2017-18

ANNUAL REPORT

INDIAN COUNCIL OF MEDICAL RESEARCH

NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH

BHOPAL

ICMR - National Institute for Research in Environmental Health
(Indian Council of Medical Research)
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Ministry of Health & Family Welfare, Govt of India
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ANNUAL REPORT
(2017 – 2018)

ICMR - NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH

(Indian Council of Medical Research)
Bhopal – 462 001 (M.P.)

MISSION

To understand the mechanisms of chemical–induced injury through basic, clinical, translational and community research and to develop diagnostic and therapeutic tools to chemical threat agents including toxic industrial and agricultural chemicals, toxins and other chemicals

VISION

(i) To address immediate health research needs of gas exposed population with focus on respiratory diseases, eye related diseases, renal diseases, reproductive & women's health, mental health (ii) Research on cancers, genetic disorders, health status of 2nd and 3rd generation children in the exposed population and community building to cope with the disaster effects at the population level (iii) To establish a National Institute of excellence in Environmental Health with emphasis on (a) epidemiology & Public Health Research (b) Clinical & Therapeutic Research (c) Biomedical research (iv) Rapid response

CURRENT FOCUS OF RESEARCH

(i) To address immediate health research needs of gas exposed population with focus on respiratory diseases, eye related diseases, renal diseases, reproductive & women's health, mental health (ii) Research on cancers, genetic disorders, health status of 2nd and 3rd generation children in the exposed population and community building to cope with the disaster effects at the population level (iii) To establish a National Institute of excellence in Environmental Health with emphasis on (a) epidemiology & Public Health Research (b) Clinical & Therapeutic Research (c) Biomedical research (iv) Rapid response

STAFF POSITION

Director& Scientist G	:	**Dr. R. R. Tiwari**
Scientist G	:	**Dr. Anil Prakash**

Epidemiology Division

Scientist E	:	Dr. Y. D. Sabde
Scientist B (Med)	:	Dr. (Mrs.) R. Galgalekar
Scientist B (Med)	:	Dr. K. K. Soni
Technical Assistant	:	Mr. A. M. Khan
Technical Assistant	:	Mrs. M. Chaturvedi
Technical Assistant	:	Mrs. A. N. Bhavsar
Technical Assistant	:	Mrs. H. Saxena
Technical Assistant	:	Mrs. S. Khare
Technical Assistant	:	Md. S. Khan
Technical Assistant	:	Mr. V. S. Rathore
Technical Assistant	:	Mr. U. S. Chauhan
Technical Assistant	:	Mrs. R. Sen
Technical Assistant	:	Dr. (Mrs.) A. Shukla
Technical Assistant	:	Mrs. R. Yadav
Technical Assistant	:	Mrs. S. Azhar
Technical Assistant	:	Mr. D. S. Shukla
Technical Assistant	:	Mr. R. K. Srivastava
Technical Assistant	:	Mr. B.K. Dixit
MTS (Tech)	:	Mrs. A. Khan
MTS (Tech)	:	Mrs. R. Lalwani
MTS (Tech)	:	Mr. M .S. Kachhwahaq (w.e.f 19-04-2017)

Molecular Biology Division

Scientist E	:	Dr. P. K. Mishra
Scientist C	:	Dr. D. K. Sarma (w.e.f 08-02-2018)
Scientist B	:	Dr. A. K. Tripathi
Technical Assistant	:	Mr. A. Aglawe
Technical Assistant	:	Mr. A. Rahman (w.e.f 09-06-2017)

Biochemistry Division

Scientist E	:	Dr. K. C. Pandey
Scientist B	:	Dr. R. Ahirwar
Technical Assistant	:	Ms. Kamini Arya (w.e.f 02-06-2017)

Pulmonology Division

Scientist E	:	Dr. Sajal De
Technician A	:	Mr. Gagandeep Singh Kushwaha (w.e.f 10-04-2017)
Technician A	:	Mr. Dharmendra Dharway (w.e.f 03-05-2017)

Microbiology Division

Scientist C	:	Dr. Manoj Kumar (w.e.f 03-11-2017)
Technical Assistant	:	Md. Asif Mansoori (w.e.f 03-11-2017)

Statistics Division

Scientist B	:	Mrs. M. Sharma (on study leave)
Scientist B	:	Dr. S. Devika (upto 23-02-2018)
Technical Assistant	:	Mr. S. Khare
MTS (Tech)	:	Mr. M. Ahmed

Computer & Bioinformatics Division

Scientist C	:	Dr. S. Singh
Scientist B	:	Dr. Sindhuprava Rana
Technician C	:	Mr. R. Chandrasekhran Pillai
Technician C	:	Mr. S. Sharma
Technician C	:	Mr. A. K. Kori
Technician A	:	Mr. R. K. Pandey

Engineering Division

Junior Engineer (Civil)	:	Mr. Vivek Narware (17-04-2017)
Junior Engineer (Electrical)	:	Mr. Sonu Kumar (01-08-2017)

Administration

Administrative Officer (JG)	:	Mr. Yogesh Kumar (w.e.f. 11-04-2017)
Private Secretary	:	Mr. Krishnadas V.K.
Section Officer(Acctts)	:	Mr. Mohan Waldhurkar
Section Officer (Admn.)	:	Mr. Sudhir Shrivastava (superannuated on 30-10-2017)
Assistant	:	Ms. Priyanka Gupta (w.e.f. 01-08-2017)
Assistant	:	Mr. Ankit Kumar Mishra (w.e.f. 07-08-2017)
Assistant	:	Mr. Abhishek Saraf (w.e.f. 23-08-2017)
Assistant	:	Mr. Anees Vyas (w.e.f. 16-10-2017)
Assistant	:	Mr. Pushpak Shrivastava (w.e.f.16-10-2017)
Upper Division Clerk	:	Mr. S. K. Vinodiya (upto 30-11-2017)
Technician B	:	Mr. R.Kerala Varma Thampuran
Technician A	:	Mrs. Anitha S. Pillai
MTS (Gen)	:	Mr. S. Mishra
Consultant (F & A)	:	Mr. S. S. Asthana
Advisor	:	Dr. N. Banerjee

Utilities

MTS (Gen)	:	Mr. D. Ugave
MTS (Gen)	:	Mr. P. Patva
MTS (Gen)	:	Mr. A. Husain
MTS (Gen)	:	Mrs. K. Bai

Attachment from BMHRC, Bhopal

Assistant Professor	:	Dr. R. M. Samarth

Project staff

Dr. Arpit Bhargava	:	DTH-PDF
Dr. Sambhavi Tiwari	:	Junior Medical Officer
Dr. Shatrughan Singh	:	Technical Officer (Physiotherapist)
Mrs. Durga Mahor	:	Senior Research Fellow
Ms. Pranjali Borkar	:	Senior Project Research Fellow
Ms. Radha Dutt Singh	:	Senior Project Research Fellow (w.e.f 10-11-2017)
Ms. Neha Bunkar	:	Senior Research Fellow (w.e.f 20-07-2017)
Dr. Harsha Lad	:	Senior Research Fellow
Ms. Ruchita Shandilya	:	Junior Research Fellow (w.e.f 01-02-2018)
Ms. Vaishali Yadav	:	Junior Research Fellow (w.e.f 23-02-2018)
Mr. Aditya Banerjee	:	Research Assistant
Mr. Peeyush Asthana	:	Computer Programmer
Ms. Jaishree Sakre	:	Computer Programmer
Mr. Pushpendra Gupta	:	Field Worker (w.e.f 04-07-2017)
Mr. Rishi Badal	:	Lab Technician (w.e.f 05-02-2018)
Mr. Lalit Lodhi	:	Technician – B (w.e.f 12-09-2017)
Mr. Ravindra Nath Biswas	:	Multi Tasking Staff

From Director's Desk

It gives me immense pleasure to present the Annual Report 2017-2018 of the institute. This annual report is an evidence of longer strides taken by NIREH towards accomplishing its mandate for being an state of art facility for research on environmental health issues of the country.

The long term epidemiological study entered into its eight year after NIREH coming into existence. This yearly cycle of study again suggested that most of the morbidities have now reached a plateau and not much year to year variation was observed. The respiratory illness is still the leading cause of morbidity. The mortality among the exposed group and unexposed population also did not differ significantly. Another study for triangulating the morbidity data from three major data sources namely Kamala Nehru Hospital, BMHRC and NIREH revealed that cardiovascular disorders were common cause for morbidity followed by ophthalmologic problems.

This year three studies on air pollution or environmental chemical exposure related changes in epigenetics also progressed as per schedule and preliminary results were available. These preliminary results gives an indication that changes at DNA, miRNA and mtDNA occur in those exposure to area which has high degree of air pollutants.

Significant progress was made in manpower and infrastructure capacity of the institute. While the new campus of NIREH is on the verge of completion, few more scientific staff was included in the current year adding new zeal and knowledge to the NIREH academic pool. The laboratories were also strengthened with procurement of several high end and sophisticated equipments. In consonance with the National programmes such as Swachha Bharat Abhiyaan, National Environmental Day, etc. the social contribution of NIREH continued this year also through distribution of dustbins, water filters and cloth bags.

I express my gratitude to the visionary leadership of ICMR- DG, ICMR, Sr. DDG (Admn), Sr. Financial Advisor and Head, NCD for their constant support to NIREH. Special gratitude is expressed to the learned members of the Scientific Advisory Committee and various Research Expert Groups for their relentless efforts to take best out of the scientific staff of NIREH. Last but not the least I am thankful to my fellow scientists, technical, administrative and supporting staff of NIREH for their dedicated contribution to the institute.

CONTENTS

Executive Summary

- The frequency of survey was changed from 6-monthly to yearly w.e.f January 2017 in the *Population based long term epidemiological study on the health effects of the toxic gas exposure*. In the 54th round (January-December 2017) any morbidity recorded was nearly the same in severely (15.6%) and mildly (15.7%) exposed cohorts while in mildly exposed cohort (9.04%) it was little lesser than the non-exposed cohort (10.8%). Overall mortality rates recorded were 5.3/1,000 population in the exposed and 6.7/1,000 population in non-exposed cohort.
- Data mining and triangulation of 3 available databases dealing with the health of gas exposed survivors i.e. IPD records of BMHRC (2010-2015), Gas rahat hospital data base (Jan 2015-May 2017) and NIREH data base (2011-2016) was done and clilinal profilie of 17,321 gas exposed individuals was prepared under the Phase I of the study titled *A cross-sectional study on current health status of gas affected individuals of Bhopal*. The highest number of morbidities belonged to the cardio-vascular system (22.4%) followed by ophthalmic morbidity (16.9%).
- A study comparing *the Effectiveness of institutional versus domiciliary implementation of standard pulmonary rehabilitation module in Bhopal gas exposed survivors having COPD* was initiated. A total of 180 gas exposed COPD subjects were provided common training on standard pulmonary rehabilitation module and randomized in to 2 groups of 90 patients each *viz.* Institutional rehabilitation and domiciliary rehabilitation. The pulmonary rehabilitation under the supervision of a qualified Physiotherapist for one-hour at pulmonary rehabilitation centre (Group I) and pulmonary rehabilitation daily for one hour at residence (Group II) was continued along with monitoring of compliance twice a week.
- Under the study *Cytogenetic profiling of patients with chronic kidney disease* a total of 108 adult gas exposed CKD patients (Group I) and 49 adult unexposed CKD patients (Group II) were recruited for cytogenetic profiling through karyotype analysis, cytogenetic endpoints and to study genomic instability through chromosomal aberration analysis, frequencies of sister chromatid assay and micronuclei assay.
- A pilot study on *Development of a mito-epigenetic carcinogenic risk assessment model for environmental chemical exposures* was initiated. Blood samples from 15 subjects exposed to broad chemical class of pro-oxidants at *in utero* stage and 15 age and gender matched control were collected and analyzed for circulating cell free DNA, miRNA, circulating nucleosomes, mtDNA copy number, inflammatory cytokines, DNA methyl transferases, global DNA methylation profile etc. Preliminary results indicated that prenatal exposure of environmental pro-oxidants not only impairs the mitochondrial nuclear cross talk but also modulates the fetal epigenome through aberrant regulations of DNA methylation and histone modifications.
- The extramural study under IMPRINT scheme of MHRD titled *Aberrant circulating epigenomic signatures: development and validation of minimal-invasive biomarkers for trans-generational monitoring of air pollution associated cancers* was initiated to characterize the epigenomic signatures in saliva and urine among people exposed to varying quantum of particulate matter residing in high-risk, mid-risk and low-risk based on the air quality index. A total of 60 pairs of

samples (mother and son) have so far been collected and analyzed. Preliminary results inidated relatively higher levels of circulating DNA, circulating nucleosomes, circulating miRNA and circulating mt DNA in population living in high-risk region.

