from 8th-9th May 2011.

4. Organized **'Foundation Workshop on Clinical and Laboratory Medicine Research'** with Moving Academy of Medicine and Biomedicine, Pune on 26th-28th July 2011.


5. **11th Smt. Pushpa Sriramachari Foundation Day Oration** was delivered by **Prof. Avdesh Surolia** on ***'Harnessing protein folding to counter diabetes and other diseases'*** at National Institute of Pathology (ICMR) on 2nd May 2011.



6. **Professor Mukesh Verma**, Chief, Methods and Technology Branch, Programme Director, Epidemiology and Genetics Research program, National Cancer Institute (NCI), Division of Cancer Control and Population Sciences, National Institutes of Health (NIH), USA delivered a lecture on ***'Epigenetic in Cancer Control: Are we there yet?'*** at National Institute of Pathology (ICMR) on 19th December 2011.




7. **Scientific Advisory Committee (SAC)** for the year 2010-11 of National Institute of Pathology (ICMR) was held on 22nd November 2011. Students presented posters on their work for review by experts.


8. Workshop on **'Flow Cytometry**: **Technical Support and Education (TTE) Programme'** was organized by National Institute of Pathology (ICMR) and BD Biosciences at National Institute of Pathology from 15th-17th February 2012.

9. Organized one-day **'Library Training Workshop'** sponsored by ICMR and Wiley Publications on **'Cochrane Library'** at National Institute of Pathology (ICMR) on 5th September 2011.


10. On the eve of **15th August 2011** and **26th January 2012**, flag hoisting was done at National Institute of Pathology (ICMR).

11. **Post-graduate students from Government Medical College, Amritsar** visited different laboratories of the Institute to get exposure to high throughput technologies available at National Institute of Pathology (ICMR).
12. Inspection of National Institute of Pathology by **Dr. Rajiv Sen**, PGIMS, Rohtak, for **renewal of accreditation of DNB Program by NBE** on 20th July 2011.
13. **Dr. Hari S. Sharma,** Institute of Cardiovascular Research, YUMC, University Medical Centre, Amsterdam, The Netherlands, delivered guest lecture on ***'Molecular Patho-physiology of chronic lung diseases'*** on 27th September 2011.
14. **Dr. Thierrry Dameral**, Deputy CEO Inserm and **Dr. Philippe Arthets**, Deputy Director, External Relations, Inserm, France, visited National Institute of Pathology (ICMR) on 19th October 2011.
15. Organized **Vigilance Awareness Week** from 31st October 2011 to 5th November 2011 at National Institute of Pathology (ICMR).


16. **World Health Organization (WHO)-sponsored 'Training Course for Technicians and Advanced level** held at National Institute of Pathology (ICMR) from 24th November 2011 uptill 23rd December 2011 on the topic, ***'Basic Biostatistics and Epidemiology'***.
17. Organized one-day workshop on **'Application of Next Generating Sequencing (NSG) in Medical Research'**, held jointly by National Institute of Pathology and Indian Council of Medical Research at National Institute of Pathology on 28th February 2012.
18. National Institute of Pathology (ICMR) organized workshop on ***'Application of Molecular Biology in Cancer Diagnostics'*** at Dr. B. Barooah Cancer Institute jointly with BBCI, Guwahati on 28th February-1st March 2012.

# EXTRAMURAL PROJECTS (2011-12)

## NEW PROJECTS

1. **Development of new live attenuated vaccine candidates for kala-azar.**
   **Dr. Poonam Salotra- DBT (2011-14).**

2. **Study on effects of anti-cancer drugs on breast cancer stem cells.**
   **Dr. Sunita Saxena- ICMR (2011-13).**

3. **Epigenetic studies in esophageal cancer in high risk region of north-east India.**
   **Dr. Sunita Saxena, Dr. Sujala Kapur- Twining Program of DBT (2011-14).**

## ONGOING PROJECTS

1. **Genome wide analysis of genetic alterations in patients with esophageal cancer from north-east India using single nucleotide polymorphism array.**
   **Dr. Sujala Kapur, Dr. Sunita Saxena- ICMR (2011-14).**

2. **Study on the effect of siRNA mediated androgen receptor gene silencing on androgen signaling pathway in breast carcinoma.**
   **Dr. Anurupa Chakraborty- Post-Doctoral Fellowship, ICMR (2010-12).**

3. **Clinicopathological determinants in leprosy type 1 reactions.**
   **Dr. Avninder Pal Singh- ICMR Leprosy Task Force project (2010-12).**

