

Disease Specific Documents for XII Plan

Cancer Research

High Power Committee to Evaluate the Performance of ICMR, 2012-13



Indian Council of Medical Research, New Delhi

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Year of Publication 2014

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Published by the Division of Publication & Information on behalf of the Secretary DHR & DG, ICMR, Ministry of Health & Family Welfare, New Delhi

ICMR INSTITUTES WORKING ON CANCER

1. National Centre for Disease Informatics and Research (NCDIR), Bangalore
2. National Institute of Pathology, (NIOP), New Delhi
3. Institute of Cytology and preventive oncology (ICPO), NOIDA
4. Regional Medical Research Centre (RMRC), Dibrugarh

CURRENT SITUATION OF DISEASE WITH CONTRIBUTION OF ICMR

India is undergoing an epidemiological and demographic transition during the last decade. While it is still grappling with the problems of communicable diseases, the non communicable diseases like cancer, diabetes, IHD, stroke have already started taking its toll. Globally, the burden of new cancer cases was estimated to be 10.1 million representing a 20% incidence over previous decade, with projection of dramatic increase to 20 million by 2020 with 70% occurring in developing world. The estimates of cancer cases for all sites for Indian males are 462,408; 497,081 and 534,353 for the years 2010, 2015 and 2020, respectively. The corresponding estimates of cancer cases for females are 517,378; 563,808 and 614,404. Further, the total cancer cases are likely to go up from 979,786 cases in the year 2010 to 1,148,757 cases in the year 2020. In India, the International Agency for Research on Cancer estimated indirectly that about 635 000 people died from cancer in 2008, representing about 8% of all estimated global cancer deaths and about 6% of all deaths in India. The absolute number of cancer deaths in India is projected to increase because of population growth and increasing life expectancy. About half of the cases among men and one fifth of cases among women, pertain to sites mainly attributable to tobacco use. Overall, about one-third of cancers in India pertain to tobacco related sites. The most common cancer among men is lung & bronchus in Mumbai, Delhi & Bhopal; stomach cancer in Bangalore & Chennai & hypopharyngeal cancer in Barshi. However, all these cancers occupy important ranks in all the registries. The other important cancers sites among men are that of oral cavity, pharynx, larynx & rectum. Cancer of cervix followed by breast cancer are the commonest cancers among women in Barshi, Bangalore, Bhopal & Chennai. Breast cancer is the commonest cancer followed by cervix, in Delhi & Mumbai. Other common forms of cancer among women are mouth, oesophagus, ovary, & stomach. Incidence of cancer of gall bladder is very high in Delhi. India is a culturally diverse country, with huge regional and rural-to-urban variation in lifestyles and in age-specific adult death rates. Thus, understanding the geographical and social distribution of specific cancers is essential to target cancer control programmes. A very high incidence of over all cancers has been reported from different North east states. (AAR in Assam 172.2, Manipur 95.6, Mizoram 155.7, Sikkim 73.6 per 100,000 population) . Among males oesophagus is the most common site of cancer, while in Sikkim and Mizoram is stomach. Among females Breast is the most common site of cancer in Assam and Sikkim while in Mizoram is cervix uteri. In Manipur lung is the most common site of cancer both in males and females.

ICMR CONTRIBUTIONS DURING XITH PLAN

NATIONAL CENTRE FOR DISEASE INFORMATICS AND RESEARCH, BANGALORE

The Indian Council of Medical Research initiated a network of cancer registries across the country under the National Cancer Registry Programme (NCRP) in December 1981. This move followed the recognition that there was an urgent need for strengthening the existing cancer registries and organization of new cancer registries in different regions of the country. The programme was commenced with the following objectives:

- To generate reliable data on the magnitude and patterns of cancer;
- To undertake epidemiologic studies in the form of case control or cohort studies based on observations of registry data;
- Provide research base for developing appropriate strategies to aid in National Cancer Control Programme; this would be in the form of planning, monitoring and evaluation of activities under this programme;
- Develop human resource in cancer registration and epidemiology.

Data collection commenced from 1 January 1982 in the population based cancer registries (PBCRs) at Bangalore, Chennai and Mumbai, and also in the hospital based cancer registries (HBCRs) at Chandigarh, Dibrugarh and Thiruvananthapuram.

Setting up PBCRs across all the eight North East states

The registries under the NCRP provided baseline parameters with data of high quality and scientific validity. Systematic collation of cancer information albeit in a few centers, has given pointers to the burden and patterns of cancers amenable to cancer control measures. The population based survival studies conducted by the registries, for the first time in the context of a developing country have made known additional factors in the form of age and stage specific survival and mortality. Based on this important information, the Government of India formulated the **National Cancer Control Programme (NCCP)** with the following main objectives:

1. Primary Prevention of Tobacco Related Cancers;
2. Early Detection and Treatment of cancer of the uterine cervix;
3. Distribution and extension of cancer management and control services through regional cancer centres, medical and dental colleges.

With the above objectives in mind the NCCP has undertaken several district projects in different states of the country under its District Cancer Control Programme. The results in the report on 'Development of an Atlas of Cancer in India' provided several pointers towards the NCCP in general and the individual District Cancer Control Programmes in particular. The priorities for Cancer Control in the North East have also been defined because of this.

The NCRP data over the years has constituted a sound scientific and research data base. The inherent advantages of the application of Electronic Information Technology as a tool towards cancer registration, networking, patient care evaluation, multi-disciplinary cancer research and cancer control have been strikingly brought out in recent years. The project on “Development of an Atlas of Cancer in India” not only gave the stimulus for further PBCRs across the country but also revealed and provided the impetus for the development of various software applications programmes culminating in the setting up of a new permanent ICMR institute *i.e.* “**National Centre for Disease Informatics and Research**” in Bangalore in 2011.

