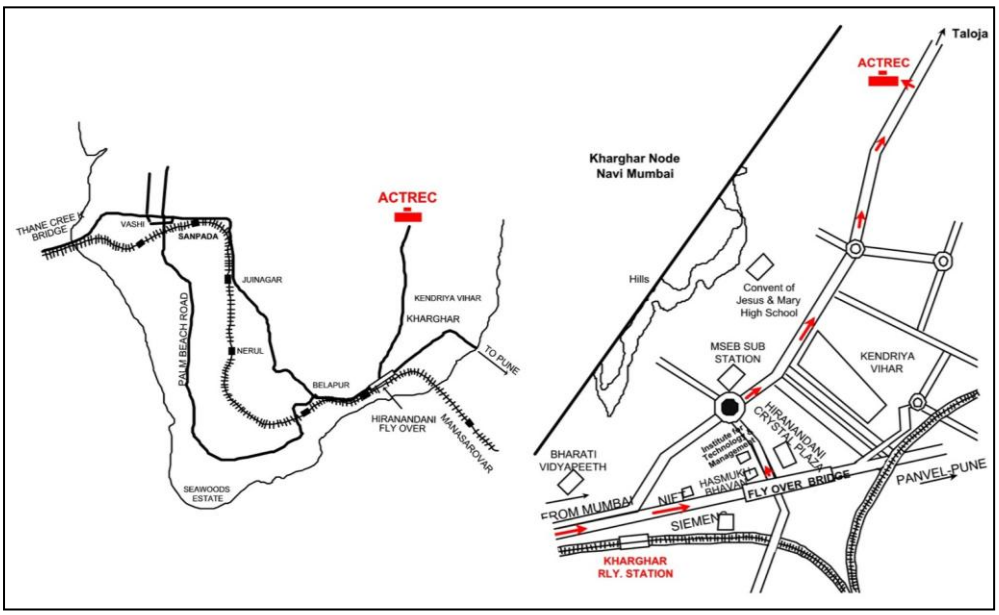
ACTREC OPEN DAY - 2011

ACTREC's 9th Open Day is scheduled to be held on Thu. 1st and Fri. 2nd December 2011.

Over this two day period, over 500 students accompanied by faculty members from around 34 science degree and medical colleges of Mumbai and Navi Mumbai will visit ACTREC. These visits have been finalized in consultation with the respective colleges. Please note that there will be no spot registration.

Posters on cancer awareness, prevention, research and treatment strategies will be on display in the entrance lobby of Khanolkar Shodhika. Following a welcome address in the lobby, batches of 12-15 students and their teachers will be taken on a tour of 10 different PI labs/ facilities/ departments of the basic and clinical research wings. In CRI, scientists and Ph.D. scholars will give poster-aided demonstrations of latest techniques and protocols used in biomedical research in cancer, *vis a vis* their on-going research projects. In the Clinical Research Centre (CRC), clinicians and technologists will demonstrate high end equipment and facilities used for cancer diagnosis and treatment.

Map & Directions to ACTREC



Demonstrations during Open Day - 2011		
1	Laboratory Animal Facility	Laboratory animals in cancer research
2	Small Animal Imaging Facility	*In vivo* imaging in cancer research
3	Sarin Lab	Polymerase chain reaction
4	Bhattacharyya Lab	Size and Shape Control Mechanism of Organelles
5	Maru Lab	Application of HPLC in carcinogenesis & chemoprevention studies
6	De Lab	Molecular functional imaging
7	Comm. Instr. Rm.	Instrumentation used in biological research
8	Ray Lab	Early diagnosis & cancer stem cell imaging
9	Radiation Oncology	Application of radiation in cancer treatment
10	Transfusion Medicine	Blood banking and transfusion in an oncology setup

1 Laboratory Animal Facility: Laboratory Animals in Cancer Research

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The main activity of the Laboratory Animal Facility (LAF) in ACTREC is to breed, maintain and supply quality rodents to in-house researchers. LAF maintains 21 different strains of mice - including transgenic, knock out, Nude and SCID, 1 rat strain, and 2 strains of hamsters for basic cancer research [http://www.actrec.gov.in/animal_main.htm]; majority are inbred strains. Standard operating procedures (SOPs) are followed in conducting all activities of LAF. Stringent programs for genetic monitoring, clinico-pathology, microbiology of laboratory rodents and animal feed are in place to ensure production of quality animals. In addition to the in-house testing, LAF, with its known expertise, provides quality control services for routine testing of biochemical markers and ELISA tests for rodent pathogens to other animal facilities in India. LAF also provides surplus animals of available strains to CPCSEA-registered animal facilities in India.

