TUMOR BIOLOGY LABORATORY

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Post Doctoral Fellow Dr. Anurupa Chakroborty, Dr. Anand

Research Areas : **Tumor Biology** : Breast cancer, genitourinary cancer, hematologic malignancies, cancers in north east India, brain tumors

Collaborators : **Dr. NK Mohanty, Dr. A Bhatnagar, Dr. Chintamani, Dr. RS Mohil, Dr. S Saluja, Dr. V Ramesh,** Safdarjang Hospital, New Delhi

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Analysis of normal and malignant tissue by conventional candidate gene approach is gradually being replaced by high throughput technology. In tumor biology, we are using both conventional and advanced genomics technology to understand the molecular mechanism, including genetic changes as well as gene-environment interactions that may be responsible for the occurrence and progression of various tumors. In addition, our aim is to validate suitable candidate biomarkers that can be clinically useful to screen for early detection, for differential diagnosis, for risk stratification and for targeted individualized therapy of cancers.

Diagnostic and Referral Services:

The Tumor Biology laboratory offers services for confirmation of specialized tumor markers for diagnosis of cancer using immnuohistochemistry for breast cancer, prostate cancer, leukemia/lymphomas and undifferentiated cancer. In addition, services for markers that have prognostic value such as estrogen receptors, progesterone receptors, and Her2neu in breast cancer are also available. New antibodies such as AMACR, a specific marker for prostate cancer, Cerb, syndecar-1 for differentiating leukemias and lymphomas, TTF-1 for lung cancer, GCDFP-15 for breast cancer and skeletal muscle myosin to specifically identify rhabdomyosarcoma has recently been introduced.

Breast Cancer:

Genetic factors and molecular mechanisms that may be involved in early onset and locally advanced breast cancer are unknown. In our earlier studies, we found an insignificant contribution of the high penetrance genes BRCA1&2 as well as low penetrance genes (AR, VDR, Cyp17) to breast cancer susceptibility. Our focus is now on gene expression profiles and methylation profiles to understand the molecular mechanism underlying the disease in Indian breast cases patients and search for suitable biomarkers that may be used for early detection and prognosis. Ongoing studies include:

- Genetic variations in high penetrance genes and low penetrance genes in susceptibility to breast cancer
- Establishment of cells lines from early onset breast cancer patients
- Global gene expression and methylation profiles associated with early onset breast cancers
- Expression of Type 1 growth factor receptor family and Multidrug Resistance (MDR) genes in response to neoadjuvant chemotherapy in breast cancer

Prostate Cancer:

Prostate cancer is one of the ten leading sites of cancer in males in all the urban registries and constitutes about 4% of all cancers. Although the disease is initially hormone sensitive, it becomes hormone resistant with progression. The cause for this is unknown. Our goal is to determine the candidate genes responsible for susceptibility to develop prostate cancer and hormone resistance with disease progression. Ongoing studies include:

- Gene polymorphisms in DNA repair genes for analyzing susceptibility to prostate cancer
- Gene polymorphisms in androgen signaling and androgen-related genes analyze hormone sensitivity and resistance

Urinary Bladder Cancer:

Superficial bladder cancer is one of the most common urinogenital cancers and characterized by high recurrence rate. In our earlier studies, we have attempted to provide individualized therapy to patients by giving intravesical therapy based on *in-vitro* cytotoxicity to reduce the recurrence and provide disease-free survival. Ongoing studies include :

- Altered patterns of expression of various tumor suppressor genes and oncogenes to identify prognostic/predictive biomarkers that determine response of these therapeutic modalities and predict recurrence.
- Role of the host immune response in preventing recurrence.