- Another extramural collaborative study under ICMR-RFBR (Russian Foundation for Basic Research) initiative titled *Development of quantum dots based nano-biosensors for detection of circulating cell-free miRNAs in environmental associated lung carcinogenesis* was initiated during the year. Complete profiling of 21 ccf miRNAs was undertaken in lymphocytes isolated from healthy individuals and treated with different concentrations of known environment associated carcinogenic pollutants. Preliminary results suggested a significant alteration in the expression of several miRNAs belonging to the tumor suppressing miRNAs and involved in the regulation of apoptotic pathways such as Let-7e, miR-202, miR-98, miR-16, miR-27, miR-29 and miR-155 in the lung cancer patients.
- The study titled *Biochemical basis of pathogenesis of chronic obstructive pulmonary disease*, initiated during the year is aiming to identify unusual proteases and analyzing differential protein expression in stable COPD patients. Blood samples were collected from 30 stable COPD patients and 15 healthy persons and 2 CKD patients (as negative control). The expression level of caspases-3, DPP IV, MMP-9, MMP-2, nutrophil elastase were estimated and serum of limited number of COPD patients was analyzed for differential protein expression analysis.
- A total of 5 Scientific cadre (3 Scientist C, 2 Scientist B), 7 Administrative cadre, 5 Technical cadre and 2 Engineering cadre incumbents joined the institute under Phsae II Staff recruitment of 57 permanent posts of NIREH.

कार्यपालन संक्षेपिका

- भोपाल गैस त्रासदी के दौरान निकली विषैली गैसों के स्वास्थ्य पर प्रभाव से संबंधित जनसंख्या आधारित दीर्घकालिक जनापदिक अध्ययन के सर्वेक्षण की आवृत्ति को जनवरी 2017 से छःमाही से बदलकर वार्षिक किया गया। 54वें चक्र (जनवरी–दिसम्बर 2017) के दौरान अत्यधिक प्रभावित क्षेत्रों के व्यक्तियों (15.6%) एवं मध्यम प्रभावित क्षेत्रों के व्यक्तियों (15.7%) के समूह में अस्वस्थता (Morbidity) लगभग समान पाई गई। साधारण प्रभावित क्षेत्रों के व्यक्तियों में यह अस्वस्थता 9.4% थी जो कि अप्रभावित क्षेत्रों के व्यक्तियों के समूह (10.8%) से थोड़ा ही कम थी। इस सर्वेक्षण में मृत्युदर 5.3/1,000 गैस प्रभावित क्षेत्रों के लोगों में तथा 6.7/1000 अप्रभावित व्यक्तियों के समूह में पाई गई।

- ऑकड़ों के खनन (Data mining) एवं गैस प्रभावित जीवित लोगों के स्वास्थ्य के संबंध में उपलब्ध 3 डाटाबेस जैसे–भोपाल स्मारक अस्पताल एवं अनुसंधान केन्द्र के आई.पी.डी. रिकार्ड्स (2010–2015); गैस राहत चिकित्सालयों का e-डेटाबेस (जनवरी 2015–मई 2017) एवं राष्ट्रीय पर्यावरणीय स्वास्थ्य अनुसंधान केन्द्र का डेटाबेस (2011–2016) का ट्राइंगुलेशन ''ए क्रास सैक्शनल स्टडी ऑन करैन्ट हैल्थ स्टैटस ऑफ गैस अफैक्टिड इंडीविजुअल्स ऑफ भोपाल'' के Phase-I के अन्तर्गत किया गया। इस अध्ययन के दौरान वर्ष में 17,321 गैस प्रभावित व्यक्तियों का चिकित्सीय खाका (clinical profile) तैयार किया गया। गैस प्रभावित जीवित व्यक्तियों में कार्डियो–वैस्कुलर सिस्टम (22.4%) एवं नेत्रीय सिस्टम (16.9%) से संबंधित अस्वस्थता सर्वाधिक पाई गई।

- ''इफेक्टिवनेस ऑफ इंस्टीट्यूशनल वर्सस डोमीसियलरी इम्पलीमैन्टेशन ऑफ स्टैन्डर्ड पल्मोनरी रिहैबिलिटेशन मॉड्यूल इन भोपाल गैस एक्सपोस्ड सर्वाईवर्स हैविंग सीओपीडी'' नामक अध्ययन के अन्तर्गत संस्थागत एवं घरेलू पल्मोनरी रिहेविलिटेशन की प्रभावशीलता का तुलनात्मक अध्ययन वर्ष के दौरान प्रारम्भ किया गया। कुल 180 गैस प्रभावित सीओपीडी व्यक्तियों को मानक पल्मोनरी पुनर्वास मॉड्यूल का प्रशिक्षण देने के पश्चात् दो समूहों में अक्रमिकरण (randomization) किया गया। संस्थागत पुनर्वास एक योग्य फिजियोथेरापिस्ट के पर्यवेक्षण में पल्मोनरी पुनर्वास केन्द्र पर (समूह–1) एवं अधिवासी पुनर्वास मरीजों द्वारा स्वतः (समूह–2) एक घण्टा रोजाना किया गया तथा सप्ताह में दो बार निगरानी अनुपालन किया जा रहा है।

- ''साईटोजैनेटिक प्रोफाइलिंग ऑफ पेसेन्ट्स विथ क्रॉनिक किडनी डिसीज'' अध्ययन के अन्तर्गत कुल 108 प्रौढ़ गैस–प्रभावित सीकेडी रोगियों (समूह–1) एवं 49 प्रौढ़ गैस–अप्रभावित सीकेडी रोगियों (समूह–2) को कैरियोटाइप विश्लेषण, साईटोजैनेटिक एण्ड पॉइन्ट तथा क्रोमोसोमल ऐबरेशन विश्लेषण के अध्ययन हेतु भर्ती किया गया।

- ''डिवेलपमेंट ऑफ ए माइटो–एपीजेनेटिक कारसीनोजेनिक रिस्क असेसमेंट मॉडल फॉर एनवॉयरोन्मेंटल केमिकल एक्सपोजर'', नामक एक अग्रगामी अध्ययन (Pilot study) इस वर्ष में प्रारम्भ किया गया। प्रो–ऑक्सीडेन्ट्स व्यापक श्रेणी के अन्तर्गत आने वाले रसायनों से गर्भावस्था में exposed 15 व्यक्तियों के रक्त नमूने एवं 15 आयु एवं लिंग मिलान नियंत्रित Unexposed व्यक्तियों के नमूने लिए गए तथा circulating cell free DNA, miRNA, circulating nucleosomes, mtDNA copy number, inflammatory cytokines, DNA methyl transferases, global DNA, methylation profile इत्यादि का विश्लेषण किया गया। आरम्भिक परिणामों से विदित हुआ कि पर्यावरणीय प्री–ऑक्सीडेंट्स का preenatal exposure न केवल माइटोकॉण्ड्रियल–न्यूक्लियर cross-talk को क्षति पहुँचाता है बल्कि गर्भस्थ इपीजीनोम को aberrant नियमन के माध्यम से DNA Methylatin एवं histone modification द्वारा प्रभावित करता है।

- मानव संसाधन विकास मंत्रालय की IMPRINT योजना के अन्तर्गत एक एक्स्ट्राम्यूरल अध्ययन ''एबरेंट सरकुलेटिंग एपीजीनोमिक सिगनेचर्स : डिवेलपमेंट एण्ड वेलीडेशन ऑफ मिनिमल इनवेसिव बॉयोमेट्रिक फॉर ट्रांस–जेनरेशनल मॉनीटरिंग ऑफ एअर पॉल्यूशन एसोसिएटिड केंसर्स'' वर्तमान वर्ष में प्रारम्भ किया गया। इसका उद्देश्य air quality index के आधार पर वर्गीकृत उच्च जोखिम, मध्य जोखिम, एवं निम्न जोखिम क्षेत्रों में रहने वाले लोगों के रक्त एवं मूत्र के नमूनों में epigenomic हस्ताक्षरों का निरूपण करना है। अभी तक 60 जोड़ों (मॉ एवं संतान) के नमूने एकत्र एवं विश्लेषित किए गए हैं। आरम्भिक परिणामों में उच्च जोखिम वाले क्षेत्र में निवास करने वाली जनसंख्या में circulating DNA, सरकुलेटिंग न्यूक्लियोसोम्स, सरकुलेटिंग miRNA एवं सरकुलेटिंग mtDNA का अपेक्षाकृत उच्च स्तर दिखाई दिया है।

- आईसीएमआर–आरएफबीआर (Russian Foundation for Basic Research) के सहयोग के अन्तर्गत एक अध्ययन ''डिवेलपमेंट ऑफ क्वांटम डॉट्स बेस्ड नेनो–बॉयोसेंसर्स फॉर डिटेक्शन ऑफ सरकुलेटिंग सेल फ्री miRNAs इन एनवॉयरोन्मेंटल एसोसिएटिड लॅग कारसीनोजेनेसिस'' वर्ष के दौरान प्रारंभ किया गया। स्वस्थ व्यक्तियों के रक्त से Lymphocytes को पृथक कर पर्यावरणीय कैंसर पैदा करने वाले pollutants की विभिन्न मात्राओं में उन्हें उपचारित कर 21 ccf mi RNAs की Profile तैयार की गई। आरम्भिक परिणाम यह बताते हैं कि बहुत सारे tumor suppressing miRNAs जैसे कि Let-7e, miR-202, miR-98, miR-16, miR-27, miR-29 एवं miR-155 के expression में महत्वपूर्ण बदलाव आया है।

- वर्तमान वर्ष में ''बॉयो–केमिकल बेसिस ऑफ पैथोजेनेसिस ऑफ क्रोनिक आब्स्ट्रक्टिव पल्मोनरी डिसीज'' नामक अध्ययन असाधारण proteases की पहचान करने तथा stable COPD रोगियों में differential protein expression का विश्लेषण करने हेतु प्रारम्भ किया गया। तीस staable COPD रोगियों, 15 स्वस्थ व्यक्तियों एवं 02 CKD रोगियों से रक्त के नमूने एकत्रित किए गये तथा उनमें Caspases-3, DPP IV, MMP-9, MMP-2, एवं न्यूट्रोफिल इलासटेस के स्तर का आकलन किया गया। साथ ही कुछ COPD रोगियों के नमूनों में differential protein expression का विश्लेषण किया गया।

- वर्तमान वर्ष में निरेह में 57 स्थाई पदों के लिए Phase II की भर्ती के अन्तर्गत 5 वैज्ञानिकों (3 वैज्ञानिक–सी एवं 2 वैज्ञानिक–बी), 7 प्रशासनिक काडर, 5 तकनीकी काडर एवं 2 अभियांत्रिकी काडर के कर्मचारी/अधिकारीगण ने संस्थान में कार्यभार ग्रहण किया।

Research Works

PROJECT 1

Population Based Long Term Epidemiological Study on the Health Effects of the Toxic Gas Exposure in BhopalInvestigators, Duration and Funding

Investigators, Duration and Funding

i. Team BGDRC(Jan 1985 to May 1994) : ICMR

ii. Team CRS (Jan 1996 to Jan 2011) : GoMP

iii. Team NIREH (Feb 2011 onwards) : ICMR

Investigators from NIREH

Dr. Y. D. Sabde, Dr. N. Banerjee, Dr. S. Singh,

Dr. K. K. Soni, Dr. R. Galgalekar, Mrs. M. Sharma

The population based long term epidemiological study on the health effects of the toxic gas exposure was continued during the year. In this over 3–decades long study the morbidity and mortality data is being collected in the assembled cohort of gas exposed and unexposed (control) families using a structured health survey questionnaire by the trained staff. However, since January 2017 the frequency of survey has been modified to once yearly in place of twice in a year in view of nearly flat trend of morbidities for the last 3-4 years.

To recapitulate, after the occurrence of Bhopal gas disaster in 1984 this study was launched in 1986 under Bhopal Gas Disaster Research Centre, ICMR (BGDRC) on a cohort of 62,706 individuals from gas exposed areas (19,260, 28,261 and 15,185 from severely, moderately and mildly exposed areas respectively) and 13,526 individuals from non-exposed areas (Control) of Bhopal. The study under BGDRC continued till 1994 and was later continued (1996-2010) by the Centre for Rehabilitation Studies (CRS), Govt. of M.P. following the same protocol on a cohort of 34,480 individuals from exposed areas (10,816 from severely, 14,137 from moderately and 9,527 from mildly exposed areas) and 7,990 individuals from unexposed control areas which were part of the original cohort. In 2011, when NIREH took over the study from CRS, a substantial part of the cohort was already lost due to a variety of reasons such as shifting of population to different places, marriage related migration, deaths etc. and only the cohort of 16,860 exposed individuals (5,658, 6,533 and 4,669 from severely, moderately and mildly exposed areas respectively) and 5,741 individuals from the non-exposed control areas was available for the follow up by NIREH. Special drives undertaken during 2013-2016 resulted in tracing and addition of about 8,380 individuals from the lost cohort.

1.1 Morbiditypattern – 54th round

During the year the 54th round (January-December, 2017) of survey was undertaken. In this round 23,379 individuals from exposedareas *viz.* severely exposed (7,813), moderately exposed (8,304) and mildly exposed (7,262) areas; and 6,310 individuals from unexposed control areas were followed up. Any morbidity recorded was same in severely (15.6%) and mildly (15.7%) exposed areas while in moderately exposed areas (9.04%) it was even lesser than the control areas (10.8%) (Fig-1). Similarly, highest magnitude of respiratory disorders (7.2%) were also recorded in mildly exposed areas while it was near identical in mildly exposed (2.0%) and unexposed control areas (1.9%).