The Laboratory Animal Facility of ACTREC is an 'Associate Member' of the International Council for Laboratory Animal Science (ICLAS) since 2004. Recently ICLAS has granted recognition to LAF as a 'Training and Education Center'. LAF inducts summer and short term trainees under its on-going quality control program; these M.Sc./ M.V.Sc. students work on small projects for their Master's dissertation. LAF regularly organizes workshops with national and international faculty to keep laboratory animal professionals within the country abreast with latest developments and to disseminate new knowledge and skills to them. Since 2005, LAF has organized six workshops in ACTREC.

2 Small Animal Imaging Facility: *In vivo* Imaging in Cancer Research

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The process of discovering and bringing a new drug to clinical application is a multi stage process. The preclinical studies with animal models are performed at the beginning and are the most important to take these molecules to end stage. Over the last couple of years molecular and functional imaging has emerged as a powerful tool for studying spatial and temporal distribution of new drugs and their target affinity non-invasively. Several Imaging modalities such as Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Ultrasound, X-ray, Magnetic Resonance and Optical; have been developed for in-vivo imaging of animals. The ACTREC has PET/SPECT and CT modalities for preclinical imaging. The recent technological developments in PET and SPECT rose to digital advanced detector systems with high-resolution image outputs and accurate quantifications of various physiological and molecular events in the underlying diseases processes. In addition to this, the functional and molecular data is mapped on an anatomical platform (PET-CT / SPECT-CT), which adds a great value in precisely locating the micro lesions of the disease involved and understanding the pathophysiology in animal models. The deep seated lesions

can be seen more accurately using PET and SPECT. Besides animals can be imaged horizontally throughout the study design without sacrificing which reduces the number of animals significantly.

3 Sarin Lab: Polymerase Chain Reaction

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In 1993, Kary Mullis received the Nobel Prize for Chemistry for the invention of Polymerase Chain Reaction (PCR). In PCR, trace amounts of DNA can be quickly and repeatedly copied to produce a quantity sufficient to investigate using conventional laboratory methods. As the name implies, it is a chain reaction for amplification of template involving denaturation, annealing and extension.

The continuous doubling of DNA is accomplished by specific proteins known as DNA polymerases using the DNA building blocks, i.e. nucleotides - consisting of the four bases (dNTPs): adenine (A), thymine (T), cytosine (C) and guanine (G). The reaction also requires primers and DNA template.

Advantages of PCR:

1. Simple
2. Powerful Technique:
   - Sensitivity
   - Specificity
   - Reliability
3. Fast

Applications:

1. Molecular diagnosis, i.e. the diagnosis of diseases based on molecular findings rather than on physiological symptoms
2. Testing of infectious diseases
3. Cancer Detection : PCR can identify genes that have been implicated in the development of cancer
4. Forensic applications: Parental testing, and Genetic fingerprinting
5. Evolution: PCR has been used to establish relationships among species

During Open Day, Sarin lab will demonstrate the PCR procedure, Visualization and Data Interpretation.

4 Bhattacharyya Lab: Size and Shape Control Mechanism of Organelles

Dr. Dibyendu Bhattacharyya dbhattacharyya@actrec.gov.in

Bhattacharyya lab is engaged in research on fundamental cell biological problems of size and shape control mechanism of organelles. Intracellular intelligence' attributes to the advanced cellular capabilities that enable a single cell to sense and maintain very fundamental features (for example - number, polarity, size and shape) of intracellular objects ranging from macromolecules to organelles. Perturbations of such fundamental features are often associated with cancer and other diseases. Bhattacharyya lab is interested in studying the intracellular intelligent process that controls and maintains the size and shape of intracellular organelles, such as Golgi apparatus or nucleus. Using advanced state of the art microscopic methods, the lab is trying to understand these problems using yeast and mammalian model systems.

