INDIAN COUNCIL OF MEDICAL RESEARCH | NATIONAL INSTITUTE OF CANCER PREVENTION AND RESEARCH

ICMR-NICPR

ANNUAL REPORT 2021

ICMR-National Institute of Cancer Prevention and Research
Ministry of Health and Family Welfare, Government of India
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FROM THE DIRECTOR'S DESK

Dear All,

Greetings and Welcome...!

ICMR-National Institute of Cancer Prevention & Research (ICMR-NICPR) is the country's premier Institute for carrying out research in the field of Cancer Prevention. It has been recognized for the contributions made in developing and validating strategies for cervical cancer screening in the country as well as in training faculty, research scholars and students for carrying out screening of prevalent cancers namely oral, breast and uterine cervix. This report presents the research and other activities carried out during the period October 2020 to June 2021.

This period was marred with the challenges of the COVID-19 pandemic. The Institute continued to support RT-PCR based COVID-19 testing in the newly established High Throughput Viral Diagnostic Laboratory for Western UP and Delhi. Till date we have tested more than 10 lakh samples. The Institute also covered the districts of Gautam Budh Nagar, Amroha and Saharanpur for carrying out four rounds of National Sero-surveillance for COVID 19. This helped in policy making at the highest level. Samples were drawn from children and healthcare workers also. The Institute supported ICMR in the follow-up of recipients of COVID vaccination in districts of Haryana. A mixed-method multicentric study on the Mental health and social stigma among healthcare personnel involved in the management of COVID-19 patients in India highlighted the various concerns of the healthcare providers. These results have important policy implications. Despite the lockdown conditions, the Institute carried out the National survey for estimating the state wise prevalence of microbiologically confirmed Pulmonary Tuberculosis in India in the states of Uttar Pradesh and few clusters of Haryana.

The WHO FCTC Global Knowledge Hub on Smokeless Tobacco generates information, knowledge and provides training, regionally and globally on smokeless tobacco. During this period, several inter-departmental research projects on tobacco control were carried out and human resource development in tobacco control was promoted by organizing training programs and meetings for policy discourse in various global tobacco control best practices. The Hub played a key role in initiating the policy reform for instituting spitting ban across several states in India as public spitting with the use of smokeless tobacco can lead to an increase in the risk of transmission of infectious diseases such as COVID 19. Further, the Hub also supported the recent COTPA (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Amendment Bill, 2020 and provided detailed feedback for its amendment to the

Union Government. Several publications in high impact journals were made. A feasibility study to integrate tobacco use screening and tobacco cessation services with routine antenatal care services has been initiated as a pilot study in district hospital of Gautam Budh Nagar.

All other flagship programmes of NICPR such as the activities of the National Tobacco Testing Laboratory, the NICPR-ECHO programme of training in-service healthcare providers for cancer screening have been continuing. A demonstration project has been initiated in Sikkim to roll out the self-sampling method of HPV testing which will provide insights on the feasibility in the public health system. NICPR continues to collect data for the Population Based Cancer Registry in District Gautam Budh Nagar.

The Institute has laid continual emphasis on primordial, primary, secondary and tertiary prevention of various cancers. The Division of Cytopathology has been carrying out cytology-based screening/ early detection of prevalent cancers. Screening for cervical and anal cancer, through cytology and HPV testing, is being undertaken in high-risk population (women living with HIV) in an effort to guide policy decisions on screening in such individuals. Training programs focused on cytology-based cervical cancer screening through virtual platform and live microscopy sessions have been initiated for capacity building of pathologists, especially in remote areas.

Scientists of the Institute have been recognized for their hard work and expertise at various forums. Dr Mausumi Bhardwaj was elected as Fellow of West Bengal Academy of Science and Technology (FAScT), 2020; Dr. Smita Asthana was awarded Best Paper Award at the National Conference of Epidemiology Foundation of India 2020; Dr. Prashant Kumar Singh was invited as an Expert to the WHO's "Equity Manual External Expert Review Group" on Sexual, Reproductive, Maternal, New-born and Child and Adolescent Health (SRMNCAH), by Department of Maternal, Newborn, Child and Adolescent Health and Ageing (MCA) and Sexual and Reproductive Health and Research (SRH), World Health Organization (WHO), Geneva in April 2021.

A total of 43 papers have been published by the Scientists during this period with a cumulative Impact Factor of 143.02. Two new Scientists have joined the Institute and positions of Technical staff and Support staff have also been filled by transfer from other ICMR Institutes.

To promote interdisciplinary research among various institutes, NICPR is committed to establish a ICMR National BioBank in its premises as a repository to store annotated biological samples and provide them for research and academic activities.

NICPR has contributed significantly both in research and capacity building during this period. The immense support of the Scientific, Technical and administrative staff of the Institute has made it possible to carry out diverse activities. The support of the Division of NCD and ICMR Hqrs for all activities deserves a special mention.

I wish the entire Team a fruitful year ahead and success in all future endeavours. .

Dr. Shalini Singh
Director
www.nicpr.icmr.org.in
www.cancerindia.org.in
http://untobaccocontrol.org/kh/smokeless-tobacco/

About the Institute

ICMR-National Institute of Cancer Prevention and Research (ICMR-NICPR), initially established as Cytology Research Centre (CRC) by the Indian Council of Medical Research (ICMR) in 1979, was elevated to the level of an Institute (Institute of Cytology and Preventive Oncology) in 1989. The Institute was granted a national status and was rechristened as National Institute of Cancer Prevention and Research in 2016 in view of its significant contribution towards cancer prevention and control in the country. The niche areas of research have included pre-cancer and cancers of the uterine cervix, breast and oral cavity with special emphasis on primary and secondary prevention. The concepts of clinical downstaging of cervical cancer, visual inspection of cervix with selective cytology screening and novel diagnostic approaches for HPV and other oncogenes were implemented by ICMR-NICPR for screening and early detection of cervical cancer. The scientists at the Institute innovated and designed a simple and economical visual device with a light source (AV Magnivisualizer) for better visualization of the uterine cervix as well as the oral cavity, to be used in community-based cancer screening programs where colposcopy facilities might be lacking. The technology has been transferred by ICMR to a private company for its commercialization.

The current major research areas at ICMR-NICPR include screening for common cancers, early detection and management of precancers, development and validation of point-of-care screening and diagnostic tests/devices, analysis of breast cancer susceptibility genes and genomic landscapes of gall bladder and esophageal cancers. With the WHO’s call for cervical cancer elimination by 2030, the Institute is undertaking a demonstration project on cervical cancer elimination in Sikkim using a multi-pronged approach.

Many multidisciplinary extramural as well as intramural comprehensive research projects are underway to accomplish these goals.

In addition to the research activities, the Institute offers diagnostic & referral services for cancer screening to various government-run hospitals across Noida. The Institute has been organizing community outreach activities including cancer awareness and screening camps in Gautam Budh Nagar district, U.P. A website "***India Against Cancer***" has been designed and hosted by the Institute to provide India-specific information on prevalent cancers to the general population as well as primary level health care workers in English as well as Hindi, to promote cancer awareness. Regular training programs on cancer prevention, screening and early detection are being carried out for different cadre of health providers through ECHO (Extension Community Health Outcomes) platform. A Health Promotion Clinic functions at the Institute for screening for non-communicable diseases including the prevalent cancers in the attendant population. These activities are supported by the provision of fine needle aspiration (FNA) of breast and other body lumps and cytology-based cervical and oral cancer cancer screening.

ICMR-NICPR has been playing a nodal role in training of different health cadre workers to facilitate the effective roll out of population-based screening of common cancers in India as outlined in the "Operational framework document" of MoHFW for screening and management of common cancers.

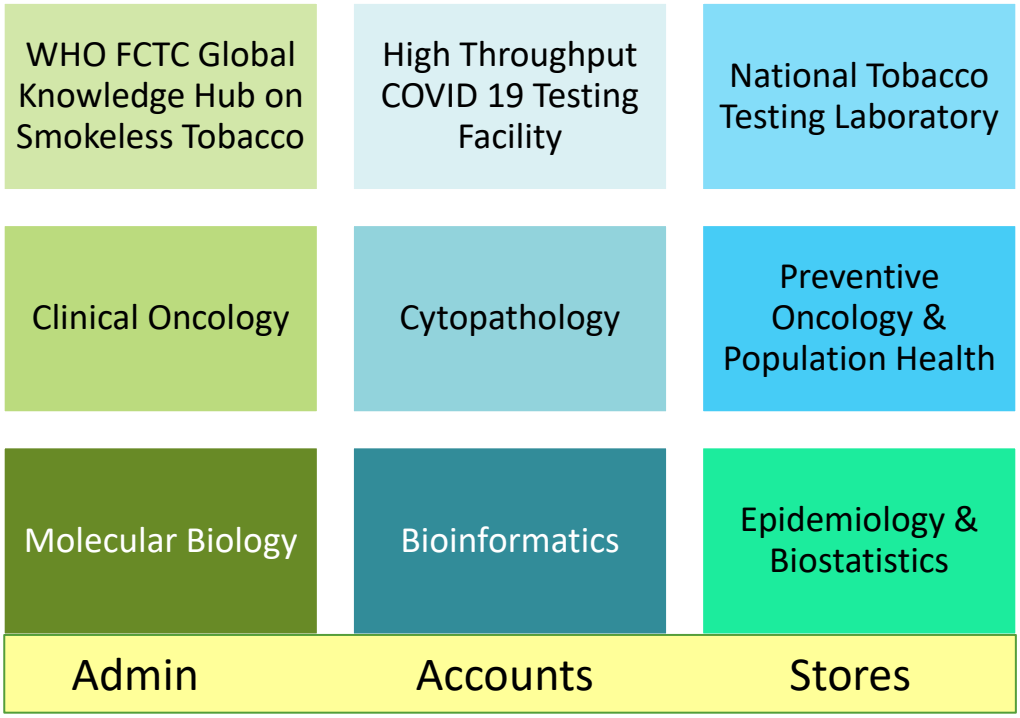
The Institute has affiliation with different universities for Ph.D. program, including, Delhi University, Banaras Hindu University and Jamia Millia Islamia. NICPR promotes capacity building in different specialities through in-service training workshops, summer training programs, MSc. project dissertation and Ph.D. programs.

ICMR-NICPR hosts the prestigious WHO FCTC Global Knowledge Hub on Smokeless Tobacco Products which generates and shares knowledge on smokeless tobacco and guides the Parties to FCTC in control of SLT use. The Knowledge Hub is working towards realizing the dream of a Tobacco-free India through creation of mass awareness, promoting cessation for all types of tobacco products, and bringing about a step-change in implementation of effective prevention and control policies. The Institute also houses the apex-level National Tobacco Testing Laboratory supported by the MoHFW for testing of tobacco samples sent by the states.

Since the beginning of 2020, the world as well as our country has been fighting with the pandemic of novel coronavirus (Covid-19). ICMR-NICPR rose to the occasion and established a High-throughput Viral Diagnostic Laboratory for RT-PCR based Covid-19 testing. This facility has conducted rgular testing during the ongoing second wave of Covid-19. More than 17 lakh RT-PCR tests for Covid-19 have been done at the facility catering to Western UP and Delhi. NICPR has also supported establishment of RT PCR testing facilities across the length and breadth of the country by providing logistics support and capacity building. Research projects on various aspects of Covid-19 are also being undertaken and proposed by the scientific staff to better understand the disease profile and its possible treatment options.

The Institute has been taking active part in the Covid-19 serosurveys being conducted by ICMR to assess the seroprevalence of Covid-19 antibodies in three districts of Western UP. NICPR has also successfully followed up the recipents of Covaxin to determine the frequency of adverse effects of the vaccine.

A Bio-bank facility is soon to be established at NICPR to promote interdisciplinary and inter-institutional research.



FACILITIES AT ICMR-NICPR

Health Promotion Clinic

The health promotion clinic has been functional at NICPR for the last seven years. It functions in the OPD rooms situated in the clinical oncology wing, ground floor. Patient data is collected in electronic format.

Activities carried out at Health Promotion Clinic:

- Creating awareness of cancer and its risk factors through kiosk displayed in the clinic area.
- Documentation of demographic details
- Screening for hypertension and diabetes
- Height, weight, and BMI estimation
- Cancer Screening services
    - Cervical cancer screening
        - Visual Inspection with acetic acid,
        - Pap smear
        - HPV DNA testing
    - Breast Cancer screening
        - Clinical breast examination
    - Oral Cancer Screening:
        - Oral Visual Examination
- Diagnostics services
    - Colposcopy examinations
    - Biopsy
- Treatment Services
    - Thermal Ablation
    - LEEP
- Symptomatic treatment

Summary of work done (Oct 2020 – Jun 2021):

- Total number of individuals screened: 1260
  (Females- 887, Males-373)
- Total number of Pap smears: 826

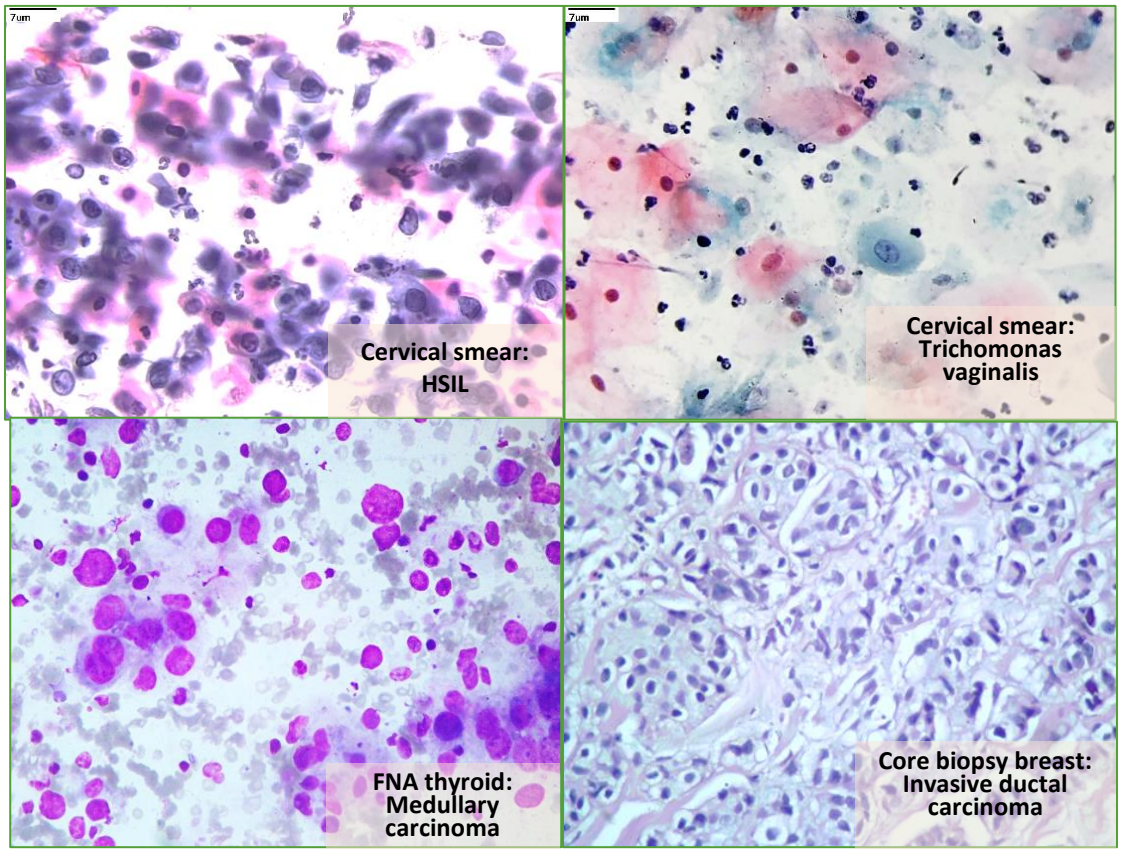
Oral Health Promotion Clinic

- A total of 1193 individuals were screened at the Oral Health Promotion Clinic.

Diagnostic and Referral Services

Diagnostic and referral services are provided to District Hospital and ESI Hospitals, Noida, Sai Sansthan and Tuberculosis centres across Noida in the following fields:

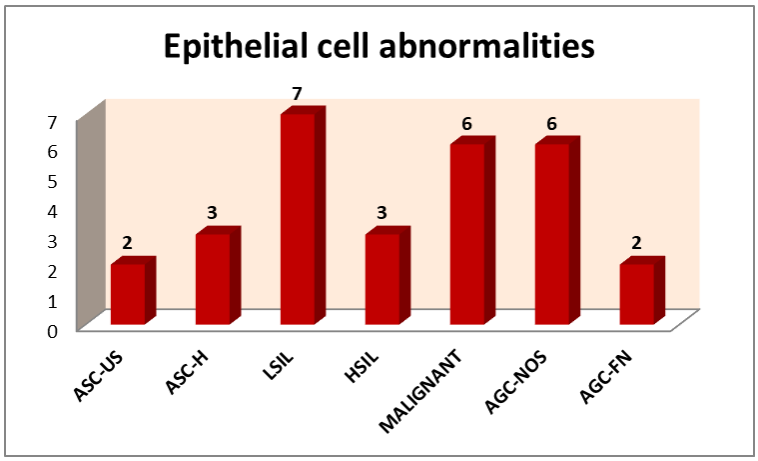
Investigation/ Procedure	No. conducted from Oct 2020 – June 2021
Pap smears	826
Fine needle aspiration cytology (FNAC)	1462
Histopathology (biopsy examination)	73
Colposcopy	30
Thermocoagulation	2
HPV testing (HC2)	773

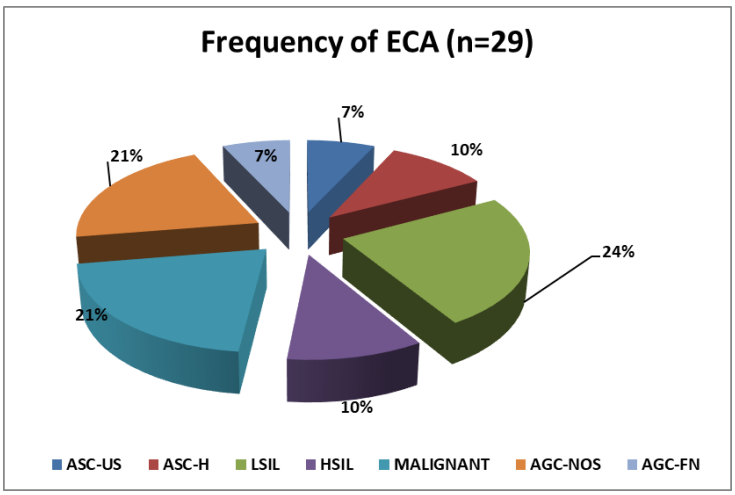


Audit of cervical smear reporting (Oct 2020 – Jun 2021)

- Total no. of cervical smears: 985
- Unsatisfactory rate: 2 (0.2%)
- Epithelial cell abnormalities (ECA): 29 (2.95%)

Epithelial cell abnormality	Number of cases	Percentage (N=983)
ASC-US	2	0.20
ASC-H	3	0.30
LSIL	7	0.71
HSIL	3	0.30
MALIGNANT	6	0.61
AGC-NOS	6	0.61
AGC-FN	2	0.20
Total	29	2.95



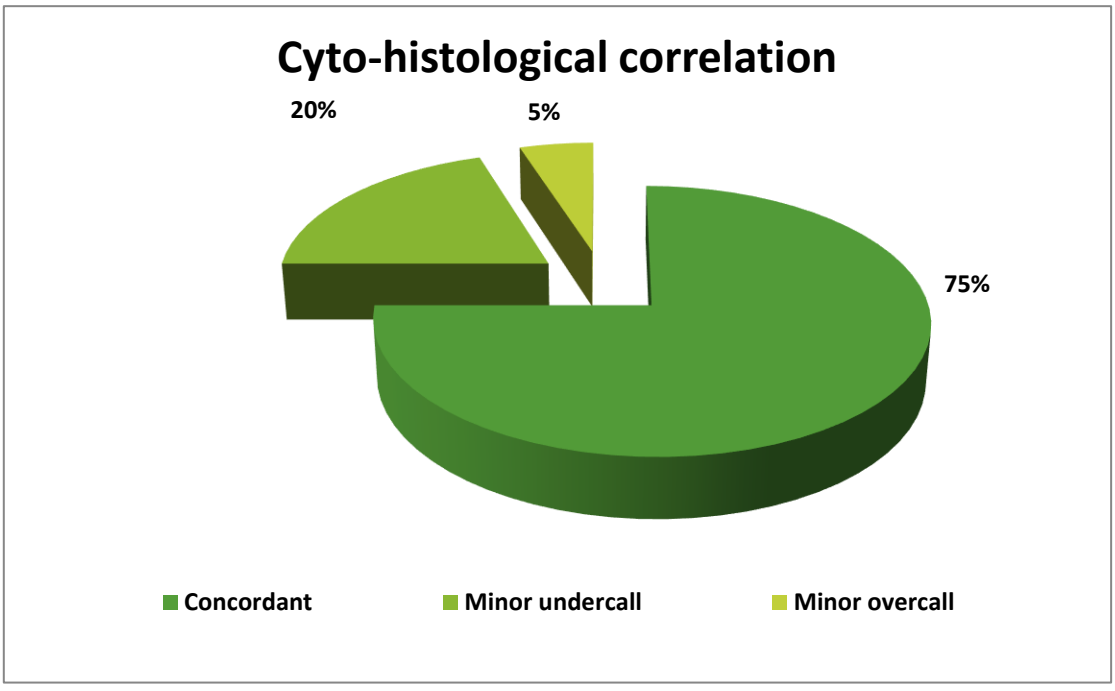


Cyto-histo correlation of cervical abnormalities *(as per American Society of Cytopathology guidelines 2017)*:

- **Cervical biopsies**: 21
  - Inadequate biopsies: 1
  - Adequate biopsies: 20

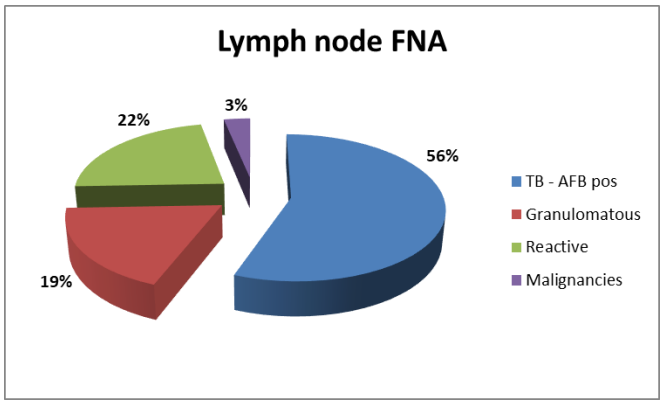
- **Cyto-histo concordance**: 15 (75% of 20)

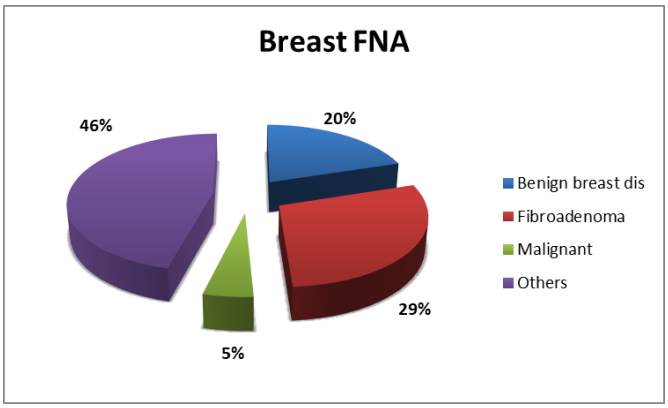
- **Discordance**:
  - Sampling error on biopsy: 1
  - Interpretative error on Pap: 4 (1 minor overcall, 3 minor undercall)

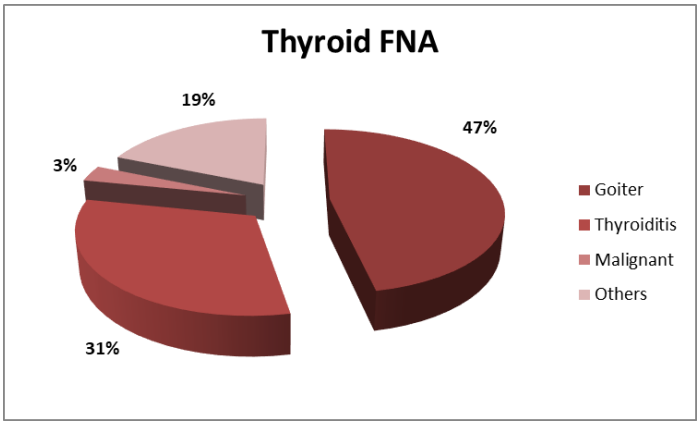


Fine needle aspiration cytology:

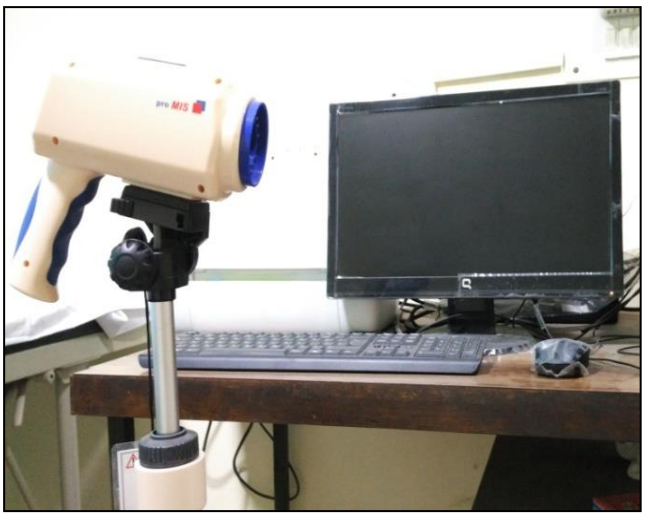
- **FNACs**: 1462
  - Lymph nodes: 645
  - Breast: 293
  - Thyroid: 32
  - Other sites: 489







Colposcopy



Colposcopy is a diagnostic procedure that involves examination of the cervix, vagina and vulva with the help of equipment named 'Colposcope'. It has a powerful light source for illumination of the area to be examined and a variable magnification ranging from 4x to 30x. The evaluation of the screen positive women (Pap smear report ASCUS and above, Hr HPV positive and VIA positive) is done using colposcopy at NICPR. If any abnormal lesion is detected on colposcopic examination, biopsy is taken and sent to the cytopathology division for reporting. Further management of the woman is undertaken based on the histology report of the biopsy.

High risk HPV detection by Hybrid Capture 2 (*HC2*)

Hybrid Capture 2 (HC2) technology serves as the platform for QIAGEN's nucleic acid hybridization assay for detection of 13 High risk human papillomaviruses (HPV).

Cervical scrapes from 773 women were tested for HR-HPV during the reporting. All the positive cases are being further analyzed for type specific HPV by PCR using HPV 16 & 18 primers. This information in conjunction with cytology report and colposcopy findings is utilized to guide patient management.

High Throughput Viral Diagnostic Laboratory (HTVDL) for COVID 19 Testing

A High throughput Viral Diagnostic laboratory (HTVDL) for COVID 19 testing was inaugurated at ICMR-NICPR in July 2020. The facility has been catering to the RT-PCR based COVID 19 testing needs of Uttar Pradesh and Delhi with an installed capacity of 6,000 samples per day.

HTVDL has worked tirelessly at the time of surge in COVID 19 cases during October, November, December 2020 and during the second wave in March, April, May 2021. During this period, HTL has adopted various modalities like sample testing with pooling strategies whenever the positivity rate came down less than 5%, adoption of manual extraction procedures and inculcating research using the available resources. NICPR-HTVDL has actively participated with the Indian SARS-CoV-2 Genomics Consortium (INSACOG) by sending positive samples for genomic sequencing.

HTVDL successfully accomplished 14 lakh sample testing for COVID 19 till June 30th 2021 and shall be completing one year of its successful functioning in July 2021.

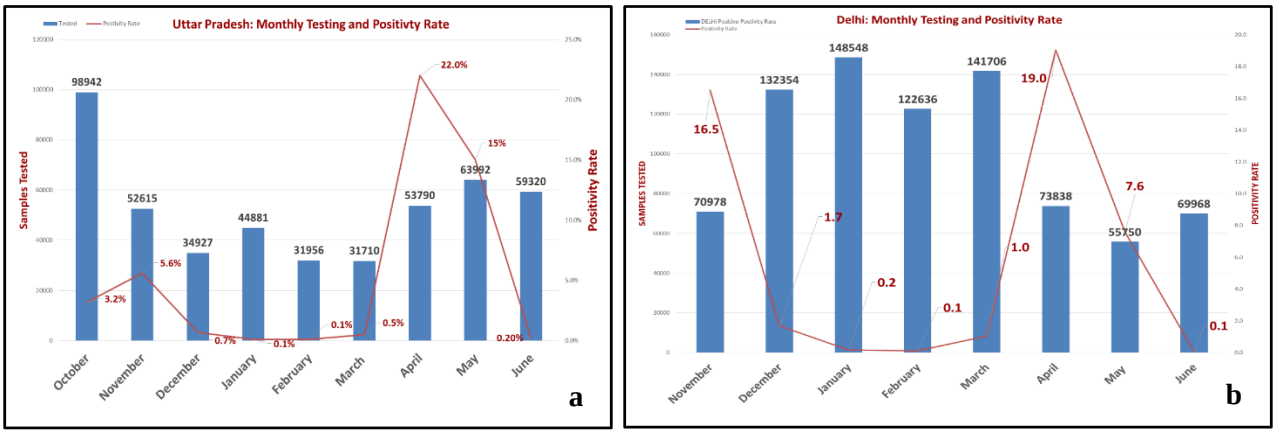


Fig: Graphical representation of NICPR-HDVTL sample testing and positive rates in UttarPradesh (a) and Delhi (b) districts during Oct 2020 – Jun 2021.

National Tobacco Testing Laboratory

The National Tobacco Testing Laboratories (NTTLs) have been established by the Ministry of Health and Family Welfare, Govt. of India at three centers: ICMR-National Institute of Cancer Prevention and Research (NICPR), Noida; Centre Drugs Testing Laboratory (CDTL), Mumbai and Regional Drugs Testing Laboratory (RDTL), Guwahati for the purpose of Tobacco Research and Testing. The NTTL at NICPR is the apex and coordination center for the other two labs first-of-its-kind in the southeast Asian region. NTTLs are envisaged as world class accredited laboratories providing analytical facilities and advisory for tobacco and tobacco products.

Objectives:

- Achieving best laboratory practices and participative compliance with Govt. recognized accredited agencies and WHO norms for standardization, regulation and monitoring.
- Estimation of toxicants present in smokeless tobacco.
- Sharing of knowledge, Expertise, Experience with world leaders on standard operating procedures, GLP, ISO etcfor tobacco testing.
- Adaptation of WHO, ISO and BIS Methods for testing of SLT products for estimation of pH, Moisture, Ammonia, Nitrates/Nitrites, Nicotine, TSNAs, Humectants, Sugars, Chlorides and Trace elements etc.
- To participate in the validation of WHO method for testing of smoked and smokeless tobacco samples.
- Generation of Scientific data for the constituents present in various forms of Smoked & Smokeless Tobacco products.
- To develop sensory materials for the development of sensors strip for detection of tobacco alkaloids.
- Development of methods for the estimation of nicotine in biological samples.