4. **Immunogenetic profile of nasopharyngeal cancer.**
   **Dr. Sujala Kapur, Dr. Sunita Saxena- DBT (2010-13).**

5. **Characterization of host immune factors associated with progression of superficial TCC of bladder by microarray analysis.**
   **Dr. Sunita Saxena, Dr. Usha Agrawal- ICMR (2009-12).**

6. **Study on gene expression and hypermethylation profiles in early onset breast cancer.**
   **Dr. Sunita Saxena, Dr. Sujala Kapur, Dr. BSA Raju- DBT (2008-11).**

7. **Protective immunogenicity of centrin KO live attenuated *Leishmania* parasite in the animal models and in the human cells.**
   **Dr. Poonam Salotra- DBT (2011-14).**

8. **New tools for monitoring drug resistance and treatment response in visceral leishmaniasis in the Indian subcontinent.**
   **Dr. Poonam Salotra- European Commission (2009-12).**

9. **Pre-clinical studies of a PSA-based human vaccine candidate targeting visceral, cutaneous and muco-cutaneous leishmaniasis and development of the associated procedures for further clinical trials.**
   **Dr. Poonam Salotra- European Commission (2009-12).**

10. **Transcriptome profiling for identification and characterization of miltefosine resistance associated genes of *Leishmania donovani*.**
    **Dr. Poonam Salotra- ICMR (2009-12).**

11. **Detection of *Chlamydia trachomatis* in synovial samples from patients with undifferentiated spondyloarthropathy / reactive arthritis.**
    **Dr. Sangita Rastogi- SRF, ICMR (2010-13).**

12. **A novel arithmetic approach for fool-proof production of growth arrest in 3T3 cells suitable for human epidermal culture.**
    **Dr. LK Yerneni- ICMR (2010-13).**

13. **Studies on epithelial-mesenchymal interactions using human epidermal keratinocyte stem cells and innovatively growth-arrested fibroblast feeders in 3-D collagen model.**
    **Dr. LK Yerneni- SRF, ICMR (2010-13).**

# COMPLETED PROJECTS

1. **Establishment of breast cancer cell lines from primary breast tumours.**
   **Dr. Sunita Saxena, Dr. Sujala Kapur, Dr. BSA Raju- ICMR Multicentric Task Force Project (2007-11).**

2. **Parasite Surface Antigen-2 (PSA-2) of *Leishmania donovani*: Studies on its role in parasite virulence, drug resistance and modulation of host macrophage function.**
   **Dr. Poonam Salotra- DST (2008-11).**

3. **Assessment of pesticide exposure in tea garden workers of north-eastern state of India (HEBM).**
   **Dr. AK Jain- ICMR (2008-11).**

# AWARDS / HONOURS

1. **Dr. Sujala Kapur** awarded '**Membership of National Academy of Medical Sciences**'.

2. **Dr. Fauzia Siraj** got '**Ramalingaswamy Award'** for the best paper on "Immunohistochemical expression of chemokine receptor CXCR3 and its ligand CXCL10 iastrocytomasin" in annual meeting of IAPM – Delhi chapter.

# PUBLISHED PAPERS


1. Ihsan R, Chauhan PS, Mishra AK, Yadav DS, Kaushal M, Sharma JD, Zomawia E, Verma Y, Kapur S, Saxena S. Multiple analytical approaches reveal distinct gene-environment interactions in smokers and non-smokers in lung cancer. **PLoS One**, 6(12): e29431, 2011.

2. Chauhan PS, Bhushan B, Singh LC, Mishra AK, Saluja S, Mittal V, Gupta DK, Kapur S. Expression of genes related to multiple drug resistance and apoptosis in acute leukemia: Response to induction chemotherapy. **Exp Mol Pathol**, 92(1):44-49, 2011.

3. Chauhan PS, Bhushan B, Mishra AK, Singh LC, Saluja S, Verma S, Gupta DK, Mittal V, Chaudhry S, Kapur S. Mutation of FLT3 gene in acute myeloid leukemia with normal cytogenetics and its association with clinical and immunophenotypic features. **Med Oncol**, 28(2): 544-551, 2011.

4. Agarwal Usha, Mishra AK, Salgia Payal, Verma Saurabh, Mohanty NK, Saxena S. Role of tumour suppressor and angiogenesis markers in prediction of recurrence of non-muscle invasive bladder cancer. **Pathol and Oncol Res**, 17(1): 91-100, 2011.

5. Bansal A, Bhatnagar A, Saxena S. Metastasizing granular cell ameloblastoma**. J Oral Maxillofac Pathol**, 16: 122-124, 2012.