Development of Software Applications Programmes

The unit has developed software to aid cancer research and development. The concept of using electronic information technology in gathering cancer data through the worldwide web was first done with the cancer atlas project which showed a remarkable degree of success. The model has been extended for the Patterns of Care and Survival Studies on three sites of cancer, *viz.*, cancer cervix, breast and head and neck cancers. Web-based data capture allows individual centres to track and get listing of patients who are on regular follow-up post treatment and those who are not. The software application has provision to provide listing of patients whose appointment is due with their telephone numbers and other details. Individual centers can generate a variety of tables on survival of their data. The PBCR Data Management software has been developed in-house and distributed to most of the 27 PBCRs. This has greatly helped in further systematizing data checking, processing and analysis. Thus the report of 25 PBCRs that was prepared during end of December 2012 is now under print.

Development of Data Base for Cancer burden and pattern

- Aizawl District in Mizoram State shows the highest AAR in both males (273.4) and females (227.8). In males, East Khasi Hills district (216.0) of Meghalaya State and in females (156.3) Kamrup Urban District follow Aizawl district.
- *Among males*, cancers of lung, mouth, oesophagus and stomach are the leading sites across all the registries. Lung cancer is the leading site in Bangalore, Chennai, Delhi, Kolkata, Tripura, Kollam and Thiruvananthapuram. All the PBCRs in Gujarat and Maharashtra states and Bhopal PBCR have mouth cancer as the leading site of cancer.
- Cancer of the oesophagus is the leading site in the registries in the states of Assam and Meghalaya. Stomach cancer is the leading site in Sikkim and Mizoram while cancer of the nasopharynx is the leading site in Nagaland.
- *Among females*, cancer of the breast and cervix are the leading sites of cancer in 18 of 25 PBCRs. Cancer of the gall bladder and cancer of the oesophagus followed cancer breast as the leading site in Dibrugrah and Kamrup respectively. Lung was the leading site in Manipur and Mizoram. Cancer of the oesophagus led the list of cancers in Meghalaya. Cancer of the thyroid followed cancer breast in the two PBCRs at Kollam and Thiruvananthapuram in Kerala state.

- East Khasi Hills District of Meghalaya had the highest relative proportion of cancers associated with the use of tobacco with 69.3% and 43.0% for males and females respectively. The proportion of cancers in childhood relative to cancers of all ages in both sexes varied from 1.1% in Meghalaya to 4.4% in Delhi.
- The data of the newer PBCRs that are being reported for the first time in this report are Nagaland, Meghalaya including Khasi Hills district, Tripura and Wardha. Among these new PBCRs, males in Nagaland show the highest AAR of 21.0/100,000 for nasopharyngeal cancer. East Khasi Hills district and Meghalaya state as a whole show the highest AAR in cancers of the oesophagus (in both males and females) and cancers of the hypopharynx and larynx in males.

NATIONAL INSTITUTE OF PATHOLOGY (NIOP), New Delhi

The National Institute of Pathology has made significant advances in its activities in Tumor Biology along with development and strengthening of its infrastructure facilities to include high throughput research technologies mainly for genomics. The major thrust is on translational research such as identifying genes that are associated with risk or serve as diagnostic tools, targets for therapy or predicting the drug response. Molecular strategies such as genomics and bioinformatics have been used to generate information that may be used for targeting the result into daily medical practice with a view to understand the biology, improving diagnosis, enhancing treatment and reducing mortality associated with cancer. The Institute is on the edge to establish proteomics, nanotechnology and stem cell facility to realize the research goals. Thrust areas of research have been **breast cancer, urologic malignancies including prostate and urinary bladder cancer, haemotopoitic-lymphoid malignancies and brain tumors with a view to understand the molecular mechanism of carcinogenesis.** More recently, studies on **cancers in Northeast region in India have been undertaken to identify risk factors for the high prevalence of cancers in this region of India and also to understand molecular mechanism.**

MAJOR ACHIEVEMENTS WITH LEADS EMERGED DURING XI PLAN

Basic Research

- Established two breast cancer cell lines using triple negative primary tumors from two young Indian breast cancer patients(<40 yrs) which would be used for understanding the molecular pathogenesis of early onset breast cancer in Indian women and identifying new drug targets.
- Identified putative high risk alleles (CYP17 A2 allele, VDR Poly AL allele and >20 CAG repeats) for breast cancer in young women.
- Consumption of tobacco and fermented betel quid in north-east region was found to contribute significantly to the development and progression of Esophageal Squamous Cell Carcinoma (ESCC). Genome-wide analysis of chromosomal alterations and gene expression profile showed over expression of FGF-12, NPY, and CTNND2 and down regulation cytokeratin 4 as important prognostic markers. Down regulation of EPHX1 has been found as an important risk factor.

- Significant familial clustering of ESCC reported in North east region. Gene expression profile in familial ESCC showed up-regulation of genes involved in β -cell receptor signaling pathway and down regulation of genes in Natural Killer cell mediated cytotoxicity suggesting that immune factors associated with familial clustering of ESCC in high-risk area. Gain of CD48 has been found as risk factor for familial ESCC.
- Germ-line sequence alterations in BRCA2 gene in familial ESCC patients from this high-risk area of India suggested that BRCA2 play a role in genetic susceptibility to familial ESCC.
- Identified Betel quid chewing by Multi Dimensional Reductase analysis as the single main risk factor for breast cancer in NE region.
- Tobacco smoking has been identified as significant risk factor for lung cancer and betel quid chewing for oral cancer, however interaction of p53 codon72 polymorphism with smoking had been found a significant risk factor for oral cancer and with betel quid a significant risk factor for lung cancer.