5 Maru Lab: Application of HPLC in Carcinogenesis & Chemoprevention Studies

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Carcinogenesis is multi-factorial, multi-step process and inhibition or slowing of any stage of carcinogenesis by other agent(s) can potentially prevent cancers from becoming clinically significant. Efforts to eliminate known human carcinogens from the environment and current cancer treatment approaches have met with limited success. A number of plant-derived antioxidants have shown anti-initiating and/or anti-promoting activities against diverse carcinogens in experimental systems. Epidemiological evidences show or suggest a good correlation between decrease in the incidence of and mortality from cancer in some organs and high consumption of green / leafy vegetable and fruits. Based on the experience with some infectious

diseases and recent progress in cardiology, prevention of diseases appears to be one of the attractive approaches.

The role of environmental agents in cancer causation and its modulation forms the main theme of the on-going research programs of this group, wherein projects are broadly grouped under: (a) Identification of exogenous and endogenous cancer risk factors and elucidation of their mechanisms of action – these encompass chemical analysis of tobacco/ tobacco smoke, exposure-related biomarkers in body fluids and biological effects using *in vitro* and *in vivo* assays, and (b) chemo-modulation of tobacco carcinogenesis – a sizeable effort is being directed towards identification, characterization and delineation of the mechanisms of chemopreventive action of plant-derived antioxidants and development of mechanism-based biomarkers and markers of drug-effect measurement.

High pressure liquid chromatography (HPLC) is one of the techniques that is employed for separation and measurements of biomolecules from mixtures. The configuration of the HPLC system and the qualitative and quantitative application in determination of curcumin an active ingredient from the spice turmeric in human plasma will be demonstrated.

6 De Lab: Molecular Functional Imaging

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Molecular imaging provides real-time visualization and quantitative measurement abilities of cellular processes at the molecular or genetic level. Functional imaging of cancer progression in experimental animal model is beneficial for translating basic research to the clinic. Our research involves miniaturized medical imaging equipments suitable for testing experimental concepts in small animal models, which can be directly translated into image-guided clinical applications to serve both cancer *diagnosis* and personalized *therapy*.

Our lab is aimed at understanding the basic biology of human sodium iodide symporter (hNIS) gene function in breast cancer. The goal of this project is to validate a hNIS based diagnostic PET imaging and targeted radioiodine therapy methods in breast cancer. We are developing experimental approaches using preclinical mouse model to predict how and up to what extent the endogenous hNIS protein expression in breast cancer can benefit PET imaging based diagnosis and radio-iodine therapy.

On another approach on imaging application to drug screening, we have developed an optimized image guided screening assay that can be used as one-stop solution in evaluating drug inhibitor effects in real-time from live cancer cells as well as from physiological animal model systems. To extract the real value of this assay in cancer research, we are pursuing design of different biosensors to assess functional changes of important cancer targeted proteins.

Demonstration on recent scientific data from the lab with respect to the above projects will be presented to the open day visitors.

7 Common Instrument Room: Instrumentation used in Biological Research

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ACTREC maintains centralized Common Instrument Rooms (CIR) in order to optimize the utilization of all major scientific instruments, and to make them available to all the staff and students of the centre. Equipment such as spectrophotometers, high speed and ultracentrifuges, HPLC, radioactivity counter, gel documentation systems, etc., are available for use around the clock on all the days, including on holidays. A team of qualified technical staff members attached to the CIR handle routine maintenance and render help to the users, thus ensuring proper usage of the equipment. With a view to reduce breakdown and consequent down time of the instruments, spares for centrifuges, CO_2 incubators, freezers, gel documentation system, etc. are procured regularly. During Open Day-2011, the following equipment having wide utility in biological research – both for general use and for specific applications/ assays, will be demonstrated to the visiting students: (1) Thermal cycler, (2) Gel documentation system, (3) Dual beam spectrophotometer, (4) Microplate absorbance reader, (5) High speed centrifuges, (6) Preparative ultracentrifuge, and (7) Sonicator.

8 Ray Lab: Early Diagnosis & Cancer Stem Cell Imaging

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In spite of incredible progress in biomedical sciences, cancer is still a challenge to clinicians due to molecular complexity and heterogeneity. Two major clinical hurdles of 21st century are to detect carcinogenesis at an early stage and prevail over the drug or radio resistance of the tumor cells. Molecular imaging is the method of visualization, characterization and measurement of biological processes at the molecular and cellular levels in humans and other living systems. The greatest advantage of non-invasive molecular imaging techniques over conventional molecular and biochemical procedures is that it enables time-resolved data acquisition of cellular events from living subjects. All these techniques have numerous potentialities of diagnosing diseases at early stages, monitoring therapies, identifying novel interactions between biological molecules and visualization of molecular processes repeatedly and non-invasively from living subjects.