Hematological Malignancies:

Although acute leukemia has a high remission rate, the disease frequently relapse. A search for biomarkers that can predict those cases that will not respond to induction chemotherapy or will relapse following complete remission has so far been unsuccessful. Our laboratory is focusing on identifying suitable markers that can predict response to induction therapy and to find suitable biomarkers for prognosis and targeted therapy. For this following work is being done:

- *In vitro* response to chemotherapeutic agents in acute leukemia- changes in cell cycle and apoptotic pathways
- Analysis of genes involved in NF-κB activation to determine if it can be used for targeted and individulazed therapy
- Expression of fusion oncoprotein such as BCR-ABL and FLT3 gene mutation in acute and chronic leukemia to determine their prognostic significance

Cancers in North-Eastern Region of India:

A high incidence of several cancers, particularly those associated with use of tobacco and pesticides have been reported for Northeastern (NE) region of India. Several risk factors such as peculiar food habits, life style, type and pattern of tobacco use and use of fermented betel nut may be involved. The role of genetic susceptibility and ethnicity in this region is unknown. Our goal is to establish link, if any between tobacco usage, exposure to pesticides and genetic susceptibility factors such as polymorphisms, mutations and gene expression changes associated with various cancers, Multicentric projects have been initiated with Institute of Pathology, New Delhi, Institute of Cytology and Preventive Oncology, Noida, Regional Medical Research Center, Dibrugarh, Assam, Dr. B Barooah Cancer Institute, Guwahati and six PBCRs of NE region (Aizawl, Gangtok, Guwahati, Silchar, Dibrugarh and Imphal) to analyze the role of gene environment interactions in this region of India. The ongoing studies include:

Tobacco Related Cancers: Oral, Esophageal, Gastric, Lung Cancers

- Gene polymorphisms in detoxifying enzymes, GSTs, CYP

- Analysis of microsatellite instability and copy number variation in tobacco-associated cancers
- Gene expression profiles associated with tobacco exposure related cancers in Northeastern India
- Gene expression profiles associated with familial predisposition to esophageal cancer in Northeastern India

Pesticide Exposure Related Cancers: Breast cancer and Lymphomas

- Genetic polymorphisms in detoxifying enzymes, GSTs, CYP genes in breast cancer
- Genetic variations in BRCA1 and BRCA2 genes in breast cancer
- Association of Bcl2/IgH translocation with occurrence of non Hodgkin's lymphoma.

Nasopharyngeal Cancers

- Immunogenetic profile of nasopharyngeal cancer

Projects Ongoing :

1. Study on Gene Expression and Hypermethylation Profiles in Early Onset Breast Cancer - **DBT**
2. Establishment and Characterisation of Cell Lines from Primary Breast Cancer - **ICMR**
3. Immunogenetic profile of Nasopharyngeal cancer- **DBT**
4. Characterization of host immune response in superficial bladder cancer by microarray- **ICMR**

Projects Completed:

International :

Genetics of Breast cancer in Indian population : **Indo-French Center For Promotion Of Advanced Research**

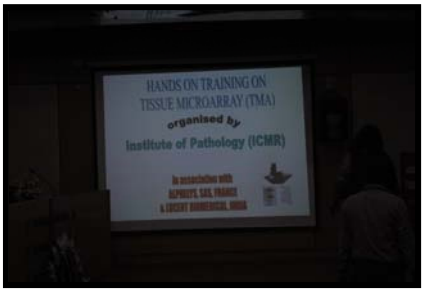
National:

1. Microsatellite instability in androgen receptor gene and p53 polymorphisms in prostate carcinoma in Indian males - **DST**
2. Cancer in north-east India -Understanding the role of tobacco - **ICMR**
3. Cancer in north-east India - Understanding the role of pesticides – **ICMR**
4. Flow cytometric assays to evaluate prognosis and patients response to chemotherapy in patients with acute leukaemia - **ICMR**

Scientific Activities ;

Workshops organized:

1. National Workshop on Microarray Technology, conducted by Institute of Pathology, Genomic Solutions Inc., USA and DSS Imagetech Pvt. Ltd., 16th –18th April 2007 at Institute of Pathology, New Delhi.
2. National workshop on "Hands-on Training on Tissue Microarray" conducted by Institute of Pathology in association with Alphelys, Sas, France & Lucent Biomedical, India, 8th – 9th June 2010.



Trainings Offered:

We offer short-term training in molecular biology techniques to young researchers and laboratory technicians in molecular diagnostic techniques.

Patient/Referral Services:

Breast Cancer: Predictive Biomarkers ER, PR, c-erbB2
Lymphomas/leukemia: IHC
Flow cytometry: AML, ALL