6. Singh LC, Chakraborty A, Kapur S, Saxena S. Study on predictive role of AR and EGFR family genes with response to neo-adjuvant chemotherpy in locally advanced breast cancer in Indian women. **Med Oncol**, 29: 539-546, 2012.

7. Singh A, Mishra AK, Ylaya K, Hewitt SM, Sharma KC, Saxena S. Wilms Tumor-1, Claudin-1 and Ezrin are useful immunohistochemical markers that help to distinguish schwannoma from fibroblastic meningioma. **Pathol Oncol Res**, DOI 10.1007/s12253-011-9456, 2011.

8. Katara GK, Ansari NA, Verma S, Ramesh V, Salotra P. Foxp3 and IL-10 expression correlates with parasite burden in lesional tissues of post kala-azar dermal leishmaniasis (PKDL) patients. **PLoS Negl Trop Dis**, 5(5): e1171, 2011.

9. Khandelwal K, Bumb RA, Mehta RD, Kaushal H, Lezama-Davila C, Salotra P, Satoskar AR. A patient presenting with diffuse cutaneous leishmaniasis (DCL) as a first indicator of HIV infection in India. **Am J Trop Med Hyg**, 85(1): 64-65, 2011.

10. Kulshrestha A, Singh R, Kumar D, Negi NS, Salotra P. Antimony-resistant clinical isolates of *Leishmania donovani* are susceptible to paromomycin and sitamaquine. **Antimicrob Agents Chemother,** 55(6): 2916-2921, 2011.

11. Ramesh V, Katara GK, Verma S, Salotra P. Miltefosine as an effective choice in the treatment of post-kala-azar dermal leishmaniasis. **Br J Dermatol**, 165(2): 411-414, 2011.

12. Selvapandiyan A, Dey R, Gannavaram S, Lakhal-Naouar I, Duncan R, Salotra P, Nakhasi HL. Immunity to visceral leishmaniasis using genetically defined live-attenuated parasites. **J Trop Med**, 631460, 2012.

13. Soni P, Prasad N, Khandelwal K, Ghiya BC, Mehta RD, Bumb RA, Salotra P. Unresponsive cutaneous leishmaniasis and HIV co-infection: Report of three cases. **Indian J Dermatol Venereol Leprol**, 77(2): 251, 2011.

14. Srividya G, Kulshrestha A, Singh R, Salotra P. Diagnosis of visceral leishmaniasis: Developments over the last decade. **Parasitol Res**, 110(3): 1065-1078, 2012.

15. Bihaqi SW, Singh AP, Tiwari M. *In-vivo* investigation of the neuroprotective property of *Convolvulus pluraicaulis* in scopolamine-induced cognitive impairments in Wistar rats. **Indian J Pharamacol,** 43: 520-525, 2011.

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17. Capoor MR, Ramesh V, Khanna G**,** Singh A, Aggarwal P. Sporotrichosis in Delhi among migrant population from Uttarakhand, India. **Trop Doct,** 41: 46-48, 2011.

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19. Jairajpuri Z, Jain I, Singh A. Papillary meningioma: A rare malignant variant. **Indian J Pathol Microbiol,** 54: 410-411, 2011.

20. Puri P, Singh A, Ramesh V. Facial nodule in a 34-year-old man. **Indian J Dermatol,** 56: 230-231, 2011**.**

21. Malhotra A, Singh A**,** Ramesh V. Basal cell carcinoma in the north Indian population: Clinicopathologic review and immunohistochemical analysis. **Ind J Dermatol Venreol Leprol,** 77(3): 328-330, 2011.

22. Mondal Shankar, Varma Saurabh, Bamola Vishwa Deepak, Naik Satya Narain, Mirdha Bijay Ranjan, Padhi Madan Mohan, Mehta Nalin, Mahapatra Sushil Chandra. Double-blinded randomized controlled trial for immunomodulatory effects of Tulsi (*Ocimum sanctum Linn*) leaf extract on healthy volunteers. **Journal of Ethanopharmacology**, 136: 452-456, 2011.

## BOOKS / MONOGRAPHS

1. Mishra AK, Chakraborty A, Saxena S. Significance of vitamin D receptor polymorphisms in breast cancer- Multinomial logistic regression analysis. In: Vitamin D: Nutrition, Side Effects & Supplements. Ed.: Malone Stephanie R.

2. Saxena Sunita. Molecular and genetic aspects of lung cancer. chapter 13, pp. 141-148. In: Pathological & Occupational Lung Health. Eds.: Vijyan VK, Tazelaar HK, Kulshrestha Ritu.