Our group is interested in early diagnosis of acquired chemoresistance in ovarian carcinoma using the conventional molecular and biochemical methods and the contemporary molecular imaging techniques. Ovarian cancer could be successfully cured if detected early or overcome the drug resistance. Unfortunately, still in India and rest of the world, ovarian cancer is the fourth leading cause of cancer death amongst women. By establishing dynamic models of chemoresistance in ovarian cancer cells, we are trying to identify the early molecular changes in cell death, cell survival and drug resistance pathways. We are also actively investigating the role and association of Cancer Stem Cells in acquirement of chemo resistance. Our other interests are to evaluate new molecules for therapeutic intervention of ovarian cancer. An all-inclusive approach to identify early molecular alteration of acquired chemoresistance in ovarian carcinoma from live cells to live animals will be discussed.

9 Dept of Radiation Oncology: Application of Radiation in Cancer Treatment

Dr. Tejpal Gupta & Dr. Jayant Sastri Goda jgoda@actrec.gov.in

Radiation therapy uses high energy ionizing radiation for the treatment of cancerous tumor because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of exposed tissue. Radiation therapy can be given by teletherapy also called external beam radiotherapy or by brachytherapy in which radioactive sources are kept close to the tumor or inside the tumor tissue.

The field of radiation therapy traces its earliest roots 100 years back with the discovery of x-rays by Wilhelm Rontgen in 1895. However, its medical use began to grow in the early 1900's after the ground breaking discovery of polonium and radium by Marie Curie. For the next 50 years, radium was the only radioactive substance used for medical radiation therapy. However, in the early 1950's, cobalt units came into existence and replaced radium. In the late 1950's, medical linear accelerators generating high energy x-rays were introduced to treat deep seated tumors inside the body.

Although the cobalt machines still form the workhorse of a radiotherapy department, continuous innovations in field of imaging and delivery of radiation therapy has allowed us to treat tumors located at complex locations using 3D conformal therapy and intensity modulated radiotherapy (IMRT) with the help of image guidance (IGRT).These advances allow us to see and target tumors in a better way, resulting in better treatment outcomes and fewer side effects.

The Department of Radiation Oncology at ACTREC is a tertiary care referral centre which endeavors to exploit these technological innovations to deliver the most advanced forms of radiation treatments to its cancer patients. These include 3DCRT, IMRT, IGRT, Stereotactic Radiotherapy (SRT), Stereotactic Radiosurgery (SRS), etc.

10 Dept of Transfusion Medicine: Blood Banking and Transfusion in an Oncology Setup

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The department of Transfusion Medicine (DTM) at ACTREC with its doctrine of vein to vein concept (donor to patient) provides services of blood collection from voluntary donors, processing the collected blood into components, testing, storage and issue prior to administration of blood to patient. DTM also provides specialized services like plateletpheresis, peripheral blood stem cell (PBSC) and granulocyte harvest. Special attention is given to the quality and sterility of blood and blood components that are supplied to patients admitted not only at ACTREC but also at other hospitals and nursing homes. To provide additional safety, bacterial screening of packed red cells and platelets by eBDS has been introduced. Currently this facility is provided to all bone marrow transplant patients. DTM also meets the requirements for specialized blood products such as leucoreduced, gamma irradiated cellular components and single donor platelets for treating transplant patients. DTM has successfully met the rising demands for blood and blood components by conducting regular blood donation camps and maintaining a voluntary blood and platelet pool. The department has the following sections: Area for Blood Donation and Apheresis, Area for Medical & Physical Examination and Donor Counselling, Red Cell Serology (RCS) laboratory, Transfusion Transmitted Infections testing laboratory, Blood Component laboratory, and Quality Control laboratory. DTM has three cell separators [apheresis devices - Comtec (Fresenius), Amicus (Baxter) and Cobe Spectra (Gambro)] that enable plateletpheresis, PBSC harvest as well as therapeutic apheresis procedures to be performed here. A blood irradiator (BI – 2000) is used for gamma irradiation of all cellular blood components issued to medical oncology patients. In the RCS laboratory, besides routine blood grouping and cross matching, all immunohematological workups like Coombs test, antibody screening, antibody titration, transfusion reaction workup, etc is performed. ELISA is used for testing of all blood units. Eighty percent of all units are made into components. One percent of all blood and blood components are routinely tested for quality. The issue of blood and blood products is conducted routinely round the clock.