Activities: During the reporting period, the NTTL-NICPR shared the research experience on SLT samples with the Director, WHO TobLabNet, Dr. Nuan Ping (through MoHFW) for improvement/ modification of SOPs for analysis of nicotine, moisture and pH in SLT samples and also analyzed the reference sample received from Dr Nuan Ping for method validation. The NTTL analyzed the legal SLT samples from Food Safety Officers, Govt. of Karnataka and Bihar. The Lab at NICPR performed analysis of 153 SLT samples for various parameters such as Nicotine, Humectants, Moisture, Total sugars, Ammonia, Volatile Bases, Chloride, and pH for about 900 tests in triplicate (approximately 2500 tests).

The scientific officers at NTTL-NICPR attended the following webinars/ meetings:

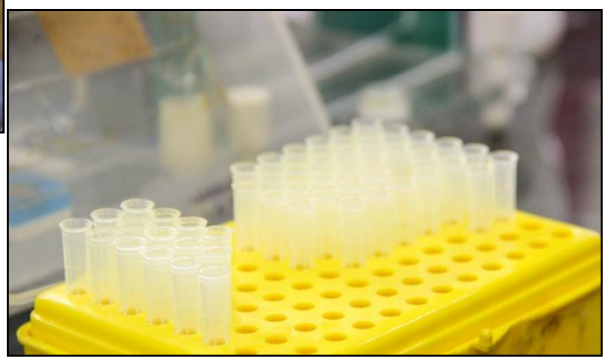
- Agilent SLIMS: An integrated LIMS and ELN solution to digitally transform your lab by Agilent Technologies, 13th October, 2020.

- "Scope of modifications to your existing Apparatus and Autosampler for varying Automation & compliance requisites" by Agilent Technologies, 15th October, 2020.
- "Advance GC solutions to detect adulteration in Flavour & Fragrance of Essential Oils" by Agilent Technologies, 15th October, 2020.
- Webinar entitled "Understanding Gas Chromatography" by Agilent, 9th December, 2020.
- Curtain raiser events by ICMR- National Institute of Cancer Prevention and Research for IISF, 11th December 2020.
- Webinar entitled "Building Blocks for a Robust GC Method" by Agilent, 11th December, 2020.
- Webinar entitled "Advancement in Analytical Techniques" by Lab India, 14th December, 2020.
- Webinar entitled "Robust Agilent Solutions for GC Applications" by Agilent, 15th December 2020.
- Webinar entitled "Introduction to Ion Mobility and the SELECT SERIES Cyclic IMS by Waters, 27th January, 2021.
- Meeting of Technical Committee to handhold the NTTLs, by MoHFW, 2nd February, 2021.
- Joint meeting of Scientific Support Group and National Tobacco Regulators Forum by MoHFW, 4th February, 2021.
- Webinar entitled "Understanding the language of liquid chromatographic results by Agilent, 11th February, 2021.
- Webinar - Column Selection and Efficient Method Development Approach, by Waters, 26th February, 2021.
- Webinar on "Transform Your GC & GC-MS Results" by ThermoFisher Scientific, 3rd March, 2021.
- Webinar on Agilent SLIMS: An integrated LIMS solution to digitally transform your lab, 5th March 2020.
- Meeting of Technical Committee to handhold the NTTLs, by MoHFW, 6th April, 2021.
- Webinar on Article 5.3 organized by WHO FCTC Global Knowledge HUB on Smokeless Tobacco at ICMR-NICPR, Noida, 15th April, 2021
- Webinar on Myths & Facts about H2O & its impact on your test results by Milli-Q, Merck Life Science Private Limited, 28th April, 2021.
- Webinar on Effective Pipetting: Every drop counts-Best practices for liquid handling by IKA, 25th May, 2021.

Future Plans:

- Preparation of Standard Operating Procedure (SOP) for analysis of smoked and smokeless tobacco products marketed in India.
- Designing of Research Project on tobacco product analysis.
- Up-gradation of NTTL facility with major and minor equipments.
- Accreditation of NTTL by NABL.
- Development of new methods of tobacco product analysis according to the SLT products available in India.

RESEARCH PROJECTS



CERVICAL CANCER

Prevalence of concurrent cervical and anal cytologic abnormalities and High-risk HPV infections in HIV infected women: An exploratory study

Principal Investigator: Dr. Sanjay Gupta, Scientist G, Division of Cytopathology

Other Collaborating Institutes: District Hospital, Noida

Funding Agency& Budget: ICMR, Rs 25,53,790/-

Project Duration: Jul 2019- Dec 2021

Brief background & rationale: High risk Human papillomavirus (HR-HPV), the primary cause of cervical cancer, is also associated with the development of anal cancers. Rates of cervical and anal human papillomavirus (HPV) infection and abnormal cytology are high in HIV-infected women. It is established that HPV infection can be transmitted to women through receptive anal intercourse. HR-HPV subtypes have been detected in 99% of cervical cancers and 80 to 90% of anal cancers It is possible that the pathogenesis of anal cancer is similar to that of cervical cancer, that is, anal HPV infection, in conjunction with other factors, leads to development of high-grade anal intra-epithelial neoplasia (HGAIN), a likely precursor to anal cancer. Despite the considerable data on cervical neoplasia and HPV infection in HIV- infected women in India, there is limited data on anal neoplasia and anal HPV infection in this population. Also, there is no Indian literature on concomitant cervical and anal HPV infections and cytological abnormalities in HIV positive women.

Objectives:

- To determine the prevalence of anal epithelial abnormalities in HIV-infected women, through cytology
- To determine the prevalence of anal HPV infection in HIV infected women
- To identify the risk factors associated with anal HPV infection in the study population.
- To determine the association of anal HPV infection with concurrent cervical HPV infection, and concurrent cytological abnormalities

Brief Methodology: This is an exploratory cross-sectional study including 130 HIV-positive women (cases) and 150 HIV-negative women (control group) attending Integrated Counselling and Testing Centre (ICTC) of District Hospital, Noida and willing for Genital examination and anal sampling.

Eligibility criteria:

- Documented serologic evidence of HIV infection as per National Guidelines
- Absence of any illness that may preclude a pelvic and /or anal examination
- No prior history of screening or treatment for anal neoplasia
- No prior hysterectomy
- No h/o HPV vaccination

After obtaining written informed consent, a detailed sexual and medical history for gynecological health care and risk factors for the development of anal neoplasia is collected. All women undergo sampling for cervical Pap smear and for cervical HPV testing (by HC2). Concurrent sample collection from anal canal for cytology and HPV testing is also be done. Samples testing positive for high-risk HPV shall be further analyzed by PCR for HPV 16/18 genotyping. Additionally, women receive a symptom directed physical examination followed by testing and care as indicated. Women are asked to return to the clinic after a week to receive results of cervical and anal cytological examinations or any other investigations and undergo referrals for any medical/Gynae condition to appropriate tertiary care centres. Women found to have cervical or anal epithelial cell abnormalities are referred for appropriate management.

Work done:

The funding for the second year of the project was received in March 2021. Participant recruitment was continued from the Integrated Counselling and Testing Centre (ICTC), District Hospital Noida. For all the participants, the clinical proforma and questionnaires (attached) were completed. In view of the ongoing Covid-19 pandemic, hospital services at the District Hospital Noida were curtailed for a significant amount of time during the reporting period leading to a lag in recruitment of participants in the study.

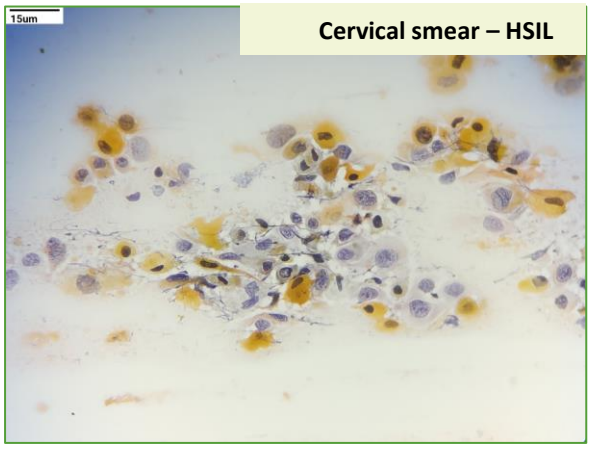
Table Summary of the anal and cervical cytological abnormalities and HR-HPV testing results in HIV-positive and HIV-negative women

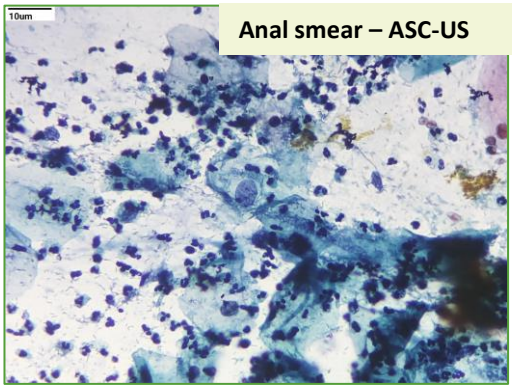
	No. of participants	**Cervical cytology**	**Cervical HR-HPV (HC2) N (%)**	**Anal cytology**	**Anal HR-HPV (HC2)**
HIV-negative (controls)	90	3 ASC-US 87 NILM	8 Positive (8.89) 82 Negative	1 ASC-US 89 NILM	7 Positive (7.78) 83 Negative
HIV-positive (cases)	50	3 HSIL 1 ASC-H 3 LSIL 7 ASC-US 36 NILM	19 Positive* (41.3) 27 Negative	3 ASC-US 47 NILM	19 Positive* (41.3) 27 Negative

*HR-HPV: High risk HPV; ASC-US: Atypical squamous cells – undetermined significance; ASC-H: atypical squamous cells – cannot exclude HSIL; NILM: Negative for intraepithelial lesion or malignancy; LSIL: Low grade squamous intraepithelial lesion; HSIL: High grade squamous intraepithelial lesion. *15 samples concurrently positive for HRHPV in cervical and anal samples*

The mean age of HIV-positive cases was 35 (±11.5) years while that of the HIV-negative controls was 32.7 (±7.9) years, with no statistical difference. No significant difference was noted between the cases and controls for parameters such as age at menarche, age at first childbirth, and the past or current history of sexually transmitted disease (STD) in the participant or the spouse.
On statistical analysis of the data collected so far, anal HPV infection was found to be significantly associated with abnormal cervical cytology (ASC-US or higher) as well as cervical HPV detection concurrently ($P < 0.05$ for both). However, no association was found between anal HPV and past or current history of STD in the participant or the spouse.

Among HIV-infected women, cervical cytological diagnosis of ASC-US and above demonstrated a positive association with the participant having more than one sexual partner (P<0.001) but not with other socio-demographic parameters.





Translational Potential: The study shall:

a) Determine the prevalence of anal HR-HPV with or without cervical HPV shedding in HIV infected women in India.
b) Delineate the spectrum of anal and cervical epithelial abnormalities in HIV infected women.
c) Determine risk factors for anal HPV in HIV infected women.
d) Establish feasibility of Anal HPV testing and cytologic examination for anal cancer screening.

Development of a Low-Cost Automated Screening System for Cervical Cancer (CerviSCAN II) – a collaborative project of CDAC(T) and RCC-T

Site Investigator: Dr. Sanjay Gupta & Dr. Ruchika Gupta, Division of Cytopathology

Other Collaborating Institutes: Centre for Development of Advanced Computing (C-DAC), Regional Cancer Centre Thiruvananthapuram

Funding agency & budget approved: DHR and MeitY, 314 lakhs (NICPR: 17.25 lakhs)

Project Duration: Jun 2018 – Apr 2020 (extended to Jul 2021)

Brief background & rationale: Cervical cancer is the second most common cancer among females in India. It can be detected early during the precancerous phase by screening through one of the three methods – Pap smear, visual methods, or HPV testing. Organized cytology-based cervical cancer screening program could not be implemented in India due to limited trained manpower, ie cytotechnicians and cytopathologists. The commercially available automated screening systems for cervical cancer are very expensive for resource-constrained countries. C-DAC(T) and RCC-T developed a low-cost automated system, CerviSCAN in their earlier project. However, the slide imaging was manual and wide variation in slide preparation was noted. Hence, this project aims to develop technology for low-cost automated slide scanning system, cyto-centrifuge and auto-stainer as a complete automated cervical cancer screening system with field trials at three centres, including NICPR.

Objectives:

- To develop a low cost and high throughput scanning system with automatic focus control for digitizing the slides
- To develop a low cost cyto-centrifuge for preparing monolayer slides using Mega Funnel Technique
- To develop a low cost auto-stainer for uniform staining of slides
- To enhance the existing algorithms of CerviSCAN and optimize for processing speed
- To conduct multi centre field trials of the complete system at RCC, Thiruvananthapuram and other three identified centres

Work done:

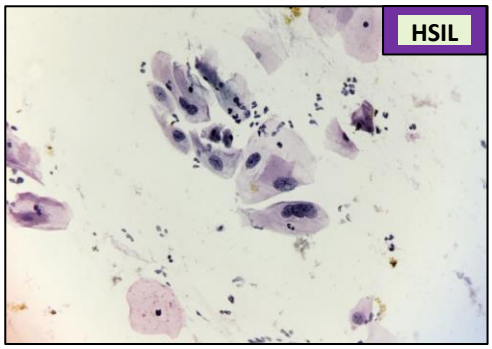
CDAC(T) has developed an indigenous slide digitizer, DiGiSmear AS20, with motorized XY and Z axes along with indigenous auto-stainer and cytocentrifuge for the project. Artificial intelligence-based algorithm for detection of abnormal cells using deep learning approach has been developed and tested against screening of cervical smears by cytotechnologists at RCC-T.

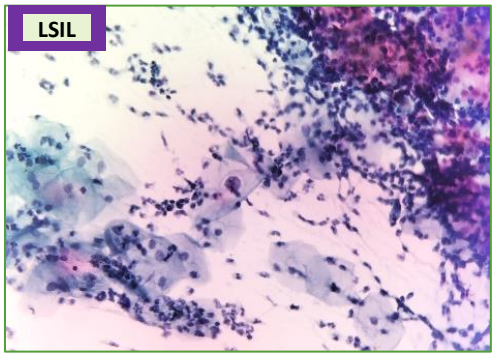
From NICPR, a total of 3569 cervical samples collected in liquid medium have been transported to RCC-T for processing by megafunnel technique and utilization in refining of the algorithm for cervical cancer detection, of which 3562 were satisfactory for evaluation.

Table Frequency of cervical epithelial lesions detected among 3562 cervical samples

S.NO	Cervical Cytologic Abnormality	No. of Cases	% (out of 3562 samples)
1	**Squamous**	**85**	**2.38**
	ASC-US	23	0.64
	ASC-H	5	0.14
	LSIL	35	0.98
	HSIL	11	0.31
	Malignant	11	0.31
2	**Glandular**	**27**	**0.76**
	AGC-NOS	24	0.67
	AGC-FN	3	0.08
	TOTAL	112	3.14

A PRSG meeting held in December 2020 approved the project extension till July 2021. The installation of the system at NICPR is awaited for field trial.





Translational Potential: The proposed system being developed in this project can be deployed as a complete system with limited dependencies on the external vendors or suppliers for the components like slide scanners, etc. The low-cost automated screening system could augment the cervical screening coverage in low resource settings like ours.

Molecular Evaluation of Anticancer and Antiviral properties of Thuja Occidentalis

Principal Investigator: Dr. R. Suresh Kumar, Scientist E, Molecular Biology Group

Other Collaborating Institutes: School of Life Sciences JNU, Central Council for Research in Homeopathy (CCRH)

Funding agency & budget: Ministry of AYUSH, 45 lakhs

Project Duration: Jan 2017 – Dec 2020 (extended till 2021)

Brief background & rationale: Thuja Occidentalis has been used to treat warts in homeopathy system. Human papilloma virus consists of 8kb genome which contains early and late genes. The E6 and E7 are considered as oncogenes which degrade or inactivate P53, pRb respectively andinduce cell cycle and proliferation. The present project intends to assess the anticancer and anti viral potential of Thuja Occidentalis in HPV infected cancer cells and its molecular mechanism in transcriptional regulation in controlling HPV transcription. The rationale is to control the transcription of E6 and E7, therby controlling the carcinogenesis process. HPV transcription is controlled by host transcription factors like AP1 and NFKb, and these transcription factors can be modulated by many of known phytochemicals. The present study tries to identify whether Thuja could modulate transcription factor and thereby control its transcripts and protein synthesis.

Objectives:

- To study the anti cancer effect of active component extract/mother tincture of Thuja occidentalis in cervical cancer cell lines infected with HPV.
- To study the phenotypic characteristics, candidate gene signatures, induction of apoptosis, population doubling time in treated cell lines.

Brief Methodology: Antioxidanat assay was performed using DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) a free radical method, which is based on electron transfer that intiates development of violet color in ethanol. Total flavnoid was determined by Aluminium Chloride method where 1 ml of test samples, 4 ml of water, 5% sodium nitrite, and 10% aluminium chloride were added. After 6minutes of incubation at RT, 1ml of sodium hydroxide was added to reaction mixture. The final volume was made to 10 ml and the absorbance was measured against Blank at 510 nm using spectrophotometer. Total Phenolic component was estimated by folin Ciocalteau reagent. Thuja extract 0.5ml was taken and was mixed in 1.5 ml Folin ciocalteu reagent (diluted 1/10). After 5 minutes incubation, 5ml of 5% sodium carbonate solution was added. The volume was made to 10 ml with distilled water. Absorbance of samples was measured at 750 nm using spectrophotometer. HeLa Cells were treated with Thuja (30C) for 48 hrs and cells were maintained in Co2 under standard condition of maintenance. The treated and untreated cells were maintained

in parallel. The cells were taken off from the petri dishes under cold condition; the cells were immediately pelleted and stored in -80C. The protein isolation was carried out using commercial kit. The proteins were quantitated and filtered through designated columns. In-solution digestion by trypsin was carried out. The samples were processed by Delhi University South campus proteomics facility.

Work done:

We have assessed Phenolic, flavanoid contents of the Thuja using thin layer chromatography and spectrophotometer methods. In addition, we have tested the alteration of proteomic contents by LC-MS/MS in Thuja-treated cells. We found exclusively expressed genes which are very less in number and need to revalidate the experiments.

Translational Potential: The preliminary study will be elaborated on transcriptional regulation of HPV in treated cells, there by controlling the HPV replication, propagation, and control of cell cycle.

Scaling up of implementation of primary HPV screening by self-sampling

Principal Investigator: Dr. Roopa Hariprasad, Scientist E, Division of Clinical Oncology

Funding agency & budget: ICRC-ICMR, 1 crore 47 lakhs

Project Duration: Nov 2020 – Oct 2023

Brief background & rationale: India is working towards achieving the target set by the World Health Organization (WHO) for cervical cancer elimination by 2035.Cervical Cancer is the second common cancer among females in India. Globocan 2018 estimates the incidence of cervical cancer in India as 96,922 and mortality as 60,078. Sikkim state is the first state in our country which has successfully included HPV vaccination in their immunization program for girls between 9-14 years of age and completed 2 doses of vaccination (first dose in August 2018 and second dose in April 2019). HPV testing is considered the most effective screening approach for cervical cancer. Our study focuses on feasibility of primary HPV DNA testing on self-collected samples in Sikkim.

Objectives:

- To evaluate the acceptance of home-based self-collection by the women, compliance of the women to further assessment.
- To evaluate the acceptance of the home-based screening by the ASHA workers, the facilitators and barriers faced by them to motivate women.
- To assess the feasibility of setting up a centralized HPV test facility in a district hospital with appropriate training of the laboratory technician.
- To assess the feasibility and effectiveness of a referral mechanism, through which the screen positive women will be managed at the district hospital.

Brief Methodology: Women aged 30-65 years, residing in East district of Sikkim would be offered HPV test on the self-collected samples. ASHAs shall collect the self-collected HPV samples and transport it to district hospital where the HPV testing facility would be placed. One rural and one urban PHC in this district have been selected; eligible women would be about 6000.

Work done: Ethics committee approval has been obtained. Project staff has been recruited. IEC materials have been translated, equipment purchased, and stakeholders sensitized. Online training in cervical cancer screening for Medical Officers, Gynaecologists at the implementation site has been conducted.

Translational Potential: The results of this implementation study can be used to replicate in other states who are ready for primary HPV screening and the various challenges faced in the implementation will become clearer and help GoI and the states to make necessary changes during implementation of the population cancer screen.

Is the Age Group 30–65 Years Optimum for Cervical Cancer Screening in Low-Resource Settings?

Intramural Research Study by Division of Cytopathology, NICPR

Background: An Operational Framework document for population-wide screening of common cancers in India was launched in 2016. The target age for screening has been decided as 30–65 years for cervical cancer.

Objectives: To determine if we are likely to miss significant cervical abnormalities by focusing on this age group alone.

Brief Methodology: A retrospective review of all satisfactory cervical smears (*n* = 79,896) received over a ten-year period (2010–2019) was conducted. Three age bands were defined: 21–29 years, 30–65 years and > 65 years. The frequency and distribution of the various epithelial cell abnormalities (ECAs) across these three age bands were calculated separately and compared.

Main Findings: Of the total 1357 ECAs (1.7% of all smears), about 16.9% were seen in the age band 21–29 years, while 4.5% presented in women >65 years of age. Among the total 512 significant high-grade and malignant (squamous and glandular) lesions, 5.6% presented in women 21–29 years, while 10.1% were seen in women >65 years of age. About 80% of the abnormalities seen in younger women were low-grade squamous lesions, while 75% of lesions in women >65 years were high-grade squamous abnormalities.

Though the majority of the significant cervical lesions would be picked up if the screening focuses on the 30–65 years age group, we are likely to miss about 19% of significant high-grade squamous preneoplastic lesions and 13% of preneoplastic glandular lesions if we exclude screening for women in the age bands 21–29 years and >65 years. The cost of screening incurred by including these age groups needs to be weighed against the benefits derived, especially in resource limited settings. Pending the implementation of universal implementation of HPV immunization, there is a felt need to enhance cervical cancer awareness and encourage screening, more so in high-risk category and symptomatic females beyond the selected age group.

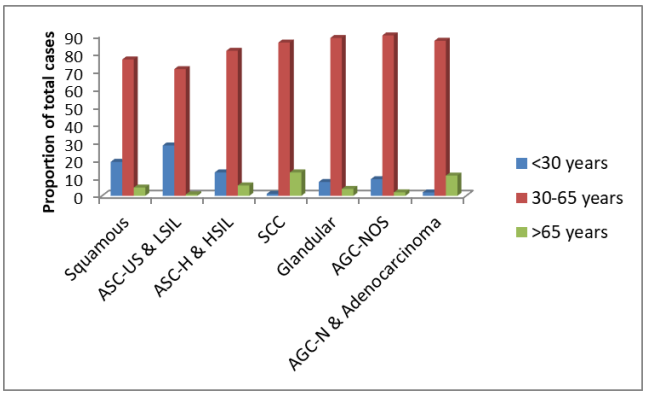


Fig. Proportion of squamous and glandular epithelial cell abnormalities detected in the different age bands.

Impact assessment of cytology based cervical cancer screening training workshops for the pathologists.

Intramural Research Study by Division of Cytopathology, NICPR

Background: Paucity of trained cytopathologists is a deterrent to effective implementation of cervical cancer screening program in resource constrained settings. Although training workshops are organized by a few centres, there is no documented report on their impact on improving the knowledge and skills of the attending pathologists in this field.

Objectives: To evaluate the efficacy of training workshops on the pathologists' knowledge, practice, and skills in cervicovaginal cytology.

Brief Methodology: Data was collected from the 10 cytology-based cervical cancer screening workshops for pathologists conducted by our division over last 5 years, with pre- and post-training evaluation using digital images and a questionnaire (knowledge score). Feedback on diagnostic skills was taken at a 1-month and 6-month interval post-workshop using a separate set of digital images of cervical lesions. A Google form questionnaire was made to seek the participants' feedback on the perceived improvement in knowledge and skills. All the data were analyzed to assess the efficacy of these workshops in imparting the desired knowledge and skills.

Main Findings: A total of 350 participants were enrolled in these workshops. The average knowledge score improved from 10.56 (± 3.23) pre-training to 21.17 (± 2.41) in the post-training evaluation (100.5% increase ($P < 0.001$)]. Similarly, the diagnostic accuracy on digital images was enhanced from 8.6 (± 2.12) to 19.5 (± 4.28) immediately post-training and was maintained at 17.6 (± 3.87) at 1-month and 16.4 (± 4.26) at a 6-month interval ($P < 0.001$). Majority of the participants reported fair to a marked improvement in their knowledge, practice, and confidence in reporting cervical cytology in the response to form-based questionnaire.

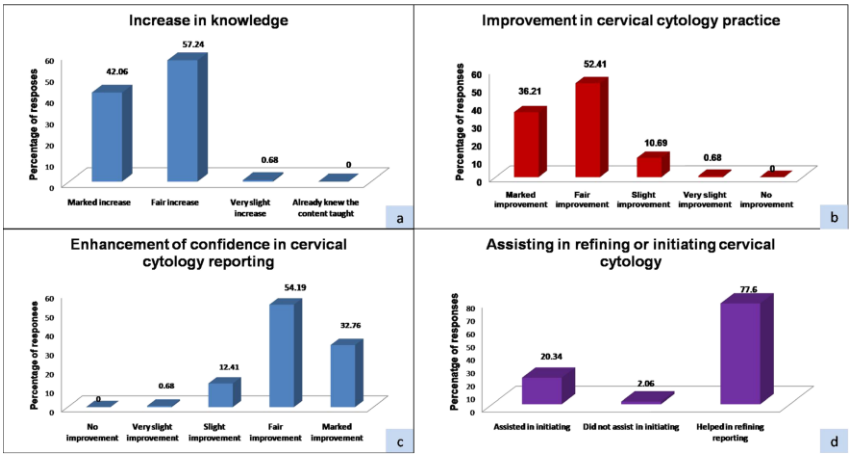


Fig: Graphical representation of response on improvement in knowledge (a), cervical cytology reporting practice (b), enhancement in confidence of reporting (c) and assistance in initiation or refining of cervical cytology practice in their respective setup (d).

Incidence and trends of breast and cervical cancers: A joinpoint regression analysis

Intramural Research Study by Division of Epidemiology and Biostatistics

Objectives: Breast and cervical cancers are two major cancers affecting women's health. Breast cancer is the most invasive cancer, and cervical cancer is the fourth most leading cause of death among women. Analysis of updated incidence data and their trends would help policymakers in planning and organizing programs to reduce the burden. This study aims to present regional variations in recent years and study trends of both the cancers in India.

Brief Methodology: For recent incidence rates of cervical and breast cancers, data were obtained from the National Cancer Registry Programme (NCRP) reports (2009–2011) for 25 registries and of 2012–2014 for 27 registries. Trends were studied for data obtained from different NCRP reports for the years 1982–2014 in six major registries. Number of persons who developed cancer and the annual percentage change in incidence were calculated along with the trend analysis for both the cancers. The Joinpoint Regression Model was used for trend analysis.

Main Findings: The age-adjusted rate (AAR) of incidence of breast cancer in South India was 36.78 in 2009–2011 as against the North region with 41 in 2012–2014. Number of breast cancer cases remained highest in the North-East region but changed from 167 in 2009 to 200 in 2012. Cervical cancer was also the highest in the North-East region during 2009 and 2012. There was an increase in the overall cervical cancer incidence with 24.3 AAR in 2009 to 28.0 in 2012 and one in 200 who develop cervical cancer in 2009 to 250 in 2012. The trend analysis for six major registries showed an increase in the incidence of breast cancer, with the highest increase in New Delhi (3.22), and decrease in the incidence of cervical cancer, with the highest decrease in Mumbai (−1.21). Hence, there has been an exponential increasing trend in breast cancer and a steep declining linear trend in cervical cancer, conferring an inverse relationship between the two cancers. This trend was present in all the major cancer registries.

Cervical Cancer Incidence and Mortality in South East Asia: Evidence from Globocan 2020

Intramural Research Study by Division of Epidemiology and Biostatistics

Objectives: Cervical cancer is one of the leading malignancies among females in Southeast Asian region (SEAR) as defined by WHO. This study aims to examine the cervical cancer burden in SEAR using recently released Globocan 2020 estimates.

Brief Methodology: Age and country wise incidence and mortality estimates for cervical cancer were obtained for 11 SEAR countries using data available from Globocan 2020. Age specific disease burden was analysed using incidence, mortality, and MI ratio (mortality/incidence). Data on human development index (HDI) was extracted from United Nations Development Programme report. Bivariate correlation analysis was done for HDI in relation to Incidence, Mortality and MI ratio separately.

Main Findings: In SEAR cervical cancer estimates for the year 2020 were 190874 cases and 116015 deaths. Age-standardized incidence rate (ASIR) was 18.1/100,000 and age-standardized mortality rate (ASMR) was 11.1/100,000. India was the leading country with 123907 cases and 77348 deaths. ASIR was highest among 50-55 years age group whereas ASMR was maximum in 55-59 years age group. Association between HDI and MI ratio was negative with significant correlation ($r=-0.664$, $p=0.026$). Association between ASIR and HDI as well as ASMR and HDI though negative, was found to be non-significant. To reduce cervical cancer burden in Southeast Asian region, main challenges are lack of cancer awareness, lack of systematic screening, late stage at disease presentation and poor treatment facilities. Mortality was higher in older age group. There was an inverse relationship between HDI and cervical cancer incidence and mortality in the SEAR.

A molecular understanding of the role of oral contraceptives in the pathogenesis of cervical cancer

Principal Investigator: Dr. Anamika Priyadarshini Sil, WOS
Mentor: Dr. Showket Hussain, Molecular Biology Group

Funding Agency: DHR – WOS
Duration of Project: 2017-2020 (concluded in Feb 2021)

Background: Cervical cancer is caused by the persistent infection with high-risk Human papilloma viruses that leads to the development of carcinoma in situ from normal epithelial cells, but not to invasive cancer. Cofactors seem to be necessary for this last step. In this context, a detailed study is ongoing to find out an interplay between viral and cellular genes, and also the role of oral contraceptives (cofactors) in HPV positive and HPV negative cervical cell lines which ultimately lead to malignancy.

Objectives:

- To study differential expression of E6/E7 oncogene on human cervical cell lines on steroid treatment.
- To study the change in the global gene expression in human cervical cell lines with and without OCs treatment followed by their functional validation

Brief Methodology:

Human-derived cervical cell lines were treated with steroid hormones and following assays were done: Cell proliferation assay, Invasion assay, Expression of E6/E7 by RT-PCR and Western Blotting, EMT marker assay by RT-PCR, RNA sequencing and Analysis, Screening of differentially expressed genes, and Functional validation.

Main findings:

The RNA sequencing and analysis showed several dysregulated genes between treated HPV16,18 positive and HPV negative cell lines and untreated cell lines. Functional validation by immunoblot, invasion assay and real time PCR results shows the there is a sharp increase in expression pattern of E6/E7, Bcl-2, Bax genes and ERK-1 genes in treated cell compared to untreated cells.
In addition to this, the Gene ontology (GO) enrichment analysis revealed that most of the genes that are affected are involved in angiogenesis, morphogenesis of branching epithelium and structure, extracellular structure organization, tube morphogenesis, muscle tissue development and organ morphogenesis.