Clinical Research

- Identified androgen receptor as independent predictive marker for response to neoadjuvant chemotherapy in locally advanced breast cancer cases.
- A Th2 dominant host immune profile was shown to have association with recurrence of tumour in bladder cancer patients. Combination panel of immunohistochemical markers (p21/waf1/VEGF/CD105) was more effective in predicting recurrence of bladder cancer than a single marker.
- Reported downregulation of MMR genes in Indian patients with carcinoma prostate (CaP), Loss of hPMS2 expression serves as significant prognostic marker for CaP.

Epidemiological/Operational Research

- Distribution of GST polymorphism in NE Indian population was found different from rest of India and similar to those reported from China. GSTT1 null genotype was found to be a risk factor for oral and gastric cancer in Assam while mutations in EPHX1 gene were found risk factor for ESCC and lung cancer in North east region.

Translational Research

- EMA, WT1, ezrin, claudin 1 & SPARC have been identified as potentially useful markers for differentiation of fibroblastic meningioma from schwannoma in brain tumors.
- A novel MLH1-93G>A polymorphism in Carcinoma Prostate patients may serve as potential diagnostic marker differentiating it from atypical hyperplasia prostate and loss of hPMS2 expression serves as significant prognostic marker for poor outcome.

INSTITUTE OF CYTOLOGY AND PREVENTIVE ONCOLOGY, NOIDA

Institute of Cytology and Preventive Oncology (ICPO) is the premier cancer research institute of Indian Council of Medical Research (ICMR) under the Ministry of Health and Family Welfare, Govt. of India. ICPO was instituted with the main aim of promoting research in the field of cancer that are most prevalent in India with an emphasis on their early detection and prevention. The thrust areas of research include precancer and cancer of the uterine cervix and breast in women. Multidisciplinary studies involving epidemiological, behavioral, clinical, cytomorphological, cytogenetics, biochemical, virological, immunological and molecular biological aspects are being undertaken in order to understand the natural history, biological behavior and mechanisms of carcinogenesis. ICPO has since made significant contributions in the field of cervical cancer research. The concept of high risk lesions, clinical down staging, visual inspection of cervix with selective cytology screening and development of novel molecular diagnostic approaches for screening HPV and other cancer causing and cancer suppressor genes have been introduced for early detection of cervical cancer. Transcriptional control of viral gene expression and preliminary work on HPV DNA vaccine and development of protocol for HPV vaccine trial in India, analysis of mutation and transcription of breast cancer susceptibility genes are some of the major research areas being undertaken. The institute has evolved as a National Reference Centre for HPV and cervical cancer and provides specialized diagnostic referral services. The institute is a member of International Union Against Cancer (UICC), Geneva, and a WHO collaborating centre for research and training in cytology and HPV vaccine.

MAJOR ACHIEVEMENTS WITH LEADS EMERGED DURING XI PLAN

HPV studies

- a. WHO's Regional HPV Reference Laboratory (HPV LABNET Programme in South East Asian region) was established at ICPO as there was an urgent global need for harmonization of laboratory assays for HPV DNA diagnostics and serology for HPV surveillance for implementation and monitoring of vaccine response.
- b. Molecular screening for cervical cancer: ICPO developed multiplex PCR to detect various HPV types in one PCR reaction saving biological material, cost and time. It also carried out studies pertaining to variant HPV types in Indian population for the purpose of developing HPV vaccines.
- c. Therapeutic strategies for HPV infections: ICPO participated in phase-I clinical trial of polyherbal Neem cream and tablet-Praneem in women with HPV infection and successfully demonstrated that polyherbal formulation possessed potent anti HPV properties. In addition, it also participated in a DST funded multi-centric trail for studying the anti HPV properties of Curcumin.

- d. Prophylactic vaccines against HPV: ICPO was selected as one of the trial sites for HPV vaccine (GARDASIL-MERCK). The study, however, was suspended in between. Now ICPO is involved in an Indo-German programme for development of Chimeric DNA based vaccine against HPV 16.
- e. Interaction of host genes in HPV mediated carcinogenesis was studied.

Genetic Studies in carcinogenesis:

- a. For genetic susceptibility the role of genetic polymorphism of genes involved in Phase-I and Phase-II detoxification system was studied especially with regards to GSTM1 and GSTT1 genes.
- b. Genetic pathways and SNP's in the development of various cancers along with genetic markers were studied; more specifically SNPs of Cytokine genes, Cyclin D1 gene, FHIT & RASSF1A, Homocysteine levels and MTHFR gene and allelic variation of CYP2D6 gene were studied with respect to susceptibility to cervical cancer. In addition, study on Cyclin D1 gene polymorphism was carried out for assessing the risk of oesophageal cancer in Kashmir valley.

Clinico epidemiological studies and screening for cervical and oral cancer:

- a. Development of clinical base and colposcopic networking for early detection of cervical cancer and its precursors.
- b. Evaluated test characteristics of different screening modalities.
- c. Two community based projects initiated at Dadri (UP). One is funded by ICMR using aided visual tests and the other one is funded by PATH (USA) to evaluate a newly developed HPV detection kit for the field settings.
- d. Developed a magnifying device (Magnivisualizer) with an inbuilt source of light for use in the field conditions.
- e. Developed modified protocols for PAP staining with minimal alcohol use.
- f. Field trial of magnivisualizer for early detection of precancerous lesions of oral cavity.
- g. Development of training manual for early detection of cervical cancer.

Bioinformatics.

- a. Established a new division of Bioinformatics at ICPO.
- b. Development of first ever Cervical Cancer Gene Database.

Behavioural Oncology

- a. Psychological Disorders in women undergoing post operative radiation and chemotherapy for breast cancer in Delhi were studied.