Glimpses of epidemiological survey

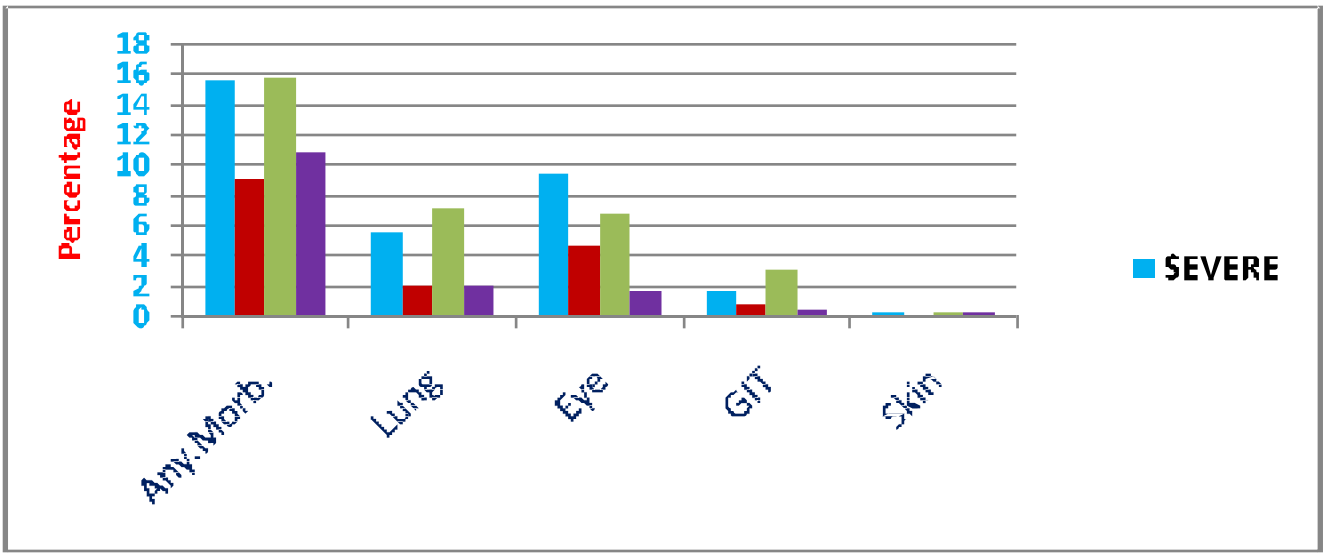


Fig-1: Morbidity pattern recorded in 54th round of survey

1.2 Mortality pattern– 54th round

Overall mortality rates in the 54th survey were 5.3/1,000 population in the exposed and 6.7/1,000 population in control areas (Table-1).

Table-1 : Primary causes of death recorded in 54th round of survey

Cause of death	Number (%)	
	Exposed Area	Control Area
Accident &Injuries	03(2.4%)	04(9.5%)
Child birth & Pregnancy	02(1.6%)	0(0.0%)
Fever	04(3.3%)	01(2.4%)
Digestive disorders	06(4.9%)	00(0.0%)
Respiratory disorders	35(28.5%)	06(14.3%)
C.N.S. disorders	05(4.1%)	02(4.8%)
C.V.S. disorders	16(13.0%)	12(28.6%)
Other system disorders	19(15.5%)	07(16.7%)
Senility	21(17.1%)	06(14.3%)
Cause unknown	12(9.8%)	04(9.5%)
Total deaths	123	42
Mortality rate (per 1,000)	**5.3**	**6.7**

1.3. Mortality data analysis (2012 - 2016)

A total of 1,292 deaths occurring during 2012-2016 in the registered followed up cohort (males 803, 62.2%, females 489, 37.8%) were analyzed. Distribution of deaths according to gas exposure cohorts is given in Table 2. Of the 1,011 persons died in exposed areas, 595 (58.8%) died before 70 years of age. Proportion of deaths before 70 was in fact higher in unexposed control areas (64.1%) though the difference was not significant. Significantly higher proportion (71.3%) of deaths before 70 years was contributed by males.

Table - 2 : Different exposure level area wise deaths in before and after 70 years of age

Age at death (yrs)	Severe		Moderate		Mild		Control		Total	
	No	%	No	%	No	%	No	%	No	%
Upto 69	206	66.5	237	55.8	152	55.1	180	64.1	775	60.0
70 and above	104	33.5	188	44.2	124	44.9	101	35.9	517	40.0
Total	310		425		276		281		1292	100.0

1.3.1 Cause of death

The most prevalent cause of death was vascular diseases (52.4%). Majority of the victims of vascular diseases died with acute myocardial infarction (80.8%) followed by cerebral haemorrhage (11.9%). The proportion of deaths claimed by vascular diseases was similar among males and females (53.4% and 52.4% respectively). However, the proportion of males dying due to vascular diseases before

70 years (67.5%) was significantly higher as compared to their female (54.3%) counterparts ($p < 0.01$, Pearson Chi-Square test df = 1). Chronic respiratory ailments i.e. chronic lung conditions and tuberculosis claimed 4.68% and 4.41% deaths respectively. The proportion of lives claimed by chronic lung conditions was higher in severely exposed areas as compared to unexposed control areas ($p < 0.001$) (Table-3)

Table-3 : Top 10 causes of death in age 30 - 69 years

Rank	Cause of Death	No	%
	Severely exposed area		
1	Cardiovascular diseases	111	53.9
2	Respiratory diseases	24	11.7
3	Malignant and other Neoplasms	20	9.7
4	Tuberculosis	13	6.3
5	Digestive diseases	8	3.9
6	Genito-urinary diseases	7	3.4
7	Diarrhoeal diseases	4	1.9
8	Unintentional injuries: Motor Vehicle Accidents	4	1.9
9	Intentional injuries: Suicide	4	1.9
10	All other causes	11	5.3
	Total	**206**	
	Moderately exposed area		
1	Cardiovascular diseases	141	59.5
2	Malignant and other Neoplasms	22	9.3
3	Tuberculosis	15	6.3
4	Respiratory diseases	14	5.9
5	Diarrhoeal diseases	9	3.8
6	Digestive diseases	9	3.8
7	Ill-defined/ All other symptoms,signs and abnormal clinical and laboratory findings	9	3.8
8	Genito-urinary diseases	7	3.0
9	Respiratory infections	2	0.8
10	All other causes	9	3.8
	Total	**237**	
	Mildly exposed area		
1	Cardiovascular diseases	93	61.2
2	Diarrhoeal diseases	14	9.2
3	Digestive diseases	9	5.9
4	Malignant and other Neoplasms	7	4.6
5	Respiratory diseases	6	3.9
6	Unintentional injuries: Motor Vehicle Accidents	5	3.3

7	Respiratory infections	4	2.6
8	Intentional injuries: Suicide	4	2.6
9	Tuberculosis	3	2.0
10	All other causes	7	4.6
	Total	**152**	
	Unexposed area (Control)		
1	Cardiovascular diseases	84	46.7
2	Malignant and other Neoplasms	21	11.7
3	Digestive diseases	12	6.7
4	Tuberculosis	8	4.4
5	Genito-urinary diseases	8	4.4
6	Intentional injuries: Suicide	8	4.4
7	Respiratory infections	7	3.9
8	Unintentional injuries: Other Than Motor Vehicle Accidents	7	3.9
9	Diarrhoeal diseases	6	3.3
10	All other causes	19	10.6
	Total	**180**	

The analysis suggested that the exposed cohort didn't differ much from the unexposed population in terms of CDR and SMR. The distribution of top 10 causes of death is also similar among all exposure categories and similar to the national data.

PROJECT 2

A cross-sectional study on current health status of gas affected individuals of Bhopal: Phase I- Data triangulation to understand health status of gas exposed survivors of Bhopal

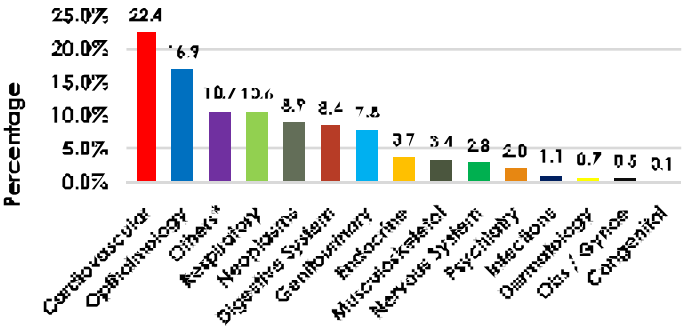
Investigators : Dr. Anil Prakash (PI) ; Dr. N. Banerjee, Dr. S. Singh, Dr. R. Galgalekar, Dr. K. K. Soni, Mrs. M. Sharma (NIREH, Bhopal) ; Mr. K. K. Dube, Dr. Sanjay Jain (KN Hospital, Bhopal); Mr. Nitin Bhatia (BMHRC, Bhopal)

Duration : 1 ½ Years (January 2017 – June 2018)

Funding : ICMR (IM)

Health care to the gas exposed survivors and their progenies is being provided free of cost by Gas Rahat Department of Govt of MP through its six well equipped hospitals & 18 Day Care Centres; and Bhopal Memorial Hospital and Research Centre (BMHRC), a 350-bedded super specialty hospital of Govt of India along with its 8 mini units. Consequently, the information on the health conditions of gas exposed survivors is although voluminous yet fragmented lacking synergy among the available data bases due to various operational and technical constraints. As a result clarity is missing on the extent of the adverse health effects being experienced by the gas exposed survivors. Therefore, this study, attempted to document the pattern of morbidities with particular reference to the intensity of exposure, disease chronicity among available gas exposed survivors in Bhopal through data mining, triangulation and linking of the available major data bases.

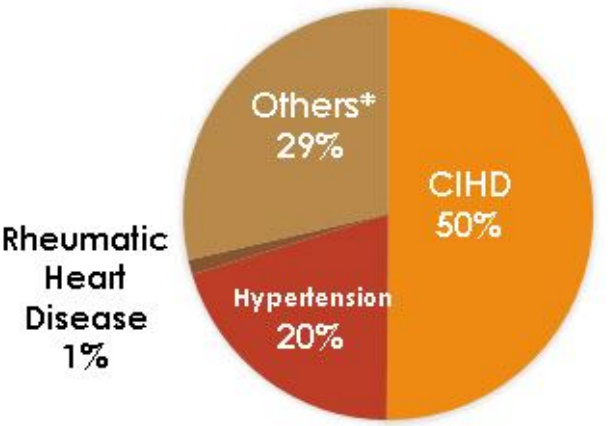
Three databases related to the health of gas exposed survivors (i) randomly selected 38,527 IPD records (belonging to 17,321 gas exposed survivors) obtained from BMHRC (2010-2015) (ii) Gas Rahat hospitals data base (Jan 2015-May 2017) and (iii) NIREH database of Long term epidemiological study (2011-2016) were linked after bringing as much uniformity as possible in the 3 data bases. From Gas Rahat hospitals database, 2,997 subjects and from NIREH's database, 584 subjects could be linked to BMHRC data base and after data cleaning three data bases were merged to form a single master list and disease profile of 17,321 gas exposed survivors was prepared. The highest no. of morbidities belonged to the cardio-vascular system (22.4%) followed by ophthalmic morbidity (16.9%) (Fig-2).



* includes ENT, blood disorders, poisoning, injury etc.

Fig-2: System wise distribution of morbidities (based on 38,527 visits of 17,321 individuals)

Among cardiovascular system related morbidities almost half (50%) of the subjects had chronic ischemic heart diseases (Fig-3).



* others include pulmonary embolism, non-rheumatic valve disorder, cardiac myopathy, cardiac arrest, heart failure, haemorrhoids

Fig-3: Distribution of cardiovascular system related morbidities (n=8,629)

Nearly 85% individuals (14,700 of the 17,321 subjects whose disease profiling was prepared) were found to be suffering from a single chronic morbidity while multimorbidity (2 or >2 chronic morbid conditions) accounted for 15% cases. The distribution pattern of single chronic morbidity is shown in Fig-4.

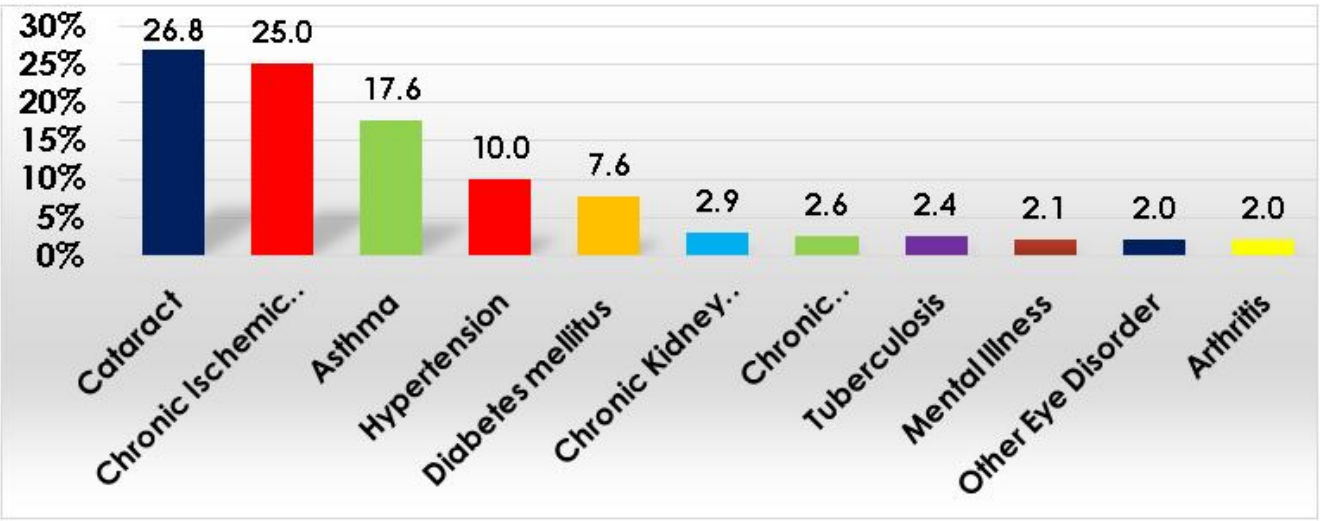


Fig-4 : Distribution of single chronic morbidity pattern (n=14,700 morbid individuals)

The study is progressing. Linking and disease profiling of another 11,000 patients is underway.

