

The Cancer Research Institute (CRI) - then located at the Tata Memorial Centre's Parel, Mumbai campus, organized its first 'Open Day' to showcase its research programs before the undergraduate and graduate students from science colleges of Mumbai in 1995. This tradition is continued uninterrupted and with the same vim and vigor even after CRI moved to the newly established Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) in Kharghar, Navi Mumbai, in 2002. CRI and the Clinical Research Centre (CRC - established in 2005) actively participate in ACTREC's Open Day.

This year, ACTREC is organizing its Open Day on 1st and 2nd of December 2022 to showcase its facilities to the invited group of students and accompanying faculties from science, pharmacy, medical and allied colleges of Mumbai and Navi Mumbai. During these two days (four sessions of half-day each) over 500 students are expected to visit the Centre. Each session will begin with a poster display on cancer research, various diagnosis and treatment modalities and prevention of cancer, followed by an introductory talk about ACTREC highlighting the Center's research, clinical and academic programs.

After the introductory talk, visit to eight laboratories to witness the live research experiments and observe high-end equipment and their importance in cancer research will start. The volunteers will lead each batch of 15 students and their faculties to the demonstrating research labs. Each demonstration will focus on the technological platform used to further cancer research or clinical research programs. The students will get an opportunity to see cutting-edge research and a chance to interact with scientists, clinicians, and research scholars.

Demonstrations for Open Day 2022

| No. | Demonstration Labs | Title of Demonstration |
|-----|--------------------------------|--|
| 1 | Academics (ACTREC students) | Academics @ ACTREC by Students Council of ACTREC |
| 2 | Composite Lab (PS) | Serum protein electrophoresis |
| 3 | Lab Animal Facility | Laboratory Animal Models for Cancer Research |
| 4 | Macromolecular Crystallography | Protein Structure for Drug Discovery |
| 5 | Microbiology Dept (PS) | Clinical utility of advanced cross-sectional imaging (MRI) |
| 6 | Nandini Lab | Use of 3D Spheroids assays in cancer research |
| 7 | Rukmini Lab | Multi-OMICS approach to identify alternate therapeutic targets in drug-resistant CML |
| 8 | Sanger sequencing | Demonstration of DNA Sequencing by Sanger's chain termination method on an automated sequencer (capillary electrophoresis) |
| 9 | Small Animal Imaging Facility | Comparative Oncology Program and Small Animal Imaging Facility |

Demo: Academics @ ACTREC Students Council of ACTREC

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This year, on the occasion of ACTREC's Open Day, the Students Council of ACTREC (SCA) has taken the initiative to hold an informal discussion with the visiting groups of young students who may be interested in pursuing their careers in research or academics. During this session, representatives of SCA will share their experience on cancer research at ACTREC from a student's perspective. There will be an open discussion in which students will be informed about different career options available after graduation/ post-graduation. And various competitive exams whih help students to get entry into the Ph.D. programs at ACTREC and other science institutes across India. The session will cover the following:

<u>Training program at ACTREC</u>: Students will be informed how 6 weeks summer training in the College break during undergraduate studies or 3-6 months research training after graduation/ post-graduation will help them to decide whether a research career is suitable.

<u>Openings after graduation (B.Sc. / B.Tech.)</u>: Various Masters's degree programs offered and available at different universities across India will be briefed. Major competitive exams for which students after their graduation can appear for exams to pursue their research career in the domains of Biological Sciences, Biotechnology, Biochemistry, Life Sciences, Microbiology and others, including the institutes which are offering Masters by research will be briefed.

<u>Openings after post-graduation (M.Sc. / M.Tech.)</u>: National-level competitive and entrance exams to pursue research, lectureship and fellowships such as NET/SET, JGEEBILS, CSIR-UGC, DBT, ICMR, BARC-DAE (OCES/DGFS), TIFR for getting enrolled into the Ph.D. programs will be briefed.

<u>Openings after Ph.D.</u>: The session will briefly touch upon the post-doctoral programs available in India and abroad, along with openings in academia or R&D in Pharma and other industries.

Demo: Composite Lab - Serum protein electrophoresis Dr. Preeti Chavan, Office-In-Charge, Composite Lab, CRC, ACTREC E-mail: pchavan@actrec.gov.in

Composite Laboratory is the central diagnostic laboratory of ACTREC-TMC and processes samples for routine hematology, clinical chemistry including immunoassay tests and emergency laboratory services. For the demonstration purpose, we will be displaying the functioning of an equipment called Serum Protein electrophoresis.