REGIONAL MEDICAL RESEARCH CENTRE, NORTH EAST REGION, DIBRUGARH

Situated in Dibrugarh, Assam, the Regional Medical Research Centre, (RMRC, Dibrugarh) conducts research on cardio vascular diseases, Rheumatoid heart disease, cancer, haemoglobinopathies, mosquito borne diseases (malaria, filariasis, Japanese encephalitis, Dengue), influenza, trematode infection, hepatitis, HIV & AIDS in the North eastern (NE) region. Population at NE region represents not only entire India but also the bordering countries due to migration which is reflected by disease diversity in this region. This centre is conducting studies on epidemiological and genetic risk factors associated with high incidence various cancers in this region.

Studies on current situation of the disease/disease burden:

Among different type of cancers in north-eastern region of India, cancer of nasopharynx (NPC) has been found to be 10 times higher than the national average and within the region, 55% of total NPC cases are reported from Nagaland followed by Manipur (22.1%). Cancer of oesophagus reported from Assam is highest in the country and Mizoram reports highest stomach cancer which is second in the world. Lung cancer in Mizoram and Nagaland are no. 1 cancer in both the sexes.

Achievements made with leads emerged out during XI plan

Risk factors for oesophageal cancer in Assam, stomach cancer in Mizoram, oral cancer in Meghalaya and Assam, lung cancer in Manipur and Mizoram were investigated along with genetic and molecular epidemiological studies. Link between various cancers and tobacco use, pesticide exposure, genetic variation including polymorphism/mutations associated with ethnic variations was studied.

Research Papers Published

| | | |
|---|---|-----|
| 1. National Centre for Disease Informatics and Research (NCDIR) | : | 430 |
| 2. National Institute of Pathology, New Delhi | : | 88 |
| 3. Institute of Cytology and Preventive Oncology, Noida | : | 107 |
| 4. Regional Medical Research Centre (RMRC), Dibrugarh | : | 11 |

TECHNOLOGIES TRANSFERRED TO INDUSTRY

Institute of Cytology and Preventive Oncology : 1

TECHNOLOGIES READY FOR TRANSFER

Institute of Cytology and Preventive Oncology : 5

LIST OF PATENTS FILED

| Sr. No. | Year of filing | Title of Patent | Institute |
|-------------------------------|----------------|--|-----------------|
| | 2011 | Two primary breast cancer cell lines established from tumor tissue of two young breast cancer patients | NIOP, New Delhi |
| Application No. 1216/DEL/2010 | 2010 | Magnivisualizer | ICPO, Noida |

MANPOWER TRAINED

NEW HUMAN RESOURCE GENERATED

NCDIR

Organized workshops and Training-cum-Orientation Training Programmes on Development of An Atlas of Cancer in Punjab State at Shri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Mohan Dai Oswal Multispeciality and Cancer Hospital, Ludhiana, Regent Park Hotel, Jalandhar and Bathindha

NIOP

DNB : 10
PhD : 19
WHO training for Pathologist : 5
WHO training for technicians : 24
Summer Training for MSc/MD : 65

Students

Various workshops organized on Flow-cytometry, Basic Molecular biology techniques, Tissue and DNA Micro-array technologies to train medical and basic scientists.

ICPO

Man power trained -- 500 Total including students,

RMRC

- a) A Workshop on Cancer Registration – Using Data Sets for Research, Analysis and Publications in collaboration with National Cancer Registry Programme (NCRP) was organized by the Centre from 10th to 13th June, 2007. This was attended by 15 participants from population based cancer registries operational in north-east India
- (b) One student completed and 2 pursued their Ph.D. work on cancers during the XIth plan period in the Centre

Table 1. Status of Completed Research Studies undertaken during XI Plan

| Sr. No. | Thematic area and Title of the Study | Objectives | Completed with outcome of the study | If off-shoot, Refer to XII th plan study | Institution |
|-----------------------|--|---|--|---|-----------------|
| Basic Research | | | | | |
| 1 | Establishment and characterization of breast cancer cell lines from primary breast cancers | To establish cell lines from primary breast tumors of Indian women | Established two breast cancer cell lines using triple negative primary tumors from two young Indian breast cancer patients(<40 yrs) which would be used for understanding the molecular pathogenesis of early onset breast cancer in Indian women and identifying new drug targets. | Study on microRNA signature associated breast cancer stem cells and their role in drug response. | NIOP, New Delhi |
| 2 | Study of candidate genes associated with breast cancer susceptibility | To identify high and low penetrance genes associated with risk of breast cancer in Indian women | Identified putative high risk alleles (CYP17 A2 allele, VDR Poly AL allele and >20 CAG repeats) for breast cancer in young women. | Follow-up study initiated- "Study of gene expression and Hypermethylation profile of Early onset breast cancers". | NIOP, New Delhi |