PROJECT 3

Effectiveness of Institutional versus domiciliary implementation of standard pulmonary rehabilitation module in Bhopal gas exposed survivors having COPD

Investigators : Dr. Ruma Galgalekar (PI) ; Dr. Lalit Kumar, Dr. Mahesh Rathore (BMHRC)

Duration : 2 Years 3 months (Jan 2017 - March 2019)

Funding : ICMR (IM)

As pulmonary rehabilitation is a lifelong process, emphasis should be to develop community based pulmonary rehabilitation programmes near the residence of such patients so that continuous rehabilitation and educational programmmes can be provided to them. This study is comparing the effectiveness of pulmonary rehabilitation among gas exposed survivors in the management of COPD cases in two different settings *viz.* under supervision in a health facility and unsupervised at domestic level. For providing supervised rehabilitation a Pulmonary Rehabilitation Centre, equipped with rehabilitation kit comprising of stationary bicycle, Treadmill, Quadriceps chair, shoulder wheel, portable oxygenator, T.E.N.S., T-pully, weight cuffs, spirometer (triflo), was established in JLN Gas Rahat Hospital which is in close vicinity of the gas exposed localities, thus, providing better accessibility to the enrolled subjects. Enrollment of 180 gas exposed COPD subjects belonging to different exposure categories satisfying inclusion and exclusion criteria has been completed (Table-5). After providing common training on standard pulmonary rehabilitation module the recruited subjects were randomized in to 2 groups of 90 patients each. One group continued to undertake rehabilitation exercises under the supervision of a physiotherapist (institutional rehabilitation) while the other group was asked to continue the pulmonary rehabilitation at their home (domiciliary rehabilitation). During follow ups 2 subjects in Institutional Group and 6 subjects in Domiciliary Group were found expired, thus, leaving 88 and 84 subjects in the two Groups respectively. The study is continuing.

Table-4 : Details of the subjects enrolled in the study

Exposure category	Institutional Group	Domiciliary Group
Mildly exposed	37	29
Moderately exposed	22	28
Severely exposed	31	33
TOTAL	**90**	**90**

PROJECT 4

Cytogenetic profiling of patients with chronic kidney disease: Evaluation of genomic instability

Investigators : Dr. R.M. Samarth (PI); Dr. Gopesh Modi (Nobel Hospital, Bhopal), Dr. Sharique Hasan (BMHRC, Bhopal), Dr. M.L. Banjare, Dr. Sanjay Jain (KN Hospital, Bhopal)

Duration : 3 Years (Oct 2016 - Sept 2019

Funding : ICMR (IM)

In patients with chronic kidney disease (CKD) the presence of massive genome damage has been repeatedly demonstrated, possibly due to accumulation of uraemic toxins, oxidative stress mediators and other endogenous substances with genotoxic properties. Therefore, it is necessary to explore the factors associated with the presence and background levels of genetic damage in CKD cases.The present study is aiming to prepare cytogenetic profile of toxic gas exposed and non-exposed patients with chronic kidney disease through karyotype analysis and cytogenetic endpoints. Further, the genomic instability in patients with chronic kidney disease is being assessed through chromosomal aberration analysis (CAA), frequencies of sister chromatid exchange (SCE) and micronuclei (MN) assay.

CKD patients, fulfilling the inclusion and exclusion criteria, belonging to four groups *viz.* Adult exposed CKD patients (Group-I); Adult unexposed CKD patients (Group-II); Adult exposed non-CKD patients (Group-III) and Normal healthy adults (Group-IV) are proposed to be enrolled in this study. During the year a total of 157 CKD Patients attending Department of Nephrology, Kamla Nehru Hospital, Bhopal /Nobel Hospital, Bhopal, belonging to Group-I i.e. Adult exposed CKD patients (n=108:59 males, 49 females) ; and Group-II Adult unexposed CKD patients (n=49: 31 males, 18 females)were recruited after obtaining written consent. From each subject 3 ml peripheral blood was collected in sterile sodium heparin vacutainer by vene-puncture for chromosomal study. 0.5 ml peripheral blood was cultured, after adding 4 ml RPMI 1640 medium supplemented with 20% fetal bovine serum and phytohaemagglutinin (PHA), at 37°C for 72 hrs. Cultures were set up in duplicates and in three separate sets for each individual. Preliminary analysis of chromosomal aberrations in 62 subjects was carried out (Table-5).

Table-5: Frequency of chromosomal aberrations in cultured peripheral blood lymphocytes of toxic gas exposed and non exposed CKD patients

Parameters	Non-exposed CKD subjects			Exposed CKD subjects		
	Male (n=13)	Female (n=10)	Total (n=23)	Male (n=26)	Female (n=13)	Total (n=39)
Mean Age	53.56±3.62	51.33±3.23	52.44±2.37	45.85±3.22	43.69±3.40	45.79±2.41
MI	7.12±0.26	7.34±0.29	7.22±0.19	7.83±0.22	7.87±0.32	7.84±0.18
Dic.	1.46±0.22	1.40±0.27	1.43±0.16	1.35±0.11	1.23±0.23	1.31±0.10
Rings	0.92±0.21	1.20±0.36	1.04±0.19	0.88±0.22	0.69±0.31	0.82±0.18
C. Breaks	0.77±0.32	0.70±0.21	0.70±0.20	1.35±0.27	2.15±0.46	1.62±0.24*
Fragments	2.23±0.48	2.40±0.48	2.30±0.34	2.81±0.33	3.31±0.35	3.33±0.27*

*p<0.05

PROJECT 5

Development of a mito-epigenetic carcinogenic risk assessment model for environmental chemical exposures: A pilot study

Investigators : Dr. P. K. Mishra (PI) ; Dr. K. C. Pandey, Dr. Y. Sabde, Dr. Sajal De

Duration : 3 Years (February 2017 - January 2020)

Funding : ICMR (IM)

There has been substantial progress with regard to prevention and treatment options for certain cancers, however the burden of this disease is increasing owing to a growing number of environmental risk factors. The rising toll of cancer-related mortality due to different accidental or occupational environmental exposures necessitates early identification of exposed victims for their appropriate therapeutic intervention. However, this is mainly restricted by lack of precise biomarkers and effective detection methodologies. Since, mitochondria are the prime target of different environmental chemical exposures, this sub-cellular organelle offers possibilities of using it for developing effective exposure associated strategies. The presence of unique inheritance pattern, rapid evolutionary rate, low recombination rate, higher copy number and resistance to degradation make mtDNA an important and indispensable tool for human exposome analysis. Earlier work from our laboratory has provided mechanistic insights in to the understanding of intricate molecular mechanisms of toxico-genomic implications invoked upon exposure to environmental stress signals and bio-transforming agents, especially pro-oxidants.Our findings have demonstrated that the risk of developing an environmental associated aberrant disease phenotype, such as cancer, involves complex interplay of mitochondria-retrograde signaling-induced epigenetic reprogramming which are maternally inherited. First twelve weeks of pregnancy is the critical window of developmental vulnerability as majority of mitochondrial-linked epigenetic reprogramming takes place during this stage. Therefore, in this study we proposed to translate this knowledge into an investigative framework to develop and validate a mito-epigenetic model of carcinogenic risk assessment for environmental chemical exposures in subjects exposed to highly reactive environmental pro-oxidants.

We collected blood samples from fifteen subjects from those exposed to broad chemical class of pro-oxidants at *in utero* stage. An equal number of age and gender matched healthy controls were also recruited for this study.Various parameters were examined based on the procedures previously standardized in our laboratory. Mean levels of circulating cell free DNA was recorded to be significantly higher in the exposed subjects as compared to age and gender-matched healthy control individuals ($p \leq 0.01$). The circulating cell free DNA levels in exposed group was 46.50 ± 3.16 ng/ul as compared to 11.58 ± 1.80 ng/ul in age and gender matched controls (Fig-5a and b). Quantum of miRNA in exposed group when compared to controls (Fig- 5c and d) did not show appreciable changes. However, mean circulating nucleosomes was significantly ($p \leq 0.05$) elevated in exposed subjects [0.89 ± 0.24 AU] with respect to controls [0.20 ± 0.03 AU](Fig-5e). It is understood that the balance between mitochondrial dysfunction and mitochondrial nuclear cross talk is reflected by mtDNA copy number, therefore, we assessed the mtDNA copy number using a quantitative real time PCR based approach. The result showed

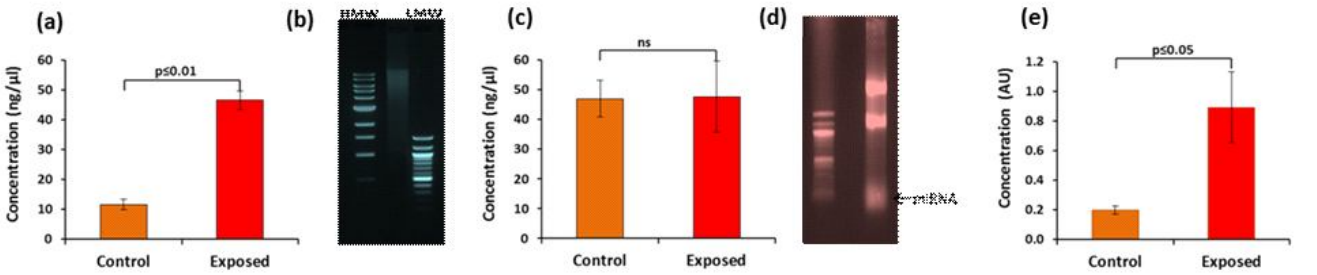


Fig - 5: (a) Quantitative measurements of circulating cell-free DNA; (b) Agarose gel profile of circulating cell-free DNA (c) Quantitative measurements of circulating miRNA; (d) Agarose gel profile of miRNA (e) Quantitative measurements of circulating nucleosomes in control and exposed samples

significantly lower (p≤0.01) mtDNA copy numbers in exposed subjects in comparison to controls (Fig-6a-c). The mtDNA copy number in exposed subjects was 322.23 ± 143.26 as **Fig-6: Relative copy number of circulating mtDNA using RT PCR in control and exposed group** compared to controls 2255.42 ± 269.91. A significant increase in inflammatory cytokines tumor necrosis factor (TNF)-α, interleukin (IL)-6 and interferon (IFN)-γ, was observed in exposed subjects as compared to healthy controls. In exposed individuals, mean concentrations of these circulating cytokines TNF-α, IL-6 and IFN-γ were 184.30 ±

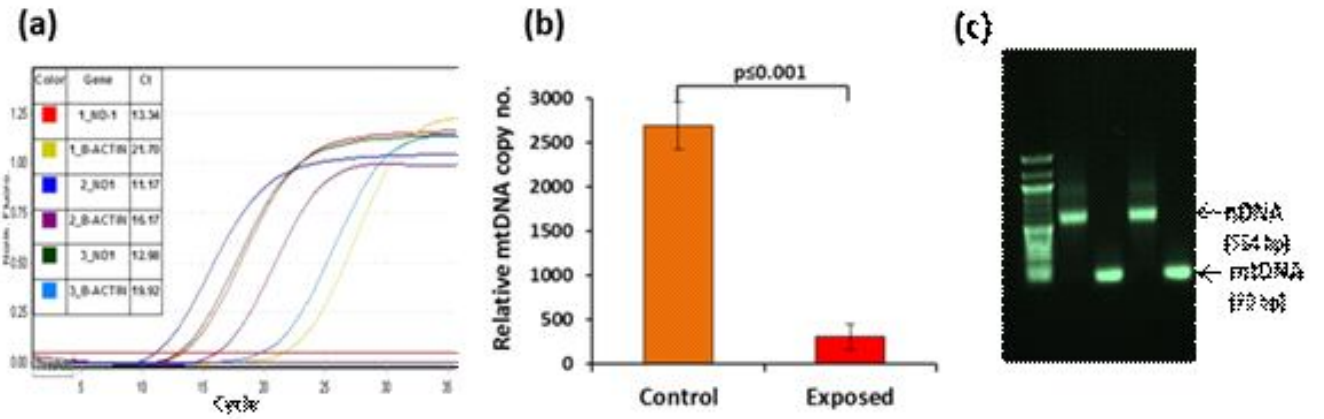


Fig-6: Relative copy number of circulating mtDNA using RT PCR in control and exposed group

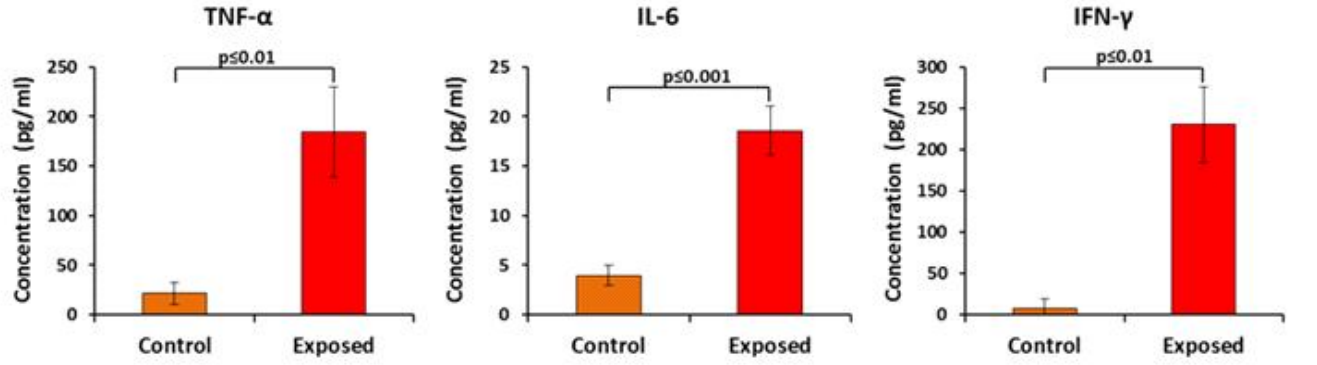


Fig-7: Quantitative assessment of tumor necrosis factor (TNF)-α, interleukin (IL)-6 and interferon (IFN)-γ by ELISA in plasma samples of controls and exposed individuals.