The HYDRAGEL 7 PROTEIN(E) gels are intended for separation of human serum proteins in human serum and urine by electrophoresis on alkaline buffered (pH 9.1) agarose gels. By design, the normal human serum proteins separate into five major fractions. The kits are used in conjunction with the SEBIA semi-automated HYDRASYS 2 Scan instrument. When proteins migrate in an electrical field, the extent of their migration and the degree of the resolution of each band depend on several factors. Two key factors that affect the migration of any protein are its pI (iso electric pH) and the pH of the buffer. The pI of any given protein is constant and dependent on its amino acid and carbohydrate content. However, the charge that the protein expresses is determined by the pH of the solution in which it is dissolved. The buffer of pH 9.2 (commonly barbital or Trisbarbital buffer) is used at which most of proteins are negatively charged and move toward the anode at a rate dependent on their net charge.

Protein electrophoresis is a well-established technique routinely used in clinical laboratories for screening of serum and some other fluids for protein abnormalities. Serum protein electrophoresis is a simple technique that is helpful in establishing a diagnosis of monoclonal gammopathies, liver cirrhosis, renal failure, hypogammaglobulinemia, and so on. Monoclonal gammopathies are due to the clonal synthesis of a unique immunoglobulin and give rise to a sharp gamma globulin band. (M band)

Demo: Laboratory Animal Models for Cancer Research

Dr. Arvind Ingle, Officer-in-Charge, Laboratory Animal Facility, ACTREC Email: <u>aingle@actrec.gov.in</u>

ACTREC has Laboratory Animal Facility (LAF) to breed, maintain and supply quality rodents for its basic cancer research programs. Available animals encompass 10 basic strains of mice, 1 hybrid strain (B6D2F1) of mice, 10 transgenic mice, 11 knockout mice, and 29 crosses of Tg and knockout mice, one each Nude, SCID and NSG mice strains; 1 strain of rat; and 1 strain of hamster, majority of which are inbred [https://actrec.gov.in/index.php/cri-research-support-facility-detail/70]. Standard operating procedures are followed for all the activities of LAF, and stringent programs are in place for genetic monitoring, clinico-pathology, and assessment of microbiological status of laboratory rodents and animal feed. An embryo freezing program has been introduced for the animal strains maintained at ACTREC. LAF offers quality control services to outside facilities and provides surplus animal strains to the CPCSEA-registered animal facilities in India. The facility is an "Institutional Member" and recognized "Training and Education Center" of the International Council for Laboratory Animal Science (ICLAS), Brussels, Belgium. Since 2005, LAF has organized eight workshops and two certificate courses for laboratory animal professionals. It also accepts M.Sc./ M.V.Sc./ MTech students as dissertation trainees under its on-going quality control program. The LAF demonstration during Open Day 2022 will introduce some of the representative animal models maintained in the Laboratory Animal Facility of ACTREC, their characteristics, and usage for the biomedical/ cancer research. The demonstrators will also detail the numbering system, environment, food and water requirements, and housing enclosure conditions for different animal models.

Demo: Macromolecular Crystallography - Protein Structure for Drug Discovery

Dr. Ashok Varma, Principal Investigator and Officer-In-Charge, Macromolecular Crystallography & X-ray Diffraction Facility, CRI, ACTREC Email: avarma@actrec.gov.in

X-ray Crystallography enables the scientist to determine precise position of each atoms and molecules present in crystallized materials. Macromolecular crystallization and X-Ray Diffraction facility has been installed and commissioned at ACTREC in 2012. This facility also has the remote access to synchrotron facility located across the world. Facility helps scientists, research scholars in protein crystallization, structure determination and refinement. Different groups from ACTREC and nearby institutions collect the X-ray diffraction from the facility. The dedicated facility has (a) Crystallization unit, (b) Microscope to visualize the crystals, (c) Microstar -Microfocus Rotating Anode and (d) Integrated computer controller motorized Image Plate detector and (e) computers to process the data and determine the crystal structure of proteins. The ACTREC facility also provides hands-on training to different university/colleges faculty and assist them to understand the structure of biological molecules.

Demo: Microbiology Lab - Clinical utility of advanced cross-sectional imaging (MRI) Dr. Vivek Bhat, Office-In-Charge, Microbiology lab, CRC, ACTREC. E-mail: <u>vbhat@actrec.gov.in</u>

The Microbiology Laboratory is the central infectious disease diagnostic laboratory of ACTREC-TMC and processes samples for routine Bacteriology, Serology, Clinical Microbiology and Mycology laboratory services.