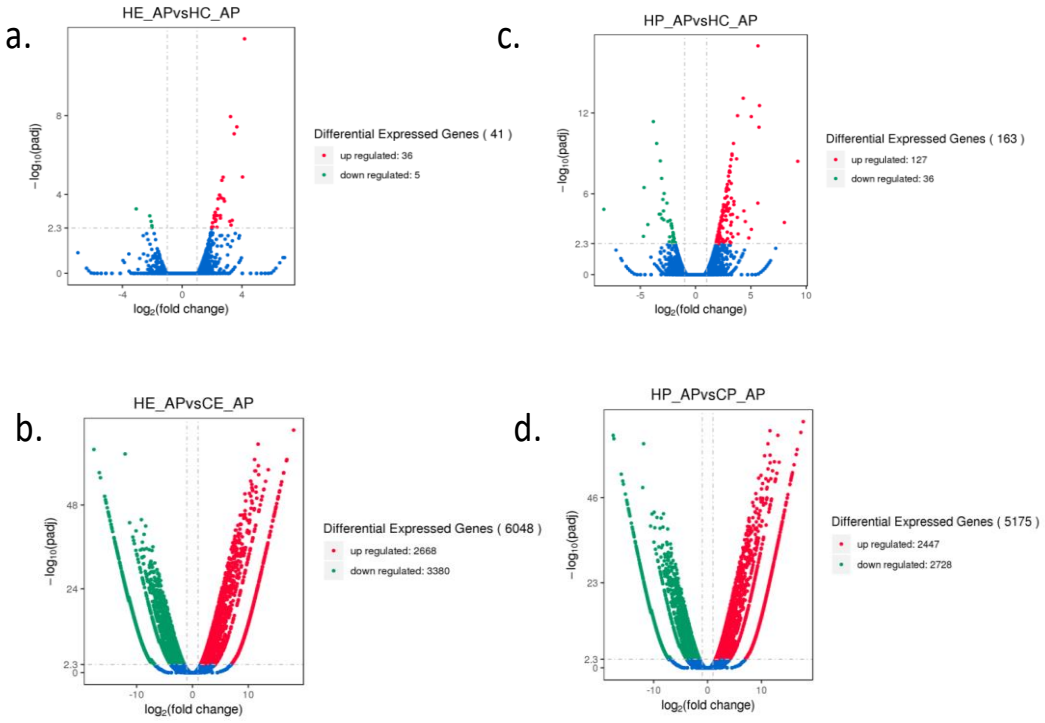


Figure: Representative volcano diagrams showing differential expression of genes

Comparative Study on Endometrial and Cervical Cancer with special reference to Human Papillomavirus type 16

Principal Investigator: Dr. Mausumi Bharadwaj, Molecular Biology Group
Research Scholar: Heena Gautam (SRF)

Funding Agency: CSIR
Duration of Project: 2018-2022

Background: Cancer of the uterine cervix and cancer of the corpus uteri are some of the most common gynaecological cancers worldwide. According to Globocan 2020, the global incidence of cancer cervix was 604,127 cases (3.1%) and corpus uteri accounted for 417,367 (2.2%) cases. Death due to cancer cervix accounted for 341,831 (3.4%) and corpus uteri accounted 97,370 (1.0%) cases. In 2020, cancer cervix accounted for 1,23,907 cases while corpus uteri for 16,413 cases in India. Human Papillomavirus (HPV) is considered one of the major etiological factors in addition to other host genetic factors for the development of cervical cancer. But the role of HPV in endometrial cancer is quite controversial. No study has been reported so far from India regarding the role of HPV in endometrial cancer.

Objectives:

- Comparative analysis of prevalence of HPV in cervical and endometrial cancer.
- Functional analysis of gene polymorphisms in endometrial and cervical cancer.
- Evaluation of HPV 16 DNA construct in murine model.
- Correlation of above findings.

Work done:

- Samples were collected and genomic DNA isolated from tissue specimens by standard Proteinase-K digestion and routine phenol-chloroform extraction procedures.
- Detection of HPV and high-risk HPVs using standard PCR methods was done but till now none was found positive for HPV infection.
- Genotyping of SNPs for some of the samples was done using allele-specific PCR for the cases and control samples.
- SNPs predicted using computational programs. *In-Silico* mapping data revealed that out of 256 nsSNPs, 08 were found to be more deleterious.

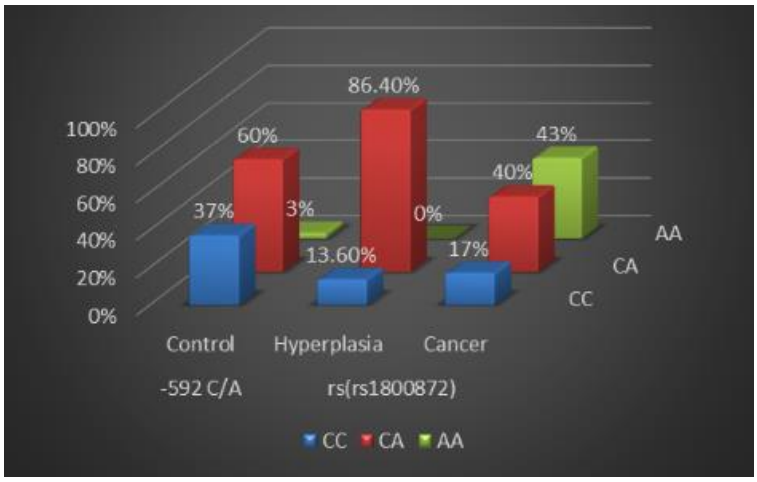


Figure: Bar diagram showing Gene SNPs in different types of clinical samples

A.A residues	**Sift**	**Snap2**	**Align-gvgd**	**Polyphen**	**Provean**	**Phd-snp**	**Snp effect**
C98Y	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect
P139H	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect
R257C	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect
C265Y	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect
S295Y	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	Increases aggregation tendency
G373C	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	Increases aggregation tendency
G373D	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect
R426C	Deleterious	Effect	C65	Probably Damaging	Deleterious	DISEASE	No Effect

To understand the mechanism of aberrant expression of miRNAs and their crosstalk with drug resistance in cervical cancer cells

Principal Investigator: Dr. Showket Hussain, Molecular Biology Group
Research Scholar: Mr. Atul Chikara, SRF

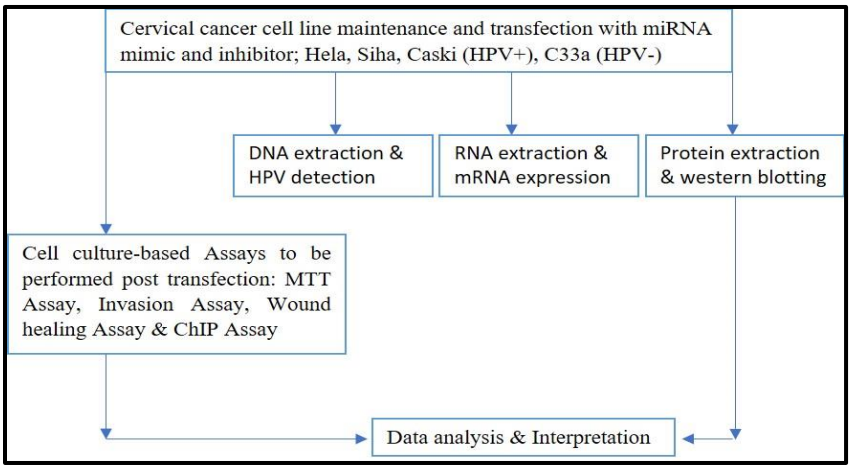
Funding Agency: ICMR – SRF
Duration of Project: 2019-2022

Background: Cervical cancer is ranked as one of the most common cancer among women worldwide and in many low-income countries, it is the most common female cancer. There are an estimated 528,000 new cases annually worldwide out of which 266,000 women succumb to their disease. To find the targeted biomarker specific in cervical cancer, we have aimed our study towards an "OncoMir" miRNA-21, which is found to play a very significant role in cancer.

Objectives:

- To evaluate the effect of miRNA-21 on epigenetic modulations of targeted gene promoters in cervical carcinoma.
- To test the role of miR-21 induced cancer drug resistance (Paclitaxel and Cisplatin) through its targeted genes in cervical cancer cells

Brief Methodology:



Work done:

Cervical cancer cell lines, HeLa and C33A were maintained in MEM medium while SiHa in DMEM and Caski in RPMI medium containing antibiotics and 10% FBS. Cell lines were transfected with mir-21 mimic and inhibited for its expression-based studies along with the targeted genes analyses. Total RNA was isolated using Trizol reagent and stored at -80°C to perform miRNA and target gene expression-based studies using Real Time PCR. Nuclear protein extraction was carried out using RIPA buffer and stored at -80°C. Furthermore, protein expression-based studies are being performed using western blotting.

To Understand the Role and Mechanism of HPV E4 And E5 Oncoproteins in Cervical Cancer Cells

Principal Investigator: Dr. Showket Hussain, Molecular Biology Group
Research Scholar: Ms. Jyoti Rani, SRF

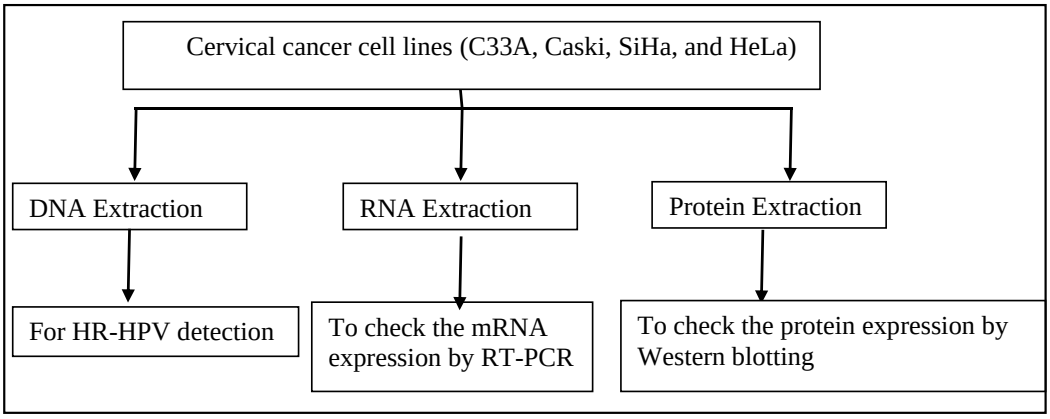
Funding Agency: ICMR – SRF
Duration of Project: 2019-2022

Background: Cervical cancer is the most common cancer as compared to other types of cancer in women. The highest numbers of cervical cancer patients are found in the rural areas due to lack of awareness, lack of medical diagnostic facilities, unhygienic conditions, low income and lack of communication. However most prominently identified is HPV. Many types of HPV are responsible for cervical cancer such as HPV types 16, 18, 31,33, 35, 39 and 45. High-risk HPV types are HPV 16 and 18. Many scientists are working on HPV E, E2, E6 and E7 ORFs. But little knowledge is available on HPV E4 and E5 ORFs. Both these ORFs play a very important role in cell proliferation, propagation of HPV and increase the HPV E6, E7 activity thereby contributing to development of cervical cancer.

Objectives:

- To study the expression pattern of HPV E4 and E5 proteins in HPV cell lines.
- To understand the mechanism by which HPV E4 and E5 regulate cervical carcinogenesis.
- To explore the target molecules of E4/E5 proteins of HPV 16 and 18 to design better therapeutics

Brief Methodology:



Work done:

DNA, RNA, and protein extraction form cervical cancer cell lines C33A, CasKi, SiHa and HeLa and basal expression pattern by RT-PCR have been done. The functional role of HPV E4 & E4 is being explored.

Development and Evaluation of CRISPR/Cas13 based diagnostic system for HPV detection

Principal Investigator: Dr. R Suresh Kumar, Molecular Biology Group
Research Scholar: Dr. Anita Kumari, PDF

Funding Agency: ICMR – PDf
Duration of Project: Jan 2021 – Jan 2023

Background: The diagnosis of HPV relies greatly on molecular biology based detection techniques. The major disadvantage of these methods is the time consumption, possibility of false positive results, sensitivity fluctuations and accessibility. So, a diagnostic test which can minimise the above-mentioned limitations would be useful for better diagnosis of HPV. To overcome these limitations, detection techniques based on Clustered regularly interspaced short palindromic repeats (CRISPR) have emerged as widely accessible and versatile method for early and easy diagnosis of HPV.

Objectives:

- In silico designing of gRNA(crRNA) against 2 targets in HPV(L1,E6) and evaluation off targets.
- Recombinase polymerase reaction (RPA) and T7 based invitro transcription of crRNA targeting HPV genes.

Brief Methodology: Cervical scrape samples shall be collected from patients diagnosed as cervical and categorized based on age, sex and stage of the disease. *In silico* target site selection shall be done and crRNA selected for the target sequences by using suitable software. Cas13a shall be expressed and purified. RPA reaction would be performed using commercially available kit. Final detection assay would be set up for detecting HPV in the samples. The efficiency of the developed diagnostic technique using Cas13 shall be validated against HPV detection by PCR.

Work done:

Designing of gRNA of the target sequence has been done. Fund release from ICMR is awaited to carry on further work.

BREAST CANCER

Comparative study of Genetic, Clinical and Epidemiological factors of Breast Cancer in Indian population (National Task Force project)

Principal Investigator: Dr. Showket Hussain, Scientist D, Molecular Biology Group

Other Collaborating Institutes: AIIMS New Delhi, NIP New Delhi, Regional Cancer Centre Thiruvananthapuram

Funding agency & budget: ICMR, Rs 1,01,45,200

Project Duration: Mar 2017 – Mar 2022

Brief background & rationale: Breast cancer is a leading cause of cancer related deaths among women in India. The incidence of breast cancer is high in urban India whereas it is low in rural areas. There are several reasons for breast cancer although the exact cause is not known. It is likely to be due to differences in lifestyle, hormonal, reproductive and nutritional habits that differ between rural and urban India. Various reports have documented alterations in some of the oncogenes and tumor suppressor genes; however, the exact molecular and genetic basis of breast cancer remains unclear.

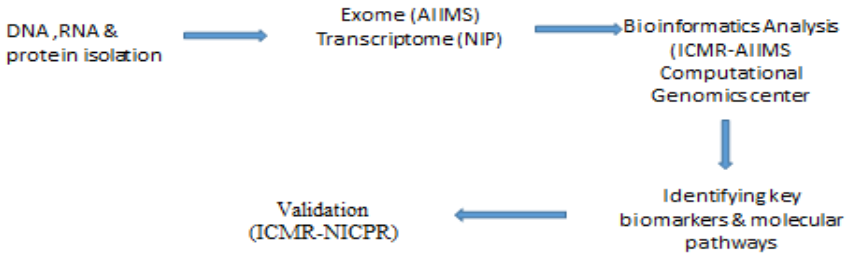
In India, the incidence of breast cancer is increasing day by day and near future it will be major health issue among women. The proposed study will help in bringing awareness about breast cancer in India. In addition, it will help in framing the policies for breast cancer prevention and for the discovery of efficient biomarkers.

Objective: To study of various clinical, hormonal, and other factors associated with breast cancer, and identification of the mutational landscape of breast cancer.

Brief Methodology:

Sample Collection:

- Patient sample collection (n=120) (tumor tissues, normal adjacent tissue & blood samples).



Work done:

The proposed sample collection has been achieved. 75-85 % of the proposed objectives have been achieved. The next generation sequencing (NGS) based data have demonstrated some of the novel genetic alterations among breast cancer patients in Indian population. Furthermore, the whole exome sequencing and transcriptome data is being validated in order to identify the potential biomarkers and explore their clinical application inbreast carcinogenesis among Indian women.

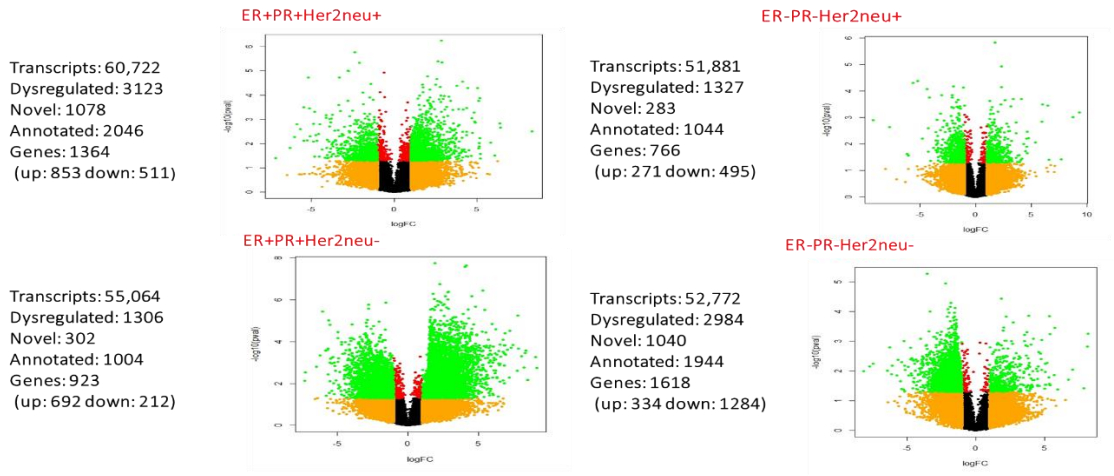


Fig: Representative images showing the novel of dysregulated genes in breast cancer patients

Translational Potential: This study may pave the way for developing indigenous diagnostic and/ or prognostic biomarkers in Indian breast cancer patients. In addition, both clinical and epidemiological data may also provide key insights about breast cancer patients in Indian population.

Evaluation of modified thermography as a tool for early detection of breast cancer in women attending breast clinic at NICPR

Intramural Research Project by Division of Clinical Oncology

Background: Breast cancer has emerged as the leading sites of cancer among women in India with an incidence of 25.8/100,000. Clinical Breast Examination (CBE) is recognized as a cost-effective measure to screen for breast cancer in LMICs. However, the major drawback of CBE is the high false positivity rate which leads to burdening of the tertiary facilities in the country. Infrared imaging of the breast or thermography is a radiation-free imaging technique which detects malignancy based on thermal changes in the body. Due to increased blood circulation and metabolic activity of the tumor, the temperature distribution around the regions of a tumor produces unique hot and warm patterns which can be used for clinical interpretation of abnormal breast conditions. However, manual interpretation of thermal images is error prone and subjective. NIRAMAI has developed Artificial Intelligence-based software (Thermalytix) to automate the analysis of thermal images and improve sensitivity and specificity of thermography. A novel algorithm is used to distinguish benign vs malignant conditions. As a final step, a machine learning classifier calibrated with results of mammography/sono-mammography and biopsy is used to generate a breast health score which can be used for automated triaging of patients in mass screening camps and the detailed report with annotated images can be used by radiologists for further diagnosis and prognosis of the disease.

Objectives: To estimate the sensitivity, specificity, and predictive values of Thermalytix© in detecting breast cancers in the women attending breast clinic at NICPR against the age appropriate 'gold-standard' test USG/mammography and/or tissue diagnosis.

Brief Methodology: This was a prospective, comparative blinded study to evaluate the effectiveness of the Thermalytix© compared to the standard screening modalities. All women attending the breast clinic underwent non-invasive Thermalytix® test by a trained technician, followed by CBE. Women found to have suspicion of breast abnormalities in either of the tests were referred for mammography or sonomammography correlation. All the results including FNAC and/ or biopsy were recorded for final comparison.

Main Findings: Till date total recruitment done: 280

Total Niramai done: 280
Total mammogram done: 199
Total ultrasound breast done: 246.

Evaluation of Breast light as a tool for early detection of breast cancer in women positive on clinical breast examination or at high risk of having breast cancer

Intramural Research Project by Division of Clinical Oncology

Other Collaborating Institutes: IARC, AIIMS New Delhi

Background: Clinical breast examination (CBE) has been proposed as an alternative to mammography screening in low-resource settings. However, it is seen that the efficacy of CBE may be substantially lower (28-36%) in practice than is reported in clinical trials. BreastLight™ (PWB Health, of Dumbarton, Scotland-model BL801) is a handheld device that trans-illuminates the breast with a visible harmless red-light (617 nm) that is absorbed by hemoglobin so that areas of high vascularity (such as malignant tumors) should appear black. As it highlights dark areas where blood is present, it is therefore quite normal to see a pattern of veins, but if there is a dark cluster, it is likely to be a potential abnormality. A cross-sectional study found BreastLight™ to have a sensitivity of 93% and a specificity of 73.7% in detection of breast cancer. Benign lesions (e.g. fibrous cysts), on the other hand, generally do not show up as positive with Breastlight™.

Objectives:

Primary Objective: To estimate the sensitivity, specificity and predictive values of Breastlight™ in detecting breast cancers in the women referred for positive CBE and mastalgia or for evaluation of contra-lateral breast in breast cancer patients against the ‘gold-standard’ test of mammography and/or tissue diagnosis

Secondary objectives:

- To develop a diagnostic algorithm that incorporates Breastlight™ in the triage of breast lumps detected on CBE to avoid unnecessary imaging and biopsy procedures for benign lumps

- To assess the agreement between Breastlight™ and ultrasonography in localizing the breast lesions correctly

Brief Methodology: This was a cross-sectional study to evaluate BreastLight™ as a triaging tool for the CBE-positive women. The study also intended to evaluate the accuracy of Breastlight™ to detect an early cancer in the contralateral breast of the women operated for breast cancer. After obtaining written informed consent, the participants were interviewed to collect the socio-demographic and reproductive variables. The Breastlight™ examination was performed by a trained provider and the results recorded. Both the breasts including the axillary tail were systematically examined in sitting position in a dark room. If a dark cluster/dark mass was visible

in the background of red colour the test was considered positive. The location of the lesion by the breast quadrant was documented. All the recruited women underwent CBE by a trained clinician or surgeon and breast ultrasound (USG) by a trained sonologist irrespective of CBE and Breast light^{TM} results. The sonologist was blinded to the Breastlight findings. All the women, except those with obvious lesion on CBE or USG had diagnostic mammography for disease confirmation. Those with suspected lesions either on USG or mammography underwent FNAC or core biopsy. Women positive for malignancy on FNAC or core biopsy underwent further investigations, staging and treatment.

Main Findings: Till date total recruitment done: 299

Total mammogram done: 239
Total ultrasound breast done: 299

Identification of molecular landscape in Familial/Sporadic breast cancer

Principal Investigator: Dr. Ved Vrat Verma (RA)
Mentor: Dr. Mausumi Bharadwaj, Scientist G, Molecular Biology Group

Funding Agency: ICMR – RA
Duration of Project: 2021 – 2024

Background: Breast cancer is one of the most commonly diagnosed cancers among women worldwide. Breast cancer forms in either the lobules or the ducts of the breast. Hereditary breast cancer caused by germline pathogenic mutations in the BRCA1 or BRCA2 genes are recently characterized as an increased risk for breast, ovarian, pancreatic, and other cancers. Differences in types of mutation and the site of mutation may partially impact cancer risk. Therefore, the following study has designed to understand the disease pathology by using In-silico tools further validated experimentally.

Objectives:

- Comprehensive literature survey and data collection on Familial/Sporadic breast cancer.
- Whole Exome Sequencing (WES) data analysis.
- Identify different novel mutations and their effect on cancer progression.
- In-silico validation specific mutations by using various in-silico approaches.
- Drug designing against highly altered and up-regulated genes identified from the proposed study.

Work done:

Comprehensive literature survey, data collection from various databases and protocol standardization is in progress.

Development of Folate Targeted Biocompatible Nanocarrier: Controlled Drug Delivery System in Combination for Breast Cancer Treatment

Principal Investigator: Dr. Ragini, PDF
Mentor: Dr. Suresh T. Hedau, Molecular Biology Group

Funding Agency: ICMR – PDF
Duration of Project: 2019-2021

Background: Chemotherapydelivers anti-cancer drugs systemically to patients for quenching the uncontrolled proliferation of cancerous cells. The main challenge of cancer therapeutics is to differentiate the cancerous cells and the normal body cells. Conventional chemotherapy fails to target the cancerous cells selectively without interacting with the normal body cells. Thus, they cause serious side effects including organ damage resulting in impaired treatment with lower dose and ultimately low survival rates. Whereas nanotechnology-based drug-delivery system should possess some basic requirements such as large loading capacity, biocompatibility, less toxicity, easily degraded by the body's metabolism, and be nanoscale in order to facilitate the release of drugs by intravenous administration with controlled manner. Besides this, for better therapeutic effectiveness, combination anti-cancer treatment has also long been adopted in clinics. For example, anthracyclines (a class of drugs) -based combination chemotherapy has shown improved anticancer activity than anthracyclines alone. This combinatorial therapy shows three types of mechanism; (1) inhibit DNA and RNA synthesis by intercalating between base pairs of the DNA/RNA strand, thus preventing the replication of rapidly growing cancer cells, (2) inhibit topoisomerase II, preventing the relaxing of supercoiled DNA, and thus blocking DNA transcription and replication, and (3) create iron-mediated free oxygen radicals that damage the DNA and cell membranes.

Objectives:

- To design a hybrid nano-carrier by using inorganic metal node and organic linker (metal organic framework, MOF), modified with folic acid decorated graphene oxide layer (MOF@GO-FA) as a targeted and combinatorial drug delivery system for breast cancer treatment.

Brief Methodology: Graphene oxide layer has been synthesized via modified Hummers' method and then functionalized with FA by using EDC/NHS coupling reaction. For further synthesis of drug loaded MOF@GO-FA, a room temperature synthesis has been used, by using zinc as a metal node, 2- methylimidazole as linker, GO-FA as covering sheet and drug molecule. Drug molecules encapsulated in situ into the micropores of framework during crystal growth via weak coordination bonds between drug molecules and zinc ions. Final drug loaded MOF@GO-FA has been collected via centrifugation.

Work done:

A comparative study has been carried out for refinement of nano-carriers and obtained results are given below. Based on results, it is concluded that DOX loaded MOF@GO-FA is better nano-carrier in comparison to GO-FA.

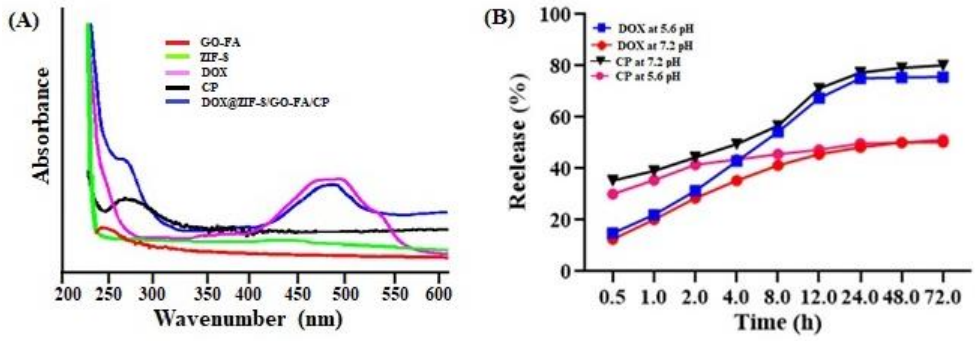


Fig: (A) UV−vis spectra of GO-FA, ZIF-8, DOX, CP, and DOX@ZIF-8@GO-FA/CP suspensions. (B) In vitro drug release profiles of DOX and CP from DOX@ZIF-8@/GO-FA/CP in phosphate buffer saline (PBS) at pH 7.2 and 5.6 separately

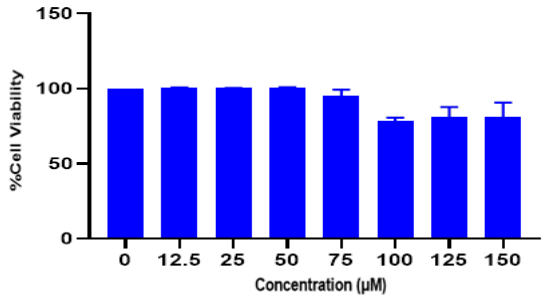


Fig: Cell viability of MCF-10A cells after incubation with MOF@GO-FA nanocarrier at different concentrations as measured using a MTT assay.

An ingenious method was developed as GO-FA functionalized MOF (ZIF-8) based nanosystem and successfully used for delivery of DOX and CP in combination (DOX@ZIF-8/GO-FA/CP). This MOF/GO-FA system showed negligible cytotoxicity and excellent biocompatibility. The FA-modification enhanced the drug uptake in cancer cells and the DOX@ZIF-8/GO-FA/CP nanosystem showed clear selection towards cancer cells and avoid healthy cells. This nanosystem showed their synergistic cytotoxic effect on MCF-7 and MDA MB-231 cells, due to controlled release of DOX and CP on a specific site under an acidic condition. We also expect that the design of the pH-responsive nanosystem can give new inspiration to the synthesis of nanoparticles with multifunctional application.

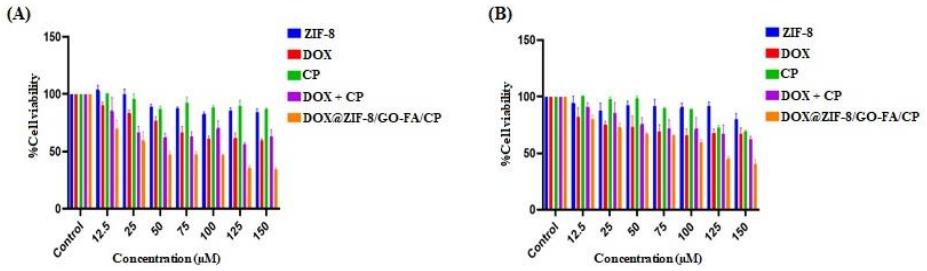


Fig: Cell viability of (A) MCF-7 and (B) MDA MB-231 cells incubated with ZIF-8, DOX, CP, DOX+CP, and DOX@ZIF-8/GO-FA/CP

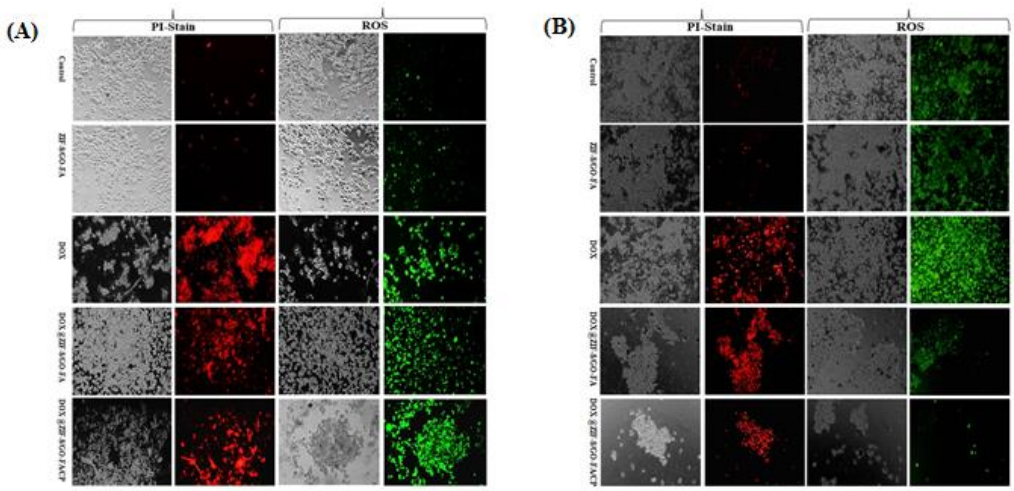


Fig: Fluorescence microscope images of PI-staining and ROS-generation after 24h incubation with control, ZIF-8/GO-FA, DOX, DOX@ZIF-8/GO-FA, and DOX@ZIF-8/GO-FA/CP at 20X magnificationin (A) MCF-7 and (B) MDA MB-231 cell-lines

Role of HDAC1 in the regulation of BRCA1 & p16 gene expression by methyl-CpG binding protein MBD2 in breast cancer cell line

Principal Investigator: Dr. Suresh T. Hedau, Molecular Biology Group
Research Scholar: Mr. Ram Krishna Sahu, SRF

Funding Agency: ICMR – SRF
Duration of Project: 2018-2021

Background: Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer related death in female worldwide. The BRCA1 protein is involved in DNA repair and transcriptional regulation in response to DNA damage. p53 protein that regulates the cell cycle and act as a tumor suppression. MBD proteins play a major role in coordinating crosstalk between DNA methylation, histone modifications and chromatin organization to achieve a coherent transcriptional program. The canonical role of MBD2 as a transcriptional repressor through interactions with other binding proteins such as the histone deacetylase complexes NuRD/Mi-2 and Sin3A has been demonstrated. HDAC1 has regulatory role in the transcription of genes involved in cell cycle and cancer progression. Histone acetylases and HDACs are responsible for the reversible acetylation of histone protein, transcription factors, DNA repair enzymes, various nuclear and cytoplasmic proteins.