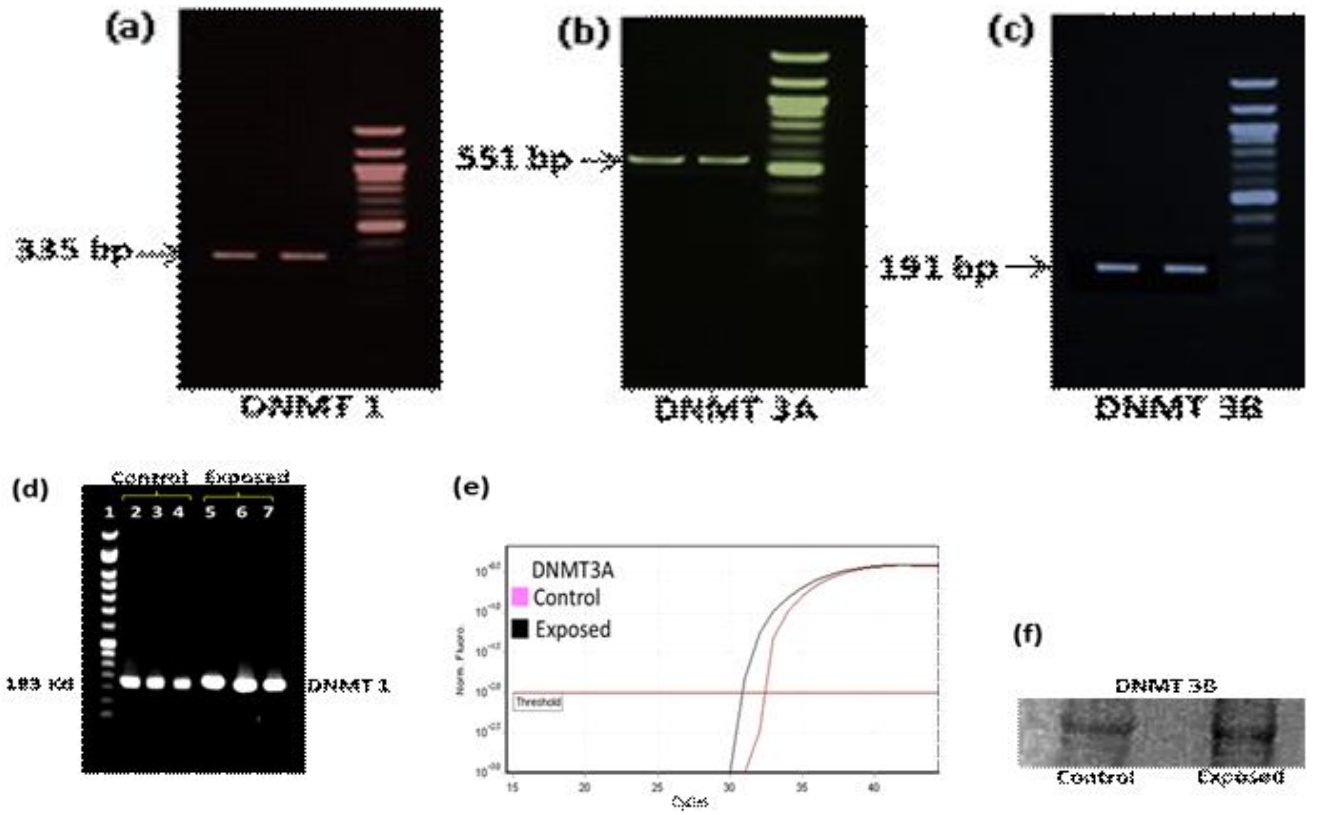


Fig- 8: (a-c) Gel pictures showing standardization of DNMT (DNMT 1, 3A and 3B) primers. (d and e) Representative picture of RT-qPCR profile and (f) Western blot profile showing comparatively high expression of DNMT gene in exposed subjects in contrast to the control

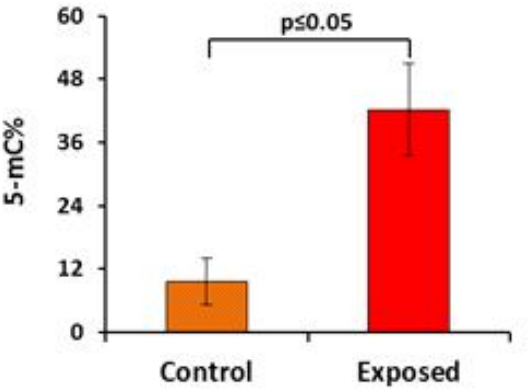


Fig-9:Bar graph shows global DNA methylation (5-mC %) levels in control and exposed groups

45.68, 18.58 ± 2.50 and 230.31 ± 42. 30 pg/ml respectively while the levels of these cytokines in controls were 21.28 ± 11. 39, 3.96 ± 1.04 and 7.44 ± 1.41 pg/ml respectively (Fig-7). The expression of DNA methyl transferases (*DNMT-1*, *DNMT-3A* and *DNMT-3B)* were assessed using reverse transcriptase PCR. Our results showed a marked increase in the expression of *DNMT-1, 3A* and *3B* in exposed subjects as compared to control group. Similar results were observed at protein expression level when assessed

using Western blot (Fig-8a-f). Covalent addition of methyl groups to cytosine in CpG dinucleotide mediated by DNMTs result in methylation of the genome. The result showed a significant ($p \leq 0.05$) increase in the global DNA methylation profiles in exposed group as compared to control group. The DNA methylation (5-mC%) in exposed group was 42.22 ± 8.77, while the level of DNA methylation in control group was 9.54 ± 4.4 (Fig-9). Post-translational histone H3 modifications that include methylation, acetylation and phosphorylation were also measured using end-point protocols. A significant increase in methylated histone marks (H3K4me1, H3K4me3, H3K27me1, H3K36me1 and H3K79me2) and a phosphorylation pattern (H3Ser10 and H3Ser28) in exposed subjects was noted with respect to controls (Fig-10a and b).

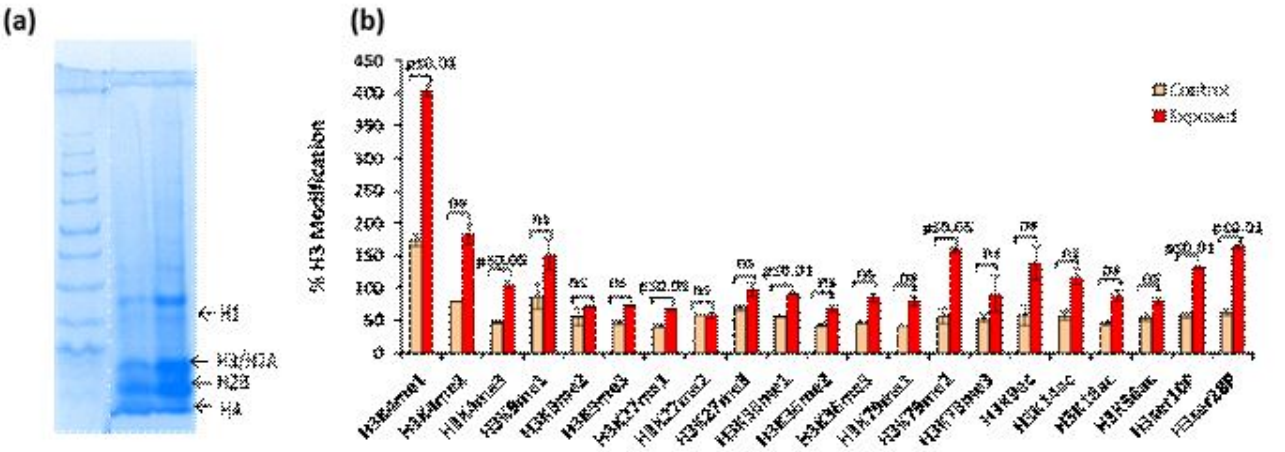


Fig-10: (a) SDS PAGE profile of total histone proteins extracts. (b) Histogram depicting comparative analysis of 21 histone H3 modifications in control and exposed individuals

The results obtained so far indicate that prenatal exposure of environmental pro-oxidants not only impairs the mitochondrial-nuclear cross talk but also modulates the fetal epigenome through aberrant regulations of DNA methylation and histone modifications. Further studies are ongoing to understand the specific epigenetic modification patterns involved in the mito-epigenomic axis evoked upon environmental pro-oxidant exposure.

PROJECT 6

Aberrant circulating epigenomic signatures: Development and validation of minimal-invasive biomarkers for trans-generational monitoring of air pollution associated cancers

Investigators : Dr. P. K. Mishra (PI- NIREH) ; Dr. Koel Chaudhury (PI-IIT Kharagpur)

Duration3 : 3 Years (March 2017 - February 2020)

Funding : EM (MHRD : Under IMPRINT scheme- domain Healthcare)

Particulate matters of different micron size are the major constituent of air pollution that triggers a diverse array of human pathologies. We have recently demonstrated that exposure to particulate matter (PM) (coarse-PM10; fine-PM2.5 and ultrafine-PM0.1) impairs mitochondrial redox homeostasis and activates phosphatidylinositol 3-kinase mediated nuclear DNA damage in human lymphocytes that can well extend beyond the genome. Despite progress in the identification of biomarkers, gene mutation based approaches still face formidable challenges as the disease evolves from a complex interplay between environment and host. Therefore, identification of an epigenomic signature might be useful for early diagnosis with the potential to reduce the environmental-associated disease burden. Non-invasive 'liquid biopsy' based epigenomic screening has recently emerged as a methodology which has potential to characterize tumor heterogeneity at initial stages. Epigenetic signatures (methylated DNA, miRNA, and post transcriptionally modified histones), known to reflect the vital cellular changes, circulate at higher levels in the individuals with cancer. Extending this idea that chromatin modification patterns are associated with different functional sequences that might manifest as aberrant epigenomic signatures in peripheral circulation, in this study we aimed to characterize the epigenomic signatures in biological fluids such as saliva and urine among defined population sets *viz.* those who were exposed to varying quantum of PM residing in high-risk, mid-risk and low-risk air-pollution zones of our country. Using a pan-India approach, cities were categorized as low-risk, mid-risk and high-risk based on the air quality index (AQI) ≤60, 60-120 and ≥120, respectively. Selected high-risk cities were Delhi and Gwalior; mid-risk cities were Bhopal and Jaipur; and low-risk cities were Sagar and Mandla. A total of 60 pairs of samples (mother and son) have so far been collected and analyzed.