3. Varma S. Tissue Transglutaminase (tTG) expression in human brain tumours: An immunohistochemical study. Lambert Academic Publications, Germany, 2011.

4. Singh A, Weng X, Nath I. Skin biopsy in leprosy. In: Skin Biopsy, InTech Publishers, 5: pp. 73-86, 2011.

## ACCEPTED FOR PUBLICATION

1. Soni A, Bansal A, Mishra AK, Batra J, Singh LC, Chakraborty A, Yadav DS, Mohanty NK, Saxena S. Functional Association of androgen signaling (AR, PSA) and metabolizing (CYP19) gene polymorphisms in prostate carcinoma in north Indian population. Genetic Testing and Molecular Biomarker.

2. Mishra AK, Agrawal U, Negi S, Bansal A, Bhatnagar A, Bhatnagar D, Chintamani, Mohil R, Saxena S. Study on expression of AR in breast cancer and its correlation with other steroid receptors and growth factors. Indian Journal of Medical Research, 2011.

3. Rastogi S, Sharma VK, Khanna G, Batra S, Kumar P. Detection of *Chlamydia trachomatis* in synovial fluid of patients with reactive arthritis. J Clin Rheum.

4. Prasad P, Singh N, Das B, Rastogi S. Involvement of superoxide dismutase in pathogenesis of spontaneous abortion in women infected with *Chlamydia trachomatis*. J Obstet Gynecol.

5. Bansal Anju, Soni Abha, Rao Punita, Singh LC, Mishra Ashwini, Mohanty N K, Saxena Sunita. Implication of DNA repairs genes in prostate carcinogenesis in Indian men. Indian Journal of Medical Research (In Press).

# SCIENTIFIC ACTIVITIES

## Dr. Sunita Saxena

1. Chaired the session on 'Disease Proteomics (Infectious Diseases)' at the IInd Annual Indian Proteomics Conference (IPCON-2011) held in New Delhi on 3rd-5th April 2011.

2. Inspected the laboratory of Dr. Yogeshwar Shukla, E-II, ECO, IITR, Lucknow on 11th April 2011 as member of ICMR team.

3. Invited to attend the meeting to discuss the policy for storage of biological samples in ICMR-funded project on 25th April 2011 at ICMR, New Delhi.

4. Invited to attend Project Review Committee meeting for Cellular and Molecular Biology and Genomics as expert on 20th May 2011 at ICMR, New Delhi.

5. Chairperson of Ethical Committee of Safdarjung hospital, New Delhi and regularly chaired the meetings of Ethics committee on alternate months.

6. Attended meetings of the Specification Committee for installing laboratory equipments and furniture for the National Institute of Research in Environmental Health, Bhopal on 6th June and 18th October 2011 at ICMR, New Delhi.

7. Invited as member of Selection Committee for the selection of candidates for ICMR-Post Doctoral Fellowship and Research Associate held on 16th June 2011 and 22nd December 2011 respectively at ICMR, New Delhi.

8. Attended meeting on Cancer Monograph in ICMR on 19th July 2011 at ICMR, New Delhi.

9. Member of Condemnation Board and attended meetings of the Condemnation Board of ICMR held on 27th July 2011 at National Institute of Medical Statistics, New Delhi.

10. Nominated to attend WG-13: Working Group of the Department of Atomic Energy (R & D Sector) held on 1st August 2011 at Mumbai, for preparation of 12th plan.

11. Attended meeting of Scientific Advisory Committee of Institute of Cytology & Preventive Oncology, Noida on 3rd August 2011.

12. Invited as Chief Guest at National conference on 'Current Trends in Advanced Biomedical Technology (CTA B-II)' organized by Department of Biosciences, Nehru Arts and Sciences College, Coimbatore, during 20th - 21st September 2011 and delivered Key-note address on *'Understanding Molecular Biology of Cancer using Genomic Approaches'.*

13. Member of Project Review Committee in Oncology (NCD) and attended meetings on 22nd–23rd September 2011 at ICMR, New Delhi.

14. Attended workshop on 'Clinical Trials Registry– India amongst the Ethics Committee' held on 26th September 2011 at India International Centre Annex, New Delhi.

15. Attended meeting of Expert Group on 'Effectiveness and safety of 2 vs 3 doses of HPV vaccine in prevention of cervical cancer: An Indian multicentric randomized trial' held on 28th September 2011 at ICMR, New Delhi.

16. Attended 2nd meeting of the PRSG to review the project 'Development of PC-based fully automatic batch analyzer for clinical chemistry' held on 17th October 2011 at CSIO, Chandigarh organized by Department of Information Technology, New Delhi.