Objectives:

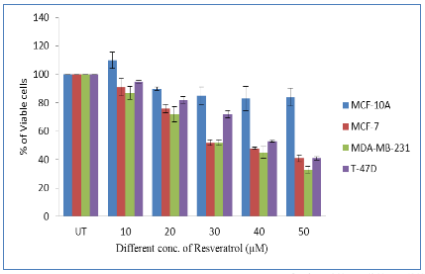
- To understand the molecular mechanism of HDAC1 in regulation of BRCA1 and p16 gene in breast cancer

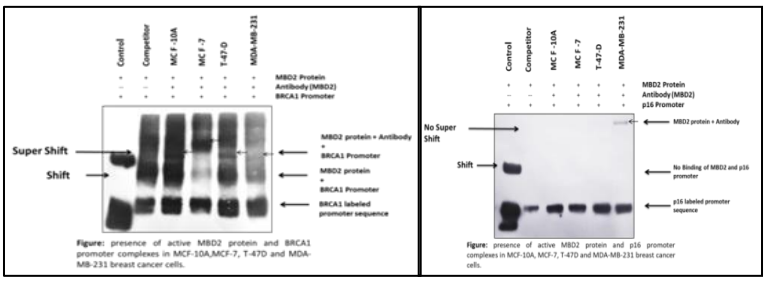
Brief Methodology: Three breast cancer cell lines (MCF-10A, MCF-7, MDA-MB-231) have been used to see the effect of resveratrol. Cell viability was measured and IC50 value was expressed as µM of resveratrol. RNA was isolated by Tri-Zol method and quantified, cDNA prepared by cDNA preparation Kit and used for Real time PCR. SDS- polyacrylamide gel electrophoresis was run to separate the proteins using tris-glycin running buffer. An electrophoretic mobility shift assay (EMSA) was used to study protein–DNA or protein–RNA interactions. Clonogenic assay was done in 6-well cell culture plate and cells were counted and seeded and allowed to attach to the plate/dish in CO2 incubator. Cells were treated with resveratrol and incubated in a CO2 incubator at 37 °C for 1-3 weeks until cells in control plates formed colonies of a substantially good size. Cell migration assay was done in 6 well plates by scratch method.

Work done:

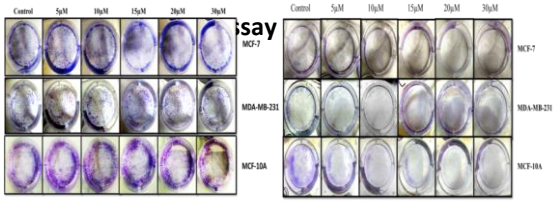
Our results suggest that MBD's proteins have binding affinity on promoter sequence of BRCA1 gene but no binding affinity for p16 gene promoter in MCF-10A, MCF-7, T-47D & MDA-MB-231 cell lines. For migration assay after treatment with 5-30µM concentration of resveratrol for 0, 6, 12 and 24hr, the cell lines significantly reduced after 24 hrs. In clonogenic assay, colony

formation was significantly reduced in cells treated with 5-30µM of resveratrol for 24hrs and maintained for 7 days, the. However, in MDA-MB-231 triple negative breast cancer cell line, the colony formation increased with increasing drug concentration. The expression analysis of MBD1, MBD2, MeCP2, HDAC1, BRCA1 & p16 genes at mRNA as well as protein level of resveratrol treated cell lines revealed that MBD2 gene expression negatively correlated with BRCA1 gene expression. Clonogenic & migration assay followed by real time PCR and western blotting of above-mentioned genes in cell lines treated with resveratrol along with HDAC1 inhibitor SAHA showed that HDAC1, MBD2 expression was significantly down regulated and BRCA1 was up regulated with increasing concentration and its effects significantly reduced the colony formation and migration at higher concentration of resveratrol along with SAHA compared to resveratrol alone in breast normal and cancer cell lines.

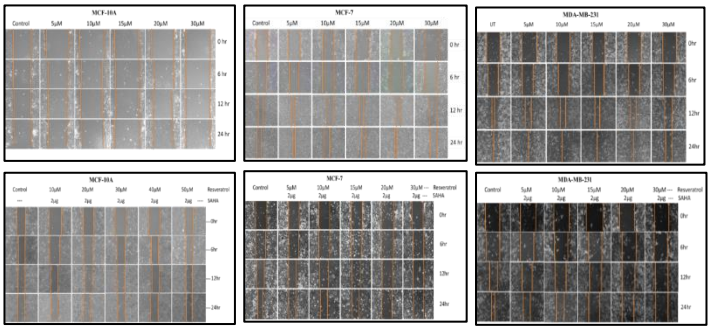




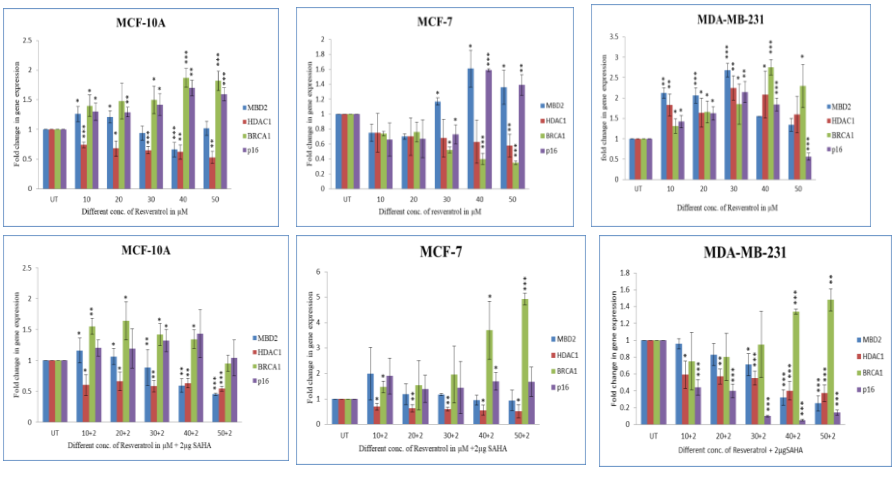
EMSA



Clonogenic Assay



Migration Assay



Real-time PCR

Role of SOX2, OCT4, KLF4 and NANOG genes in therapy resistance against multi-kinase inhibitors and their post-transcriptional regulation in Breast cancer

Principal Investigator: Dr. Binayak Kumar, Young Scientist
Mentor: Dr. Suresh T. Hedau, Molecular Biology Group

Funding Agency: DHR
Duration of Project: 2020-2023

Background: Breast cancer is one of the most common cancers worldwide. It is number one ranked in Indian female population. Various therapies are being used to cure the breast cancer but emergence of drug resistance is the major obstacle. Accumulating evidence suggest that most of the anti-cancer drug kills bulk population of tumor cells but fails to target cancer stem cells (CSCs). Eradication of cancers requires the elimination of CSCs. CSCs have self-renewal capacity and ability to differentiate into diverse progenies of tumor cells. SOX2, OCT4, KLF4 and NANOG genes are considered as pluripotency-associated transcription factors. The role of SOX2, OCT4, KLF4 and NAOG genes in iPSCs generation are well studied but in cancer therapy resistance is poorly studied. miRNA as a target candidate for these genes are studied well in context of iPSCs generation but still need to study for targeting cancer stem cells. In an earlier ICMR-PDF project of our group, Abemaciclib and Palbociclib resistant MCF-7 and MDA-MB-231 breast cancer cell models were developed. In this project, we shall evaluate the expression of SOX2, OCT4, KLF4 and NANOG genes at transcriptional level.

Objectives:

- To understand the oncogenic role of SOX2, OCT4, KLF4 and NANOG genes in therapy resistance in Breast cancer.
- To identify mi-RNAs as post-transcriptional regulatory candidates to inhibit the SOX2, OCT4, KLF4 and NANOG gene expressions which might be help to eliminate the CSCs.

Work Done:

Elevated levels of all these stem cell transcription factors in resistant cells as compared to the control (drug-sensitive) cells were found (Fig).

Literature search was conducted for the regulatory role of miRNAs on above-mentioned stem cell transcription factors. Using miR-DB database tools, we performed network analysis of miRNAs for other target genes as well as transcription factors (Fig). We found out some interesting miRNAs such as miR-429, miR-107, miR-300 and miR-200 etc. that need to be studied in detail.

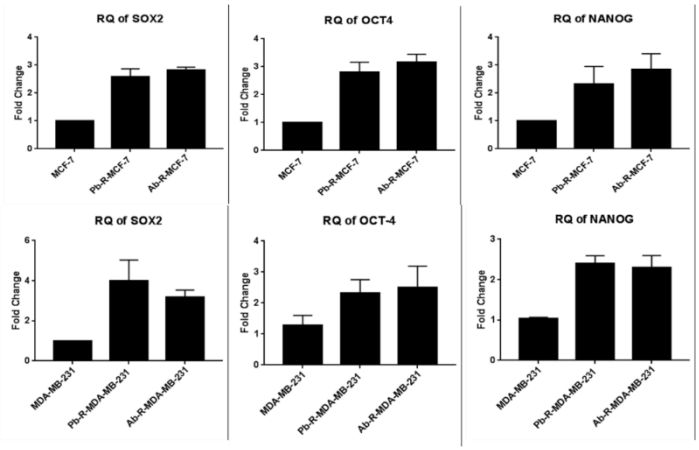


Fig: mRNA expression of SOX2, OCT4 and NANOG genes in the Ab and Pb resistant cell models.

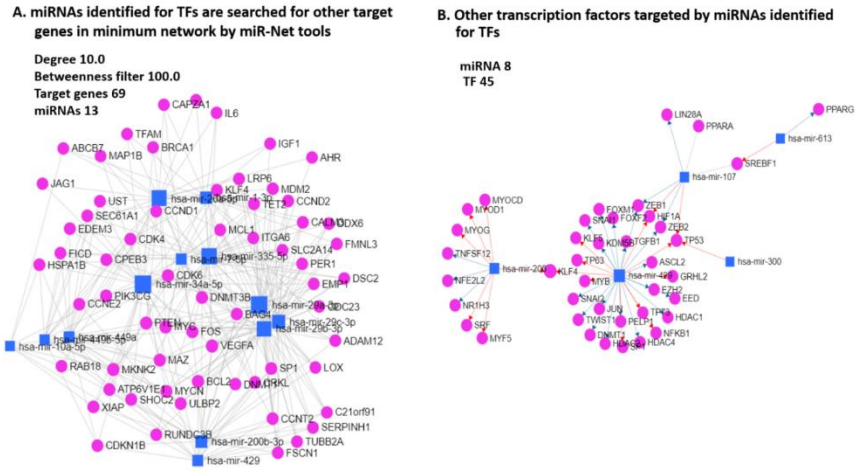


Fig: Network analysis of identified miRNAs for (a) Gene regulation and (b) other transcription factors along with SOX2, OCT4, KLF4 and Nanog.

To explore the SALL transcription factor family in breast carcinogenesis

Principal Investigator: Dr. Showket Hussain, Molecular Biology Group
Research Scholar: Mr. Sandeep Sisodiya, SRF

Funding Agency: ICMR – SRF
Duration of Project: 2020 – 2023

Background: Breast cancer is among the top ranked cancers in women worldwide including India. It is classified into several sub-types based on the histological markers or various gene expression profiles. There are several genetic factors associated with breast carcinogenesis. Among them, transcription factors are molecules that can directly regulate cancer cells by expressing or repressing certain proteins that are associated with breast carcinogenesis. The SALL family of transcription factor family consists of SALL1, SALL 2, SALL3 and SALL 4, but SALL2 is an emerging transcription factor that controls expression of various cell cycle events including apoptosis and regulation of key genes. Recent studies have suggested that SALL2 acts as a tumor suppressor that inhibits breast and ovarian cancer progression.

Objectives:

- To investigate the role of SALL2 transcription factor in ER+ PR+ and ER- PR- breast cancer cell lines.
- To study the role of SALL2 downstream target gene p21 in breast carcinogenesis.

Brief Methodology: Breast cancer cell lines (ER+ PR+ and triple negative), PCR, western blotting and promoter binding techniques (ChIP and EMSA) shall be performed.

Work done:

We observed differential expression pattern of SALL2 in ER+PR+ and triple negative breast cancer cell lines by RT-PCR. Further, the functional role of SALL2 transcription factor is being studied to establish its role in breast cancer development.

HEAD & NECK CANCER

Bioinformatics based analysis of head and neck cancer RNA-seq data for developing a database on alternative splicing events

Principal Investigator: Dr. Vishwas Sharma, RA
Mentor: Dr. Sanjay Gupta, Scientist G, Division of Cytopathology

Funding Agency: ICMR, RA
Duration of Project: 2019-2022

Background: Alternative splicing (AS) is a regulatory process during gene expression that allows a single gene to code multiple proteins. The major subtypes include cassette exon skipping (ES), intron retention (IR), mutually exclusive exon (MXE), and alternative 5′ and 3′ splice site (ASS). Sequencing of RNA (RNA-Seq) is a high throughput technology, which has been used by various studies to identify AS events in head and neck cancer (HNC). Role of AS in HNC is still not completely known. A systematic review is required to understand the role of AS in HNC. Besides, the analysis of RNA-seq data in this aspect will also help us to identify the important regions in the genome of HNC patients that could influence the biology of HNC.

Objectives:

- To identify alternatively splicing events via analysis of head and neck cancer RNA-seq dataset freely available in next generation sequencing data repositories.
- To develop a database based on the alternatively splicing events identified through literature search and analysis of RNA-seq dataset of head and neck cancer.
- To rank the identified genes and select the top candidates for functional validation as a drugs target.
- To design TaqMan probe for the top ranked candidate genes.

Brief Methodology:

A systematic literature search was performed following PRISMA guidelines to determine the AS events in HNC identified through RNA-seq. Briefly, records were screened on PubMed and Web of Science databases. A total of 323 records were obtained from PubMed, 887 records from Web of Science. The validation of AS events as seen in multiple records was performed. Additionally, the list of RNA-seq data of HNC patients from next-generation sequencing data repository GEO, SRA, ENA is being carried out. Forty-eight (48) RNA-seq oral cancer samples were analysed. The quality of reads was assessed using FastQC program. The software Trimmomatic was used for trimming the sequences and removing the adapter content. For trimming the data, HEADCROP:12 TRAILING:1 SLIDINGWINDOW:4:20 MINLEN:50 was used. The alignment, assembly, and differentially spliced gene identification was done through Tuxido pipeline. Briefly, the mapping was done through Tophat software and assembly through Cufflinks software. The programme Cuffdiff was used for indentifying DF genes

Work done:

A total of 84 genes in cancer samples of gingiva n and 40 genes in samples of tongue were found to be differentially spliced ($p<0.05$). Based on the results it is quite evident that differential spliced events play a critical role in the etiology of oral cancer.

Translational Potential: Based on the information obtained from the analysis of the RNA seq data from the HNC, hopefully a database on AS events in HNC will be developed.

Investigation of Salivary Exosomal miRNAs Differential Expression in Oral Cancer

Principal Investigator: Dr. Gaurav Verma, PDF
Mentor: Dr. Sanjay Gupta, Division of Cytopathology

Funding Agency: ICMR, PDF
Duration of Project: 2019-2021

Background: Oral cancer is the second most prevalent cancer in India among both sexes, accounting for an estimated 1,19,992 new cases and 72,616 deaths in 2018. India alone accounts for 34% of incidence and 40% of mortality of oral cancer world-wide. Interestingly, it is one of the most manageable cancers if diagnosed at an early stage. Recent scientific data suggest that "salivary exosomal miRNAs" are promising bio-molecular candidates in diagnostic and prognostic approaches for several diseases.

Objectives:

- To assess the differential expression of salivary exosomal miRNAs in normal, OPMDs and cancer by small RNA Next Generation Sequencing.
- To validate the significant differentially expressed salivary exosomal miRNAs in oral pre-cancer and cancer by qRT-PCR.
- To elucidate the correlation of differentially expressed salivary exosomal miRNAs with clinical/histopathological parameters through statistical analysis.

Brief Methodology:

Un-stimulated saliva/oral rinse samples was collected following informed consent from normal (clinically declared), OPMDs and oral cancer subjects and stored at -70°C until further processing. Samples were subjected for exosome isolation using Exosome Isolation Kit as per manufacturer's instructions. Subsequently, miRNA was isolated using miRNA Isolation Kit according to manufacturer's protocol. Qualitative/Quantitative screening of samples was performed by qRT-PCR (miR-24 as internal control). Selected normal, OPMDs and cancer samples would be processed for Small-RNA NGS to analyze differential expression of salivary exosomal miRNAs. Further, validation of differential expression by qRT-PCR would be performed in all the samples. Statistical correlation of differentially expressed salivary exosomal miRNAs would be done with clinical/ histopathological parameters.

Work done:

A. Clinical Sample Collection: Un-stimulated fresh saliva/oral rinse samples (n=120) from normal (n=50), OPMDs (n=49) and oral cancer (n=21) were collected in a 15ml sterile vial placed on ice as per protocol and stored at -70º C until further use.

B. Molecular Biology Techniques performed:

Salivary Exosome Isolation and Colorimetric analysis: Salivary exosomes were isolated from the saliva/oral rinse samples by using ExoEnrich (Saliva) Exosome Isolation Kit ExoCan (Pune, India) followed by colorimetric assay for qualitative assessment using ExoColor Exosome Colorimetric Quantification Kit ExoCan (Pune, India) as per the manufacturer's protocol.

miRNA Isolation from Exosomes: miRNA was extracted from enriched exosomes using QIAGEN's miRNeasy Mini Kit, (USA). Initially, exosome samples were lysed in QIAzol Lysis Reagent.

Small RNA Next Generation Sequencing: The extracted salivary exosomal miRNA from collected saliva/oral rinse samples was subjected to Small RNA Next Generation Sequencing via. Illumina (NEB E7580L) platform (Outsourced) in 9 samples (3 Normal, 3 OPMDs and 3 Oral Cancer). The raw data has been received and data analysis is under process for studying the differential expression of salivary exosomal miRNAs in OPMDs and cancer subjects with respect to controls (normal).

Mechanistic insights into NF-kB interactome IN HPV and / or tobacco induced tongue aquamous cell carcinoma: role of mutations in shaping protein-protein interaction

Principal Investigator: Dr. Shilpi Gupta, PDF
Mentor: Dr. Mausumi Bharadwaj, Molecular Biology Group

Funding Agency: ICMR, PDF
Duration of Project: 2018-2021

Background: Tongue cancer (TSCC) is the most prevalent head and neck cancer subtype, often associated with tobacco or HR-HPV infection. HPV-positive TSCCs possess a unique mechanism of tumorigenesis which contrasts with that of tobacco-induced TSCCs. These intra-tumour heterogeneities and associated genetic alterations in TSCC appear to be the major obstacle to the identification of effective targeted therapeutic agents. Our group's recent research established that NF-κB subunits play a significant role in tumor aggressiveness and metastasis. This suggests NF-κB along-with HPV and tobacco play a critical role in the development of tongue tumorigenesis.

Objectives:

- To identify non-canonical and/or de-novo interactions and associated mutations in HPV and/or tobacco-induced TSCCs, to identify new potential therapeutic target(s).

Protein extraction	Total and nuclear protein from all samples and cell lines will be prepared as described earlier**(Dignam, 1990)**
Immunoprecipitation	For immunoprecipitation, 3-6 mg of nuclear extract will be incubated with antibody against desired protein for overnight followed by incubation with protein A/G beads, overnight. The protein will be eluted and measured. Once quantified, proteins will be analysed using mass spectrometry.
Western Blotting	Western Blotting will be performed as described previously by **Gupta et al; 2015.**
Mass Spectrometry	***Sample Preparation for Mass Spectrometry:*** The proteins will be denatured using 50ul of 8M urea, disulfide bonds will be reduced by 1mM DTT and alkylated by 1mM iodoacetamidefollowed by Tryptic digestion. The peptides will be analyzed by mass spectrometry.
	Protocol for Mass Spectrometry: These peptides will be loaded on a 15cm long column, packed with preheated, 1.8um C_{18} beads. The peptides will be separated using a linear gradient from 5 to 35% of buffer B followed by a wash reaching 95% of buffer B. The gradient length will be adjusted to 240 mins.
Co-IP & Sequential ChIP assay	The ChIP assay will be carried out in accordance with **Kuo and Allis (1999)**.
siRNA knockdown	Knocking down will be performed using commercially available siRNAs raised against NF-kB specific genes and *de-novo* interactors will be performed according to the manufacturer's protocol (Invitrogen).
Mutation Analysis by Sequencing	Isolated DNA will be used to amplify genes coding for NF-kB family proteins & *de-novo* interactors, using primers flanking the gene body. Amplicons will be sent for sequencing and aligned against the reference human genome to identify mutations associated with the gene.

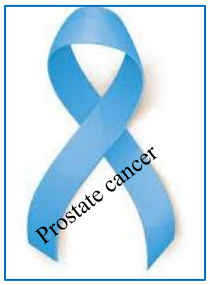
Brief Methodology:

Work done: HPV prevalence in tumor tissues was found to be 28%. PV 16 was the most prevalent type found in tumor tissue of TSCC patients.

Western Blot analysis showed a higher of expression of NF-kB family proteins (p50, p52, RELA, RELB and c-REL) in TSCC cell lines and majority of TSCC cases when compared to normal controls.

ChIP assay showed that various target genes interactions with the NF-kB/p65 and NF-kB/c-REL genes promoters were found in both HPV+ve and HPV-ve TSCC cells. Several p65/c-REL associated protein-protein interactions with CD44, BCL2, EGFR, BMI1 were identified both in-silico as well as in-vitro assays. NF-kB/p65 and c-REL binding promoters were highly enriched in these target genes. The overlapping of p65 and c-REL binding sites with key target genes indicated a possible functional interaction between p65 and c-REL and their target genes in the regulation of gene expression during TSCC. PPIN included the p65 and c-REL proteins strongly interact with AP-1 family proteins including c-Jun, JunD, Fos, Fra-1, Fra-2 and ATFs. PPIN showed that p65 and c-REL proteins are also strongly interact with other transcription factors and key target proteins such as YY1, BCL-2, NOTCH1/2, STAT, c-MYC and BMI-1.

OTHER CANCERS



Genomics of Gall Bladder Carcinoma in Indian Population

Principal Investigator: Dr. Showket Hussain, Scientist D, Division of Molecular Biology

Other Collaborating Institutes: AIIMS New Delhi, CSIR- Institute of Genomics and Integrative Biology New Delhi

Funding agency & budget: ICMR, Rs 55,34,000

Project Duration: May 2018 – May 2023

Brief background & rationale: Gallbladder carcinoma (GBC), a type of hepato- biliary tract cancer (BTC), is highly prevalent in Indian population. There are very few reports on genetic mechanism in etiopathogenesis which are restricted to inadequate sample size and lacked further validation based on their gene expression profile.

The proposed study aims to elucidate the genetic alteration in GBC etiopathogenesis using NGS platform followed by validation, in Indian population. The result of this study will help to obtain a greater insight into thegenetic mechanism(s) during GBC pathogenesis which would further elucidate specific genetic signatures involved in the etiopathogenesis of GBC in Indian population.

Objectives:

- Exome/Transcriptome sequencing of GBC cases
- Identification of candidate genes.
- Correlating the findings with disease progression

Brief Methodology:

- Collection of gall bladder tumor tissue, normal tissue, inflammatory tissue & blood sample with consent and questionnaire.
- DNA/RNA extraction through Qiagen extraction kit.
- Quality check & library preparation for downstream application.
- Whole Exome and transcriptome sequencing for collected samples.
- Data analysis, validation and establishment

Work done:

Till date, whole exome sequencing in 58 paired samples and bioinformatic analyses of 23 samples have been done. In order to identify the somatic mutations, firstly panels of normal (PONs) were created for all the available normal samples followed by the implementation of Mutect2 tool of GATK package to identify the somatic variants. Annotation was done by the implementation of ANNOVAR and SnpEff tools. From the analysis, the occurrence of missense mutations was found at highest level followed by nonsense mutations and frame shift deletions.

So far, 14 samples have been processed for RNA sequencing and a total of 40551 genes were found to be differentially expressed. After filtering the genes on the basis of log2 fold change and p value, a total number of 866 genes were found to be upregulated and 679 genes were found to be downregulated.

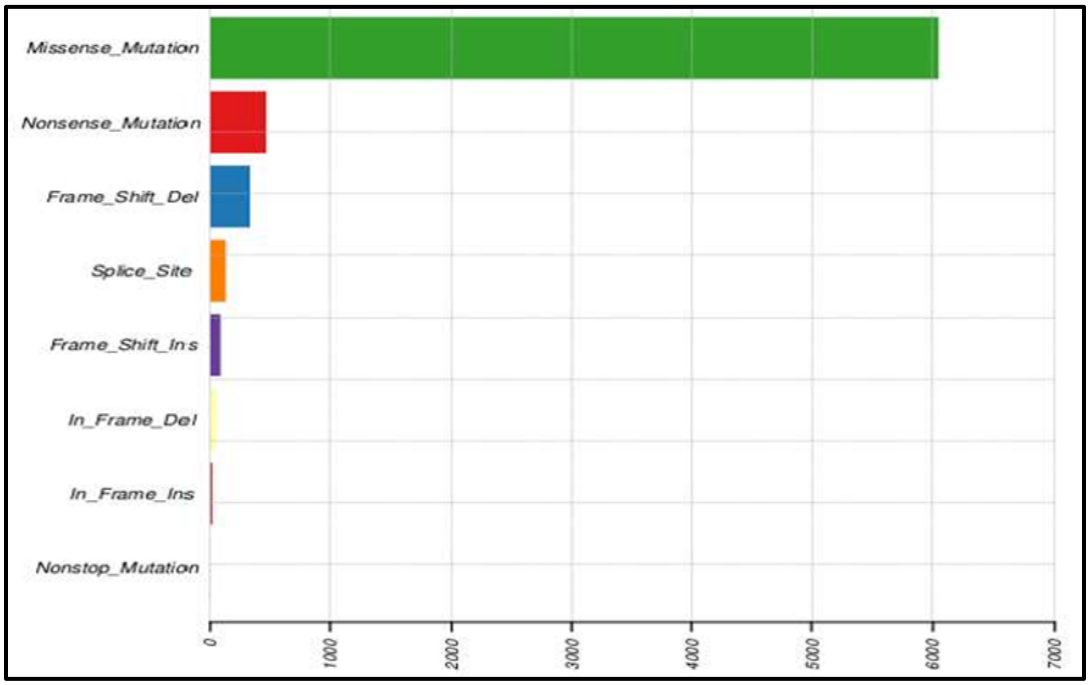


Fig: Representative images showing the frequency of mutation occurrence in gallbladder cancer patients

Translational Potential: The project has potential to develop the India specific cancer gene panel for diagnosis and prognosis of GBC. The outcome of this proposed study will be to find the novel mutational patterns and dysregulated gene expression profile among GBC patients.

Brain derived neurotrophic factor (BDNF) and its receptor, TrkB in gall bladder carcinoma: potential biomarkers and prognostic markers

Principal Investigator: Dr. Ruchika Gupta, Scientist D, Division of Cytopathology

Other Collaborating Institutes: GB Pant Institute of Postgraduate Medical Education & Research, Delhi; Hindu Rao Hospital, Delhi

Funding agency & budget: ICMR, Rs 30,08,631/-

Project Duration: Mar 2021 – Mar 2024

Brief background & rationale: Gall bladder cancer (GBC) is the most common biliary tract malignancy and fifth commonest cancer of the digestive tract with a high morbidity and mortality. Serum tumor markers like CA19-9 and CEA are commonly utilized to support a clinical diagnosis of GBC. However, these markers are usually elevated only in advanced stages and their specificity in early stages of the cancer is very low. Brain derived neurotropic factor (BDNF), a member of neurotrophin growth factor family, has been demonstrated to be overexpressed in tissues of GBC. Benign lesions such as adenomas and polyps exhibiting BDNF positivity have demonstrated moderate to severe dysplasia of the epithelium, suggesting that BDNF might play a role in the early phases of gall bladder tumorigenesis. BDNF exerts its effects through its receptor, tropomyosin-related kinase B (TrkB) and this binding leads to downstream activation of the PI3K/Akt pathway. TrkB expression has been reported in more than 90% of GBC specimens with correlation of expression at the invasive front of the tumor with clinical staging and lower overall survival. TrkB is also being explored as a target for newer anticancer drugs.

Objectives:

- To evaluate the tissue expression of BDNF, TrkB, PI3K, Akt and EGFR in chronic cholecystitis, gall bladder showing epithelial dysplasia and GBC.
- To quantitate the pre-operative serum levels of BDNF and TrkB in these three study groups.
- To correlate the tissue expression and serum levels with diagnostic markers (CEA, CA19-9) and prognostic factors (tumor grade, stage, hepatic invasion, lymph node metastasis) and patient survival.

Brief Methodology:

A total of 150 cases comprising of 60 cases of gall bladder carcinoma, 60 tissues from chronic cholecystitis samples and 30 from cases with epithelial dysplasia of gall bladder shall be included in this study. Written informed consent shall be taken from all participants.

- Detailed clinical history, including demographic data and presenting complaints shall be noted. Investigations, including serum tumor markers (CEA, CA 19-9) and radiological evaluation (ultrasound/ CT scan/ MRI) shall be recorded.

- Pre-operative blood sample of patients undergoing choelcystectomy shall be collected, serum separated and appropriately stored.
- The surgical procedure with significant intra-operative finding shall be noted from the case records. The final histopathological diagnosis shall be noted for categorization of the participant into one of the three groups: chronic cholecystitis, epithelial dysplasia or GBC.
- H&E-stained sections of cases diagnosed as GBC shall be reviewed for tumor grade, extent of invasion into the gall bladder wall, local infiltration into liver parenchyma (if included) and lymph node metastasis.
- Immunohistochemistry on paraffin-embedded sections for BDNF, TrkB, PI3K, Akt and EGFR shall be performed as per the protocol. The immunostained sections shall be evaluated for cytoplasmic (PI3K, Akt, TrkB), cytoplasmic and/or membranous (BDNF) and membranous (EGFR) positivity. For PI3K and Akt, cases with ≥50% cells staining for the antibody shall be considered as positive while at least 25% positive staining will be taken for BDNF and TrkB. And 10% for EGFR.
- Serum BDNF and TrkB shall be estimated using the sandwich ELISA technique following the kit protocol.
- Follow-up data: Further clinical work-up of the cases diagnosed as epithelial dysplasia or adenocarcinoma shall again be recorded along with the status at the last available follow-up or completion of the study, whichever is earlier.

Work done: The funds were received in March 2021. Manpower (research assistant) has been recruited. Ethics committee approval from ICMR-NICPR and Hindu Rao Hospitals have been received. Ethics committee approval from GBPIMER, Delhi is under process.

