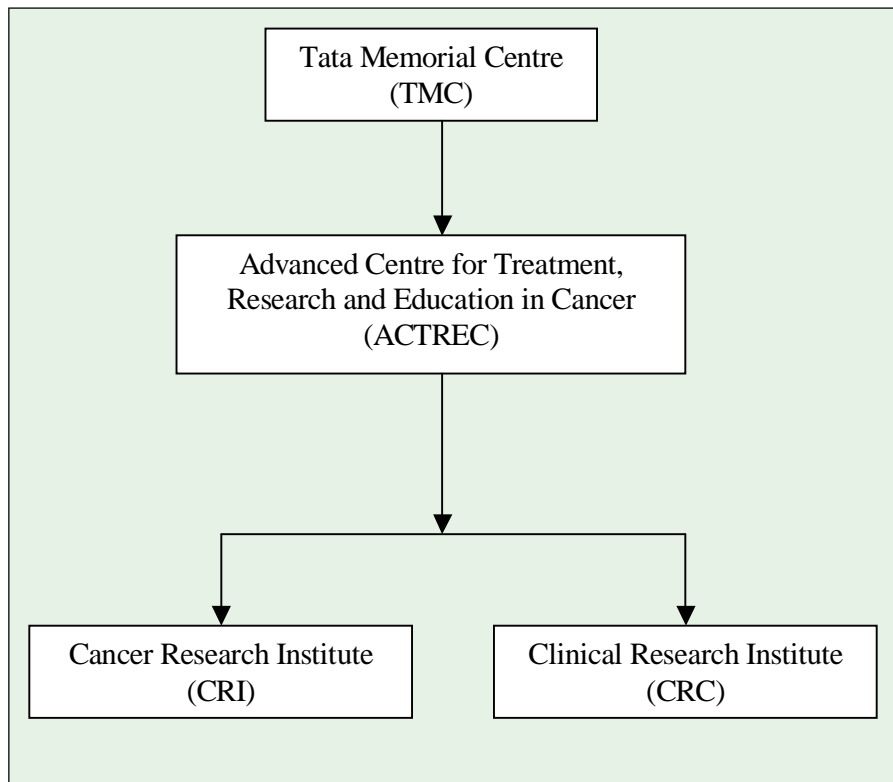


# Advanced Centre for Treatment, Research and Education in Cancer (ACTREC)

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The Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) - as it is called today - was originally established in 1952 as the Indian Cancer Research Centre (ICRC) and re-christened Cancer Research Institute (CRI) in 1966. ICRC was the brainchild of Dr. V.R. Khanolkar, then Director of Pathology and Biochemistry Laboratories, Tata Memorial Hospital (TMH). ICRC was set up under the purview of the Ministry of Health, Government of India. In 1966, CRI was amalgamated with the Tata Memorial Hospital (TMH), creating the first comprehensive cancer centre in India - Tata Memorial Centre (TMC), a grant-in-aid institution of the Department of Atomic Energy (DAE). ICRC and its alter-ego CRI were the flagships of biomedical



*ACTREC campus at Kharghar, Navi Mumbai*

research in independent India, serving as cradles for several institutions that emerged from them - Biomedical Division of BARC, Institute of Immunohaematology and National Institute for Research in Reproductive Health.

In subsequent decades, a succession of eminent scientists led the institute and guided its activities, bringing it to its present stature – where it is recognised worldwide as a premier institute for research on Cancer. In an era that brought in a revolution in biology, the institute's research programmes turned from the cellular to the molecular level. As the institute grew, gross inadequacy of space was felt at the Parel campus leading to the idea of seeking a larger campus. ACTREC was first envisaged over a decade ago, and was nurtured by successive directors of TMC.

In 2001, the Cancer Research Institute, moved to Navi Mumbai to become the basic research wing of the Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), and started functioning from its new premises from August 19, 2002.

ACTREC comprises two wings: a basic research wing - CRI and a clinical research wing – CRC.

Research at CRI is broadly grouped under the following areas: Biochemistry & Cell Biology, Chemical Carcinogenesis, Chemotherapy, Genetic Engineering,

Immunology, Neuro-oncology, Tobacco Carcinogenesis and Virology. On-going research studies at the Centre focus on human cancers relevant to the Indian subcontinent, and address basic research queries using animal models and cells in tissue culture.