17. Attended Technical Committee meetings of ICMR held on 4th November 2011, 19th January & 19th March 2012 at ICMR, New Delhi.

18. Attended Selection Committee Meeting for award of Emeritus Medical Scientist for ICMR held on 4th November 2011 at ICMR, New Delhi.

19. Nominated as member of Scientific Advisory Committee of Regional Medical Research Centre, NE region, Dibrugarh (Assam).

20. Attended Scientific Advisory Group Meeting of Division of Publication & Information, ICMR held at ICMR, New Delhi on 29th November 2011.

21. Invited to deliver talk on *'Significance of Microarray Technology in Understanding Cancer Genome and identification of Biomarker– Genome-wise approach to identify Cancer Biomarker"* in 1st Biennial Conference of IASN organized by

Agra Medical College in association of National JALMA Institute for Leprosy and Other Mycobacterial Diseases (ICMR), Agra during 30th November - 1st December 2011.

22. Invited to deliver talk on *'Application of Tissue Microarray in Pathology'* in Symposium on "Antibody–based Proteomics' on 1st December 2011 at IAP-APCON 2011.

23. Nominated as expert for Selection Committee meeting for NASI Scopus Young Scientist Award 2011 held on 5th December 2011 in New Delhi.

24. Attended Scientific Advisory Group meeting of Basic Medical Science Division of ICMR held on 26th December 2011 at ICMR, New Delhi.

25. Invited to attend panel discussion on 'Histopathological insight into DES thrombosis from large necropsy & experimental animal experiences: Can we have a safe DES?' organized by Department of Cardiology, VMMC & Safdarjang hospital, New Delhi on 26th December 2011.

26. Attended Director's Meeting held at Desert Medicine Research Centre, Jodhpur during 13th-14th January 2012.

27. Attended signing of Memorandum of Understanding between ICMR and Symbiosis International University, Pune on 23rd January 2012 at ICMR, New Delhi.

28. Invited to attend Meeting of South Asian Forum for Health Research (SAFHeR) during 5th – 7th February 2012.

29. Invited as Chief Guest to deliver a talk on *'Applications of Tissue Microarray in Pathology and Research*' in workshop organized by Dr. B. Borooah Cancer Institute, Guwahati held during 28th February - 1st March 2012.

## Dr. Sujala Kapur

### *Invited Speaker*

- *Molecular Diagnosis of Lymphomas and Leukemias*: 26th Annual Conference of Indian Association of Pathologists and Microbiologists, NIOP, New Delhi, April 2011.

- *Microarray and its application*. Students Exchange Progamme of GTB Hospital, Shahdara, October 2011.
- *Microarray: Principles and Methodology*: Joint Workshop on Molecular Biology, NIOP and BBCI, Guwahati, February 2012.

### *Workshops / Conferences / Meetings Attended*

- Workshop on Cytogenetics and Automatic Slide Scanning Workstation, organized by Carl Zeiss, 5th May 2011.
- Member, Executive Committee, 26th Annual Conference of Indian Association of Pathologists and Microbiologists, NIOP, New Delhi, April 2011.
- Workshop on Next Generation Sequencing at NIN, Hyderabad from 13th - 17th June 2011.
- Member, PRC meeting on Gastroenterology, NCD, ICMR.
- Visited BBCI, Guwahati and Imphal, Manipur for collaborative projects, August 2011.
- *'New Horizons in Cancer Research',* International AACR Conference, December 2011, Gurgaon.
- *'Analysis of redox mediated B-cell activation in BCLL'* at National Conference on Oxidative Stress and Its Complication in Human Health (NCOSH-2011), Karunya University, Coimbatore.

## Dr. Sangita Rastogi

1. Member, Selection Committee, Department of Microbiology, VMMC & SJ hospital, New Delhi for selection of Senior Research Fellow in ICMR-funded project (August 2011).
2. Convened Institutional Animal Ethics Committee Meeting at NIP on 23rd August 2011.
3. Attended Meeting for MD Project Protocol Presentation at VMMC & SJH, New Delhi on 20th September 2011.

4. Attended ICMR Centenary Symposium & Commemorative Currency Coin Release at ICAR (Pusa), New Delhi on 15th November 2011.

5. Presented paper titled, *Circulating antibodies to Chlamydia trachomatis and heat shock proteins'* in 5th Asian Congress on Autoimmunity at Singapore on 17th-19th November 2011.