Role of hepatitis B virus genotype specific X protein (HBx) in TGF-β mediated regulation of liver inflammation in hepatocellular carcinoma: an in vitro study

Principal Investigator: Dr. Manikankana Bandopadhyay, RA
Mentor: Dr. Mausumi Bharadwaj, Molecular Biology Group

Funding Agency: ICMR, RA
Duration of Project: 2018-2021

Background: Hepatocellular carcinoma (HCC) is a typical chronic inflammation-related cancer and inflammation is one of the major risk factor for HCC progression. Hepatitis B virus (HBV) X protein (HBx) encoded by HBV reported to be associated with pathogenesis of HCC. The transactivator HBx protein plays a vital role in the initiation and maintenance of hepatic inflammatory processes through interactions with components of the tumor microenvironment. Hepatic stellate cells, which are a cellular member of liver tumor microenvironment, reportedly participate in the progression from chronic liver inflammation to cirrhosis and liver cancer.
TGF-β, an inflammation-related cytokine belonging to the TGF-β superfamily, possesses significant role in cancer development. Numerous studies have confirmed a close relationship between HBx and TGF-β. Initiation and progression of HCC are highly reliant on viral genomic heterogeneity In India. Hence, developing information in the Indian context becomes imperative for rational design of newer diagnostic/therapeutic interventions for overall management of HBV related HCC. So studying effect of HBx protein of different HBV genotype found in Indian population on TGF-β mediated regulation in the context of hepatic cancer is of utmost importance .

Objectives:

- Study of activation of hepatic stellate cells by HBx of viral genotypes prevalent in the Indian population.
- Analysis of TGF- β expression in hepatocyte cell lines.

Work done:

HBV X gene region was amplified from 1.3mer HBV plasmid of Genotype C. The ligated X gene in TA cloning kit were transformed, cloned & plasmids were isolated. Next, this ligated sample was inserted into mammalian expression vector pCXN2. For this, the plasmids were digested with KpnI and HindIII. The products were ligated by T4 ligase. The X gene construct (pCXN2 –HBx) were selected, transformed, cloned. The plasmids were isolated. DNA was sequenced bi-directionally by purifying PCR amplicons and the genotype was identified. The sequence was aligned and corrected along with reference gene bank sequence in Bioedit sequence alignment editor. HBx genotypes were identified from neighbor-joining tree constructed using Mega 6 software.

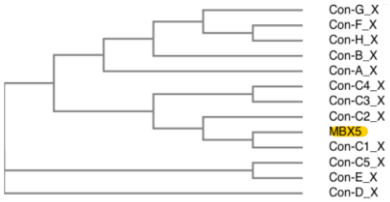


Fig: During the phylogenetic analysis, the x gene consensus sequences of different HBV genotypes were used as reference (namely Con A to Con H). For HBV genotype C, consensus of different subgenotypes were also included (Con C1 to Con C5).

Cell Culture & standardization of transfection of HepG2 cells

The hepatoblastoma cell lines, HepG2 and Huh-7 cells were grown and maintained in DMEM media supplemented with 10% FBS, at 37˚C in 5% CO2 incubator with 1% penicillin - streptomycin antibiotic cocktail. Cells were transfected using Lipofecatmine 2000 with two doses - 1 μg and 2 μg of pCXN2-HBx plasmid (The X gene construct, D genotype, constructed at first year), and empty vector. After 48 h, cells were used for RNA extraction.

LSD1 ablation regulates dsRNA and IFN responses, targeting LSD1 in combination with anti-PD-(L) 1 immunotherapy in gastric cancer cell lines & B16 cells

Principal Investigator: Dr. Soni Kumari, Young Scientist
Mentor: Dr. Suresh T. Hedau, Molecular Biology Group

Funding Agency: DHR
Duration of Project: 2020-2023

Background: Chromatin regulators play a broad role in regulating gene expression and when gone awry, can lead to variety of disease including cancer. The roles of chromatin regulators in cancer have been investigated both at the levels of cancer cell proliferation and impact on human immune system. However, the relative effects of chromatin regulation on cancer cell- intrinsic functions versus T cell functions, as well as on the overall responses to tumor to immune system, are unexplored. In this study we target the histone H3K4 demethylase LSD1 (KDM1A) which play a critical role in suppressing endogenous double stranded RNA (dsRNA) levels and IFN responses in tumor cells and demonstrate that dsRNA stress resulted from LSD1 inhibition leads to potent anti-tumor T cell immunity. LSD1 in regulating dsRNA and IFN responses, targeting LSD1 in combination with anti-PD-(L)1 may prove to be a broadly applicable new strategy in cancer immunotherapy.

Objectives:

- To investigate the role of TLR3, MDA5, RIG 1, AGO2, DICER, TRBP2, IFN, IL-28, ISG115, OASL and endogenous retroviruses in sh-control and sh-LSD1 gastric cancer cell line.
- To confirm the methylation status and stability of AGO2 in cell treated with cychlohexamide (CHX) in the presence or absence of GSK-LSD1(LSD1 inhibitor) in gastric cancer cell line.
- To investigate the Anti-tumor T cell immunity and survival rate in scramble, LSD1 KO, TCRα KO, IFN-β KO and LSD1/ TCRα DKO, LSD1/MDA5 DKO, and LSD1/ IFN-β in B16 cells.

Brief Methodology: Cell culture will be maintained as per standard protocols, gene knockdown by shRNA, RNA extract and RT-qPCR, strand specific PCR, DsRNA analysis by J2 immunoblot, protein extraction and immunoblot analysis, Protein immunoprecipetation, ELISA, Cell colony formation assay, Chip-sequencing.

Work done: qRT-PCR data revealed that AGO2 (0.07-fold), DICER (0.007-fold), TRBP2 (0.04-fold), ISG15 (0.55-fold) and MAD5 (0.09-fold) were significantly downregulated while OASL (5.76-fold) was significantly upregulated compared to internal control (18s) when AGS cells treated with LSD1siRNA compared with scrambled control. These results indicate that LSD1 positively regulate AGO2, DICER1, TRBP2, ISG15, and MAD5 and negatively regulate OASL. The frequent over expression of these genes in cancer cells may prove to be a broadly applicable new strategy in cancer immunotherapy.

Study on expression profile of miRNA in Prostate Cancer

Principal Investigator: Dr. Mausumi Bharadwaj, Molecular Biology Group
Research Scholar: Mohd Mabood Khan (SRF)

Funding Agency: ICMR
Duration of Project: 2018 – 2023

Background: Prostate cancer is one of the most prevalent malignancies worldwide among males. Adoption of the western lifestyle appears to promote prostate cancer development in India. Cancer of prostate is a multifactorial, multistep genetic transformation. Prostate Specific Antigen (PSA) is a serum biomarker widely used in prostate cancer screening. However, an increase in PSA levels can be related to non malignant disorder too. Depending upon their relative expression and its biological importance, miRNAs are presumed to be valuable diagnostic, predictive and prognostic biomarkers. miRNA may be used as a reliable diagnostic tool for prostate cancer. Prostate cancer miRNA expression profiling will give some clues about cancer pathogenesis and their correlation with the risk factors in the development of prostate cancer.

Objectives:

- Identification of miRNAs and their expression in prostate cancer.
- Validation of selected miRNA.
- Analysis of translated product of target genes.
- Correlation of the above findings.

Work done:

Prostate cancer samples were taken from patients with various demographic status (age, sex, income, disease incidence, etc.). Total RNA was extracted using a kit-based procedure. The quality and quantity of total RNA were evaluated followed by cDNA formation. The quality of the cDNA was determined by RT-PCR amplification of an endogenous control genes such as miR-16, U6 snRNA, RNU43 snoRNA, U1 snRNA, miRNA-39 from a corresponding total RNA sample. Amplification of 380 miRNAs gene was done for PCa patients' samples in a duplicate manner with above mentioned endogenous control gene.

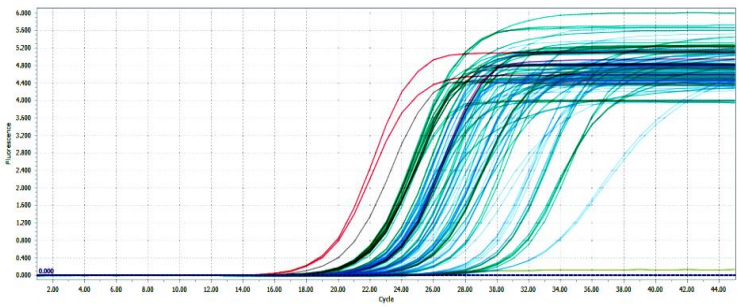


Fig: Amplification of 94 miRNA gene from prostate cancer tissue samples

Genome Wide Methylation Profiling of North Indian Gall Bladder Cancer Patients

Principal Investigator: Dr. Sonam Tulsyan, RA
Mentor: Dr. Showket Hussain, Molecular Biology Group

Funding Agency: ICMR, RA
Duration of Project: 2021 – 2024

Background: Gallbladder carcinoma (GBC) is a highly aggressive cancer prevalent in North Indian population. There are very few reports on epigenetic mechanisms in GBC etiopathogenesis which are restricted to inadequate sample size and lacked further validation on the basis of their methylation/ expression status.

Objectives:

- To elucidate the methylation profile of GBC in north Indian population by whole genome bisulphite sequencing followed by validation using quantitative methylation specific PCR.
- To correlate the methylation profile with clinicopathological characteristics of GBC patients.

Brief Methodology:

A total of 88 surgically resected tissue specimen comprising of 44 tumour tissues and 44 adjacent non-tumour tissues would be collected in 1% PBS from GB Pant Hospital, New Delhi, India. DNA isolation followed by whole genome bisulfite sequencing woud be performed. The validation of identified differentially methylated regions shall be done through quantitative methylation specific PCR.

Work done:

Till date, a total of 20 surgically resected tissue specimen comprising of 10 tumour tissues and 10 adjacent non-tumour tissues have been collected and DNA isolation is being done.

CANCER SCREENING & AWARENESS

Oral Cancer Screening: development of research partnership and feasibility study

Principal Investigator: Dr Roopa Hariprasad, Scientist E, Division of Clinical Oncology

Other Collaborating Institutes: University of Warwick, UK

Funding agency & budget: University of Warwick (UK), Rs. 21,75,588/-

Project Duration: Jan 2020 – Mar 2021

Brief background & rationale: Oral cancer screening may be useful with one large RCT in Kerala, India showing significant reduction in mortality. However, in this trial non-medical university graduates were trained to undertake visual inspection of the oral cavity and there is a need for further research on the role of community health workers in undertaking this role using mobile technology. We propose a new international, leading interdisciplinary group to: (a) develop and evaluate a novel screening strategy in resource–limited settings; (b) build national/regional capacity to conduct high quality research; (c) use this capacity to support wider prevention efforts within the region; and (d) provide robust evidence to up-scale for long-term sustainability

Objectives:

- To develop UK-India partnership on Oral cancer
- To develop novel screening strategy encompassing community health workers screening for oral cancer using mobile technology
- Train community health workers in conducting screening
- Produce preliminary data for future grants applications
- Establish dataset of photographs for further analyses
- Use Machine Learning to develop algorithms for use within the community
- To build research capacity by offering bespoke training in oral cancer prevention; sharing examples of good practice, offering mentorship
- To develop a sustainable research partnership through a strong interdisciplinary research team, establishing links with academic, governmental and advocacy organisations.

Brief Methodology:

- Study participants: Males & females aged above 30 years + Adult tobacco users <30 years registered in the house-hold survey.
- Exclusion criteria: Adult non-tobacco users aged below 30 years.
- Sample size: 1000 participants

- Study tool: After training, the ASHAs visited each household to seek consent to screen eligible adults in random selected areas. They screened them by completing a questionnaire using mobile application noting demographic/lifestyle factors; and visual oral examination. High resolution photographs were taken and downloaded at the end of the day to a secure server. Any abnormality noted was referred to local hospitals for further management which also included tobacco/alcohol cessation.

Work done:

A total of 1200 participants (52% males and 48% females) were approached by CHWs for screening with 98% uptake. Main reasons for the 22 (2%) not participating include being healthy, lack of time or interest. Of these, 1018 participants (48% females, 52% males) visited ICMR-NICPR HPC for screening by the trained dentists. Out of the total population screened, majority were aged 30-39 years (35.5%) and mean age of participants was 35years.

Translational Potential:

- Develop training material for ASHA workers on Oral Cancer Screening.
- Management of suspected oral lesions and regular follow up for tobacco users.
- Expedite the process of Oral screening by Community health workers.
- Establish dataset of photographs for analyses by screening more population and use machine learning to develop algorithms for use within the community.

Assessing the prevalence of Risk Factors for Non-Communicable Diseases Including Common Cancers among Nurses in Delhi NCR Using Digital Community Based Assessment Checklist: A Pilot Study

Intramural Research Study by Division of Clinical Oncology

Background: Majority of deaths due to non-communicable diseases (NCDs) occur in low and middle-income countries. In India, NCDs account for 63% of all deaths. Of these 27% is due to cardiovascular disease, 11% is due to chronic respiratory disease, 9% is due to cancer. Nurses are a significant workforce in healthcare. As part of their daily work, nurses experience much occupational stress, burn out, and alteration in the circadian rhythm, which predisposes them to NCDs. Hence, we planned a study to assess the risk factors for non- communicable diseases; including the three common cancers among the nurses working in government hospitals in Delhi NCR using a web based survey in this study.

Objectives:

- To assess the prevalence of NCD risk factors including three common cancers (cervical, breast and oral cancers) among nurses aged 30 years and above in Delhi NCR using a digital community-based assessment checklist.
- To educate nurses on the risk factors of three common cancers, hypertension, diabetes, obesity using pre-recorded short educational videos.

Brief Methodology: This is a descriptive cross-sectional web-based survey. Consenting nurses of age 30 years and above, working in Delhi NCR, and registered members of TNAI Delhi branch were included. A web-based, self-administered questionnaire was used for data collection. A mobile-friendly digital consent form and a validated questionnaire was sent via what's app/email to all the nurses of eligible age group. If the participants consented to participate in the study, then the questionnaire was displayed.

Work Done: Till date, the questionnaire, the CBAC form and the webpage have been developed. The questionnaire has been piloted. Data collection shall start from August 2021.

EPIDEMIOLOGY

Setting up of Population Based Cancer registry at Institute of Cytology and Preventive Oncology (ICMR-NICPR) covering GautamBudh (GB) Nagar

Principal Investigator: Dr Smita Asthana, Scientist E, Division of Epidemiology & Biostatistics

Funding agency & budget: ICMR-NCDIR, yearly budget of Rs 34.79 lakhs

Project Duration: 2017 - 2022

Brief background & rationale: Cancer registries are essential part of any national programme of cancer control ranging from etiological research through primary and secondary prevention to health care planning and patient care, to benefit individual and society at large. As there is no registry in Uttar Pradesh and ICPO is located at Gautam Buddh Nagar district of U.P and the mandate of ICPO includes primary and secondary prevention of cancer through etiological research, it is proposed to set up a population-based cancer registry for covering GB Nagar district of Uttar Pradesh in UP.

Objectives:

- To set up a population-based cancer registry at Institute of Cytology and Preventive Oncology (ICPO) covering the rural and urban population of GautamBudh Nagar (G.B. Nagar) district of Uttar Pradesh.

Brief Methodology: Information from various sources where the cancer cases are reported were obtained from Government hospitals, community health centres, private hospitals and private laboratories of the selected district. Demographic details of the cancer patient recorded and arranged in alphabetic order and thoroughly checked for duplicity. Duplicate data excluded and submitted online to NCRP on regular basis. Report preparation is being done at NCRP Bengaluru by using morbidity & mortality coding proforma. The staff attended a training workshop on Population Based Cancer Registry held on 26th March 2018 at National Centre for Disease Informatics and Research (NCDIR), Bengaluru.

Work done:

Total cancer incidence cases registered from different hospitals in Population Based Cancer Registry, G.B. Nagar till date is 1033 for the year 2018 and 2019. For the year 2019, data collection and data entry are going on.

Total registered incidence cases registered during reporting period:

Sr No	Hospital Name	Incidence (%)
1.	Apollo Hospital, Noida	25 (2.42%)
2.	CMO, Noida	46 (4.45%)
3.	Delhi State Cancer Institute	188 (18.20%)
4.	Dharamshila Hospital	13 (1.26%)
5.	Fortis Hospital, Noida	117 (11.33%)
6.	Jaypee Hospital, Noida	23 (2.23%)
7.	Max Hospital, Vaishali	51 (4.94%)
8.	Metro Hospital and Heart Institute	53 (5.13%)
9.	Neo Hospital, Noida	38 (3.68%)
10.	NICPR, Noida	13 (1.26%)
11.	Rajiv Gandhi Cancer Hospital	45 (4.36%)
12.	Safdarjung Hospital	64 (6.20%)
13.	Shanti Mukund Hospital	54 (5.23%)
14.	Sri Jagannath Charitable Cancer Hospital	32 (3.10%)
15.	Sumitra Hospital	11 (1.06%)
16.	Surabhi Hospital	21 (2.03%)
17.	Yatharth Hospital, Noida	15 (1.45%)
18.	Others	224 (21.68%)
	Total	**1033 (100%)**

Mortality data: Total cancer mortality cases registered during reporting period: **99**

Distribution of cancer data for different sites under the reporting period:

Location of Cancer	ICD10	Incidence	%
Lip, Oral Cavity and Pharynx	C0-C14	169	16.36
Digestive Organs	C15-C26	187	18.10
Respiratory System and Intratoracic Organs	C30-C39	144	13.94
Bones, Joints and Articular Cartilage	C40-C41	10	0.97
Hematopoietic and Reticuloendothelial System	C42	38	3.68
Skin	C44	10	0.97
Peripheral Nerves and Autonomic nerves system	C47	0	0.00
Retroperitoneal and Peritoneum	C48	1	0.10
Connective, subcutaneous and other soft tissues	C49	6	0.58
Breast	C50	170	16.46
Female Genital Organ	C51-C58	100	9.68
Male Genital Organs	C60-C63	60	5.81
Urinary Tract	C64-C68	54	5.23
Eye, Brain and other parts of central nervous system	C69-C72	30	2.90
Thyroid and Other Endocrine glands	C73-C75	13	1.26
Other and Ill-defined sites	C76	3	0.29
Lymph Node	C77	36	3.48
Unknown primary sites	C80	2	0.19
Total		**1033**	**100%**

National survey for state-wise prevalence of microbiologically confirmed pulmonary tuberculosis in India

Site Investigator: Dr Smita Asthana, Scientist E, Division of Epidemiology & Biostatistics

Funding agency & budget: Ministry of Health and Family Welfare, ICMR-WHO Collaborative project

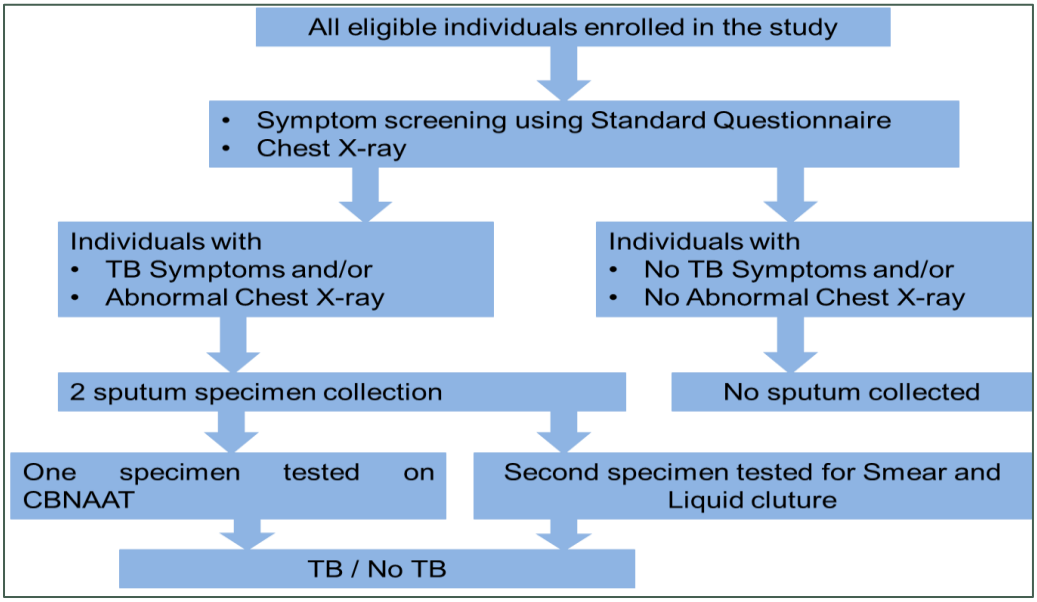
Project Duration: 2018 – 2020 (extended till July 2021)

Brief background & rationale: It is important to know the disease burden of tuberculosis at national level for monitor the progress towards TB control with the aim to 'End TB' as per sustainable development goals (SDGs). There is a diversity and variation of burden of disease across the country, so it is equally important to know state level prevalence of Tuberculosis. ICMR-NICPR is one of the Nodal institutes for Delhi and UP clusters.

Objectives:

- To estimate the point prevalence of microbiologically confirmed pulmonary TB among persons ≥15 years of age in India at national level
- To estimate the point prevalence of microbiologically confirmed pulmonary TB among persons ≥15 years of age for 20 individual states / state groups.

Brief Methodology:



Screening Strategy of the Survey

No. of clusters covered/ Total No. of clusters envisaged: Total clusters proposed at Delhi were 9, and all the clusters from Delhi was completed. At UP, total clusters were 34.

Work done so far:

In this duration, a total of 17 clusters from UP were completed. Of the total population of 17672 in these clusters, 13600 were eligible to be interviewed. Of these, 12073 people gave consented and were interviewed. X rays had been performed in 11825 people. The first sputum sample was collected in 1765 and second sputum sample collected in 1564 people. A total of 49 people were diagnosed with TB.

CAPACITY BUILDING PROJECTS

Estbalishment of a Model Rural Health Research Unit (MRHRU) at CHC Khotpura, Panipat, Haryana

Team: Dr. Shalini Singh, Dr. Sanjay Gupta, Dr. Ruchika Gupta

Funding agency: DHR

Brief background & rationale: MRHRU Scheme was approved by the Govt of India in 2013 as an initiative to develop/strengthen the health research infrastructure in the country and make the relevant health research facilities available across the country.

Objectives:

- Create infrastructure at the periphery for transfer of technology to the rural level for improving the quality of health services to rural population.
- To ensure an interface between the new technology developers (Researchers in the Medical Institutions; State or Centre), health systems operators (Centre or state health services) and the beneficiaries (communities in rural areas)
- Ensure the much-needed geographical spread of health research infrastructure in the Country.

Work done

DHR designated ICMR-NICPR as the Mentoring Institute for the MRHRU at CHC Khotpura, Panipat, Haryana.

- Land transfer for the construction of MRHRU at Khotpura, Panipat, Haryana is in process.
- A Scientific Research Advisory Committee has been constituted to examine the research proposals submitted under MRHRU.
- Research proposals were invited from the linked medical college, Kalpana Chawla Govt Medical College, Karnal. The Dept of Microbiology, KCGMC, Karnal submitted three research proposals which were discussed in a virtual meeting of the Scientific Research Advisory Committee on 16.03.2021.
- Two research projects were finalized and submitted to DHR for final approval and funding:
    - *Antimicrobial resistance surveillance in view of one health concept*
    - *Sero-prevalence of Aspergillus in patients with Chronic Obstructive Pulmonary Disease and their clinical co-relation*

.

Basic Molecular Biology Techniques Relevant to Cancer Research- Tissue Culture related Techniques

Principal Investigator: Dr. Mausumi Bharadwaj, Scientist G, Molecular Biology Group

Team members: Dr R Suresh Kumar, Dr Suresh Hedau

Funding agency & budget: DHR, Rs. 80 lakhs

Project Duration: 2019 – 2024

Brief background & rationale: Globally, cancer is one of the major public health issues. Therefore, research in preventive oncology is very important. The main aim of this project is therefore to develop human resource development towards it through bridgeing the gap between clinical practice and laboratory expertise. Hence, hands-on training on different basic molecular biology techniques relevant to cancer research to the faculties/students of Medical Colleages/ Research Institute / Universities relevant to cancer research will help to train manpower towards cancer research.

Objectives:

- Workshop in Research Methodologies (4 days)
- Short term training (4-8 weeks) in Molecular Biology Techniques-
- Long term training (6-10 Months)

Brief Methodology: Through adversiment in ICMR-NICPR website, 20 participants from different disciplines of clinical and biomedical research background are selected per workshop for two workshops in a year. For short term training, 15-20 students while 10-12 students are accepted for long term training in a year.

Work done (Oct 2020 – Jun 2021): Eight students conducted sixmonths training during this time. They got inducted with basic research methodologies togather with project work.

TOBACCO-RELATED RESEARCH

WHO FCTC Global Knowledge Hub on Smokeless Tobacco

Principal Investigator: Dr. Shalini Singh, Director, ICMR-NICPR
Nodal Officer: Dr Prashant Kumar Singh, Scientist D
Funding agency & budget: ICMR, Rs. 3 crores 33 lakhs

Project Duration: Jan 2019 – Dec 2021

Brief background & rationale: At sixth session of the Conference of the Parties (COP) of WHO-FCTC treaty (in Moscow 2014), smokeless tobacco use was recognized as a global health problem. Parties felt the need to establish a global knowledge hub to identify and support the work of controlling smokeless tobacco use, with its center based at India. The Government of India along with WHO FCTC Secretariat designated the National ICMR-Institute of Cancer Prevention & Research, Noida to serve as the 'WHO-FCTC Global Knowledge Hub (KH) on Smokeless Tobacco' with a formal launch of the hub on 6 April 2016.

Objectives:

1. To generate and share expertise, information, knowledge and provide training, regionally and globally on SLT
2. To promote and facilitate communication among the Parties to the Convention and other stakeholders on SLT
3. To support the Convention Secretariat in hosting meetings, prepare technical materials and participate in technical and subsidiary body meetings on SLT.

Activities: The Hub conducted a Webinar on "Implementation of Article 5.3 of WHO FCTC-Prioritizing Policies to prevent Tobacco Industry interference". It was attended by more than 70 participants from various ICMR institutes. The tobacco control experts gave insights into the provisions of WHO FCTC and the Code of Conduct. The participants were sensitized about the Parties' obligations under Article 5.3 and the tricks and tactics being utilized by the tobacco industry to undermine the tobacco control efforts.

To commemorate World No Tobacco Day on May 31, 2021, a virtual Webinar on "Commit to Quit Tobacco: To avoid the Deadly Quartet- Covid-19, Cardiovascular diseases (CVDs), Respiratory diseases and Cancer" was organised wherein the panel of experts deliberated on the effects of tobacco on the deadly quartet. More than 100 participants were benefitted from the interactive session.

A collaborative study between ICMR-NICPR, International Agency for Research on Cancer, University of York and The Union studied the pattern and determinants of areca nut use with tobacco and without tobacco in India. The study reported that about 23.9% of the adult population consumed areca nut, that is, approximately 223.79 million people in India. Majority of users

(14.2%) consumed areca nut with tobacco. The study also provided detailed information on socioeconomic determinants of areca nut consumption, with and without tobacco, and separately for men and women.

To identify vulnerable populations with respect to tobacco and alcohol use, sub-samples from eight mega cities of India, namely Chennai, Delhi, Hyderabad, Indore, Kolkata, Meerut, Mumbai and Nagpur, from National Family Health Survey (NFHS) conducted in 2015-2016 were taken to assess smoked tobacco use, SLT and alcohol with emphasis on urban slums. The study comprised 4970 slum dwellers and 11806 non-slum dwellers with 14,484 (86.3%) women and 2,292 (13.7%) men. Findings suggested that nearly 26% men and 3.2% women from slums consumed SLT which was higher than their non-slum counterparts (men 19.1% and women 1.3%). All the cities except Nagpur showed that a higher proportion of both men and women slum-dweller consumed SLT than their non-slum counterparts. In the case of women, a large difference in SLT use between slum and non-slum areas was evident in Mumbai, followed by Kolkata and Indore. Through regression analysis, it was revealed that the odds of smoking were 48% higher among women living in slum areas compared to women in non-slum areas. In case of SLT use, the odds were 34% higher among women living in slum areas.

A dedicated website for WHO FCTC GKHSLT is being maintained to provide information on the activities on SLT https://untobaccocontrol.org/kh/smokeless-tobacco/. This website also provides valuable information related to SLT products, epidemiology, policies, cessation etc.

Addressing Smokeless Tobacco and Building Research Capacity in South Asia (ASTRA)

Principal Investigator: Dr. Shalini Singh, Director, ICMR-NICPR

Co-PI: Dr Prashant Kumar Singh, Scientist D

Other Collaborating Institutes: University of York, Maulana Azad Medical College Delhi, ARK Foundation Bangaldesh, Aga Khan Medical University Karachi.

Funding agency & budget: National Institute of Health (UK), Rs 1 Crore 80 Lakhs

Project Duration: Apr 2019 – Mar 2022

Brief background & rationale: To date, a range of interventions have been tested to achieve tobacco cessation in different groups of ST users; these approaches include the use of behavioral interventions, pharmacologic treatment, or a combination of the two. Prospective cohort and quasi experimental studies in ST users of South Asian origin based in the UK have demonstrated nicotine replacement therapy (NRT) to be effective in achieving short-term ST cessation, however no evidence is available from South Asia itself. Similarly, culturally tailored behavioral interventions may be practical to deliver in low resource settings, but there is little evidence demonstrating its benefit in these populations. This study aims to address this research gap by testing both NRT and behavioral support (BISCA) as part of a feasibility trial.

Objectives: The main objectives of this trial are to assess feasibility of:

1. Delivering the interventions (NRT and BISCA),
2. Recruitment, randomisation and retention,
3. Methods to measure and collect the following:
    a. Baseline participant information (demographics, ST use and related behavior)
    b. ST cessation at 6, 12 and 26 weeks (using self-reported and validated abstinence)
    c. Mediators of ST cessation
    d. Adverse events and withdrawal symptoms
    e. Economic data (health resource use, quality of life)
4. Process evaluation data (context, mechanisms of impact and implementation)

Brief Methodology: The study is a 2 x 2 factorial design trial which will test the feasibility of delivering two interventions [Nicotine replacement therapy (Treatment A), and a behavioral support intervention for ST cessation-BISCA (Treatment B)] alone and in combination. The trial will be individually randomized, with and embedded process evaluation and preliminary economic assessment. Eligible and consenting individuals will be randomised to one of the following four trial arms:

Arm 1: No Intervention [VBA + self-help material on quit planning]
Arm 2: Intervention A only [8-week NRT in addition to standard VBA + self-help material (arm 1)]
Arm 3: Intervention B only [Behavioural support intervention for ST cessation-BISCA (incorporating VBA and self-help)]
Arm 4: Treatments A & B described above

Work done:

The adaptation phase of the trial has been completed. Framework data analysis was used to analyse data before a thematic synthesis was completed. Results showed that participants reported long term ST use and high dependency. All reported strong cessation motivation and multiple failed attempts because of ease of purchasing ST, tobacco dependency and lack of institutional support.

Based on findings of adaptation phase of the study, we have developed Information, Education and Communication (IEC) materials that will be provided to the SLT users during the next (main trial) phase of the study. During the reporting time we have completed all participants' recruitment, assigned different arms and provided necessary interventions as per the protocol of the study. As of now we have completed 26th week follow-up of more than half of the study participants and many participants have reported tobacco quitting.

As part of the dissemination strategy, we developed a Fact Sheet "Smokeless Tobacco Cessation in India" describing information related to current status of SLT cessation in India viz, differences between different states, demographic and socioeconomic groups, methods of cessation being used, people who attempted to quit tobacco with support and without any support. The fact sheet also describes challenges and opportunities that the study faced during COVID-19 and lessons that could be learned for future cessation studies.

We have also developed a short video showing participants who quit SLT, their experiences during the study period and what motivated them to quit SLT. The video has been uploaded to the official YouTube link of ICMR-NICPR for wider dissemination to encourage other SLT users to quit. The title of the video is "Quitters are Winners: Smokeless Tobacco Cessation @ICMR-NICPR" https://www.youtube.com/watch?v=uqKk_Qr-6_o

Translational Potential: The study would provide evidence to SLT cessation in Indian setting with combination of behavioral interventions, pharmacologic treatment, or a combination of the two. Results of the trail will provide critical inputs towards tobacco control efforts in the country.