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| 3 | Comprehensive studies in esophageal cancer in high risk region of northeast india | To elucidate the genetic and environmental risk factors associated with high incidence and familial clustering of esophageal cancer in North east region | <p>In this collaborative study RMRC, Dibrugarh carried out the case- control study involving 317 histologically confirmed oesophageal cancer cases and 317 controls in Assam. Significant risk for the development of oesophageal cancer was recorded with family history (OR 2.3; 95% CI: 1.2 - 2.61), rural place of residence (OR 3.2; 95% CI: 1.5-6.9) along with the tobacco chewing and smoking habits</p> <p>Genome-wide analysis of chromosomal alterations and gene expression profile showed over expression of FGF-12, NPY, and CTNND2 and down regulation cytokeatin 4 as important prognostic markers. Down regulation of EPHX1 has been found as an important risk factor.</p> <p>Significant familial clustering of ESCC reported in North east region. Gene expression profile in familial ESCC showed up-regulation of genes involved in β-cell receptor signaling pathway and down regulation of genes in Natural Killer cell mediated cytotoxicity suggesting that immune factors associated with familial clustering of ESCC in high-risk area. Gain of CD48 has been found as risk factor for familial ESCC.</p> <p>Germ-line sequence alterations in BRCA2 gene in familial ESCC patients from this high-risk area of India suggested that BRCA2 play a role in genetic susceptibility to familial ESCC.</p> | <p>Two studies initiated- "Genome wide analysis of genetic alterations in patients with esophageal cancer from north-east India using single nucleotide polymorphism array".</p> <p>"Epigenetic studies in esophageal cancer in high risk region of north-east India"</p> <p>"Molecular Biomarkers in Esophageal Cancer in Northeast India: validation and clinical application." Submitted for funding to DHR</p> | NIOP, New Delhi RMRC, Dibrugarh, ICPO, Noida |
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| 4 | Developed HPV detection kit for field testing | A multiplex PCR kit is being developed which needs to be validated. | | | ICPO, Noida |
| Clinical Research | | | | | |
| 1 | Type 1 growth factor receptor family : expression and correlation with response to neo-adjuvant chemotherapy in locally advanced breast cancer | To identify biomarker to predict the response to neoadjuvant chemotherapy in locally advanced breast cancer cases. | Identified androgen receptor as an independent predictive marker for response to neoadjuvant chemotherapy in locally advanced breast cancer cases. | Follow-up studies initiated initiated on the -effect of siRNA mediated androgen receptor gene silencing on androgen signaling pathway in breast carcinoma - Understanding the role of androgen receptor signalling in breast cancer -Multicentric validation of role of Androgen receptor as independent predictive marker for response to neoadjuvant chemotherapy in locally advanced breast cancer cases. | NIOP, New Delhi |
| 2 | Microsatellite instability in androgen receptor gene, p53 gene polymorphisms/ mutations and expression profile of mismatch repair genes (mrr) in prostate cancer. | To study the role of AR and MMR genes in development and progression of CaP. | Reported downregulation of MMR genes in carcinoma prostate (CaP), Loss of hPMS2 expression can serve as significant prognostic marker for CaP. | "Genome wide analysis of genetic alterations and gene expression profile of Hormone sensitive and hormone refractive prostate cancer". Submitted for funding. | NIOP, New Delhi |

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| 3 | Clinical trial of polyherbal neem cream and tablet Praneem in women with HPV infection. | Anti HPV molecules Praneem- a polyherbal compound has shown promising results. Further studies need to be carried out for validation. | | | ICPO, Noida |
| 4 | Molecular screening for cervical cancer. | Potential biomarkers like p53, bcl2, and Cyclin D1 has been studied for early detection of cervical cancer. | | | ICPO, Noida |
| 5 | Evaluated test characteristics of screening modalities for cervical cancer | In a resource limited setting where organized mass screening by cytology or HPV DNA testing is difficult, VIA appears to be viable cost effective screening alternative with a reasonably comparable sensitivity (87% vs 91%) and specificity (97% vs 91%) to that of cytology. | | | ICPO, Noida |
| Epidemiological/Operational Research | | | | | |
| 1 | Two community based projects for cervical cancer detection initiated At Dadri (UP) | | Development of preventive oncology field stations at Dadri (UP). This will be useful for cancer control programmes. | | ICPO, Noida |
| 2 | Development of first ever cervical cancer gene database. | | Database developed with 537 genes. It will be very useful in designing new projects involving genetic aspects. | | ICPO, Noida |

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| 3 | Cancers in north-east India: Understanding the role of tobacco (2005-10) | To investigate the link between the cancers and carcinogenic contents of tobacco used in north-east India and genetic variation including polymorphism/ mutations associated with ethnic variations | In this collaborative study RMRC, Dibrugarh carried out the case-control study involving 2,027 cases of 4 major tobacco related cancers viz. oral cavity (n = 735), oesophagus (n = 529), stomach (n = 333) and lung (n = 430) from the six population-based cancer registry areas of north-east India with equal number of age, sex and place of residence matched controls. Tobacco chewers with habit of alcohol consumption (OR 1.04; CI 0.29-3.76) ; and those consuming alcohol along with smoking habit (OR 1.55; CI 0.35-6.81) were found at higher risk of developing oesophageal cancer. Smokers with habits of tobacco chewing and consuming alcohol (OR 8.24; CI 0.90-75.22) were more prone to develop stomach cancer. Combination of smoking with alcohol consumption | Three studies planned and submitted to DHR for funding-“Metastatic Potential and Molecular Differentiation of Precursors of Gastric Cancer in High Risk Northeast Indian Population” “ Validation of role of EPHX1 gene as risk factor for esophageal and lung cancer in North east region”- “Validation of molecular biomarkers in prediction and prognosis of Breast Cancer in Northeast | RMRC, Dibrugarh NIOH, Ahmedabad; NIOP, New Delhi ICPO, Noida |
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| | | | <p>(OR 2.39, CI 0.25-22.70); and alcohol consumption with tobacco chewing habit (OR 2.49, CI 0.27-22.49) Tobacco smoking has been identified as significant risk factor for lung cancer and betel quid chewing for oral cancer, however interaction of p53 codon72 polymorphism with smoking had been found a significant risk factor for oral cancer and with betel quid a significant risk factor for lung cancer.</p> <p>Distribution of GST polymorphism in NE Indian population was found different from rest of India and similar to those reported from China. GSTT1 null genotype was found to be a risk factor for oral and gastric cancer in Assam. while mutations in EPHX1 gene were found risk factor for ESCC and lung cancer in North east region</p> <p>Betel quid chewing was identified as the single main risk factor for breast cancer in NE region Copy Number analysis showed alterations in Drug Metabolism, Molecular Transport and Nucleic acid Metabolism pathways with involvement of AKR1B10, AKR1B1 and ETS2 genes in betel quid chewing associated breast cancer in North east India.</p> | | |
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| 4 | Cancers in north-east India: Understanding the role of pesticides (2005-2010) | To investigate the link between cancers and the exposure to pesticides and genetic variation including polymorphism/mutations associated with ethnic variation in north-east India | In this collaborative study RMRC, Dibrugarh conducted the case-control study involving 842 cases of two major sites of pesticide related cancer viz. Breast cancer (n=585) and NHL (n=257) with equal number of age, sex and place of residence matched controls from the six population-based cancer registry areas of north-east India. The risk of occurrence of breast cancer among females was higher among farm workers, especially those handling fertilizers (OR 2.94; CI 1.61-5.36), pesticides (OR 2.42; CI 1.31-4.48), other chemicals while working with animals (OR 1.75; CI 1.32 -2.33), as compared to non-farm workers. Illiteracy (OR 2.63; CI 1.34-5.14), smoking in the past (OR 1.89; CI 1.01; alcohol consumption in the past (OR 2.51; CI 1.51-4.18), working in the farm (OR 2.19; CI 1.44-3.33), especially handling fertilizers (OR 2.84; CI 1.57-5.12) emerged as significant risk factors for the development of NHL cancer. | No | RMRC, Dibrugarh; NIOH, Ahmedabad; NIOP, New Delhi ICPO, Noida |
| Translational Research | | | | | |
| 1 | Developed clinical base and colposcopic networking for screening of cervical and oral cancers. | - | Development of clinical base and colposcopic networking for early detection of cervical cancer and its precursors was initiated and will continue in the 12 th Plan which will help in wider coverage of screening programme for prevention and better management of cervical, breast and oral cancer. | | ICPO, Noida |