6. Participated in conference on 'Nucleic acids in disease & disorder' at Indian Institute of Technology, New Delhi on 7th-9th December 2011.

7. Reviewed STS project proposals for 'Short-Term Studentship Program' of ICMR (2011-12).

8. Attended CME on 'Diagnosis of autoimmune disorders: The continuing dilemma' at LNJP, New Delhi on 10th-11th December 2011.

9. Participated in International Symposium on Molecular Pathology at Manekshaw Centre, New Delhi on 28th-29th January 2012.

10. Participated in 'National CME in Obstetrics & Gynecology' at AIIMS, New Delhi on 24th-25th March 2012.

## Dr. Poonam Salotra

1. Presentation at Woods Hole Immuno-parasitology meeting at MA, USA in April 2011.

2. Participated in the Steering Committee Meeting of *Leishmania* Kala Drug Project at Strathclyde University, Glasgow, U.K. in June 2011.

3. Invited participant in meeting to finalize the specifications of equipment for medical colleges, held at ICMR, in June 2011.

4. Participated in the Steering Committee Meeting of *Leishmania* Kala Drug Project at Berlin, Germany in August 2011.

5. Invited by Applied Biosciences for the inauguration of Technologies Torrent Personal Genome Machine Training Facility, at Gurgaon in August 2011.

6. Attended PRC meeting on Malaria, Filariasis & Leishmaniasis held at ICMR, New Delhi in September & November 2011.

7. Organized International Project Review Meeting of European Commission-funded project (Rapsodi) partners from France, Spain, Peru, Tunisia in New Delhi, 26th-28th September 2011.

8. Invited speaker at 'Advanced WHO-IRTC/UNIL Course on Immunology, Vaccinology and Biotechnology applied to Leishmaniasis' at Lausanne, Switzerland in October 2011.

9. Participated in ICMR Awards Presentation Ceremony held at DRDO Bhawan, New Delhi, in November 2011.

10. Participated in ICMR Centenary Symposium, Commemorative Currency Coin Release held at NASC Complex, ICAR, Pusa Road, New Delhi in November 2011.

11. Participated in International Symposium Vaccines: From Discovery to Translation held at Surajkund, Delhi, November 2011.

12. Participated in INSA Fellow Awards in December 2011 at Tezpur, Assam.

13. Invited speaker in meeting on 'Monitoring of clinical outcomes of Kala-azar in the health & surveillance of drug resistance' held at Surajkund, January 2012.

14. Participated in the Steering Committee Meeting of *Leishmania* Rapsodi Project at Toulon, France during 6th-12th February 2012.

15. Organized Training Program on Flow Cytometry in February 2012 at NIP, New Delhi.

16. Invited speaker in Meeting on 'Diagnostics of Public Health Importance in India' held in February 2012 at National Institute of Immunology.

17. Participated in second Brain Storming Meeting of Vector Science Forum on Japanese Encephalitis and Visceral and Cutaneous Leishmaniasis, held at NIP during February 2012.

18. Participated in Kala-Azar Alleviation Initiative: 1st Annual meeting held at Maples Hotel, New Delhi, March 2012.

## Dr. Usha Agrawal

1. Organizing Secretary of 26th Annual Conference Delhi Chapter, IAPM held on 17th April 2011 at VB Patel Chest Institute, North Campus, New Delhi.

2. Attended conference on 'IPCON-2011' organized by the Proteomic Society of India and Jawaharlal University from 4th-6th April 2011 at Hotel Parkland, New Delhi.

3. Attended 'Data Curation and Bioinformatics Workshop' organized by Shodhaka-ICMR-NIRRH at Mumbai from 31st May to 3rd June 2011.

4. Deputed to visit Tissue Repository Facility at ACTREC, Khargar, Navi Mumbai on 6th June 2011.

5. Facilitated the inspection for renewal of DNB Accreditation in National Institute of Pathology on 20th July 2011, by Dr Rajiv Sen, PGIMS, Rohtak.

6. Served as expert on Selection Committee for Research Associate (Pathology) held on 22nd July 2011.

## Dr. LK Yerneni

1. Attended Workshop on Cytogenetics & Automated Slide Scanning Workstation conducted by Carl Zeiss, India on 5th May 2011, at Hotel Parkland, New Delhi.

2. Attended a Public Consultation meet on stem cell guidelines for northern region held on 17th December 2011 at Chinmaya Mission auditorium, New Delhi.

3. Attended several rounds of discussions at ICMR Headquarters during 2011 held amongst NRDC, ICMR and a Hyderabad based pharmaceutical company regarding transfer of epidermal culture technology to industry.