ICMR Task Force Study on Smokeless Tobacco and reproductive & Maternal Health (ICMR SLT-RMH Study)

Principal Investigator: Dr. Prashant K Singh, Scientist D, Division of Preventive Oncology & Population Health

Other Collaborating Institutes: ICMR Hqrs, RMRC Bhubaneshwar

Funding agency & budget: ICMR, Rs 1 Crore 39 Lakhs

Project Duration: 2019 – 2022

Brief background & rationale: Smokeless Tobacco (SLT) and areca nut use remains to be neglected among females, especially pregnant women, despite causing much preventable morbidity in mothers and the neo-nates. Hence, this study aims to understand SLT use among women of reproductive age as a means to develop training and behaviour change intervention models for cessation.

Objectives:

- To examine the socioeconomic factors associated with SLT and areca nut use among women of reproductive age and adverse pregnancy outcomes using Demographic and Health Surveys in selected south Asian countries.
- To understand the socioeconomic and cultural norms along with inter-generational linkages of SLT and areca nut use among women of reproductive age group in two study sites (Noida, Uttar Pradesh and Bhubaneswar, Odisha).
- To develop Behavioural Change Intervention (BCI) strategies for SLT and areca nut cessation among women belonging to reproductive age group

Brief Methodology:

- For the first objective, data from latest rounds of Demographic and Health Surveys (DHS) on the consumption of SLT among the women from the reproductive age group (15 - 49 years) from Afghanistan, Bangladesh, India, Nepal and Pakistan were included.
- For the second objective, an attempt to understand the socio-cultural context and determinants of SLT and areca nut use among target population would be undertaken. It would examine the role of social network, family history, occupation on current use along with knowledge and awareness regarding its adverse effects and quitting intentions.
- For the third objective, utilising the insights obtained from the above two studies, SLT cessation behavioural change intervention (BCI) tool shall be developed using Information, Education and Communication (IEC) strategy which shall be tested for cultural acceptability at a local cessation centre.

Work done:

Findings from Primary Data Collection

Demographic Characteristics: Of the 237 women enrolled so far, majority belonged to age group 18-35 years. Many of the women were illiterate, primarily home-makers or worked as house-helps or as unskilled labourers. Most of the women were unaware about the existing government-funded health-care schemes.

Field Observations and Preliminary Findings

- The most commonly used SLT products included Gutkha, Areca Nut, Khaini and Gul Manjan of an array of brands. Friends, family and neighbors had an influence on initiating SLT use. Pregnancy related nausea, dental issues, and addiction were cited as major reasons for using SLT products during pregnancy/lactation.
- While some of the participants were oblivious of adverse health effects of SLT use, those who were aware did express their intention to quit. However, the high dependency and low-priced SLT products supplanted the motivation among the users' to seek tobacco cessation counselling.

Table: Number of participants screened and interviewed during the field visits, February 2021 to April 2021

Total No. of individuals interacted			**237**			
Total No. of individuals screened			71			
Total No. of Consent Forms Obtained			65			
Sub-group Type	Never Used	Currently Pregnant	Recently Delivered/ Lactating	Recently Quit	ASHA/ ANM/ NGO Worker/ AWW /Doctor	Total Sample Size
No. of Interviews to be conducted	20	20	20	20	20	100
No. of Interviews Conducted	11	13	18	2	17	61

Observations of Community Health Workers on SLT Use among Pregnant and Lactating Women:

- 22.7% (5 of 22) of the healthcare workers themselves reported using SLT or areca nut products, however, one of the doctors reported smoking and nicotine addiction.
- The women visiting the health facility who consumed SLT and/or Areca nut products were counselled for cessation of the habit by suggesting healthier alternatives such as fruit juices, biscuits, candy and mixture of saunf (aniseeds) with sugar candy and jaggery.

- However, only 7 of 22 (25.92%) of the CHWs assisted the women users to tobacco cessation clinics (ICMR – NICPR). Of these., only 2 had assessed the women's willingness to quit.
- Approximately, 14 of 22 (63%) of the FHWs and Community stakeholders had received training on SLT/Areca nut cessation. Majority of the participants perceived oral cancer (5 of 22; 22.72%) as the foremost adverse health consequence of SLT and/or Areca nut use followed by other illness such as low birth weight, anaemia, pre-mature delivery, lung cancer, stunted growth, risk of developing cancer in the foetus, asthma and other types of cancer.
- FHWs were considerably well cognizant about the determinants of SLT use among pregnant and lactating women such as addiction, lack of knowledge, less price sensitive and perceived health benefits. In addition, the other factors such as peer influence, surrogate advertisements and easy accessibility were articulated by the participants.

Table: Details of the recruited Health Workers for the field study

Study Participants	Number	Education
Accredited Social Health Activist (ASHA)	10	Elementary education to graduation
Auxiliary Nurse Mid-Wife (ANM)	7	Senior Secondary school to Post-Graduate
Workers from Non-Governmental Organizations (NGO)	6	Graduates to Post-Graduate
Doctors from Primary Health Centers	4	MBBS

Secondary data analysis (National Family Health Survey)

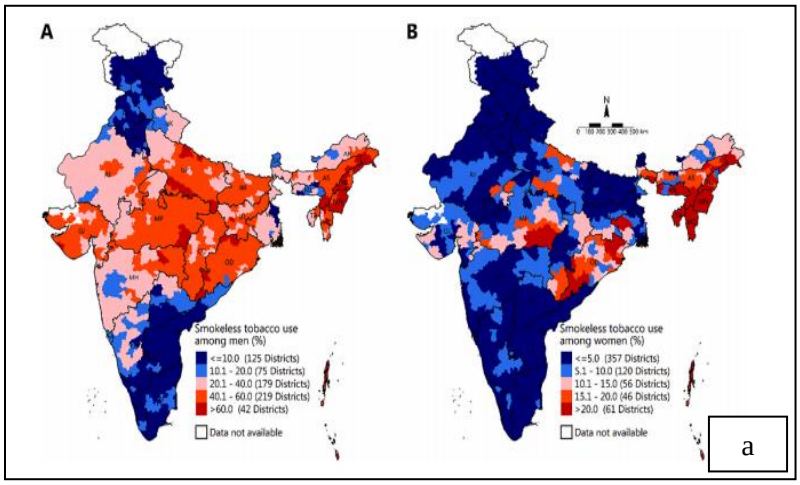
Mapping smokeless tobacco use among reproductive age women in 640 districts of India

o A quantitative analysis was carried out to assess the sex-stratified prevalence of different forms of smoking and SLT and alcohol among adults aged 15-49 at the district level. The study utilized the available data on 28521 communities across 640 districts of India, from the NFHS conducted in 2015-16. The study sample included 1,03525 men and 6,99,686 women. Different forms of SLT products were also mapped. Multilevel logistic regression models were applied to quantify the variation at district and community-level in smoking and consumption of SLT and alcohol.

o The prevalence of smoking, SLT and alcohol was higher among men than women. However, in many districts across states of India, a significant proportion of women were found to be using different forms of tobacco and alcohol. Out of 100 top districts with the higher prevalence of any form of tobacco or alcohol consumption among women, 41 districts were concentrated in three states, namely Assam (14 districts), Arunachal Pradesh (14), and Chhattisgarh (13). In 108 (out of 640) districts, over one-fifth of women consumed any form of tobacco or alcohol. In 61 districts, consumption of smokeless tobacco was over 20% among women. Gutkha/paan masala with

tobacco and khaini were the most commonly used product among men and women in Gujarat, Uttar Pradesh, Bihar, Jharkhand, Chhattisgarh, Odisha, West Bengal, northeast region and parts of Madhya Pradesh, Maharashtra and Rajasthan.

o The study found considerable sex-differentials in inter-individual variations with respect to smoking, SLT and alcohol consumption. Study findings suggested that both forms of tobacco among women were largely influenced by community or neighbourhood contextual characteristics.



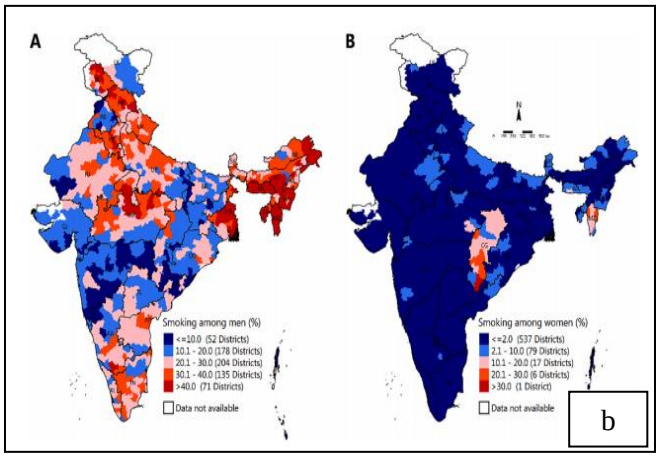


Figure: Prevalence of any Smokeless tobacco use (a) and smoking (b) among (A) men aged 15-49; (B) women aged 15-49 across districts of India, 2015-16)

Translational Potential: The study will provide scientific understanding about the usage of SLT and areca nut among the reproductive age women including its associated cultural and socio-economic determinants. The study would also contribute towards development of a behaviour change intervention tool that is culturally sensitive and locally contextualised with the help of relevant stakeholders.

Feasibility of integrating tobacco use screening and tobacco cessation services with routine antenatal care services: a pilot study in district hospital of Gautam Budh Nagar

Principal Investigator: Dr. Shalini Singh, Director, NICPR; CoI Dr Ekta Gupta, Scientist E

Funding agency & budget: ICMR, Rs 40 lakhs

Project Duration: Mar 2021 – Feb 2024

Brief background & rationale: It is a well-established fact that tobacco use is contra-indicated in pregnant women. The health hazards of using tobacco during pregnancy range from intrauterine growth restriction to perinatal mortality. In India, as per the latest Global Adult Tobacco Survey (GATS) 2016-17, prevalence of tobacco use among pregnant women was as high as 7.5%. It has also been documented that advice by a healthcare professional is a potent motivation for quitting tobacco use. Pregnant women meet the healthcare providers several times during their pregnancy (antenatal visits). This is possibly the first study in the Indian public health system which aims to explore the portals for smooth integration of tobacco cessation services with antenatal care services.

Objectives:

- To measure the prevalence of tobacco use (smoking and smokeless form) among pregnant women
- To study the pattern of use of tobacco products during pregnancy and lactation
- To develop a comprehensive behavioral intervention module for tobacco cessation in women
- To assess the tobacco quit rate during pregnancy using behavioral intervention
- To study adverse pregnancy outcomes among tobacco users (including in mothers and newborns)

Brief Methodology:
The study would be carried out in the District Hospital Noida, in the antenatal clinic as a mixed methods study. The quantitative part of the study will be a case-control study. Women registered in the antenatal clinic shall be screened for tobacco use and their anthropometric and biochemical parameters and followed up till delivery for pregnancy outcomes. The tobacco users shall be administered a tobacco cessation intervention plan to support quitting tobacco use and followed up for quit rate documentation using urine cotinine levels and breath analysis. The qualitative part of the study would include Focus Group Discussions (FGDs) among the pregnant women (both users and non-users) to understand the knowledge, awareness, triggers for initiating use, risk perception of harms from tobacco use, support women need to help quitting tobacco use. In-depth interviews (IDIs) of doctors, nurses, and FGDs of ANMs and ASHAs would also be carried out

among the health care providers for designing suitable intervention which can be integrated easily into the health care system. This data would provide inputs for the special needs of pregnant women on support needed for quitting and will be used in the behavioural intervention.

Work done:

A global review is being undertaken to assess the available behavioural intervention tools that have been used among pregnant women for tobacco cessation. Also, development of study tools is under process for pilot testing prior to start of main survey.

Translational Potential: The study will demonstrate the feasibility of incorporating tobacco cessation services in antenatal clinics in public healthcare settings and this model can be replicated in other hospitals and in the national program. The study would also provide the evidence for risk factors for adverse pregnancy outcomes (if any) recorded during the tenure of the study. The behavioral intervention developed during the study can be translated into other Indian languages for use in the Indian context.

Strengthening, biochemical, research policy, capacity building and cessation support to advance and smokeless tobacco control in India

Principal Investigator: Dr. Mausumi Bharadwaj, Scientist G, Molecular Biology Group

Funding agency & budget: ICMR, 4.3 crores

Project Duration: May 2019 – May 2023

Brief background & rationale: Due to use of smokeless tobacco (SLT), a non-combustible form of tobacco, more than 3.5 lakh SLT users die every year globally. But currently in India SLT use is also one of the major health issues. Hence, control of SLT use is now needs specific strategies to deal with. Though there are various challenges but effort has been initiated to curb the SLT menace. Therefore, given the extent and multiple faces of the SLT use epidemic in the country, a comprehensive study has been designed for better understanding of the mechanism

Objectives: For better understanding of the mechanism a holistic approach will be involved including microbiological, chemical and behavioural aspects of SLT products

Brief Methodology: In first phase of the study, characterization of common microbiome present in SLT products will be performed by Next Generation Sequencing (NGS)

Work done: The physio-chemical properties of smokeless tobacco products (STPs) showed pH values ranging between 5.36 - 10.27. The STPs had a mean moisture value of 18.19 ± 1.17% and the highest moisture content was recorded in Moist snuff products. The mean alkaloid content was 20.74 ± 1.62 mg/g in STPs and Khaini category contained the maximum alkaloid content. Further, some STPs exhibited Aflatoxin-B1 and OchartoxinA.
Next, the microbiome of STPs was established and a total of 22 bacterial phyla were identified in all STPs. The 536 genera were identified in all SLT products. Furthermore, the mycobiome analysis reveals that the fungal genera rich in STPs were Pichia, Sterigmatomyces, Rhizoctonia, and Apiotrichum. The taxonomic characterization of the microbiota of STP users showed that the genera like Streptococcus, Prevotella, and Neisseria prevailed in SLT users and Bacillus genus level was decreased in SLT users as compared to non-users. The number of microbes belonging to fungal genera Candida, Mortierella, Pichia, Cladosporium, Fusarium, and Rhizophlyctis were decreased in SLT users. Finally, the effect of smokeless tobacco extract (STE) on cell lines showed that morphological alterations of CAL-27 cells in the 2.5% STE treated group were observed unhealthy, as compared to untreated or lower concentration treated group. While 0.6% of STE treated cells remained healthy like untreated cells.

Translational Potential: The identification of harmful microbes and toxins in STP will provide information to concerned scientific and regulatory bodies regarding the processing and storage of STPs. Further, identification of changes in the microbial profile of STP users as compared to healthy (non-users) will lead to the identification of putative microbes (probiotics) or their products (prebiotics) for the prevention or treatment of oral diseases in STP users.

Identification of oral microbial genes as potential molecular diagnostic markers of tobacco exposure

Intramural Research Study, Dr. Anuj Kumar, Molecular Biology Group

Background: Oral cancer is the third most common cancer in India and use of tobacco is main and preventable cause of oral cancer. Tobacco is mainly used in two forms – smoked tobacco and smokeless tobacco (SLT). As the number of smoked tobacco users is declining, the number of SLT users are reported to be rising in India, as per GATS, 2017. Though a range of intervention studies have been published, there is a need for South-east Asia-specific interventions. The interventions need to be assessed by markers, such as cotinine. However, cotinine as a tobacco marker has limitations like marker of short-term exposure, individual differences, need of expensive instruments. Thus, there is need to investigate other markers of tobacco exposure. Approximately 256 chemical compounds have been associated with smokeless tobacco. These compounds enter the mouth of SLT user and are metabolized by the enzymes and oral microbiome during mastication. Nicotine and cotinine are mainly accumulated in the saliva. In this study, we aim to investigate the binding of nicotine and cotinine to these enzymes. Several studies have enlisted the microbiome of the oral cavity, however there is a lack of knowledge on the metabolism of tobacco alkaloids by the oral microbes.

Objectives:

- To investigate and compare the bacterial population in oral cavity of SLT users and non-users.
- To delineate the genes involved in the metabolism of tobacco compounds through comparison between SLT users and non-users.

Brief Methodology: Aliquoted of saliva samples were collected and stored in cryovials stored at -20 C. For determining the cotinine level in aliquoted salivary samples, samples were thawed at room temperature. Samples were thoroughly vortexed and then spun to settle debris. Then diluted 10 times as per the protocol of the commercial. The standard curve was prepared in the pilot experiment. The level of cotinine in each samples was determined by commercially available kit.

Main Findings:

Cotinine level was determined in saliva samples of subjects, who have self-reported tobacco exposure (smokeless tobacco level). The level of cotinine was found higher than average. The level of cotinine showed significant variation among self-reported tobacco exposure status of subjects.

Studies on the Impact of Microbial Treatment on Tobacco Specific Nitrosamines in Indian Smokeless Tobacco Products

Principal Investigator: Dr. Nivedita Mishra, WOS
Mentor: Dr. R. Suresh Kumar, Molecular Biology Group

Funding Agency: DHR – WOS
Duration of Project: 2019-2022

Background: Smokeless tobacco products are highly injurious to health causing various types of cancers and many other non-communicable diseases. As successful quitting percentage is very low among tobacco users, reducing the harmful contents of products can be a better approach.
The microbial populations are responsible to a large extent for generation of carcinogenic Tobacco Specific Nitrosamines in tobacco products. We propose to elucidate the possible role of microbes in reducing the amount of carcinogenic chemicals among ready-to-use Indian smokeless tobacco products.

Objectives:

- To identify and characterize the microflora present in different Indian ready-to-use smokeless tobacco products using conventional microbiological and molecular methods.

Brief Methodology: Initial identification would be done using conventional microbiological procedures such as colony and cell morphology followed by various biochemical tests. Molecular methods for microbial identification would be employed using universal primers for species level identification, the sequences shall be compared with the GenBank database using BLAST. Community dynamics study shall be done using appropriate PCR primers and analysed using available software (eg. PEAR, PANDAseq etc.).

Chemical contents of different smokeless tobacco products such as nitrite, various TSNA compounds and other chemicals would be estimated on LC-MS/MS. Statistical analysis will be performed using ANOVA followed by suitable post-hoc analysis to compare chemical profiles of various tobacco products. The selected microbial strains will be sprayed on tobacco products and after enrichment the chemical contents will be determined.

Work done:

The study of physical and chemical parameters of 20 smokeless tobacco products available in Indian market was completed. The results have confirmed the heterogeneous nature of tobacco products available in Indian market. Nitrate reducing bacteria were isolated as pure culture from different SLT samples. Morphological, biochemical, and genetic studies of these microbes are under progress to understand their microbial nature. DNA extraction was done from 20 SLT samples. Genetic analysis and community structure study is under progress to understand the microbial community structure.

PHYTOCOMPOUND RESEARCH

Predicting the anti-cancer potential of phytomolecules against different cancers using knowledge of natural products

Principal Investigator: Dr Subhash Agarwal, Scientist E, Division of Bioinformatics

Funding agency & budget: ICMR, Rs. 21 lakhs

Project Duration: Jan 2020 – Jan 2023

Brief background & rationale: Continuous efforts are being made globally by researchers and pharmaceutical companies to discover and develop anti-cancer therapeutic agents from phytomolecules as they represent one of the richest sources of high chemical diversity and provide novel scaffold structures that can serve as starting points for rational drug design. This has necessitated the need for developing computational knowledge resources which enable discovering leads from phytomolecules.

Objectives:

- Collection and compilation of phyto-molecules with their anticancer activity from literature.

Brief Methodology: To identify the plant-derived naturally occurring compounds with reported anti-cancerous activity, we have searched PubMed and collected the relevant literature. A number of journals pertaining to medicinal plant and natural product research were collected and we have read through the full text of each article to catalogue information like compound name, information pertaining to its in vitro/in vivo biological activity (IC_{50} etc), the cell line used for in vitro cytotoxicity assays, the model system in case of in vivo experiments and the protein target as documented in the references along with its tracking number (PMID).

Work done:

- Presently, detailed data for 2063 molecules has been collected and information on their structure, experimentally determined invitro and invivo biological activity, cancer type, cell lines, inhibitory values (IC50, ED50, EC50, GI50), molecular targets, and drug likeness of compounds has been collated.
- Details for 411 cancer cell lines corresponding to about 6923 compound-cell line interactions has been collected.
- Also, data on 2239 experimentally validated compound-target interactions i.e. protein targets that effect growth of cancer cell lines is available with us.
- Our analysis indicates that compounds having activity reported against various cancers like lung, breast, colon, haematopoietic, nasopharyngeal, skin, prostate, liver, ovarian etc is available (Fig. 1).
- We could collect maximum number of compounds against Lung and Breast cancer, which are number one cancer in males and females of India, respectively.

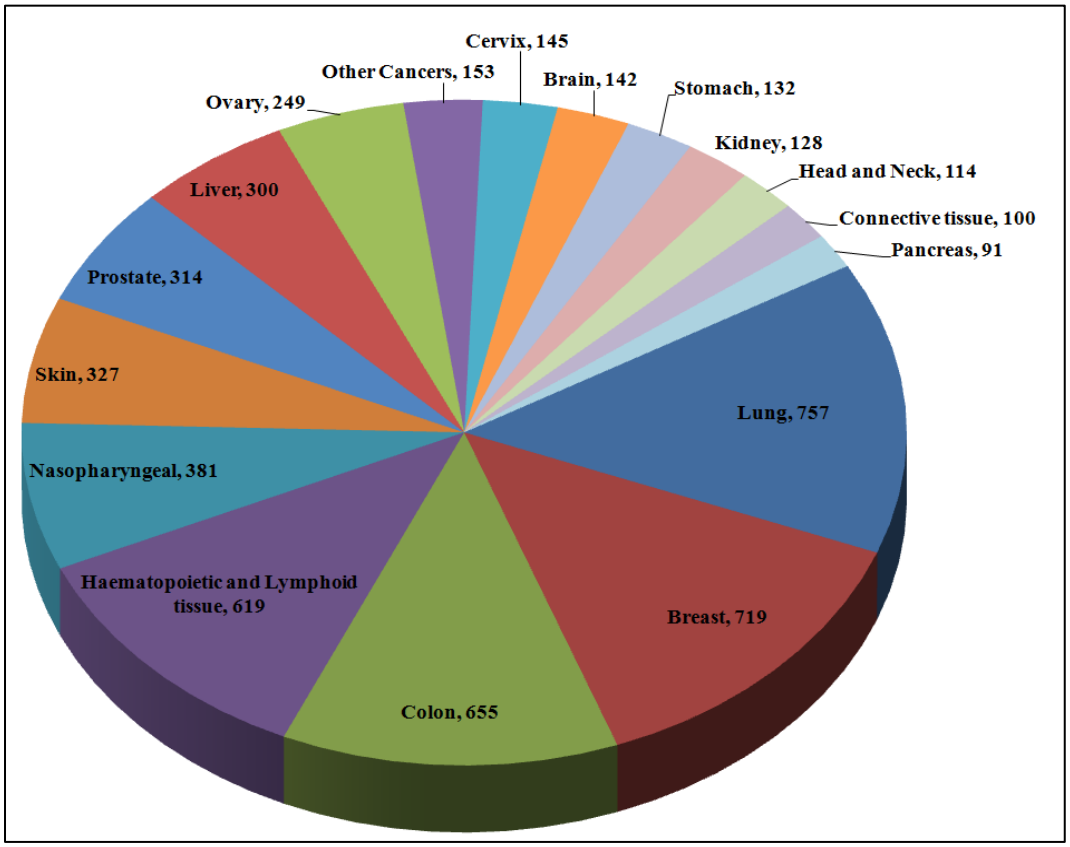


Fig: Distribution of phytomolecules in different cancers

Translational Potential: We have been able to generate a computational knowledge resource that has bioactivity and structure information of known anticancer phyto-molecules, which can be utilised in silico screening and identification of scaffolds against anti-cancer drug targets.

Develop machine learning models to identify isoform specific inhibitors against EGFR and HER2, the therapeutic targets in Lung and breast cancer

Intramural Research Study by Division of Bioinformatics

Background: The EGFR kinase pathway is one of the most frequently activated signalling pathways in human cancers. EGFR and HER2 are the two significant members of this pathway, which are attractive drug targets of clinical relevance in lung and breast cancer. Therefore, identifying EGFR and HER2 specific inhibitors is one of the important challenges in cancer drug discovery.

Objectives: To design isoform specific classification models using machine learning approach that can predict the specificity of a compound as an EGFR or HER2 specific anticancer agent.

Brief Methodology: A dataset of 519 compounds having inhibitory activity against both the isoforms i.e., EGFR and HER2, was collected from literature and developed a knowledge-based computational classification model. Seventy-two classification models using nine fingerprint types, four classifiers (IBK, NB, SMO and RF) and two different datasets (EGFR and HER2 isoform specific) were developed. The performance of the models was validated using five-fold cross-validation technique and external validation technique. Once the models were validated, the Applicability Domain was evaluated to check whether the predictions for test set molecules are reliable. In addition, the best selected models were validated using Y-randomization test.

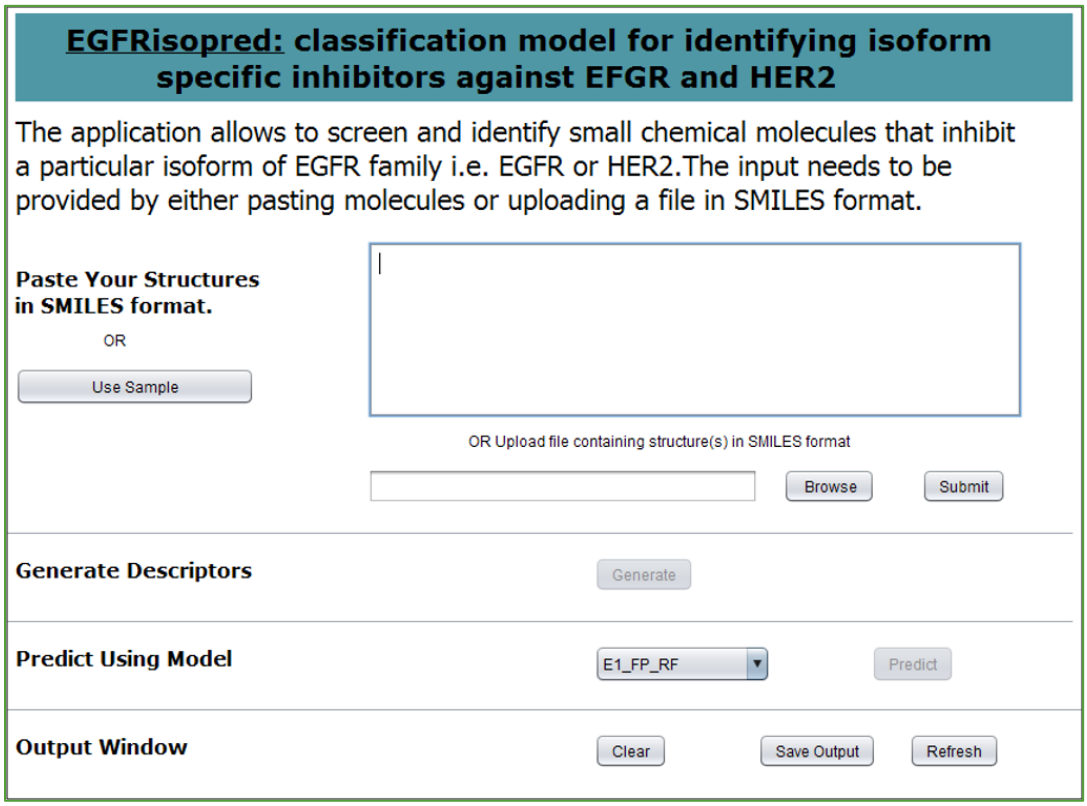
Main Findings:

- EGFR specific model: The two models developed using Random forest classifier with CDK and CDK extended fingerprint showed >80% accuracy and >0.60 MCC on the validation dataset.

- HER2 specific model: The two best models developed using IBK classifier with CDK and CDK extended fingerprint showed ~85% accuracy and ~0.70 MCC on the validation dataset.

- We also identified the major structural scaffolds prevalent in the EGFR and HER2 dataset. The five top-most framework that cover nearly 75% of the molecules in the EGFR specific dataset were: 4-anilinoquinazoline (33%), 4-anilinoquinoline (16%), 4-anilinopyrimidine (11%), pyrrolo-triazine (9%) and thieno[3,2-d]pyrimidine (6%). Similarly, the most prevalent chemotypes in HER2 specific datasets covering nearly 75% of the molecules are: Pyrrolo[3,2-d]pyrimidine (34%), thieno[3,2-d]pyrimidine (13%), 4-anilinoquinazoline (11%), pyrazolo-pyrimidine (10%) and anilino-quinoline (8%).

- The performance of the models was also evaluated using the decoy datasets and it was observed that the accuracy of the two EGFR models was 76% and 72%, while that of HER2 models was 68% and 75%.



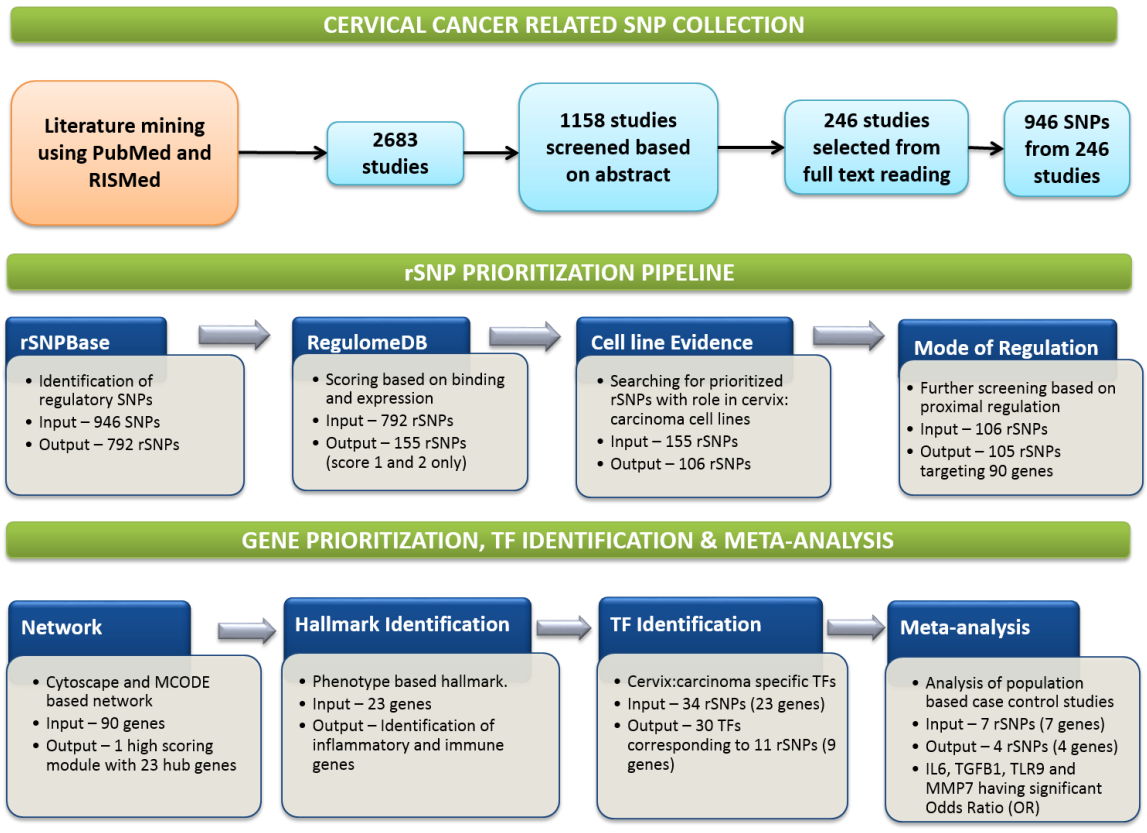
Identification of regulatory SNPs responsible for increased cervical cancer risk using meta-analysis

Intramural Research Study by Division of Bioinformatics

Background: Cervical cancer is a leading women cancer. Its increased risk has been linked with genetic variations like single nucleotide polymorphisms (SNPs). Although, the effect of one or few SNPs have been studied in a few candidate genes, however the role of a comprehensive pool of non-coding regulatory SNPs (rSNPs) in cervical cancer is not available. So, this study was undertaken to prioritize the important regulatory SNPs and evaluate their effect in cervical cancer patients using population-based studies.