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| 2 | Developed a magnifying device (Magnivisualizer) with an inbuilt source of light for use in field conditions for detecting precancerous and cancerous lesions of cervix and oral cavity. | - | Magnivisualizer offers an alternative means of detecting most of the early cancerous lesions of cervix and oral cavity in field conditions (sensitivity 82% vs 79%) and specificity (94% vs 99%) for detecting high-grade lesions of cervix. Further for oral cavity screening it can detect high grade lesions more than twice compared to torch light. Improved commercial version of this device with inbuilt source of light was developed. Patent has been applied by the IPR unit of ICMR in 2010 (Application No. 1216/DEL/2010 dated 25/5/2010). Validation of the instrument has also been initiated under translational research programme of ICMR. Digital image capturing device will also be integrated in the existing Magnivisualizer with suitable modifications to capture the image while diagnosis the case in field setting. | | ICPO, Noida |
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Table 2. Important and essential activities which need to be continued in XIIth Plan

| Sr. No. | Thematic area and Title of the Study | Justification | Time Frame | Deliverable outcome with public impact | Institution |
|-----------------------|---|---|------------------------|--|--|
| Basic Research | | | | | |
| 1 | Study on gene expression and hypermethylation profiles in early onset breast cancer | DBT funded study for duration 2008-2012 | 2008-2012 Completed | Study has highlighted differential gene expression and methylation profile of early onset breast cancer in Indian women along with molecular pathways involved. The bioinformatics analysis is undergoing. The study has helped in understanding molecular pathogenesis of early onset breast cancer and would help in identifying risk factors for this group of patients | NIOP, New Delhi |
| 2 | Genome-wide analysis of genetic alterations in patients with esophageal cancer from north-east India using single nucleotide polymorphism array | Extramural ICMR project initiated in 2011 | 2011-2014 | The study would help in identifying genetic risk and prognostic factors and new drug targets. | NIOP, New Delhi RMRC, Dibrugarh |
| 3 | Epigenetic studies in esophageal cancer in high risk region of northeast India | Extramural DBT project initiated in 2011 | 2011-2014 | The study would help in identifying epigenetic biomarkers (histones/methylated genes) for risk/ progression and new drug targets. | NIOP, New Delhi RMRC, Dibrugarh |
| 4 | Immunogenetic profile of nasopharyngeal cancer (NPC) in a high-prevalence region of north-east India | Extramural DBT project initiated in 2010 | 2010-2013 | The study would help in understanding etiopathogenesis and the role of EBV and HLA haplotypes in development and prognosis of NPC in this region which would further help in stratification of genetic and environmental risk factors. | NIOP, New Delhi |

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| 5 | Development of prophylactic DNA based vaccine with high antigenic potential against Human Papilloma Virus- HPV 16 and HPV 18 | We have identified ten major variants of HPV 16, which have been characterized and cloned in mammalian expression vector. | To evaluate these characterized vaccines constructs in an animal model before clinical trials. | | ICPO, Noida |
| 6 | Role of Genetic polymorphism of genes involved in Phase I and Phase-II detoxification genes in different cancers and Cytokine genes in Oral cancer and Cyclin D1 in Bladder cancer, FHIT & RASSF1A in colorectal cancer. | <i>Genetic polymorphisms of these genes have been found to be associated with one or the other cancer indicating susceptibility to cancer development.</i> | To understand the exact mechanism of cancer development among carriers of these high risk alleles. Validation in different ethnic populations. | | ICPO, Noida |
| Clinical Research | | | | | |
| 1 | Patterns of Care and Survival Studies on Cancer Breast, Cancer Cervix and Head and Neck Cancers | Seventeen centres participating in this study. Data on over 65,000 cases of these three sites of cancer received and interim analysis done. Developed software programmes to monitor follow-up and survival analysis. | 10 years | For the practice of, evidence based medicine, help develop treatment protocols and possibly conduct clinical trial. Costs for treatment of cancer are extraordinarily high. Standardisation of treatment protocols for Indian conditions and patients with evaluation of costs and benefits measured through treatment outcome studies is a necessary step. | NCDIR, Bangalore |
| 2 | Characterization of host immune profile associated with progression of superficial Transitional cell carcinoma(TCC) of bladder by microarray analysis | Extramural ICMR project for duration 2009-2013 | 2009-2013 | Study has helped us in identification of urinary immunologic biomarkers(IL-1RA, IFNgamma, PDGF and RANTES) associated with recurrence of superficial TCC | NIOP, New Delhi |