4. Visited a Pharma industry, Hyderabad, on 19th October 2011, as an inventor member of an ICMR-NRDC team to ascertain the suitability of their laboratories for undertaking the epidermal culture work towards clinical trial and the subsequent commercial exploitation of the technology.

## Dr. AP Singh

1. Presented a paper titled *'Clinicopathological correlations in leprosy type 1 and type 2 reactions'* at 26th Annual IAPM- Delhi Chapter Conference held on 17th April 2011 at National Institute of Pathology-ICMR, New Delhi.

2. Participated in 6th International CME in Dermatopathology from 11th-13th November 2011 at India Habitat Center, New Delhi.

3. Delivered an invited talk on *'Tissue microarray in pathology'* at CME in Pathology held on 8th October 2011 at Maulana Azad Medical College, New Delhi.

4. Presented a paper titled *'Immunohistochemical expression of chemokine receptor CXCR3 and and its ligand CXCL10 in gliomas'* at Annual IAPM Delhi Chapter, IAPM Conference held at Maulana Azad Medical College on 25th February 2012.

## Dr. AK Mishra

1. Faculty for the course no. BIO-G532 'Biostatistics and Biomodelling' under the off-distance Campus Ph.D. programme of National Institute of Pathology (ICMR) in collaboration with BITS, Pilani for the academic session 2011-2012.

2. Faculty as Co-supervisor for DNB (Pathology) thesis dissertation work: Role of epithelial mesenchymal transition in progression of bladder cancer: An immunohistochemical analysis. Course successfully completed by the candidate.

3. Involved as Co-Investigator in the extramural research project entitled, 'Immunogenetic profile of NPC– Nasopharygeal Cancer in a high prevalence region of northeast India', funded by Department of Biotechnology, Ministry of Science of Technology, Government of India.

4. Involved as Co-Investigator in the extramural research project entitled, 'Epigenetic studies in esophageal cancer in high risk region of north-east India' funded by Department of Biotechnology, Government of India, Ministry of Science of Technology.

5. Submitted application as a candidatureship for American Cancer Society for

Beginning Investigator (ACSBI), to Union for International Cancer Control (UICC) for the research proposal entitled, 'Designing and implementing community based breast cancer screening programme for early detection and prevention and downstaging in northern part of India.

6. Served as a resource person for the 'National Seminar on Scientific Writing', organized by Bakson Homoeopathic Medical College and Hospital, Greater Noida, sponsored by Commission for Scientific and Technical Terminology, Ministry of Human Resource Development, Government of India on 2nd March 2012.

7. Attended one-day workshop on 'Application of Next Generating Sequencing (NSG) in Medical Research (ICMR)', held jointly by National Institute of Pathology (ICMR) and ICMR at NIP on 28th February 2012.

8. Attended lecture on 'Application of algebraic statistics in statistical genetics' by Professor MB Rao, University of Cincinnati, USA at All India Institute of Medical Sciences (AIIMS) on 9th December 2011.

9. Served as Faculty for the World Health Organization (WHO)-sponsored Training Course for Technicians and Advanced level held at National Institute of Pathology (ICMR) from 24th November 2011 to 23rd December 2011 for the topic, 'Basic Biostatistics and Epidemiology'.

10. Served as faculty for the Foundation Workshop on Clinical and Laboratory Medicine Research, held at National Institute of Pathology (ICMR) from 26th-28th July 2011 and delivered talk on '*Statistical Softwares'.*

11. Contributed to the research methodology towards proposal development for the research project entitled 'Cholinergic and non-cholinergic toxicity in tea-garden workers due to organophosphate pesticide exposure during pregnancy and its correlation with expression of serotonin receptors, SERT and PON1', submitted to ICMR for extramural grant.

12. Contributed to the research methodology towards proposal development for the research project entitled, 'Study of genetic alterations in extracellular matrix related genes in Chronic Obstructive Pulmonary Disease (COPD)', submitted to ICMR for extramural grant.

# PDF SCHOLARS

## Dr. Anurupa Chakraborty

1. Attended Workshop on Basics of Cell Culture and Stem Cell Techniques, DBT MSUB- ILSPARE Vadodara, 28th February - 3rd March 2012.

# SCIENTIFIC ACTIVITIES BY Ph.D. STUDENTS

1. Ms. Regina Devi Thoudam presented poster in American Association of Cancer Research (AACR) International Conference on 'New Horizons in Cancer Research: Biology to Prevention to Therapy', 13th-16th December 2011, Gurgaon.