**Oral Cancer:** This cancer represents about 30% of cancers in the country and is associated with chewing of tobacco and pan masala/gutkha. On-going investigations on oral cancer have included study of alterations in oncogenes and tumour suppressor genes, analysis of gains and losses of chromosomes, gene and protein expression, gene alterations in DNA repair/xenobiotic metabolizing enzymes, role of intermediate filament proteins in epithelial cell transformation, presence of novel HPV (human papilloma virus), molecular mechanisms in immune surveillance, and development of single chain antibodies against tumour antigens.

Animal studies show that gutkha has tumour promoting/progressor activity suggesting that gutkha consumption poses carcinogenic risk to chronic habitués.

Studies on tobacco-mediated carcinogenesis have encompassed chemical analysis, examination of the bioactivity of various tobacco products, transplacental carcinogenesis and biomonitoring of habitués and bidi workers.

Data from studies providing a sequence of genetic events leading from leukoplakia to frank cancer have led to a multi-institutional study of specific molecular markers, which can predict the onset/prognosis of oral cancer.

ACTREC is a partner in the global analysis of genes and proteins along with five leading national institutions, thus contributing to CSIR's new Millennium Indian Leadership Technology Initiative (NMITLI).

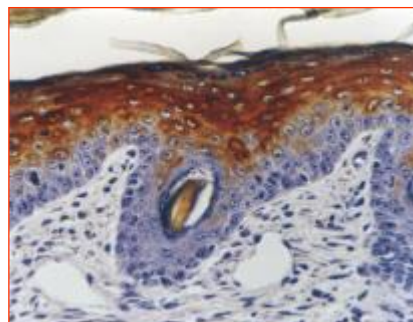
A xenograft model of human oral cancer has also been developed in nude mice for studies on gene therapy. The Centre has also initiated a programme to use a 'suicide gene' to kill oral cancer cells.

**Breast Cancer:** Studies have investigated the importance of human leukocyte antigen (HLA) in breast cancer predisposition in ethnic groups such as Parsis and Maharashtrians, and its relation to age at onset of the disease, since ~5% of breast cancer patients show an early onset familial pattern. Specific genetic alterations and weakened immune responses have also been identified as potential markers for the identification of individuals with a high risk for breast cancer. Epigenetic mechanisms regulating genes involved in cell proliferation have also received attention.

**Other Cancers:** On-going investigations include analysis of cytokine profiles, role of antibodies to viral E6 and E7 proteins and Human Papilloma Virus analysis in **cervical cancer**, cytokine imbalance in **lung cancer**, significance of T-cell repertoire in **T-ALL**, and urinary cytokines in intravesical BCG therapy of superficial **bladder cancer**. The role of HPV in **esophageal cancer** and HHV6 in **lymphoproliferative disorders** is also under investigation,



*Pre-clinical Studies for Gene Therapy of Oral Cancer using a Xenograft Nude Mouse Model of Squamous Cell Carcinoma of Pyriform Fossa and HSV/tk-GCV Strategy*



*Transgenic mice generated by injecting pK14-EF into single cell embryos.*

while studies in **liver cancer** assess the utility of viral mRNA for HBx gene and circulating antibodies towards HBx protein as markers of chronic hepatitis B virus infection.

The Centre was the first to develop transgenic mice. Further studies have revealed that this mouse model, carrying a gene for a growth factor modulator, can serve as a good animal model for squamous cell carcinoma.

Chemoprevention studies have shown that the dietary constituent 'haldi' and its active component curcumin have chemopreventive effect. Interesting leads are expected for the prevention of cancer with the components of tea and grapes.

Studies using cultured cells address queries about chromatin structure, signal transduction pathways, molecules and intermolecular interactions mediating

cell proliferation, cell death and functional differentiation - many of which are altered during cellular transformation. A national facility for screening anticancer drugs using a panel of human malignant cell lines has recently been established at ACTREC. This facility also undertakes in vivo drug testing using murine tumours and human tumour xenografts in nude mice.

Other studies involve cultivation of Indian isolates of HIV-1 and HIV-2, and in-depth study of HIV-2 biology with a view to develop an indigenous retroviral vector for gene transfer. An indigenous sero-diagnostic Western blot kit for HIV-1 and HIV-2 has been developed with support from Department of Biotechnology (DBT) and a private party.