Objectives: To prioritize and identify regulatory polymorphisms that increases the risk of cervical cancer.

Brief Methodology: A search was conducted in PubMed up to February 2020 for identification of articles with information on SNPs in the non-coding region. These SNPs were then analysed through rSNPBase and RegulomeDB for identification of regulatory SNPs. Afterwards, a regulatory module was constructed using protein-protein interaction data and a hub of highly interacting target genes corresponding to important rSNPs was identified. To further understand the mechanism of action their transcription factor information with respect to cervical cancer was



retrieved. Also, to evaluate the pooled effect in cervical cancer patients of the important polymorphisms, a meta-analysis was performed.

Main Findings:

- As our goal was to identify regulatory polymorphisms that induce changes and increase the risk of cervical cancer, a pool of 946 non-coding SNPs were collected by text mining the literature in the last 30 years.
- Prioritized 105 functional and regulatory SNPs in cervical cancer using the ENCODE based tools rSNPBase and RegulomeDB.
- A network of 90 targeted genes (corresponding to 105 rSNPs) was constructed to identify a hub of twenty-three highly interconnected genes.
- To further understand the mechanism of action of the 34 rSNPs, their transcription factor information with respect to cervical cancer was checked.
- Finally, to evaluate the pooled effect in cervical cancer patients, a meta-analysis was performed which identified the polymorphisms in IL6 (rs2069837), TGFB1 (rs1800469), TLR9 (rs187084) and MMP7 (rs11568818) are significantly ($p < 0.05$) associated with cervical cancer.
- In summary, it was found that rSNPs targeting immune and inflammation associated genes are important role for increasing the risk of cervical cancer.

Study on Reversal of Multidrug Resistance (MDR) and role of P-gp in different cancer cell lines Using Natural Chemo preventive agents

Principal Investigator: Ms. Indu Kumari, WOS
Mentor: Dr. R. Suresh Kumar, Molecular Biology Group

Funding Agency: DHR – WOS
Duration of Project: 2018-2021

Background: Drug resistance has been a major problem in cancer therapy. Almost all therapies (except surgery) being used in the treatment of cancer can result in resistance. Unfortunately, there is a large group of patients that either do not respond to the therapy (intrinsic resistance) or become resistant during therapy (acquired resistance). Various mechanisms involved in multidrug resistance (MDR) like alterations in the cell cycle, reduced apoptosis, decreased uptake of drug have been identified. One of the proteins in the family of ABC transporters, P-glycoprotein (P-gp) acts as an ATP-dependent efflux pump to remove cytotoxic drugs from cytoplasm.
Phytochemicals may serve as an alternative option in management of many diseases including cancer. Identification of phyto inhibitors and reversal of MDR using natural compounds may help in reducing the cancer burden and easy to use for successful cancer chemotherapy.

Objectives:

- To Study on drug tolerant and drug resistant phenotypes in cancer cells (breast carcinoma cell line, lung carcinoma cell line, and oral carcinoma cell line) through progressive in vitro drug exposures.
- To study on the expression profile of ABC drug transporters (p Glycoprotein) and its role in drug resistance pathway.

Brief Methodology: In-silico methods were used to screen phytochemicals against target protein. Colony formation assay, MTT assay and Trypan blue dye exclusions were performed with compound No 4 to investigate the growth in non - treated and treated normal breast cancer and resistant MCF-7 cells. Drug uptake capability of resistant breast cancer cells was explored by Rhodamine assay in phytochemical treated cells. Expression of proteins was evaluated by Western blot against targeted genes related to multidrug resistance. Pulse Resistance cells are being developed with known chemotherapeutic drug.

Work done:

From MTT result we evaluated the cytotoxic effect and IC50 value of phytocompound as 60µM and 40 µM Ver., for both MCF-7 and MDA MB-231 cell lines. Morphological analysis of MCF-7 from trypan blue exclusion dye showed significant effect of HAR, an inhibitor ligand drug as increasing concentration of drug. Trypan blue exclusion showed increasing proliferation inhibition with increasing dose of phytocompound (drug) in treated and untreated cell for normal MCF-7 and resistant MCF-7/ 5-FU cells. Wound healing assay result showed inhibition of cell migration as increasing dose of drug for both MCF-7 and MCF-7/5FU. From FACS result we

concluded that drug arrest G-M phase of cell cycle. From result of Rhodamine assay we determined that HAR significantly reverse /sensitize the 5-FU resistant breast cancer cell (MCF-7/5-FU). Western blot analysis of MCF-7 positively support the Rhodamine results as increasing the dose of drug decreasing the expression of target transporter protein, drug resistance marker, MAPK/ERK pathway related proteins.

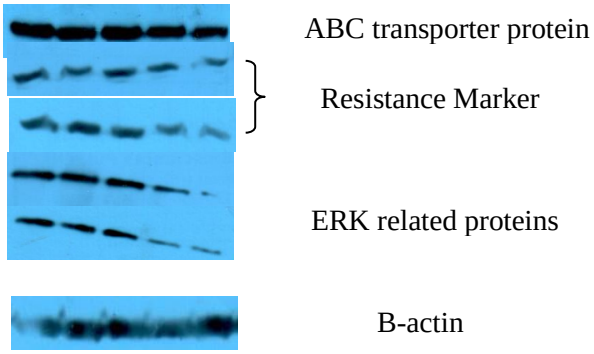


Fig: *Expression of various proteins following treatment of normal breast cancer cells MCF-7 with HAR compound for 48hr*

Fig: *Expression of various proteins following treatment of normal and drug resistant breast cancer cells MCF-7 and MCF-7 /5FUR with HAR compound for 48hr*

.

COVID-19 RELATED RESEARCH

National population-based sero-surveillance for SARS-CoV-2 infection transmission in India: Third round (December 2020) and Fourth round (June-July 2021)

Institutional Coordinator: Dr. Shalini Singh, Director

Team Leader: Dr Smita Asthana, Scientist E, Division of Epidemiology & Biostatistics

Funding agency & budget: ICMR

Project Duration: 19th Dec 2020 – 19th Jan 2021 (Round 3) and 28th June 2021 – 4th July 2021 (Round 4)

Objective: To estimate the sero-prevalence for SARS-CoV-2 infection in the general population at the national level and determine the trend over time among general population above 10 years of age and health workers. During fourth round of serosurvey a subset of samples was also collected from 6 to 10 years children.

Work Done:

Results of sample collected during third round of sero survey

Sr. No.	District	General Population			Health Care Worker		
		Sample Tested	Positive	Negative	Sample Tested	Positive	Negative
1.	Gautam Buddha Nagar	398	109 (27.39%)	289 (72.61%)	100	28 (28.00%)	72 (72.00%)
2.	JyotibaPhule Nagar	395	80 (20.25%)	315 (79.75%)	100	23 (23.00%)	77 (77.00%)
3.	Saharanpur	397	52 (13.1%)	345 (86.91%)	100	13 (13.00%)	87 (87.00%)
	Total	**1190**	**241 (20.25%)**	**949 (79.75%)**	**300**	**64 (21.33%)**	**236 (78.67%)**

Results of sample collected during fourth round of sero survey

Sr. No.	District	General Population			Health Care Workers		
		Sample Tested	**Positive**	**Negative**	**Sample Tested**	**Positive**	**Negative**
1	Gautam Buddha Nagar	399	266 (66.67%)	133 (33.33%)	100	86 (86.00%)	14 (14.00%)
2	Jyotiba Phule Nagar	400	205 (51.25%)	195 (48.75%)	100	89 (89.00%)	11 (11.00%)
3	Saharanpur	399	275 (68.92%)	124 (31.08%)	100	91 (91.00%)	9 (9.00%)
	Total	**1198**	**746 (62.27%)**	**452 (37.73%)**	**300**	**266 (88.67%)**	**34 (11.33%)**

Mental health and social stigma among healthcare personnel involved in the management of COVID-19 patients in India

Principal Investigator: Dr. Prashant K Singh, Scientist D, Division of Preventive Oncology

Other Collaborating Institutes: ICMR Hqrs

Funding agency & budget: ICMR, Rs 3.52 lakhs

Project Duration: Sept – Nov 2020

Brief background & rationale: Healthcare personnel working in COVID-19 wards face tremendous pressure owing to concerns about their personal safety, safety of loved ones, and shortage of equipment such as ventilators and protective gear. Prior studies have documented similar adverse psychological reactions during the 2003 SARS outbreak. However, evidence-based interventions for healthcare personnel during epidemics are scarce. Identification of factors associated with mental health issues among healthcare personnel would inform such interventions. The present study seeks to address this knowledge gap.

Objectives:

- To assess the occurrence of psychological distress, including depression, burnout, anxiety and other associated mental health outcomes among healthcare personnel (doctors, nurses, laboratory technicians, etc.). engaged in COVID-19 management.
- To understand the extent of social stigma faced by the healthcare personnel engaged in the management of COVID-19 and its effect on their mental health status.
- To identify the coping mechanisms adopted by the healthcare personnel to mitigate the psychological effects of handing the COVID-19 infected.
- To explore the perception and expectations of healthcare personnel on interventions that could mitigate the stigma associated with the COVID-19.

Brief Methodology:

This is a mixed-method study with both quantitative data collection as well as qualitative indepth-interview among the selected participants. The quantitative component will provide the proportion of subjects suffering from psychological distress, including depression, burnout, anxiety and other associated mental health and the qualitative component will provide answers to the extent of social stigma, perceptions and coping mechanism of health care providers. For the quantitative study, different cadres of 90 healthcare workers including doctors, nurses, ambulance emergency response teams, lab personnel, and others who are directly involved in patient care from COVID 19 designated hospitals. Study also includes frontline health workers who are involved in case identification, contact tracing, prevention and control measures for COVID 19.

Work done: Overall, 52.9% of the participants had risk of psychological distress that needed further evaluation. Psychological distress was found to be more among female staff, those found working in isolation of COVID cases (57.9%), caring the patients with symptoms (58%), in the intensive care units (58.3%), involved in contact tracing (60.1%) and screening (59.9%) and in transporting COVID patients. About 4.7% of the HCWs were overextended (Emotional exhaustion score>18); 6.5% were disengaged (Depersonalisation>8) and 9.7% HCWs were showing signs of burnout. Being a female increased the risk of psychological distress by 1.4 times, longer working hours increased the risk by two times; being a doctor and nurse increased the risk by 1.6 times, emotional exhaustion by nearly 4 times and high depersonalisation nearly twice.

The qualitative analysis shows that HCWs report major changes in work-life which influenced their family life and well-being to a large extent. This included excessive workload with erratic timings, periods of quarantine thereafter, and long durations away from home accentuated with the personal protection equipment (PPE) which was cumbersome. Family-related issues were manifold; the main challenge being separated from family, the challenge of caregiving especially for females with infants and children and fears around infecting family. Stigma from neighbours, friends, and relatives exhibited itself in various ugly faces from verbal abuses to stigmatizing actions such as avoidance, rejection, and even being asked to vacate from their residences. Coping strategies were mainly dependant on support from peers, family and friends and taking solace in electronic communication to substitute in-person communication. The perceptions on the way forward were largely organizational related with a call for a conducive working environment, a platform for their problems to be heard, time for the family through a rotation of workforce and more staff, incentivization, debunking of false information, involvement of HCWs in COVID-19 sensitization activities to allay fears and prevent stigma and finally need-based psychological support for them and their families.

Translational Potential: This study finding would provide insight and understanding of the mental health and social stigma faced by the healthcare professionals due to COVID management at different levels. This understanding could help in evolving feasible acceptable and timely need-based interventions for health care providers that address these concerns.

Adverse Events Following Immunization (AEFI) Surveillance of Covaxin

Intramural Research Study initiated by ICMR

Background: During the Covid-19 pandemic, the second global pandemic witnessed on record by human race, India indigenously developed a vaccine for this deadly disease. Keeping in view the urgency and need to vaccinate Indian citizens when the World was facing a huge vaccine shortage, the DCGI gave Covaxin – EUA under clinical trial mode for Indian health workers in the first phase. ICMR along with its Institutes partnered with Minitry of Health & Family Welfare to mitigate any risks associated with an unprecedented event like this.

Objectives:

- To conduct a follow-up of all the beneficiaries receiving Covaxin during Jan to April 2021
- To provide medical and epidemiological support to the Ministry to mitigate adverse outcomes.

Brief Methodology: All the beneficiaries who received Covaxin between January to April 2021 were followed up telephonically on day 7 & day 28 of their first and second dose, respectively. The subjects were interviewed for various signs and symptoms for minor, moderate and severe adverse events as the primary outcome.

Main Findings:

The data analysis is in progress.

Development of multiplex RT-qPCR for rapid diagnosis of COVID-19 samples

Intramural Research Study, Dr. Pramod Kumar, Scientist C, Molecular Biology Group

Background: Considering the mounting burden of COVID-19 cases in the country, newer/improved diagnostic modalities developed in India is urgently required to scale-up. The probes with most conserved region or newly designed primers and probes targeting two viral regions (E gene /N gene/Orf1ab and RdRp) with two different fluorophores on the respective probes need to be multiplexed with one host gene transcript (labelled with a third fluorophore on respective probe) according to the compatibility of the fluorophores channels available in qPCR machines.

Objectives: To develop a multiplex RT-qPCR for diagnosis of SRAS-CoV-2 and evaluate its performance for diagnosis of COVID-19 samples.

Brief Methodology: Extracted viral RNA from throat/nasal swab samples from positive and 1% of negative (including inconclusive) COVID-19 cases (upto 200) diagnosed by RT-qPCR received at NICPR were used for performance evaluation (Sensitivity and specificity). Sensitivity and specificity was determined against the WHO protocol involving RT-qPCR targeting RdRp using RdRp-SARS primers (forward and Reverse) and P2 probe (confirmatory) using known positive and negative COVID-19 cases.

Main Findings:

Development of duplex RT-qPCR development is in process with improved diagnostic sensitivity.

Standardization of RNA extraction method for high-throughput diagnosis of COVID-19 samples

Intramural Research Study, Dr. Pramod Kumar, Scientist C, Molecular Biology Group

Background: The rapid and global spread of the virus following its first appearance in China pressed India to take effective preventive measures. The virus has been named “SARS-CoV-2” and the disease it causes has been named “coronavirus disease 2019” (abbreviated “COVID-19”). Considering the mounting burden of COVID-19 cases in the country, newer/improved diagnostic developed in India is urgently required to scale-up diagnostic efficiency and self-reliance of the country in tackling COVID-19. We propose to establish manual RNA extraction protocol to enhance testing capacity along with automated extraction systems.

Objectives: To develop a rapid inhouse RNA extraction method and evaluate its performance for diagnosis of COVID-19 samples using RT-qPCR.

Brief Methodology: A manual RNA extraction protocol based on magnetic beads will be optimized. Extracted viral RNA from throat/nasal swab samples from 100 positive and 100 of negative (including inconclusive) COVID-19 cases diagnosed by RT-qPCR received at NICPR were used for performance evaluation (Sensitivity and specificity).

Main Findings:

Manual RNA extraction protocol using magnetic bead has been established. Optimization of the buffers composition for extraction is in process.

ACADEMIC ACTIVITES

JOURNAL CLUB PRESENTATIONS

Date	Presenter	Mentor	Title of paper presented
15.04.2021	Dr. Ragini	Dr. Suresh T Hedau	Electrochemical Determination of Naloxone Using Molecularly Imprinted Poly(para-phenylenediamine) Sensor
15.04.2021	Mr. Ram Krishna Sahu	Dr. Suresh T Hedau	NSD3-induced methylation of H3K36 activates NOTCH signaling to drive breast tumor initiation and metastatic progression
29.04.2021	Dr. Sonal Srivastava	Dr. Mausumi Bharadwaj	Repurposing dextromethorphan and metformin for treating nicotine-induced cancer by directly targeting CHRNA7 to inhibit JAK2/STAT3/SOX2 signaling
29.04.2021	Mr. Arpit Singh	Dr. Prashant K Singh	Economic Costs of Diseases and Deaths Attributable to Tobacco Use in India, 2017–2018
13.05.2021	Dr. Jigisha Chaudhary	Dr. Prashant K Singh	Overcoming Challenges to Treating Tobacco use During Pregnancy - A Qualitative study of Australian General Practitioners Barriers
13.05.2021	Mr Satyander Yadav	Dr. Smita Asthana	Introduction to R software
27.05.2021	Dr Gaurav Verma	Dr. Sanjay Gupta	miRNA- and cytokine-associated extracellular vesicles mediate squamous cell carcinomas
27.05.2021	Dr. Binayak Kumar	Dr. Suresh T Hedau	CHD4 Promotes Breast Cancer Progression as a Coactivator of Hypoxia-Inducible Factors
10.06.2021	Dr Md Sajid	Dr. Mausumi Bharadwaj	Dysbiosis of oral microbiota during oral squamous cell carcinoma development
10.06.2021	Ms. Arpita Singh	Dr. Prashant K Singh	Tobacco control policies in the 21st century: achievements and open challenges
24.06.2021	Dr.Neha Nimkarde	Dr. Smita Asthana	Smokeless tobacco-associated cancers: A systematic review and meta-analysis of Indian studies

PhD/ MD/ MS Thesis Enrolled/ Completed

Dr Mausumi Bharadwaj, Molecular Biology Group

- **PhD Thesis**

S.No.	Name of student	Title of Thesis	
1	Upma Sharma	Role Of Immuno Modulatory Genes In Oral Squamous Cell Carcinoma In Indian Population	Completed in 2020

Dr. Subhash Agarwal

- **PhD Thesis**

S.No.	Name of student	Title of Thesis	
1	Mr Agneesh Pratim Das	Identification of Inhibitors Targeting Epidermal Growth Factor Receptor (EGFR) Mutants: A Therapeutically important Target in Cancer	2020-2024

Dr. Showket Hussain, Molecular Biology

- **PhD Thesis**

S.No.	Name of student	Title of Thesis	
1	Vishakha Kesharwal	Functional role of NF-kB and HPV infection in esophageal carcinoma	2020 – 2024

MD Thesis

S.No.	Name of student	Title of Thesis	
1	Dr. Nitin Singh	Expression of E26 transformation specific Sequence 1 (ETS-1) and human papilloma virus (HPV) in oral cancer	Ongoing
2	Dr. Gopal Puri	Association of different modalities of treatment with the expression of various subset of T lymphocytes in patients with breast cancer and their clinical outcome	Ongoing
3	Dr. Nighat Nasreen	Comparative Evaluation of MMP-9 Expression in Oral Squamous Cell Carcinoma using Immunohistochemistry, Western Blotting and Reverse Transcription Polymerase Chain Reaction Techniques	Ongoing

POST-DOCTORAL FELLOWS/ RESEARCH ASSOCIATES/ TRAINEES/ DISSERTATIONS

Dr Mausumi Bharadwaj

S. No.	Name of student	Fellowship	Project
1.	Dr. Vineeta Sharma	ICMR- RA	Functional evaluation of Toll like receptors and Interleukin SNPs in association with Reproductive tract infections
2.	Dr. Upma Sharma	ICMR-RA	Evaluation of Functional role of Identified Novel SNPs of IL-10 gene and their interaction with miRNAs (miR-27a/mir-98) in Oral Carcinoma
3.	Dr. Ved Vrat Verma	ICMR-RA	Identification of molecular landscape in Familial/Sporadic Breast cancer

Dissertation Trainees under Dr. Mausumi Bharadwaj:

S. No.	Name of student	University enrolled	Duration
1.	Lalit Bhargava	Amity University	6 months
2.	Sarita Singh	Gautam Budha University	6 months
3.	Alishan Maqsood Khanam	Gautam Budha University	6 months
4.	Sona Rawat	Jaipur National University	6 months

Dr R Suresh Kumar

S. No.	Name of student	Fellowship	Project
1.	Ms. Indu Kumari	DHR-WOS	Study on Reversal of Multidrug Resistance (MDR) and role of P-gp.in different cancer cell lines Using Natural Chemo preventive agent
2.	Dr. Nivedita Mishra	DHR-WOS	Studies on the Impact of Microbial Treatment on Tobacco Specific Nitrosamines in Indian Smokeless Tobacco Products
3.	Dr. Anita Kumari	ICMR-PDF	Development and Evaluation of CRISPR/Cas13 based diagnostic system for HPV detection
4.	Dr. Mayank Maheshwari	ICMR-PDF	Investigating potential modulation of P21 (Cip/Waf1) mediated Autophagy via Ros induced endoplasmic stress

Dissertation Trainees under Dr. R Suresh Kumar:

S. No.	Name of student	University enrolled	Duration
1.	Rupal Sarup	Amity University	4 months

Dr. Subhash Agarwal

S.No.	Name of student	University enrolled	Duration
1	Ms. Shristi Tyagi	Jaipur National University	6 months
2	Ms. Nisha Chaudhary	Jaipur National University	6 months

Dr Smita Asthana

Dissertation Trainees:

S. No.	Name of student	University enrolled	Degree pursuing
1.	Dr Neha Vilas Nimkarde	IIHMR	PGDHM
2.	Dr SaimaZubair	IIHMR	PGDHM
3.	Mr. Ahmed Siddique	IIHMR	PGDHM
4.	Dr Shabnam	IIHMR	MPH
5.	Mr. Panwar	IIHMR	PGDHM
6.	Dr RenuDofe	IIPH, Gandhinagar, Gujarat	PGDHM

Dr Showket Hussain

S. No.	Name of student	Degree pursuing	Project/ Study title
1	Dr. Anamika Priyadarshini Sil	PDF	A molecular understanding of the role of oral contraceptives in the pathogenesis of cervical cancer
2	Dr Sonam Tulsyan	ICMR-RA	Genome Wide Methylation Profiling of North Indian Gall Bladder Cancer Patients

Dissertation/ Summer Trainees under Dr. Showket Hussain:

S. No.	Name of student	University enrolled	Duration
1.	Ummi Abiha	Amity University	6 months
2.	Nidhi Singh	Gautam Buddha University, Greater Noida	6 months

Dr Prashant Kumar Singh

Dissertation Trainees:

S. No.	Name of student	University enrolled	Duration
1.	Ms. Isha Joshi	TERI University	5 months
2.	Ms. Rupal Jain	TERI University	5 months
3.	Ms. Vasundhra Singh	TERI University	5 months
4.	Ms. Kriti Luthra	TERI University	5 months
5.	Ms. Pratiti Choudhury	TERI University	5 months
6.	Ms. Manshi Wadhwa	TERI University	5 months

Dr Pramod Kumar

S. No.	Name of student	Degree pursuing	Project/ Study title
1	Dr Sristy Shikha	ICMR-PDF	Preparation, encapsulation of recombinant multiepitope protein/peptides of SARS-CoV-2 in nanoparticles and their immunogenic studies

Dissertation/ Summer Trainees under Dr. Pramod Kumar:

S. No.	Name of student	University enrolled	Duration
1.	Ms Aditi Dhingra	Amity University	6 months

Dr Anuj Kumar

Dissertation/ Summer Trainees:

S. No.	Name of student	University enrolled	Duration
1.	Ashok Tiwari	Jaypee Institute of Information Technology	4 months
2.	Krati Garg	Sharadha University, Greater Noida	5 months

PUBLICATIONS

1. Adhikari T, Gulati BK, Juneja A, Nair S, Rao MVV, Sharma RK, Saha KB, Singh S. Development of behaviour change communication model for improving male participation in maternal and child health services among Saharia Tribes in Gwalior district of Madhya Pradesh: a mixed method approach. International Journal of Community Medicine and Public Health 2020;7(12):5134-43.
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5. Bondhopadhyay B, Sisodiya S, Chikara A, Khan A, Tanwar P, Afroze D, Singh N, Agrawal U, Mehrotra R, Hussain S. Cancer immunotherapy: a promising dawn in cancer research. Am J Blood Res 2020; 10: 375-385. **IF 3**
6. Chhabra A, Hussain S and Rashid S. Recent trends of tobacco use in India. J Public Health 2021; 29: 27-36. **IF 2.341**
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11. Hussain S, Tulsyan S, Dar SA, Sisodiya S, Abiha U, Kumar R, Mishra BN and Haque S. Role of Epigenetics in carcinogenesis: Recent Advancements in Anticancer Therapy. Semin Cancer Biol 2021June 26 (Online) **IF 15.707**
12. Khan A, Das BC, Abiha U, Sisodiya S, Chikara A, Nazir SU, Das AM, Rodrigues AG, Passari AK, Tanwar P, Hussain S, Rashid S, Rashid S. Insights into the role of complement regulatory proteins in HPV mediated cervical carcinogenesis. Semin Cancer Biol. 2021 Jun 1:S1044-579X(21)00161-9. **IF 15.707**
13. Kumar R, Kumar R, Tanwar P, Rath GK, Kumar R, Kumar S, Dash N, Das P, Hussain S. Deciphering the impact of missense mutations on structure and dynamics of SMAD4 protein involved in pathogenesis of gall bladder cancer. J Biomol Struct Dyn. 2021 Apr;39(6):1940-1954. **IF 3.3**
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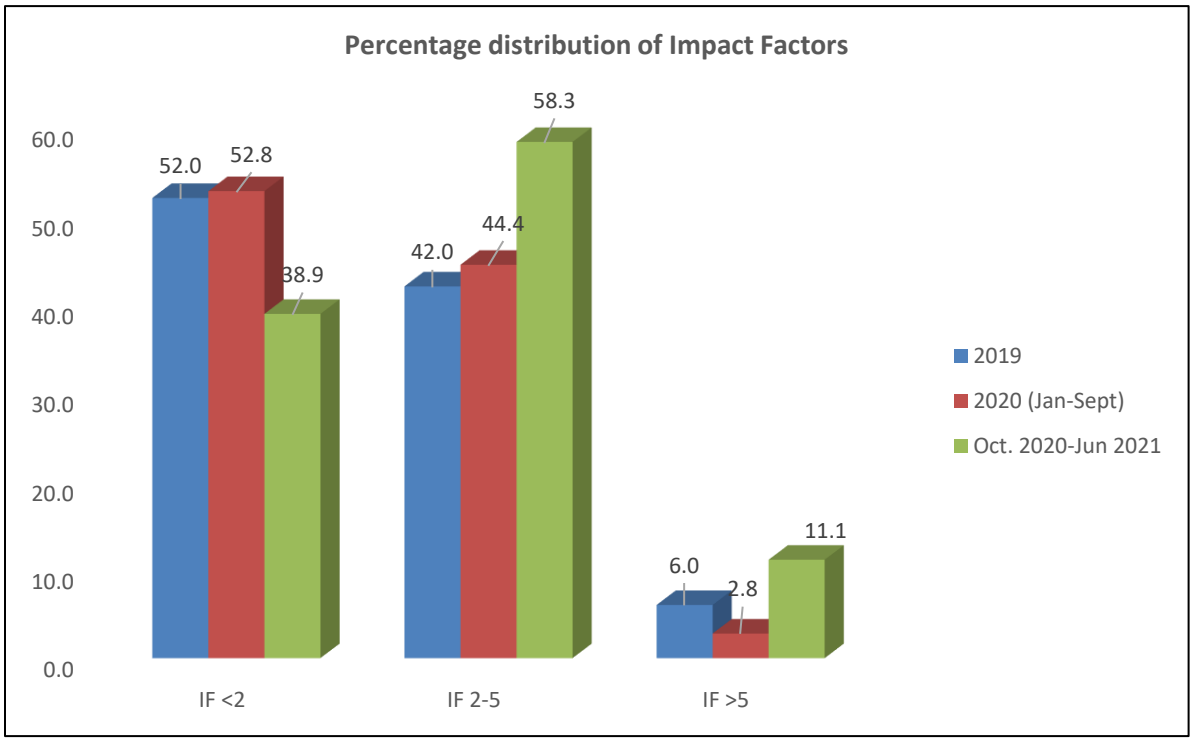


Percentage distribution of Institute's Publication Impact Factors over given periods

WORKSHOPS ORGANIZED

DIVISION OF CLINICAL ONCOLOGY

1. Webinar on Breast cancer awareness for teachers, 16 Oct 2020
   Participants: 60
2. Training of Master Trainers from the state of Chattisgargh for Medical officers and Staff nurses, 7 Jan & 14 Jan 2021
   Participants: 51 + 48
3. Webinar on Cervical cancer awareness for general public, 19 January 2021
   Participants: 70
4. Training on cervical cancer screening for Gynaecologists, 19-20 May 2021
   Participants: 35
5. Training on cervical cancer screening for Medical Officers, 11-12 June 2021
   Participants: 52

Training of master trainers (TOTs) of Madhya Pradesh Medical Officers and Nurses	8-10 February 2021	59
	15-17 February 2021	45
	1-3 March 2021	47
	8-10 March 2021	39

Capacity building of various cadres of Health Care Providers in cancer screening through NICPR-ECHO program	Medical Officers	16 Sept 2020 – 16 Dec 2020	45
	Dentists	17 Sept 2020 – 24 Dec 2020	112
		13 Oct 2020 – 19 Jan 2021	118
		6 Jan – 14 Apr 2021	125
	Nurses	17 Aug 2020 – 19 Oct 2020	45

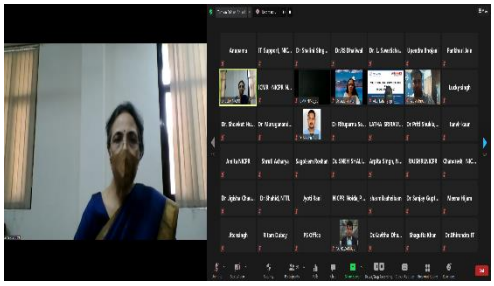
DIVISION OF EPIDEMIOLOGY AND BIOSTATISTICS

• **National Workshop on Research Methodology** co-organized with the All India Institute of Medical Sciences, Deoghar, 16-20 February 2021
Participants: 100

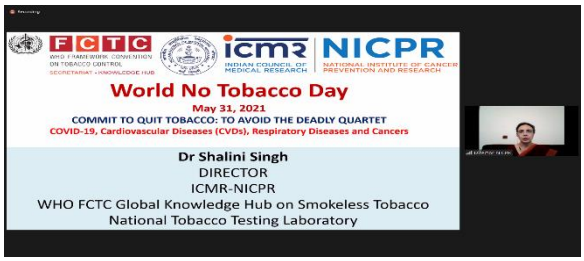
DIVISION OF PREVENTIVE ONCOLOGY

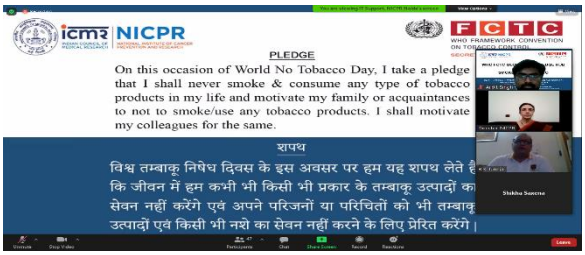
- Webinar titled "**Implementation of Article 5.3 of WHO FCTC- Prioritizing Policies to prevent Tobacco Industry interference**", **April 12, 2021**

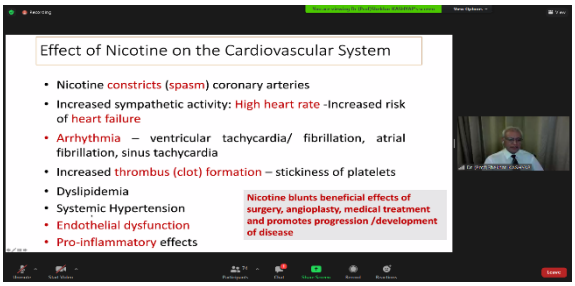
Participants: 72

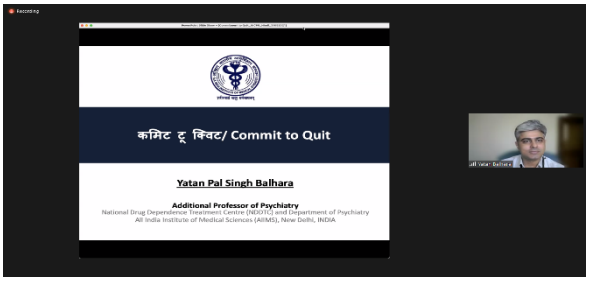


- Webinar on the topic "**Commit to Quit Tobacco: To avoid the Deadly Quartet- Covid-19, cardiovascular diseases (CVDs), respiratory diseases and cancer**", **May 31, 2021**









AWARDS, FELLOWSHIPS & RECOGNITIONS

AWARDS, FELLOWSHIPS & RECOGNITIONS

- **Dr. Mausumi Bharadwaj** was elected as Fellow of West Bengal Academy of Science and Technology (FAScT), 2020.