2. Mr. Sandeep Verma presented poster titled, *'Role of Parasite Surface Antigen-2 gene of Leishmania donovani in antimony resistance'* in 'International Conference of Human Infectious Disease and Immunity' held during 14th-15th October 2011 at Karunya University, Coimbatore.

3. Ms Arpita Kulshreshtha presented poster on *'Transcriptome profiling for identification and characterization of miltefosine resistance associated genes in Leishmania donovani'* at MICROCON-2011 conference organized by Indian association of Medical Microbiologists held at BHU, Varanasi from 23rd-26th November 2011.

4. Mr. Avishek Srivastava attended 'Basic Course training on Flow Cytometry' conducted by BD Biosciences, from 4th-6th April 2011 at Gurgaon.

5. Ms Nitu Kumari attended the Indian Proteomics Conference and Post-Conference Hands-on Workshop at JNU, New Delhi during 4th-9th April 2011.

6. Ms. Nitu Kumari attended the Bio-Plex User Advance Training on 10th August 2011 at Bio-Rad House, Gurgaon.

7. Ms. Asheema presented poster titled, *'Association between polymorphism of xenobiotic-metabolizing genes and the risk of acute leukemia'* at AACR's first conference in India 'New Horizons in Cancer Research: Biology to Prevention to Therapy' held at Gurgaon during 13th-16th December 2011.

8. Ms Namita Singh attended IPCON-2011 'The Indian Proteomics Conference' at JNU, New Delhi during 3rd-5th April 2011.

9. Ms Namita Singh participated in "Hands-on Workshop on Proteomics Techniques" at JNU, New Delhi during 6th-8th April 2011.

10. Ms Priya Prasad attended IPCON-2011 'The Indian Proteomics Conference' at JNU, New Delhi during 3rd-5th April 2011.

11. Ms Priya Prasad presented poster titled, *'Role of superoxide dismutases in spontaneous aborters infected with Chlamydia trachomatis'* at International Symposium on Molecular Pathology held in New Delhi during 28th-29th January 2012.

12. Mr. Praveen Kumar attended Indian Proteomic conference on "Trends in Translational Proteomics" organized by Proteomics Society (India) in collaboration with JNU, New Delhi during 3rd-5th April 2011.

13. Mr. Praveen Kumar attended hands-on workshop on 'Basic Molecular Biology Techniques Relevant to Cancer Research' at ICPO (ICMR), Noida during 8th -12th August 2011.

14. Mr. Praveen Kumar attended lecture entitled "Rheumatoid arthritis- The search for next generation therapies" by Dr. Anwar Murtaza (Senior Scientist III, Worcester, USA) at AIIMS, New Delhi on 3rd November 2011.

15. Mr. Praveen Kumar attended CME on 'Diagnosis of autoimmune disorders: The continuing dilemma' at GB Pant Hospital, New Delhi on 10th-11th December 2011.

# DNB/ Ph.D PROGRAMME

## DNB Programme

The Post-graduate Level Training Programme in the speciality of Pathology continued during 2011-12. During the year, the following four students who appeared for the DNB Exam held in 2011-12 have come out with flying colours:

1. **Dr. Sherry Khan**
2. **Dr. Ila Jain**
3. **Dr. Disha Arora**
4. **Dr. Manpreet Bhatia**

As per guidelines of the National Board of Examination, the Institute conducted Review Examinations of the DNB students in July 2011. **Dr. Rajiv Sen**, PGIMS, Rohtak, appointed as Inspector by NBE came as reviewer to NIP.

## Ph.D. Programme

- **Mr. Gajender Katara** submitted his Ph.D. thesis on *"Studies on host immuno-determinants modulated during active disease in kala-azar and post kala-azar dermal leishmaniasis"* in 2011.
- **Mr. Pradeep** submitted his thesis on *"Genetic alterations and multidrug resistant gene expression profile of acute leukemia"* in February 2012.
- **Ms Regina** submitted her thesis on *"Genetic analysis and gene expression profile of gastric cancers in high risk region of north-east India"* in March 2012.
- **Mr. Dhirender** submitted his thesis *"Genetic variations and gene expression profiling of oral cancer associated with tobacco correlation"* in March 2012.

During 2011-12, National Institute of Pathology further attracted young researchers-Research scholars with CSIR Junior Research Fellowships (1), and one woman scientist has joined the Institute during this period.

## OTHER ACADEMIC ACTIVITIES

As part of academic activities, the Institute organized journal clubs, slide seminars and seminars by various experts from both within and outside the country.


**NATIONAL INSTITUTE OF PATHOLOGY (ICMR)**

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