Our preliminary results showed that the levels of circulating DNA ($p \leq 0.0001$), circulating nucleosomes ($p \leq 0.01$), circulating miRNA and circulating mtDNA ($p \leq 0.0001$) in population living in high-risk region is comparative higher (Fig-11). Trends showed significantly higher circulating nucleosomes levels among mother and son from the high-risk zone as compared to the mother and son from low-risk zone. Mean levels of circulating nucleosomes in mother and son in high-risk, mid-risk and low-risk cities were 3.177±0.270, 2.313±0.227; 2.914±0.318, 2.127±0.521; and 1.025±0.384, 0.696±0.264 respectively ($p \leq 0.01$) (Fig -12). The levels of circulating mtDNA copy number was significantly higher in the high-risk zone as compared to the low-risk zone ($p \leq 0.0001$). The maximum mtDNA copy numbers were observed in the mother & son from high-risk zones i.e. 1319.10±107.41, 1179.94±125.77, while mtDNA copy numbers in mother & son from mid-risk and low-risk cities were 204.95±40.04, 139.50±12.64 and 18.49±3.57, 14.02±1.45 respectively (Fig.-13). Comparatively higher levels of 5-methyl Cytosine (5-mC) was observed in the high-risk group as compared to the low-risk group. Upon quantitative analysis, mean levels of 5-mC in the mother & son from high-risk zones measured were 20.36±2.78, 24.05±1.93. For

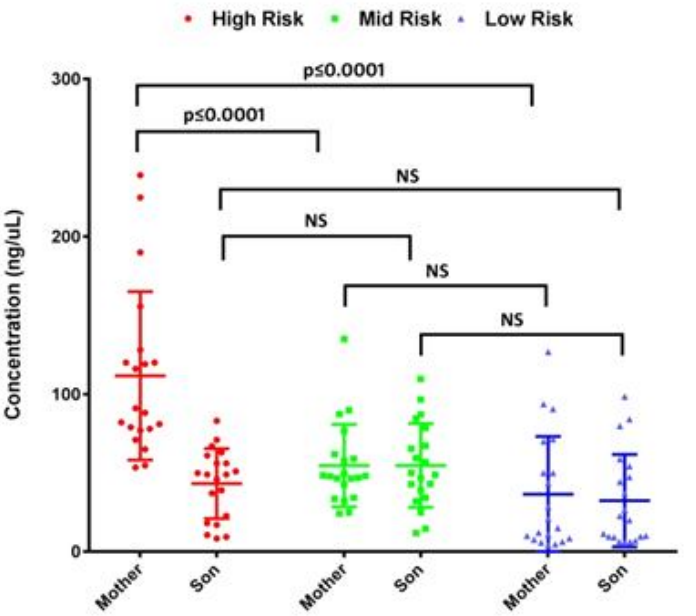


Fig-11: Scatter plot showing the levels of circulating DNA (ng/uL), in mother & son from high-risk, mid-risk & low-risk cities

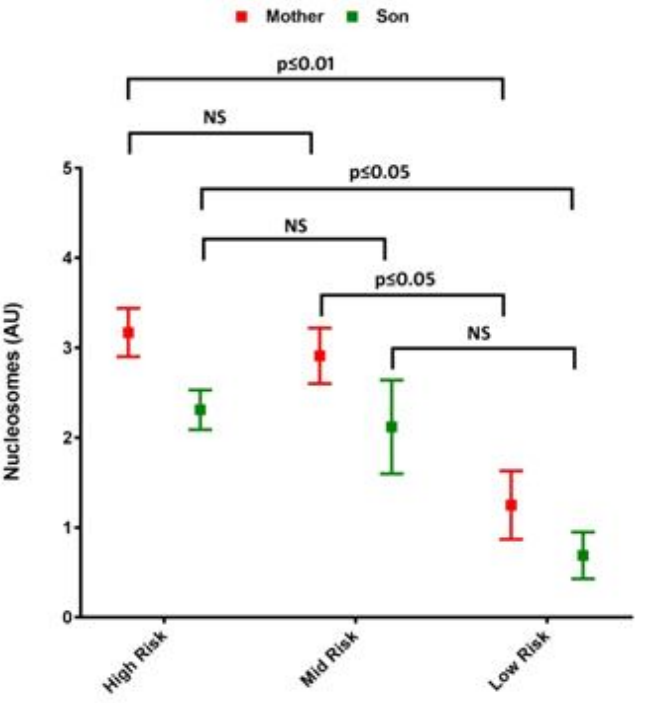


Fig-12: Graph showing the levels of circulating nucleosome (AU) in mother & son from high-risk, mid-risk & low-risk cities

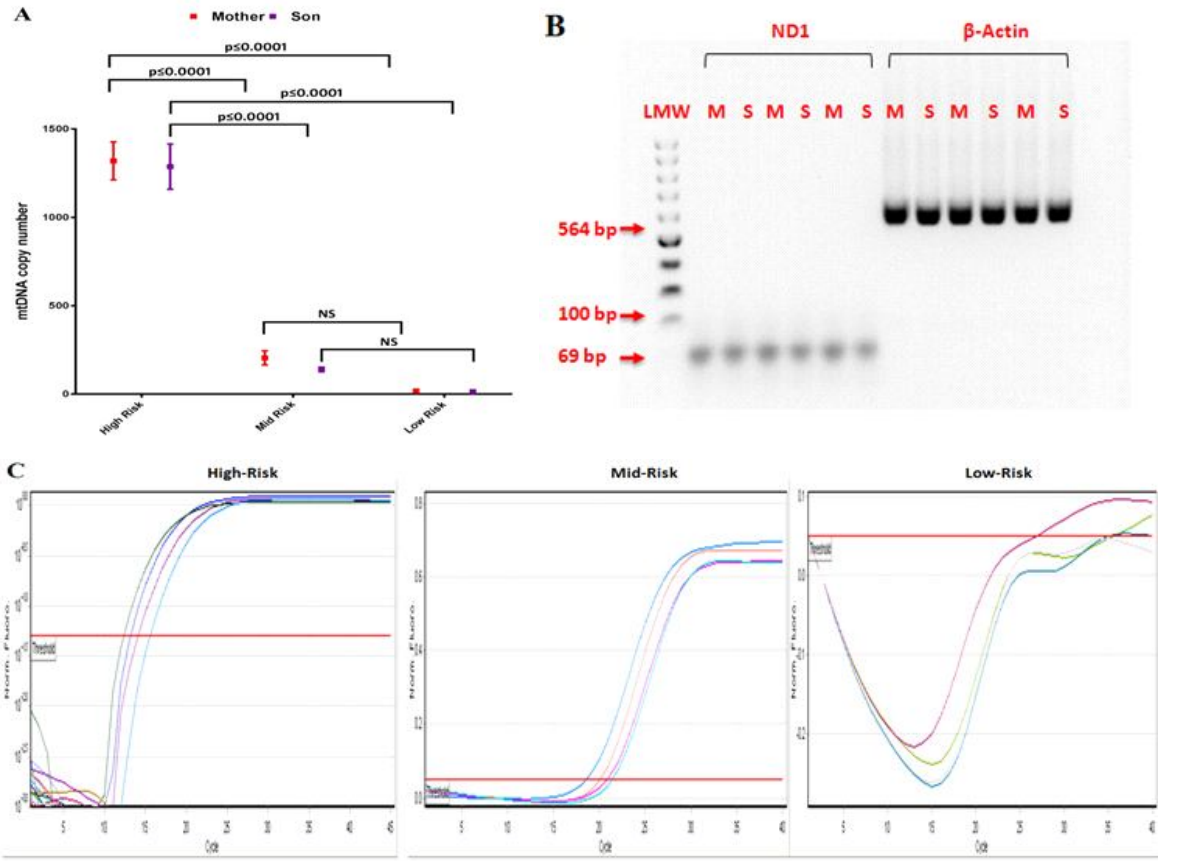


Fig-13: (A) Graph showing the levels of circulating mtDNA copy numbers in mother & son from high-risk, mid-risk & low-risk cities. (B) Gel image of ND-1 and β-actin in mother (M) and son (S) from high-risk, mid-risk & low-risk zones. LMW; {ND1 [high-risk] - Lane 1, mother; Lane 2, son]; [mid-risk - Lane 3, mother; Lane 4, son]; [low risk] - Lane 5, mother; Lane 6}; {β-Actin [high-risk] - Lane 1, mother; Lane 2, son]; [mid-risk - Lane 3, mother; Lane 4, son]; [low risk] - Lane 5, mother; Lane 6}. (C) Real-time PCR analysis of mtDNA copy number in high-risk, mid-risk and low-risk zone

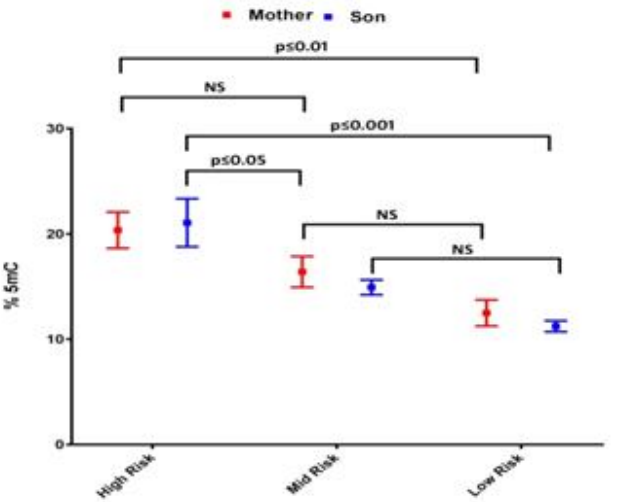


Fig- 14: Graph showing global % 5-mC in circulating DNA of mother & son from high-risk, mid-risk & low-risk cities.

mid-risk and low-risk cities, 5-mC were 14.75±0.76, 12.50±2.20; 8.88±0.60, 11.24±0.49 respectively (p≤0.01) (Fig-14). Relative gene expressions of DNMT1 and DNMT3a in high-risk, mid-risk & low-risk cities were quantified by RT-PCR using cellular mRNA with respective primers. Higher band intensity observed among high-risk group as compared to the low-risk (Fig-15). Total 21 H3 modifications including mono-, di- and tri-methylation of lysine 4, 9, 27, 36 and 79; acetylation of lysine 9, 14, 18 and

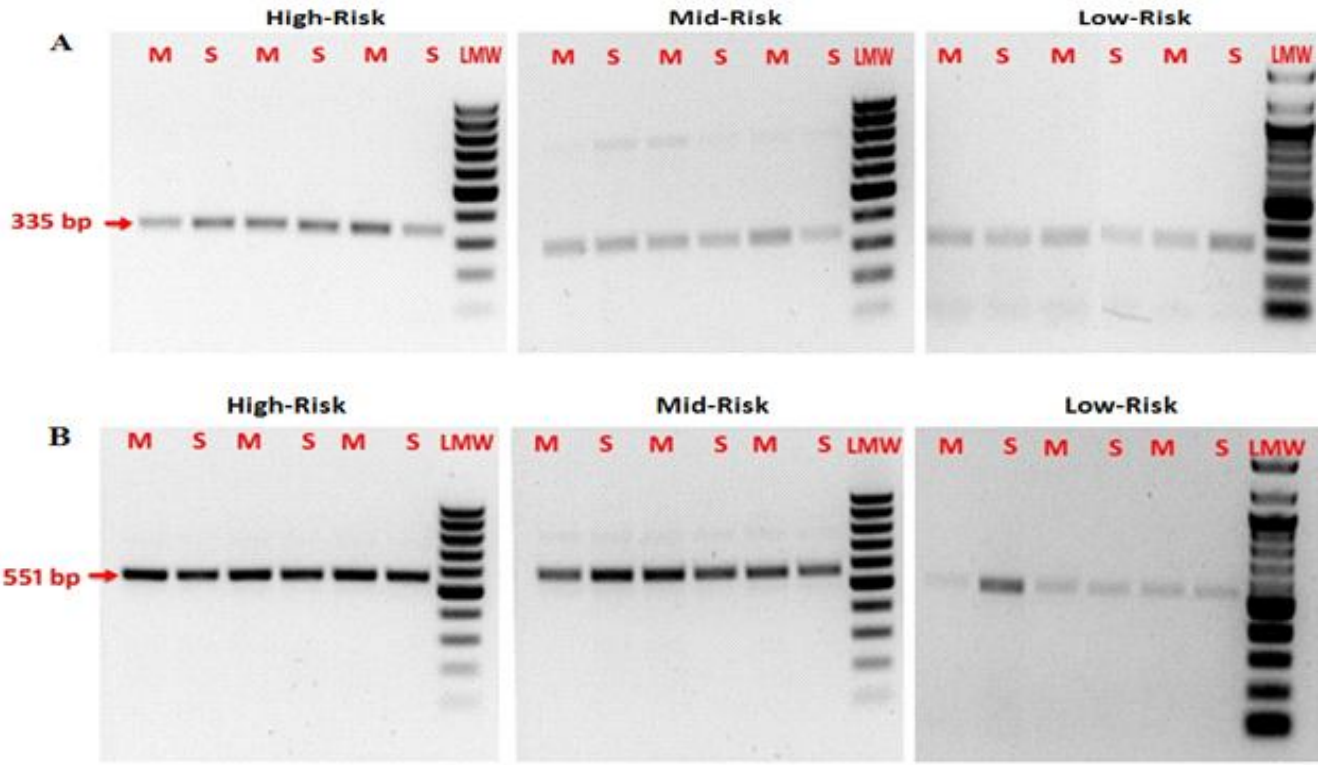
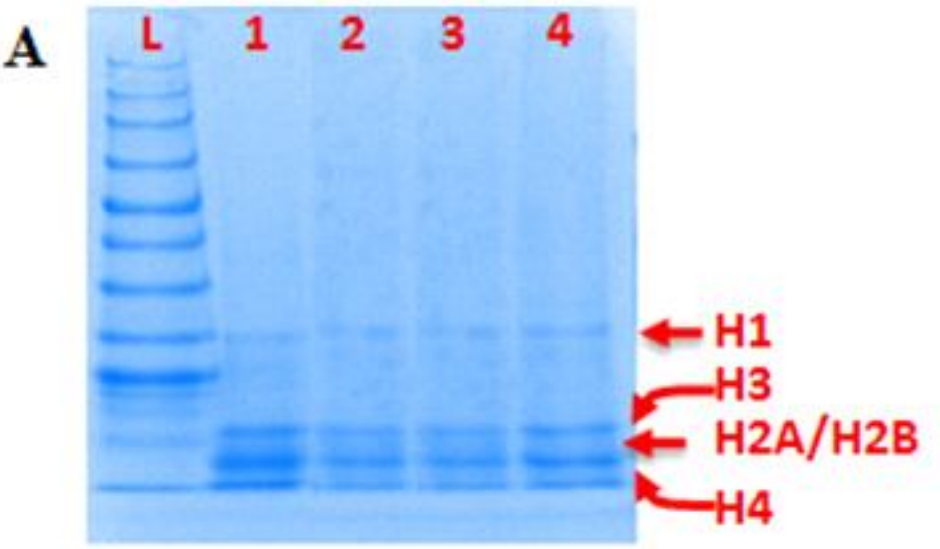