- **Dr. Smita Asthana** was awarded Best Paper Award at All India Institute of Medical Sciences (AIIMS), Rishikesh., EFICON 2020 National Conference of Epidemiology Foundation of India (EFI), 19th - 20th December, 2020.

- **Dr. Smita Asthana** was recognized as a "Women Warrior of ICMR" on e-Samvaad for Women scientists leading India's fight against COVID-19, ICMR's Special edition on International Women's Day, March 8, 2021.

- **Dr. Prashant Kumar Singh** was invited as an Expert to the WHO's "Equity Manual External Expert Review Group" on Sexual, Reproductive, Maternal, New-born and Child and Adolescent Health (SRMNCAH), by Department of Maternal, Newborn, Child and Adolescent Health and Ageing (MCA) and Sexual and Reproductive Health and Research (SRH), World Health Organization (WHO), Geneva, April 2021.

CONFERENCES/ WORKSHOP ATTENDED

Dr Shalini Singh

- "ICMR National Ethical Guidelines with special reference to Epidemiological Research", conducted by ICMR, 3rd November 2020.
- Information Toolkit on the Knowledge Hubs, meeting organized by WHO FCTC Secretariat, 4th December 2020.
- Public Lecture titled 'Breast Cancer Awareness and how to prevent it' delivered by Prof Anurag Srivastava, Head, Dept of Surgery, AIIMS, New Delhi at NICPR, Noida, 30th December 2020.
- Speaker at Guidelines and Draft Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) [COTPA] Amendment Bill 2020 for Pre-legislative consultation Organized by MoHFW, 5th January 2021.
- CME organized by Noida Obstetrics and Gynaecology Society, 16th January 2021.
  Talk delivered: Preinvasive Lesions: What next when a Pap Smear Comes Abnormal
- World Cancer Report Webinar Series - Social Inequalities and Cancer, organized by International Agency for Research on Cancer (IARC), 21st January 2021.
- E-symposium organised by ICMR-NIRRH on HPV Vaccination organized by ICMR-NIRRH, Mumbai, 29th January 2021.
- Cancer e-Summit Organized by IHW Council, 4th February 2021
  Talk delivered: Role of Nutrition, lifestyle and awareness to fight Cancer
- Speaker at International Childhood Cancer Day Celebrations organized by SSPHPGTI, Noida, 15th February 2021.
- Communicating Science Workshop series: Synthesizing Science for Parliamentarians organized by Global Health Strategies and ICMR, 19th February 2021.
- National Consultation on "Women and Tobacco – Issues-gaps and Challenges and Way Forward organized by Strategic Institute for Public Health Education and Research (SIPHER), Resource Centre for Tobacco Control, PGIMER-Chandigarh, 27th March 2021.
- Publishing Webinar - Tips from the Editors, organized by ICMR and Elsevier, 30th March 2021.
- International Symposium and Workshop on OneHealth organized by ICMR Hqrs, 12th April 2021.
- Speaker on Facebook Live in the programme Chaupal talk titled "India Quit Tobacco", 30th May 2021.
- Speaker at the National Training Workshop On Strengthening Monitoring and Evaluation of NTCP/MPOWER in the country- prioritising and reorienting Public Health Institutes and National Institutes of Eminence, 10th – 12th June 2021.
- South Asian Colloquium on WHO FCTC Article 5.3, titled "How immune are we against the tobacco industry interference?", 18th June 2021.

- 17th World Congress of IFCPC 2020, 25th June 2021.

  Panelist in the discussion on Preparing India's Roadmap Towards Cervical Cancer Elimination - Implementing Optimal Screening Strategies.

Dr. Sanjay Gupta

- Talk on " Cancer and Heart Disease - different stems and branches but a common root" by Dr (Prof) Shekhar Kashyap, on World Cancer research day 24th September 2020 at NICPR.

- IAC Jewel 50 series lecture "Time to change form 1M to 3M" Delivered by Prof Kusum Verma, 21st November 2020.

- IAC Jewel 50 series lecture "Best of Journal of Cytology" Dr Panna Chaudhary Award winner papers, 9th January 2021.

- IAC Jewel 50 series lecture 'Pancreatic solid tumors- the John Hopkin's Experience' delivered by Prof Syed Ali, 23rd January 2021.

- IAC Jewel 50 series lecture 'Yokohama System of reporting FNAB cytopathology and recent developments in cytopathology reporting systems' delivered by Prof Andrew Field, 20th February 2021.

- 'We Hope' Seminar on 'Cervical Cancer Screening effective with two tests or one- Co- testing vs Primary LBC' organized by BD India, 24th February 2021.
  Invited as a Panelist for discussion on this topic

- International Women's Day celebrations 8th March 2021, ICMR-NICPR, Noida.
  Acted as Judge for Painting competition with theme of women empowerment.

- IAC Jewel 50 series lecture 'EBUS FNA of lung tumors: emerging opportunities' delivered by Prof Nirag Jhala, 20th March 2021.

- Meditation session by a yoga teacher, Mr. Amit Sawhney, organized by ICMR-NICPR, 8th April 2021.

- Webinar titled "Reducing Health inequities in NCDs – towards a healthier Nation" organized by ICMR-NCDIR, 7th April 2021.

- Webinar focussing on Article 5.3 of WHO Framework Convention on Tobacco Control (WHO FCTC), organized by ICMR-NICPR, 12th April 2021.

- International Symposium & Workshop on "One Health in India: Research Informing Biosafety, Preparedness and Response" 12th April 2021. Speaker: Dr Harsh Vardhan, Union Minister for Health and Family Welfare.

- Webinar on "Molecular Markers in Prostate Cancer", organized by Datar Cancer Genetics Ltd. 16th April 2021.

- Webinar on 'Hypertension, Covid 19 and Tobacco- A deadly triad' by Dr Shekhar Kashyap, 17th May 2021 – World Hypertension Day.

- Webinar on Augmented Reality/ Virtual Reality in context of NICPR- 23rd May 2021.

- Webinar on "Commit to Quit Tobacco- To avoid the deadly quartet of COVID 19, CVDs, Respiratory diseases and Cancer" on 31st May 2021 - World No Tobacco Day.

- Webinar on "Evolving Paradigm in Breast Cancer": Bench to Bedside. Organized by Emcure, 8th June 2021.

- Lecture on" Rajyoga for emotional stability in the time of Covid 19" by Sister B. K Shivani, organized by ICMR on International Yoga Day, 21st June 2021.

- Webinar on "Training-cum-awareness" program of ERMED resources Access / Download articles from NML-ERMED consortium 2021 Webinar" organized by WILEY, 22nd June 2021.

Dr. Mausumi Bharadwaj

- Annual Conference of Indian Association for Cancer Research (IACR) February 2020.

- International Conference on emerging trends in Life Sciences, 18th-19th February 2021.

- Live Webinar: Ovarian Cancer- Quest for a Better Tomorrow organized by the Association of Gynecological Oncologist of India, 21st February 2021.

- International Conference on "Challenges and strategies in reproductive and environmental health with special reference to COVID-19 Pandemic" at the 31st Annual meeting of the Indian Society for study of Reproductive and Fertility (ISSRF), 19th – 21st February 2021.

- 40th Annual Conference of Indian Association for Cancer Research (IACR-2021), 1st March 2021.

Dr. Smita Asthana

- Invited guest faculty for 3 M.Sc programmes - Cellular & Molecular Oncology, Stem Cell Science & Technology and Molecular Medicine & one undergraduate program (B.Sc (Hons) Biochemistry) at Amity Institute of Molecular Medicine & Stem Cell, Noida.
  Lectures taken for BSc and MSc classes on Research Methodology.
- Attended Webinar on by ICMR and NDQF (National Data Quality Forum) Measuring dietary intake using 24-hour recall method in the current times: Accuracy, Validity and Quality on 30th November 2020.

- Guest Speaker for three days workshop on Research Grant Writing organised by Santosh University, Ghaziabad under aegis of Dr. Padam Singh Research and Development Scheme in collaboration with Institute of Applied Statistics (IAS) on 10th – 12th December 2020
  Talk given on "Understanding the financial aspects".
- Invited as a Resource Person for the session on "Systematic Review and Meta-Analysis" at One Week Online Training Program on Biostatistics, 21st – 27th February 2021 at Science Tech Institute, Lucknow.
- Addressed a virtual session on 'Numbers Don't Lie' organized by Fortis International Oncology Centre with Noida Obstetrics and Gynaecology, 16th January 2021.
- Webinar on "Planning a Scientific Study and Protocol Writing" co-organized with Biostatistics Consortium of India (BCI), 4th – 5th March 2021.
- Webinar on Augmented Reality/ Virtual Reality in context of NICPR, 23rd May 2021.

Dr Raj Narain

- COVID and Oncology- An Exclusive Session by Tata Memorial Centra, 19th August 2020.
- Online CME on Telemedicine Practice Guidelines, 19th August 2020.
- Online training course entitled 'healthy ageing for in the impact 21st century", September - December 2020.
- COVID-19 vaccination online training for health workers, 25th December 2020.
- Online course on Infection Prevention and Control (IPC) for COVID-19 Virus, 22nd December 2020.
- Publishing webinar tips from editors at ICMR, 30th March 2021.

Dr. Showket Hussain

- ICMR FICCI health technology accelerated commercialization program H: TAC, 11th July – 8th August 2020.
- Webinar on Article 5.3 of WHO Framework Convention on Tobacco Control and the Code of Conduct organized by WHO FCTC Global Knowledge Hub on Smokeless Tobacco, 16th April 2021.
- Commit to Quit Tobacco- To avoid the deadly quartet of COVID 19, CVDs, Respiratory diseases and Cancer, ICMR-NICPR, 31st May 2021.
- Webinar on "Publishing Webinar-Tips from the Editors organised by Elseiver, 30th March 2021.
- Journal Citation Reports (JCR) Training & Certification Program organized by Clarivate, 15th June 2021 & 17th June 2021.

Dr Prashant Kumar Singh

- "ICMR National Ethical Guidelines with special reference to Epidemiological Research", conducted by ICMR, 3rd November 2020.
- "Information Toolkit on the Knowledge Hubs", meeting organized by WHO FCTC Secretariat, 4th December 2020.
- "Public Lecture titled "Breast Cancer Awareness and how to prevent it" delivered by Prof Anurag Srivastava, Head, Dept of Surgery, AIIMS, New Delhi at NICPR, Noida", 30th December 2020.
- "World Cancer Report Webinar Series - Social Inequalities and Cancer", organized by International Agency for Research on Cancer (IARC), 21st January 2021.
- "Communicating Science Workshop series: Synthesizing Science for Parliamentarians", organized by Global Health Strategies and ICMR, 19th February 2021.
- "National Consultation on "Women and Tobacco – Issues-gaps and Challenges and Way Forward", organized by Strategic Institute for Public Health Education and Research (SIPHER), Resource Centre for Tobacco Control, PGIMER-Chandigarh, 27th March 2021.
- "Publishing Webinar - Tips from the Editors", organized by ICMR and Elsevier, 30th March 2021.
- Webinar on "Ensuring immunization for all in the context of COVID-19" organised by Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, 24th – 25th April, 2021.
- Webinar on "Illicit trade and tobacco industry interference: a serious threat to the transparency, economy, and health?" organised by WHO FCTC Secretariat, 29th April 2021.
- Webinar on "Showcasing SDG Target 3. a in Parties' Voluntary National Reviews", organised by WHO FCTC Secretariat, 21st June 2021.
- Workshop on "National Training Workshop (Virtual) on Strengthening Monitoring and Evaluation of NTCP/MPOWER in the country – Prioritising and Reorienting Public Health Institutions and National Institutions of Eminence", organised by The Union – South & East Asia regional office New Delhi, 10th – 12th June 2021.

Dr Ruchika Gupta

- Talk on " Cancer and Heart Disease - different stems and branches but a common root" by Dr (Prof) Shekhar Kashyap, on World Cancer research day 24th Sept 2020 at NICPR.

- IAC Jewel 50 series lecture "Time to change form 1M to 3M" Delivered by Prof Kusum Verma, 21st Nov 2020.

- Online CME 2020 on Bone and Soft Tissue Tumors organized by SNMC, Agra, 13th Dec 2020.

  Talk delivered: An interesting case in aspiration cytology

- IAC Jewel 50 series lecture 'Pancreatic solid tumors- the John Hopkin's Experience' delivered by Prof Syed Ali, 23rd Jan 2021.

- Webinar on "Important amendments in GFR-2017: Regarding procurement of Goods & Services in view of Atmanirbhar Bharat initiatives of Govt. of India" organized by the National Productivity Council, 17th Feb 2021.

- IAC Jewel 50 series lecture 'Yokohama System of reporting FNAB cytopathology and recent developments in cytopathology reporting systems' delivered by Prof Andrew Field, 20th Feb 2021.

- IAC Jewel 50 series lecture 'EBUS FNA of lung tumors: emerging opportunities' delivered by Prof Nirag Jhala, 20th March 2021.

- 'We Hope' Seminar on 'Cervical Cancer Screening effective with two tests or one- Co- testing vs Primary LBC' organized by BD India, 24th Feb 2021.

- International Women's Day celebrations 8th March 2021, ICMR-NICPR, Noida.

  Participated in the painting competition with theme of women empowerment.

- Meditation session by a yoga teacher, Mr. Amit Sawhney, organized by ICMR-NICPR, 8th April 2021.

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- Webinar focussing on Article 5.3 of WHO Framework Convention on Tobacco Control (WHO FCTC), organized by ICMR-NICPR, 12th April 2021.

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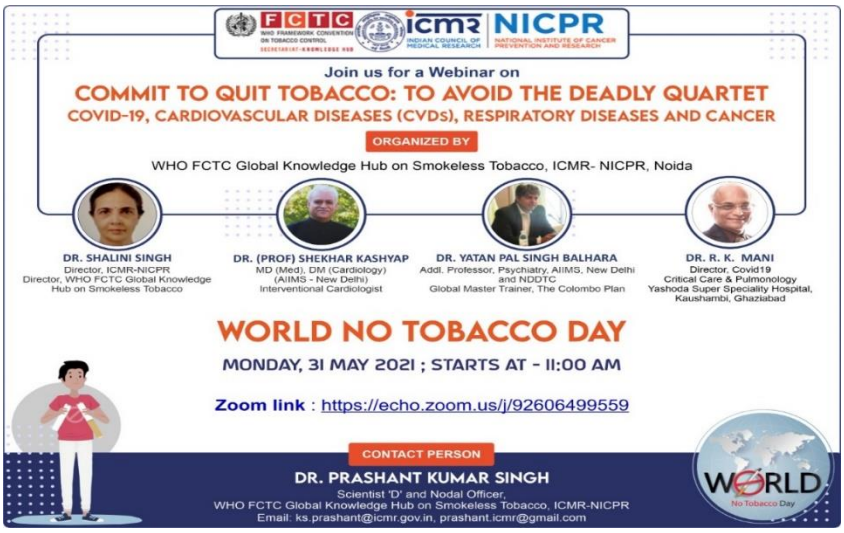
- Webinar on “Evolving Paradigm in Breast Cancer”: Bench to Bedside. Organized by Emcure, 8th June 2021.

- Lecture on” Rajyoga for emotional stability in the time of Covid 19” by Sister B. K Shivani, organized by ICMR on International Yoga Day, 21st June 2021.

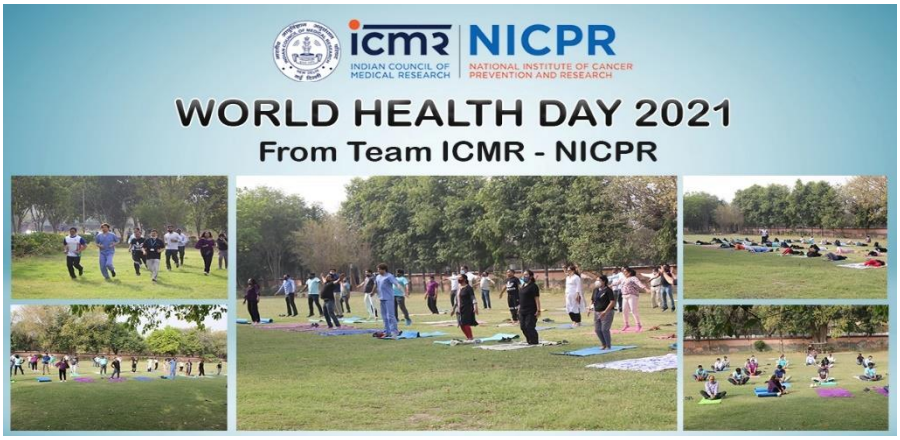
- 39th Annual National CME (Virtual) organized by Dept of Pathology, JNMC, Belgavi, 24th – 26th June 2021.
  Poster presented: Aspiration cytology of extraskeletal osteosarcoma in the arm: report of a rare case posing diagnostic dilemma

EVENTS ORGANIZED

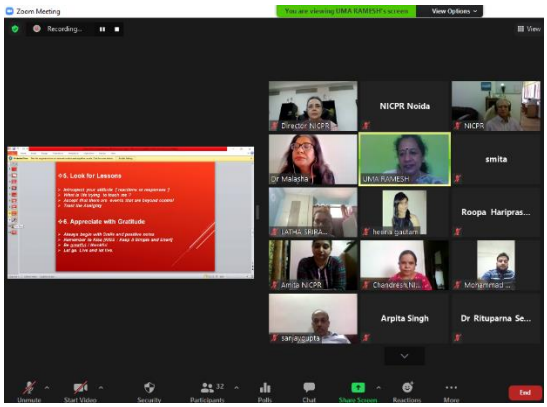
World No Tobacco Day celebrated on 31st May 2021



World Health Day, 8th April 2021

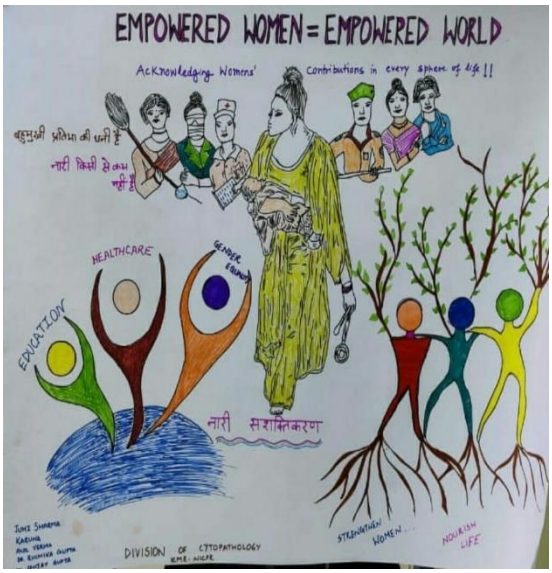


International Women's Day, 8th March 2021



Webinar

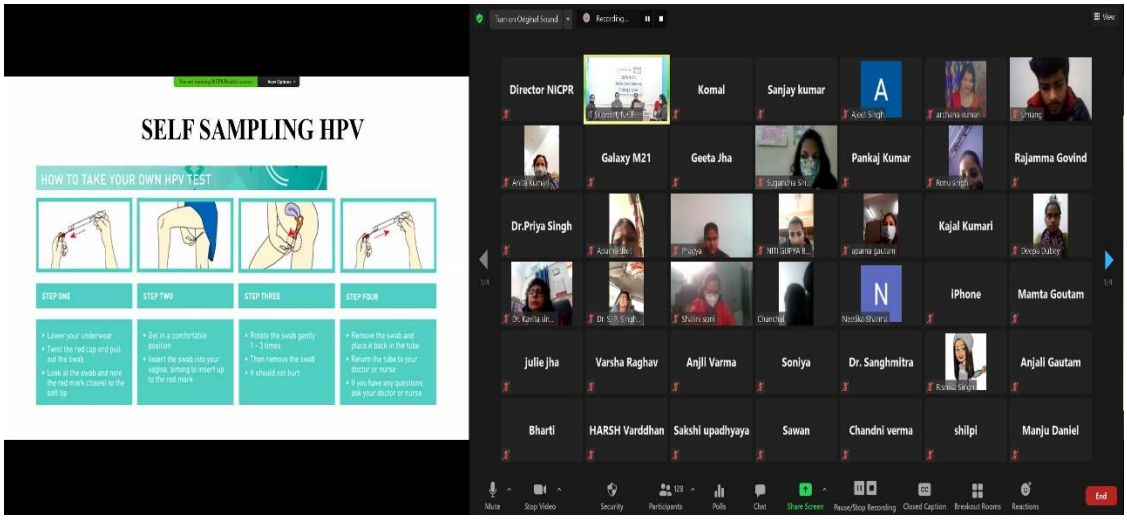
Nukkad Natak



Painting Competition
Theme: "Women Empowerment"

Repbulic Day Celebration, 26th January 2021

“Cervical Cancer Awareness Month” celebrated with a webinar, 19th January 2021



Annual Day Celebrations of ICMR-NICPR, 14th January 2021

Sports Activities

Rangoli competition

Team Building Workshop

Felicitation Ceremony

Community outreach for tobacco cessation (Noida Golf Course), 23rd – 25th November 2020

National Cancer Awareness Day celebrated at Morna Bus Depot, Noida, 6th – 7th November 2020

जागने के लिए नशे की लत का बहाना छुड़ाएगा कैंसर संस्थान

चालक-परिचालकों को बताएगा तंबाकू छोड़ने का तरीका

शोहदात्तर हिशाल ● नोएडा

मोरना बस डिपो में राष्ट्रीय कैंसर जागरूकता दिवस पर स्क्रीनिंग

प्रोग्राम में 200 से अधिक बस चालकों व परिचालकों की स्क्रीनिंग की गई। स्क्रीनिंग में यह बात सामने आई कि कई चालक रात के समय बस चलाते समय नींद से बचने के लिए तंबाकू का सेवन करते हैं। इनमें चालकों ने तंबाकू छोड़ने की इच्छा जताई है। इसलिए इन चालकों की नशे की लत छुड़ाने के लिए फालोअप किया जाएगा। यह बातें राष्ट्रीय कैंसर रोकथाम एवं अनुसंधान संस्थान (एनआइसीपीआर) की

मोरना डिपो पे स्वास्थ्य शिविर में जांच कराते चालक-परिचालक ● सौ. शिक्षिका

निदेशक डॉ. शालिनी सिंह ने कहीं।

उन्होंने बताया कि शुक्रवार और शनिवार को आयोजित कैंसर जागरूकता शिविर में चालक-परिचालकों की स्क्रीनिंग की गई है। स्क्रीनिंग में बड़ी संख्या में लोगों ने बीड़ी, सिगरेट, हुक्का के साथ धुआं रहित तंबाकू जर्दा, खैनी, गुटखा, तंबाकू वाला पान, गुल हत्यादि का सेवन करने की बात कही है। चूंकि इन सभी के सेवन से मुंह के कैंसर होने की संभावना अधिक होती है। साथ ही दूसरी बीमारियों के जल्द होने की संभावना होती है। इसलिए उन्हें इस खतरे से अवगत कराया गया है। कई चालकों ने तंबाकू छोड़ने की इच्छा जताई है। इसलिए ऐसे लोगों का फालोअप किया जाएगा।

चालक को नींद आने पर होती है दुर्घटना सबसे ज्यादा : रात या भोर में रोडवेज बस चालकों को नींद आ जाने के कारण सड़क हादसे होते रहते हैं। इसे ध्यान में रखते हुए उत्तर प्रदेश परिवहन निगम ने कई प्रयास किए हैं, पर स्थिति नहीं बदली। कई बार नशे का सेवन करने के लिए भी चालकों का ध्यान भटक जाता है। सड़क हादसे की संभावना बढ़ जाती है। इसलिए सरकारी बसों के चालकों को तंबाकू के सेवन छोड़ने से सड़क हादसे की संभावना भी कम होगी।

Community outreach for cancer prevention and tobacco cessation (Government Degree College, Noida), 16th October 2020

ICMR-NICPR STAFF

SCIENTIFIC STAFF

	NAME	DESIGNATION
1.	Dr. Shalini Singh	Director
2.	Dr. Sanjay Gupta	Scientist –G
3.	Dr. Mausumi Bharadwaj	Scientist –G
4.	Dr. Smita Asthana	Scientist –E
5.	Dr. Subhash M. Agarwal	Scientist –E
6.	Dr. R. Suresh Kumar	Scientist –E
7.	Dr. Suresh T. Hedau	Scientist –E
8.	Dr. Roopa Hariprasad	Scientist –E
9.	Dr. Deepika Singh Saraf	Scientist – E
10.	Dr. Ekta Gupta	Scientist – E
11.	Dr. Raj Narain	Scientist –D
12.	Dr. Kavitha Dhanasekaran	Scientist –D
13.	Dr. Prashant Kumar Singh	Scientist – D
14.	Dr. Showket Hussain	Scientist –D
15.	Dr. Ruchika Gupta	Scientist – D
16.	Dr. Shamsuz Zaman	Scientist – D
17.	Dr. Malasha Kumari	Scientist –C
18.	Dr. Pramod Kumar	Scientist – C
19.	Dr. Anuj Kumar	Scientist – B
20.	Dr. Dinesh Kumar	Scientist - B

TECHNICAL STAFF

1.	Mrs.Latha Sriram	Principal Technical Officer & Administrative Officer-in-Charge
2.	Smt.Rajshri	Technical Officer-C
3.	Mr. Chidambarmurthy Joshi	Technical Officer-C
4.	Dr. Pragya Sharma	Technical Officer-C
5.	Mrs. Amita	Technical Officer-B
6.	Mrs.Reena Diwedi	Technical Officer-B
7.	Mrs.Chandresh P. Verma	Technical Officer-B
8.	Mr. Himanshu Rohilla	Technical Officer-B
9.	Mr. Deep Kumar	Technical Officer-A
10.	Mrs. Kalpana Verma	Technical Officer-A
11.	Mr. Neeraj Dubey	Technical Assistant
12.	Mrs.Sangeeta Batra	Jr. Librarian
13.	Mrs.Karuna	Sr. Technician-3
14.	Mr. Bhopal Singh	Technician-C
15.	Mr. Dharmender Kumar Sharma	Technician-1
16.	Mr. Mritunjay Kumar	Technician-1
17.	Mr. Danial Das	Lab.Assistant-1
18.	Mr.D.K.Roy	MTS(LT)
19.	Mr. Ram Chander Das	Lab. Assistant
20.	Mr. Ram Phool Meena	Lab. Assistant
21.	Mr. Anil Kumar Verma	Lab. Assistant
22.	Mr. Satya Pal Singh	Lab. Assistant
23.	Mr. Jitender Singh	Lab.Attendant-1
24.	Mr. Rahul Tiwari	Lab.Attendant
25.	Mr. Vinod Kumar Dhyani	Lab.Attendant-1
26.	Mr. Yogesh Kushwah	Lab.Attendant
27.	Mr. Ajay Singh	Lab Attendant
28.	Mr. D. K. Roy	MTS (LT)
29.	Mr. Sandeep Kumar	MTS (Tech)

ADMINISTRATIVE STAFF

Sl. No.	Name	Designation
1	Mr. Dinesh Soni	Administrative Officer
2	Smt.Latha Sriram	Admn.Officer In-Charge
3	Mr.M. L. Meena	Accounts Officer
4	Mr. Sanjeev Kumar	Private Secretary & Accounts Officer-in-Charge
5	Mrs.Sonia Khattar	Section Officer
6	Mr. Jiwan Singh Bisht	Section Officer
7	Mr. Rajesh Kumar	Section Officer
8	Mr. Rakesh Kumar	Section Officer
9	Mr. Vijay	Assistant
10	Mr. Monu Sharma	Assistant
11	Mr. Sant Ram	Assistant
11	Mrs.Krishna Magoo	Personal Assistant
12	Mr. Ramesh Kumar	UDC
13	Mr. Avinash Malhotra	UDC
14	Mr. Sidharth Yadav	UDC
13	Mr. Naveen Kumar	UDC
14	Mr. Paras	UDC
15	Ms. Neha Kaushik	UDC
16	Mr. Ram Prakash	Sr. Technician-3 (Sr. Driver)
17	Mr. Kailash Kumawat	Staff Car Driver Grade-I
18	Mr. Tarachand Gurjar	Staff Car Driver Grade-I
19	Mr. Dheeraj Rajaura	Staff Car Driver Grade-I
20	Mr. Roopchand	MTS (Gen)
21	Mrs.Anoop Devi	MTS (Gen.)
22	Mr. Jai Prakash	MTS (Gen)

SUPERANNUATED TECHNICAL & ADMN STAFF

Mr. Mohinder Singh, LDC – March 2021

Mr. Mohanan T., AO – May 2021

STAFF TRANSFERRED FROM NICPR

Mr. Harsh Agnihotri, Assistant – October 2020

Dr. Nisha Thakur, TO-B – December 2020

Mr. Akhileshwar Sharda, TO-B – February 2021

Mr. Dinesh Kumar, TO-A – February 2021

Mr. Rajesh Solanki, MTS – March 2021

Mr. Harkesh Gupta, Technician-B (DOJ at NICPR-12.03.2021) – April 2021

Dr. Sneh Shalini, TO-B (DOJ at NICPR-09.02.2021) - June 2021

LIST OF SAC MEMBERS

Prof. Maqsood Siddiqi, Chairperson **Chairman MC and Managing Director** **Cancer Foundation of India** **1120, Tagore Park** **Tiljala, Kolkata-700 039** **West Bengal.**
Dr R Sankarnarayanan Advisor, Reserch Trinagle International 43, Padma Nabha Nagar, Airport Road, Coimbatore - 641014
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Dr. Shyama Jain Director Professor, Department of Pathology Maulana Azad Medical College New Delhi - 110002

Dr. RS Dhaliwal **Scientist- G and Head** **NCD** **Indian Council of Medical Research** **Ansari Nagar** **New Delhi-110 029.**
Special Invitee **Prof. Sanghamitra S. Acharya** Centre of Social Medicine and Community Health, School of Social Sciences Jawaharlal Nehru Univesity, New Delhi
Member Secretary **Dr. Shalini Singh** Director ICMR-NICPR, I-7, Sector 39, NOIDA.


I AM
AND
I WILL
Together,
all of our
actions
matter
World
Cancer Day
4 February