For demonstration purpose, we will be displaying the functioning of automated blood culture system called BacT/ALERT® 3D. The BacT/ALERT® 3D provides an optimal environment for the recovery of a wide range of pathological organisms including bacteria, yeasts and mycobacteria. Bottles are tracked by the computer and must be loaded using the computer and barcode. If microorganisms are present in the test sample, carbon dioxide is produced as the organisms metabolize the substrates in the culture medium. When growth of the microorganisms produces CO2, the color of the sensor in the bottom of the bottle changes from green to yellow. Each bottle contains a carbon dioxide sensor that is monitored continuously using solid-state reflectometers. This information is transmitted to a computer where it is compared to the initial CO2 level in the bottle. If there has been a sustained acceleration in the rate of CO2 production, high initial CO2 content and/or unusually high rate of CO2 production, the sample is determined to be positive. If after a specified number of days the CO2 level does not change significantly, the sample is determined to be negative.

Demo: Nandini Lab - Use of 3D Spheroids assays in cancer research.

Dr. Nandini Verma, Principal Investigator, Nandini Lab (KS-231), CRI, TMC-ACTREC E-mail: nverma@actrec.gov.in

The complex nature and behavior of cancer cells present inside a tumor in patients makes them extremely complicated to study due to unavailability of model systems that can mimic tumours in vitro. In recent years, a multicellular tumor spheroid (MCTS) model has become a commonly adopted method in cancer biology. MCTS models provide an accurate representation of the physiology of tumors and are gradually making a significant contribution to our understanding of cancer biology.3D multicellular tumor spheroid (MCTS) as a useful model to study cancer biology.

Spheroids have several structural, functional and physiological similarities to tumors in vivo. Both are made up of heterogeneous cells and have similar secretory and metabolic activity. MCTS models generally use spheroids between 200–500 μ m and are grown in a 3D culture as opposed to a monolayer.

This 3D system exposes cells, enabling them to communicate with each other as well as their surroundings, providing an optimal environment for the cells to respond like they would in a tumor. Within such a representative environment, having cell to cell contacts, 3D architecture, spheroids are able to express chemical gradients of various nutrients, oxygen & catabolites found in a tumor – something that can assist in understanding tumor growth, drug response & resistance.

One of the most defining features of a tumor is its hypoxic core, and this is also replicated in spheroids. As the tumor grows, the cells will often run out of adequate blood supply, leaving the center of the tumor with a very low oxygen and nutrient concentration. These oxygen starved cells grow very slowly, are acidic and tend to be resistant to therapy. Many researchers believe that this hypoxic core is the culprit behind the failure of cancer drugs and treatments to date.

Benefits of 3D cancer models

3D tumor models are extensively used as systems for studying various types of solid cancers such as breast, colon, lung, pancreatic, cervical, and prostate. These systems can be derived from already established cancer cell lines. Sometimes it is also possible to expand these 3D cell cultures directly from patient tumor cells or excised biopsies offers tremendous advantages, these are called organoids or tumoroids. These tumoroids may have the potential to function as mediators for 2D culturing models and also for developing in vivo tissue xenografts.

Tumor spheroids are able to meticulously reproduce the core properties of solid human tumors. They can induce micro-metastasis formation and have the potential to display cancer-like microenvironment features e.g., cell-cell, cell-ECM exchanges, local nutrients transportation, gases, and growth factors. Therefore, these models give a great opportunity to ask experimental biology questions that will have more physiologically relevant answers in cancer biology.

Demo: Rukmini Lab - Multi-OMICS approach to identify alternate therapeutic targets in drug resistant CML

Dr. Rukmini Govekar, Principal Investigator, Rukmini Lab, CRI, ACTREC E-mail: <u>rgovekar@actrec.gov.in</u>

Identification of global molecular alterations has proved to be useful in identification pathways involved in normal cell physiology and pathology. In our studies, we have used this approach to identify alternate therapeutic targets for cases of chronic myeloid leukemia (CML) resistant to the existing targeted therapy that uses tyrosine kinase inhibitors (TKIs) such as imatinib. CML is associated with recurrent reciprocal chromosomal translocation between chromosome 9 and chromosome 22 [t9;22 (q34;q11)] with a resultant fusion gene BCR/ABL which encodes a constitutively active tyrosine kinase. Inhibition of kinase activity of Bcr/Abl with imatinib is the most successful therapy for CML. However, patients in advanced stages of CML - termed blast crisis (BC), are known to show resistance to treatment with imatinib. Our research projects are aimed at identifying alternate or supplementary therapeutic targets for CML-BC using multi-'OMICS' analysis of representative cell lines (viz. K562) as well as CD34+ cells from CML patients. Integration of genomics and proteomics approach has allowed for identification of the mechanism of imatinib resistance in CML-BC.