Fig-15: Representative gel images display the comparative levels of (A) DNA methyltransferase 1 (DNMT1) and (B) DNA methyltransferase 3a (DNMT3a)



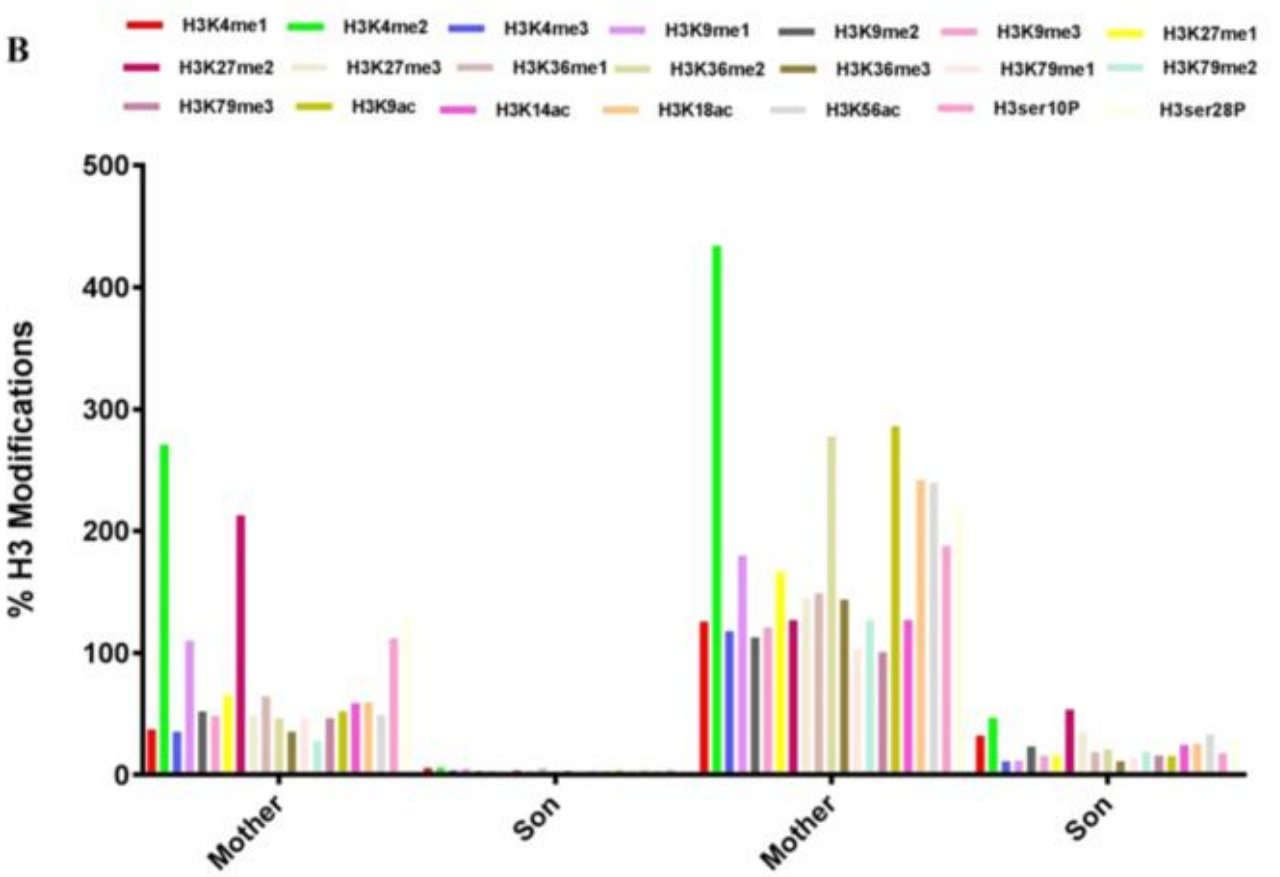


Fig- 16: (A) SDS-PAGE gel image of histone extracts. Protein marker; Lane 1, high-risk mother; Lane 2, high-risk son; Lane 3, mid-risk mother; Lane 4, mid-risk son. (B) Histogram shows changes in histone 3 modifications.

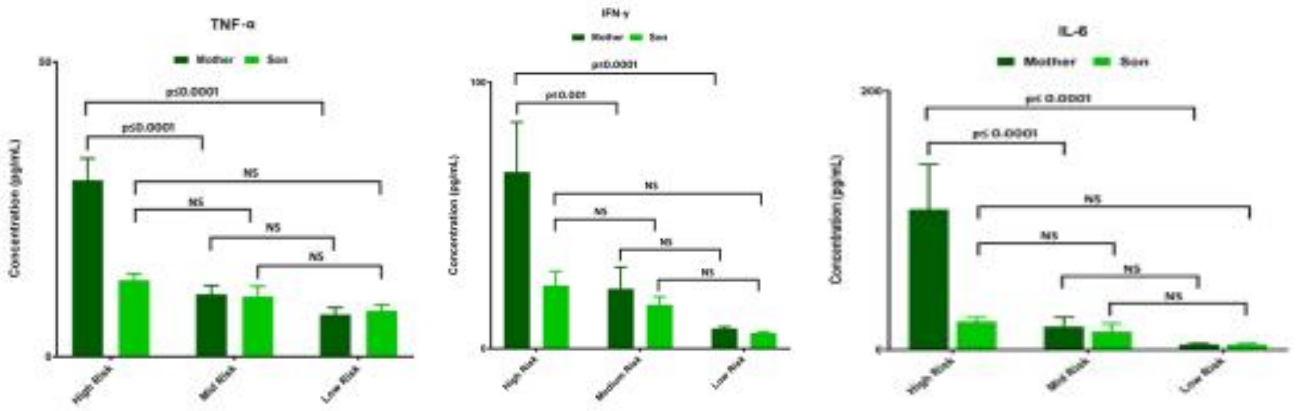


Fig- 17: Graph showing the secreted levels of pro-inflammatory cytokines i.e. tumor necrosis factor-α (TNF- α), interferon-γ (IFN-γ), and interleukin-6 (IL-6) of mother & son from high-risk, mid-risk & low-risk cities

56; phosphorylation of serine 10 and 28 were studied in mother and son belonging to the high-risk and mid-risk zones. Higher levels of histone modifications were observed in the mothers of both zones in contrasts to their sons (Fig.-16). Status of secreted levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), interferon-γ (IFN-γ), and tumor necrosis factor-α (TNF- α) in mothers and sons from high-risk, mid-risk & low-risk air pollution zones showed an increasing trend (Fig-17). Upon measurement of oxidative DNA damage marker 8-OH-dG (ng/mL), we observed higher formation of modified nucleotide base among high-risk group as compared to the low risk (p≤0.0001) (Fig- 18). Results of glutathione-S-transferase M1 and T1 (GSTM1/T1) gene polymorphism with internal control β-actin showed interesting findings as few individuals were detected having wild type of genotype in contrast to the higher number of mutated or mixed type of genotypes (Fig 19). The study is continuing.

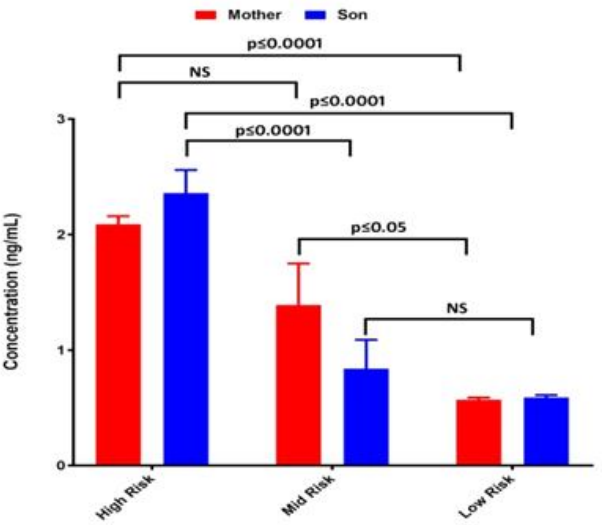


Fig-18: Bar graph shows higher formation of 8-hydroxy-2-deoxyguanosine (ng/mL), a modified nucleotide base among high-risk group as compared to the low risk

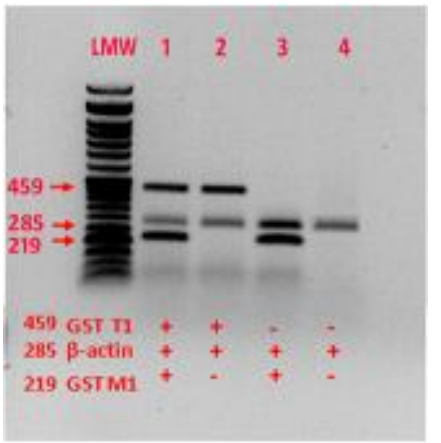


Fig-19: A representative image showing the glutathione-S-transferase M1 and T1 (GSTM1/T1), and β-actin gene polymorphisms done using multiplex polymerase chain reaction (PCR). Lane M, 50-bp DNA low molecular weight marker; Lane 1, GSTM1/T1 (+/+) genotype; Lane 2, GSTM1/T1 (+/-) genotype; Lane 3, GSTM1/T1 (-/+) genotype; Lane 4, GSTM1/T1 (-/-) genotype

PROJECT 7

Development of quantum dots based nano-biosensors for detection of circulating cell-free Mi RNAs in environmental associated lung carcinogenesis

Investigators : Dr. P.K. Mishra (PI- NIREH) ; Prof. Irine Yu Goryacheva (RFBR-SU-RUSSIA)

Duration : 3 Years (July 2017 - June 2020)

Funding : EM (Russian Foundation for Basic Research, Russia)

Clinically recommended diagnostic and screening modalities for lung cancer include low-dose computed tomography (also called a low-dose CT scan, or LDCT), biopsy, magnetic resonance imaging (MRI) and Positron emission tomography (PET) which are associated with several limitations such as over-diagnosis, excessive cost, and risks associated with radiation exposure that questions their application for reliable population-based screening of lung carcinogenesis. Therefore, the identification of a non-invasive biomarker, able to detect the presence of lung malignancy or to predict tumor aggressiveness, might be useful for early diagnosis with the potential to reduce disease burden.

microRNAs (Mi RNAs) are short, non-coding, single stranded RNAs with ~22-23 nucleotide that play an essential role in gene expression and several cellular processes. However, they exhibit unique expression patterns in various pathophysiological conditions such as cancer, providing an ease in differentiation in cancerous and healthy tissues. Presence of circulating miRNA in the body fluids has emerged as a potential biomarker for the development and implementation of clinically relevant minimally-invasive technology for risk assessment, early detection and monitoring therapeutic responses in lung cancers. Evidence of disease-specific circulating cell-free miRNAs in different patho-physiological conditions such as lung cancer could act as a potential biomarker for diagnostic applications. Despite the availability of various methods for the detection of miRNA such as qPCR method in the biological samples where the miRNA templates are amplified and measured using fluorescent probes, detection through NIR imaging via quantum dots based strategy in the biological system preferably eliminates the need for PCR and other complicated techniques and its variants. Quantum dots are semiconductor nanomaterials that exhibit size-tunable fluorescence along with photostability superior to conventional fluorescent dyes presenting their potential candidature as effective biosensors. In this study we are aiming to develop quantum dots based nanosensors for detecting lung cancer specific circulating cell free miRNAs.