## Patents

- I An alternate method for synthesis of methotrexate
- I Isolation of topoisomerase inhibitor podophyllotoxin
- I A 2kb-nucleotide sequence specific for the early detection of oral cancer.

## Education

Young researchers who have just completed Ph.D./M.D. and are interested in pursuing a career in Cancer Research are inducted into ACTREC as Research Associates .

The Centre is recognised by the University of Mumbai for the M.Sc. and Ph.D. degrees. At present, 15 scientists of CRI are recognised guides for Ph.D. in Applied Biology / Biochemistry, and 45 students are registered for the PhD degree. Affiliation to the University of Mumbai allows scientists of the Centre to participate in teaching activities, by delivering lectures in their area of specialisation at degree colleges/departments of the University.

Each year, over a 2-month period during their summer break, ~20 M.Sc/ M.B.B.S. students undertake short projects supervised by mid-level/senior scientists of ACTREC. The trainees learn a specific basic technique used in cancer research, use it to answer a small scientific query and present their results in a project report, which earns them points that are added to their overall percentage by their college. This programme has helped create in the minds of bright youngsters an awareness of cutting-edge research, attracting them towards cancer research as a full time career.

Once a year, ACTREC holds an Open House where students and professors of colleges affiliated to

Mumbai University visit the Centre. After an introductory lecture on the thrust research areas at ACTREC, they are taken to different departments/facilities where scientists from each group demonstrate latest techniques used in Cancer Research. This activity has helped focus the attention of youth on research in general as well as cancer research programs and career opportunities available at the Centre.

### **Future Challenges**

ACTREC has been established as a specialised centre for frontline basic and clinical research in cancer to meet the challenges of the new millennium. Basic research at CRI will henceforth focus on genomics, proteomics, bioinformatics, gene therapy, vector development, molecular immunology, immunotherapy/immunodiagnosics, targeted drug development, molecular carcinogenesis, chemoprevention, signal transduction and glycobiology.

CRC will specialise in pediatric oncology and cancer genetics. Being fully equipped with a 50 bed-hospital, phase I/II clinical trials of new anti-cancer drugs developed nationally/internationally will be carried out; this will also cover emerging areas of single chain monoclonal antibodies and gene therapy. Molecular Pathology and Pharmacokinetics will also receive attention. An important focus of ACTREC will be the application of cutting-edge technologies to address the problem of cancers relevant to our country and, where there are internationally competitive opportunities, the use state-of-the-art technology in joint partnership with industry and leading institutions in India and abroad. Another important mandate of ACTREC will be to conduct educational programs and undertake human resource development in different disciplines of oncology.

## **Accreditation of Laboratory For Personnel Monitoring Of Radiation Workers Using Thermoluminescence Dosimeter (TLD)**

Indigenous development of TLD devices at BARC has provided a simple and accurate technique for country wide personnel monitoring service for radiation workers incurring exposure to X, Gamma and Beta radiation. This service is in use at BARC for more than twenty-five years. Two accredited laboratories performing similar service are already operational. The equipment needed for monitoring are developed indigenously and are commercially available. As the monitoring service is economically viable and could be carried out by competent agencies other than BARC, it was decided to grant accreditation to interested agencies/institutions/ such as radiation therapy centres, regional/national laboratories, private agencies manufacturing radiation equipment etc. Private agencies must have good financial background and experience or interest in radiation protection work. The accredited laboratory will work under the supervision of BARC.

*Further details can be had from :*

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## **The 2<sup>nd</sup> National Symposium on Advances in Control and Instrumentation (SACI)- 2005**

The DAE-BRNS Symposium on Advances in Control and Instrumentation (SACI – 2005) will be held at Mumbai during February 16-18, 2005. This symposium will act as a forum for researchers and practitioners interested in the areas of modelling, design, analysis and simulation of control and instrumentation systems of nuclear reactors and processes. SACI – 2005 aims to strengthen relations between industry, research laboratories, and universities. It is being organised by BARC and sponsored by the Board of Research in Nuclear Sciences, Mumbai.

For details please see <http://www.barc.ernet.in/webpages/brns/brns1.html>.