Demo: Sanger Sequencing - Demonstration of DNA Sequencing by Sanger's chain termination method on automated sequencer (capillary electrophoresis)

Dr. Pradnya Kowtal, CRI, TMC-ACTREC

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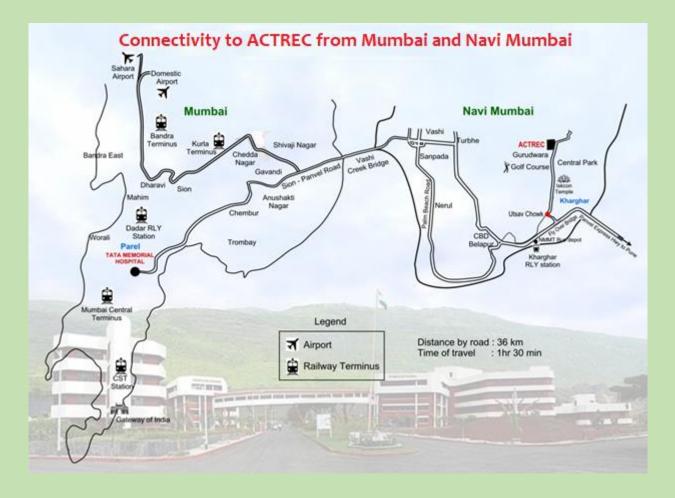
The chain termination sequencing method for DNA sequencing is based on the principle of addition of nucleotides to a primer by DNA polymerase to synthesize a DNA strand complementary to the template. Dideoxynucleotides (ddNTP) are nucleotides that lack a 3' hydroxyl group –OH that is required to form a phosphodiester bond to add nucleotides to the growing chain. The DNA chain terminates whenever a ddNTP is incorporated. The automated DNA sequencers use ddNTPs tagged with fluorescent dyes which are detected by a laser and an output as a chromatogram is seen. The primary sequence obtained from the chromatogram is compared with a normal or reference sequence to detect any changes/variations/mutations in the DNA sequencers from Thermofisher. During the Open Day, setting up of sequencing reactions, data viewing and analysis will be demonstrated. The analysis will include detection of variants / mutations.

Demo: Small Animal Imaging Facility - Comparative Oncology Program and Small Animal Imaging Facility

Dr. Pradip Chaudhari, Scientific Officer G, CRI, ACTREC E-mail: <u>pchaudhari@actrec.gov.in</u>

Preclinical research is the backbone of modern medicine and new drug discoveries. The use of small-animal models in basic and preclinical sciences is a major keystone for these kinds of research and development strategies, representing a bridge between discoveries at the molecular level and clinical implementation in diagnostics and/or therapeutics. The high-resolution in vivo imaging technologies provide a unique opportunity for studying diseases in real-time, quantitatively, at the molecular level non-invasively. ACTREC has got state-of-art imaging facility having PET (positron emission tomography [PET] and SPECT (single photon emission computed tomography) and ultrasound. Each modality has intrinsic advantages and limitations. The focus of the facility is on preclinical animal imaging and research on radiopharmaceuticals. Diagnostic radionuclides such as technetium-99m and fluorine-18 complexes are being evaluated for their utility in imaging and monitoring cancer in various mouse xenograft and orthotopic models.

In the arena of the Comparative Oncology Program - Animal Cancer Care Centre (Kukkuripa) provides diagnosis and treatment of pet animals suffering from spontaneous cancer. Also, it examines comparative aspects of animal and human cancers. The animal cancer biorepository maintains biological specimens such as blood, fresh-frozen or formalin-fixed or formalin-fixed paraffin-embedded tissues collected during diagnosis/ treatment, and uses it for comparative oncology research.



Trains on Harbour Line ply between Mumbai CST and Panvel stations. Nearest stations to reach ACTREC are Kharghar or CBD Belapur.

NMMT bus routes from Kharghar: 45 and 54; from CBD Belapur: 52 and 55

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