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| 3 | Participated in multicentric trials for studying the anti HPV properties of Curcumin. | Developed a novel therapeutic approach to control pathogenic HPV infection by using potent antioxidative agents such as Curcumin. | To identify the potential use of Curcumin for treatment of cervical cancer infected with HPV. | | ICPO, Noida |
| 4 | WHO Labnet programme | Global proficiency panels were acquired for establishing comparable and reliable HPV genotyping services for vaccinology worldwide | To establish comparable and reliable HPV serology and genotyping services for vaccinology. | | ICPO, Noida |
| Epidemiological/Operational Research | | | | | |
| 1 | Population Based Cancer Registries | Commenced 7 new PBCRs. Collection of data in a systematic way provides actual incidence of cancer and not estimates. Identified areas for Epidemiological Research and Published 2004-2005 and 2006-2008 reports. Developed PBCR-DM software, being used by 24 out of 27 PBCRs. | 20 years | Need to expand to other states and continued in existing places to provide trends in incidence rates over time and indicators for cancer control. | NCDIR, Bangalore |

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| 2 | Hospital Based Cancer Registries | Commenced 2 new HBCRs. Contributes to PBCRs and Patient Care. Published 2004-2006 report. Developed HBCR-DM software, being used by 41 centres. | 20 years | Need to have HBCRs to monitor and evaluate patient care and also help in having Patterns of Care and Survival Studies | NCDIR, Bangalore |
| 3 | Development of An Atlas of Cancer in North East Region | 6 PBCRs have been commenced in the North East but to cover several areas of Assam State this project has continued | 10 years | Needs to be continued to know the patterns of trends of incidence of cancer in areas not covered by PBCRs of North East. | NCDIR, Bangalore |
| 4 | Development of An Atlas of Cancer in Punjab State (Collaborating centres in Delhi, Chandigarh, Rajasthan and Punjab) | To know patterns of cancer in Malwa region of Punjab. 48 centres have registered and sending data. Software for dynamic monitor of data capture developed. | 10 years | Project is just a year old and minimum of 3 years data is required to provide meaningful interpretation | NCDIR, Bangalore |
| 5 | Risk factors of lung cancer in RMRC, Manipur and Mizoram (2008-2012) | The proposed study duration was 2008-2011. However, due to the later release of funds one year extension was granted | Completed in Nov 2012 | This case-control study involving 315cases & 606 controls in Manipur and Mizoram states assessed the epidemiological risk factors of primary lung cancer and the lung cancer risk imposed by inheritance of polymorphic alleles of GSTM1 & CYP1A1 genes. Tobacco smoking (specially Zozial) and chewing with or without betel nut were found deterministic risk factors for lung cancer. GSTM1 null genotype was significantly associated with lung cancer. | RMRC, Dibrugarh, RIMS, Imphal; Civil Hospital Aizawl |

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| 6 | Study of genetic and molecular epidemiology of oral cancer in 2 states Assam & Meghalaya (2009-2012) | The study was initiated in the later part of the 11 th plan and by default the 3 rd year of the study fell in to 12 th plan period | Completed in Nov 2012 as per original time frame | This case-control study involved 171 cases & 172 controls in Assam & Meghalaya. GSTM1 null genotype and MSP 1 mutant genotype of CYP1 A1 gene were independent risk factors of oral cancer. Chewing of tobacco and smoking enhanced the risk of oral cancer in subjects with GSTT1 null genotype | RMRC, Dibrugarh; BBCi, Guwahati; AMCH, Dibrugarh; NEIGRIHMS, Shillong |
| 7 | Study of genetic and molecular epidemiology of stomach cancer in Mizoram (2009-2013) | By default the 3 rd year of the study (2012) fell in to 12 th plan period. Subsequently the study was extended for 1 year due to operational reasons | The study will be completed in May 2013 | This study, being carried out in a case-control design is expected to throw light of genetic and molecular epidemiology of stomach cancer in Mizoram | RMRC, Dibrugarh, Civil hospital, Aizawl |
| 8 | Study of genetic and molecular epidemiology of breast cancer in 2 states Assam & Meghalaya of NE India & Comparative study of genetic, clinical and epidemiological factors of breast cancer in rural and urban India (2009-2013) | By default the 3 rd year of the study (2012) fell in to 12 th plan period. Subsequently the study was extended for 1 year due to operational reasons | The study will be completed in May 2013 | Studies will throw light on genetic and molecular epidemiology of breast cancer in Mizoram, Tripura, Assam and Meghalaya states. So far, results have indicated betel nut chewing with or without tobacco as an important risk factor. No association of family history or genetic polymorphism of BRCA1 and XRCC1 genes with increased risk of breast cancer has been found | RMRC, Dibrugarh, BBCi, Guwahati; NEIGRIHMS, Shillong, Civil Hospital, Aizawl, RCC, Agartala |

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| 9 | Northeast Cancer Registry programme (2002-2012) | Longitudinal data collection to be continued for monitoring cancer burden in NE India | Through whole of XII th Plan | The study is generating reliable data on the magnitude and pattern of various prevailing cancers in different north-eastern states. A total of 12 registries are functional of which 6 were opened during XIth Plan period | NCDIR, Bangalore |
| Translational Research/Techniques | | | | | |
| 1 | Task Force Project on Translational Research | Developing software for Cancer Registries and Patterns of Care and Survival Studies has been a major activity of the centre. It has helped among other things to monitor data capture, standardisation of the same in quick time and reduced the time gap between calendar year of data and year of report publication. | 10 years | Software is in the evolving process. Merging of various modules and integrating with the Hospital Information Management System and Electronic Medical Records is a big challenge that needs to be continued as a long term activity. | NCDIR, Bangalore |

Table 3. New Proposals to be undertaken during XIIth Plan

| Sr. No. | Thematic area and Title of the Study | Off-shoot of an earlier completed programme (name the completed programme) | De Novo idea which is either nationally relevant or it is likely to lead to a new scientific breakthrough. | Time frame | Deliverables | Instt. |
|--------------------------|---|--|--|------------|--|------------------|
| Basic Research | | | | | | |
| 1 | Study on microRNA signature associated breast cancer stem cells and their role in drug response. | Establishment and characterization of breast cancer cell lines from primary breast cancers. | | 2012-2015 | Established cell lines would be used to identify new drug targets for novel therapeutic approaches in young breast cancer patients. | NIOP, New Delhi |
| 2. | Targeted sequencing of breast cancer specific genes in early-onset breast carcinoma | Study on gene expression and hypermethylation profiles in early onset breast cancer | | 2013-2015 | Study would help in identification of new biomarkers for risk stratification, early diagnosis and new drug targets in early onset breast cancer. | NIOP, New Delhi |
| Clinical Research | | | | | | |
| 1 | Patterns of Care and Survival Studies : (a) Childhood Cancer (b) Lymphoid and Haemopoetic malignancies (c) Gynaecological tumours. | Patterns of Care and Survival Studies are an important need for Evidence Based Medicine and evolving treatment patterns and costs. These three sites of cancers are important because most of Childhood Cancers and several of Lymphoid and Haemopoetic malignancies and Gynaecological tumours are curable Cancers. | | 10 years | | NCDIR, Bangalore |

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|---------------------------------|--|--|---|----------|---|------------------|
| 2 | Existing participating centres using HBCR-DM software | | | 10 years | | NCDIR, Bangalore |
| 3 | Setting up of Population Based Cancer Survival Study on Cancer Breast and Cancer Cervix across the country and Infrastructure for Coordinating Unit of NCRP, Bangalore | | | 10 years | | NCDIR, Bangalore |
| 4 | Genomic and proteomic analysis for early diagnosis of gall bladder cancer | | New project planned de novo based on the high incidence of Gall bladder cancer in Northern India with poor prognosis. The study is planned to identify early diagnostic biomarker and new therapeutic targets. Project submitted to DBT for extramural funding. | | To identify risk factors, early diagnostic biomarker and new therapeutic targets. | NIOP, New Delhi |
| Epidemiological Research | | | | | | |
| 1 | Population Based Cancer Registry at Hyderabad | There is no PBCR or HBCR in Andhra Pradesh state. Since lifestyles and dietary habits of population vary from place to place there is a need to have a PBCR in Andhra Pradesh state. | | 20 years | | NCDIR, Bangalore |

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| 2 | Hospital Based Cancer Registries – to evolve into PBCRs in Regional Cancer Centres | Several states of the country do not have a HBCR or PBCR. As a first step HBCRs in Regional Cancer Centres could be commenced to expand to PBCRs wherever there is not one. | | 20 years | | NCDIR, Bangalore |
| 3 | Development of An Atlas of Cancer in Kerala State | | | 10 years | | NCDIR, Bangalore |
| 4 | HBCRs in Sources of Registration of already existing PBCRs at Bangalore, Chennai, Delhi, Mumbai and Kolkata Chennai, Delhi, Mumbai and Kolkata | | | 10 years | | NCDIR, Bangalore |
| Translational Research | | | | | | |
| 1 | Identification and characterization of putative urinary proteins as biomarkers in urothelial carcinoma | Characterization of host immune profile associated with progression of superficial TCC of bladder by microarray analysis | | Submitted for funding | Identification of non invasive urinary biomarker to predict recurrence of superficial TCC of bladder | NIOP, New Delhi |
| 2 | Validation of molecular biomarkers in prediction and prognosis of Breast Cancer in Northeast Indian Population | Effect of tobacco and pesticide exposure in causation of cancer in north east india. | | Submitted for funding to DHR Translational project call | The biomarkers identified by genome-wise studies would be validated at larger sample size | NIOP, New Delhi |
| 3 | Molecular Biomarkers in Esophageal Cancer in Northeast India: validation and clinical application. | Comprehensive studies in esophageal cancer in high risk region of northeast India | | Submitted to DHR translational project call | The biomarkers identified by genome-wise studies would be validated for their clinical applications viz risk,prognosis and drug targets at larger sample size | NIOP, New Delhi |

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|---|---|--|--|---|--|-----------------|
| 4 | Metastatic Potential and Molecular Differentiation of Precursors of Gastric Cancer in High Risk Northeast Indian Population | Role of tobacco use in causation of cancer in North east India | | Submitted to DHR translational project call | The biomarkers identified by genome-wise studies would be validated at larger sample size for their metastatic potential precursors of gastric cancer. | NIOP, New Delhi |
| 5 | To establish tumour tissue repository(TTR) at NIOP | | To establish TTR at NIOP by collecting tumors which are usually discarded after diagnosis. This would include fresh/ paraffin embedded tumour tissues, blood, serum, urine and saliva. | Submitted for funding to DHR | A TTR with well annotated tumour tissue samples would be of great use to scientists at institute and other centers. At present there are limited TTR at national level in India. | NIOP, New Delhi |