The isolation of circulating cell-free miRNAs from the plasma samples was done as per our laboratory's standardized protocols. The profiling was carried out using conventional and one step PCR method. For validation of the study lymphocytes were isolated from healthy individuals and treated with different concentrations of known environmental associated carcinogenic pollutants such as benzopyrene (B[a]P), a non-carcinogenic compound, anthracene (ANT) and air-borne particulate matter (PM 10, PM 2.5 and PM 0.1). Subsequently, miRNAs were isolated, characterized and complete profiling was carried out for 21 ccf miRNAs (U6, Let-7a, Let-7b-5p, Let-7d, Let-7e, miR-202, miR-98, miR-221, miR-17, miR-200c, miR-29a, miR-128-2, miR-34a, miR-155, miR-24, miR-27, miR-28-5p, miR-150, miR-142-5p, miR-16-5p, miR-451a). The profiling exhibited significant changes in the expression of some miRNAs

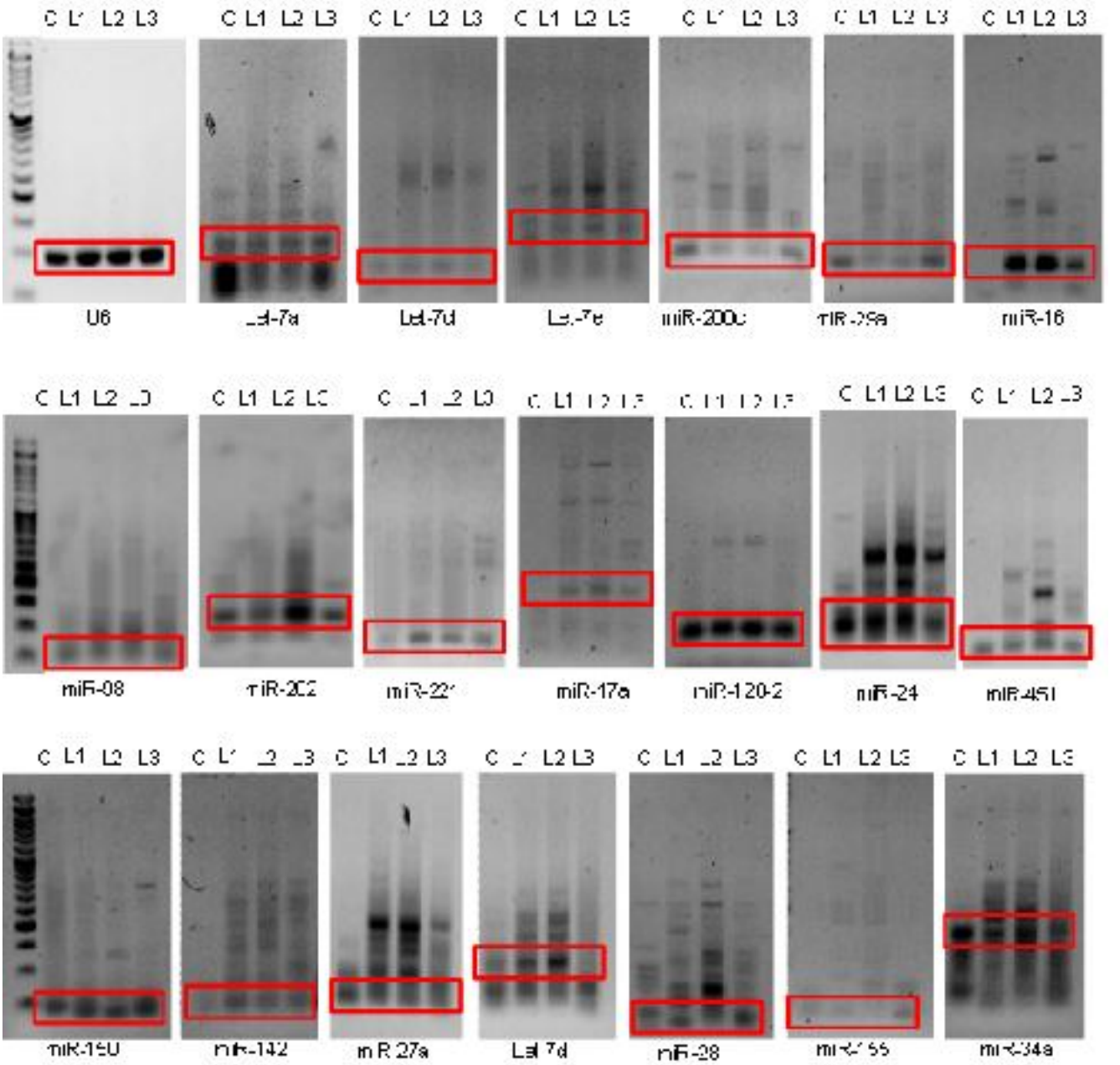


Fig-20: ccf-miRNA profiling of lung cancer samples through conventional PCR with enblocked bands representing the specific miRNA positions.

under observation. While miR-98, miR-200c, and miR-29a were found to be down-regulated , miR-202 and 221 were significantly up-regulated (Fig-20). For the validation of the obtained results, expression profiles of the above-mentioned miRNAs were assessed through real-time qPCR method. Through the real-time qPCR method, the expression profiles of several miRNAs showed noteworthy changes such as downregulation of miR-98, miR-24, miR-34, miR-128, miR-155, miR-16 and miR-29 with 0.33, 0.28, 0.48, 0.058, 0.22, 0.49 and 0.02 fold change respectively (Fig- 21). B[a]P treatment of the lymphocytes resulted in substantial alteration in the expression profiles of Let-7e, miR-98, and miR-202. Upregulation of expression miR-16, miR-27 and miR155 down-regulated expression was observed (Fig. 22 & 25). ANT

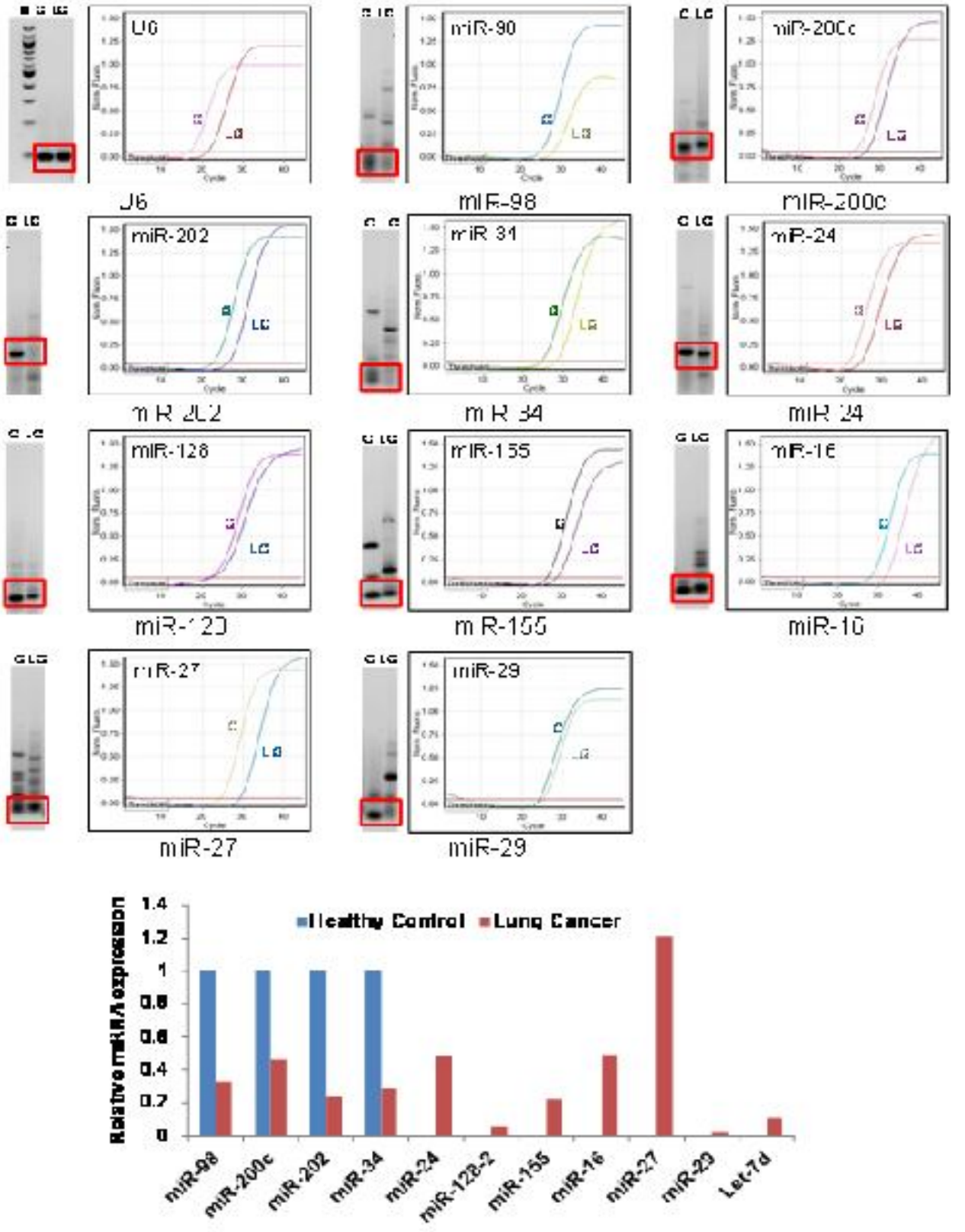


Fig-21: ccf-miRNA profiling in lung cancer samples through quantitative one-step PCR method with enblocked bands representing the specific miRNA positions.

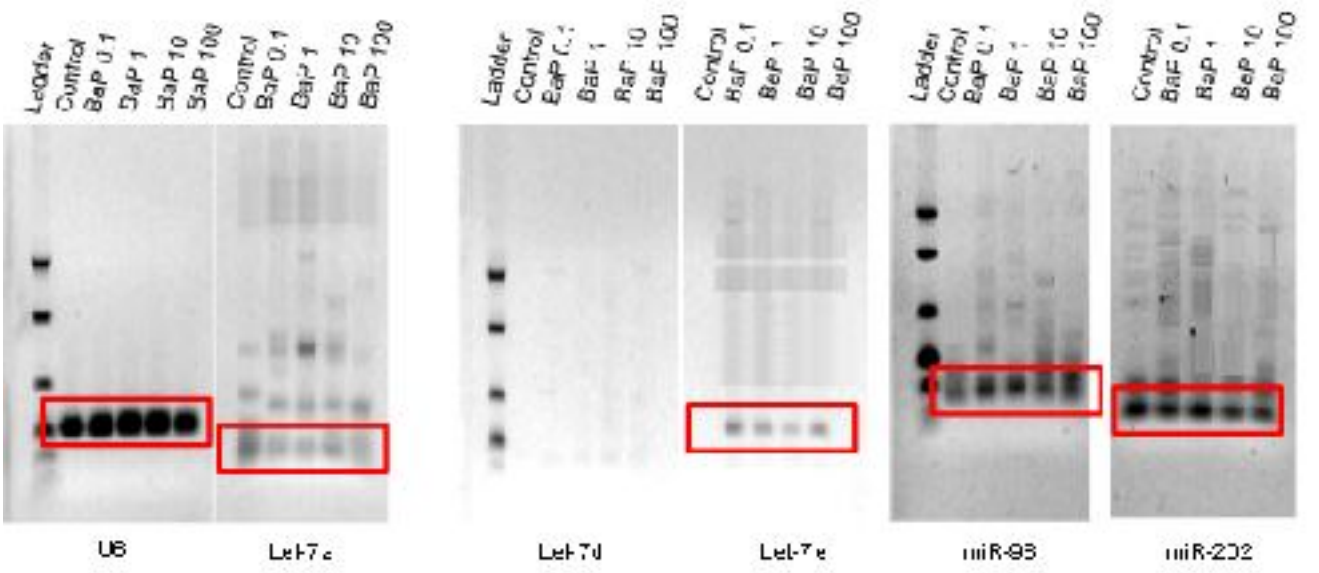


Fig-22: Cellular miRNA profiling in B[a]P treated lymphocytes through conventional PCR method. The enblocked bands represent the specific miRNA positioning

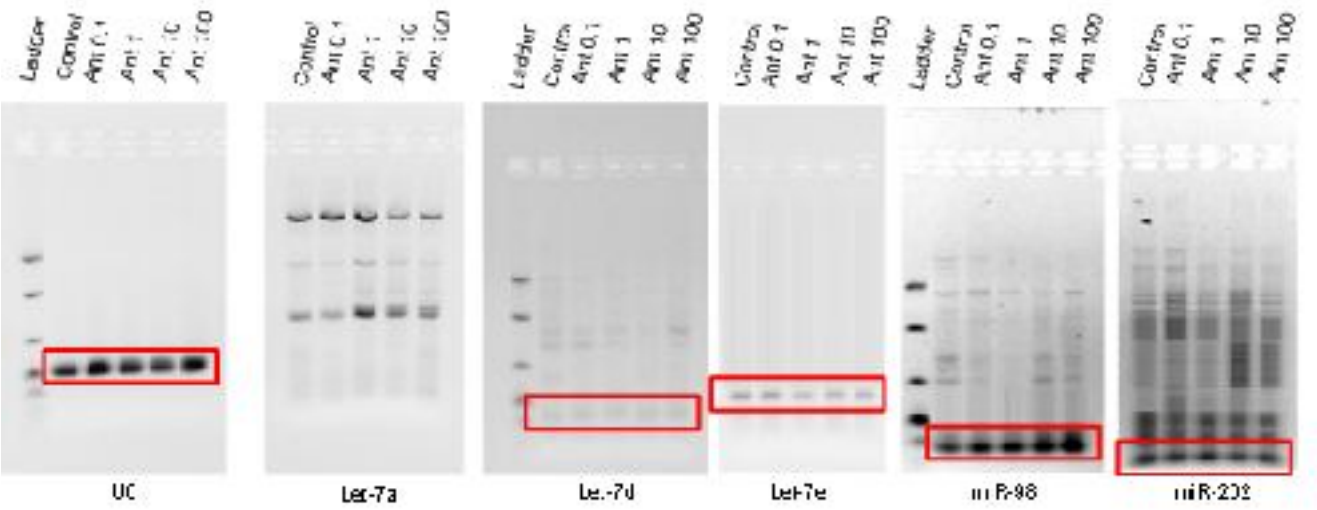


Fig - 23: Cellular miRNA profiling in ANT treated lymphocytes through conventional PCR method. The enblocked bands represent the specific miRNA positioning

treated lymphocytes exhibited increased expression profiling of miR-98 (Fig-23), miR-16, miR27, miR-29, and miR-155 (Fig. 23 & 25). Lymphocytes treated with different concentration of PM (0.1, 2.5, 10) demonstrated a significant increase in the expression of miR-7d along with miR-16, miR-27, and miR-155. A reduction in the expression profile of miR-29 was also observed (Fig. 24 & 25). Early observations from this study suggested a significant alteration in the expression of several miRNAs in the lung cancer patients such as Let-7e, miR-202, miR-98, miR-16, miR27, miR-29, and miR-155, that belong to the tumor

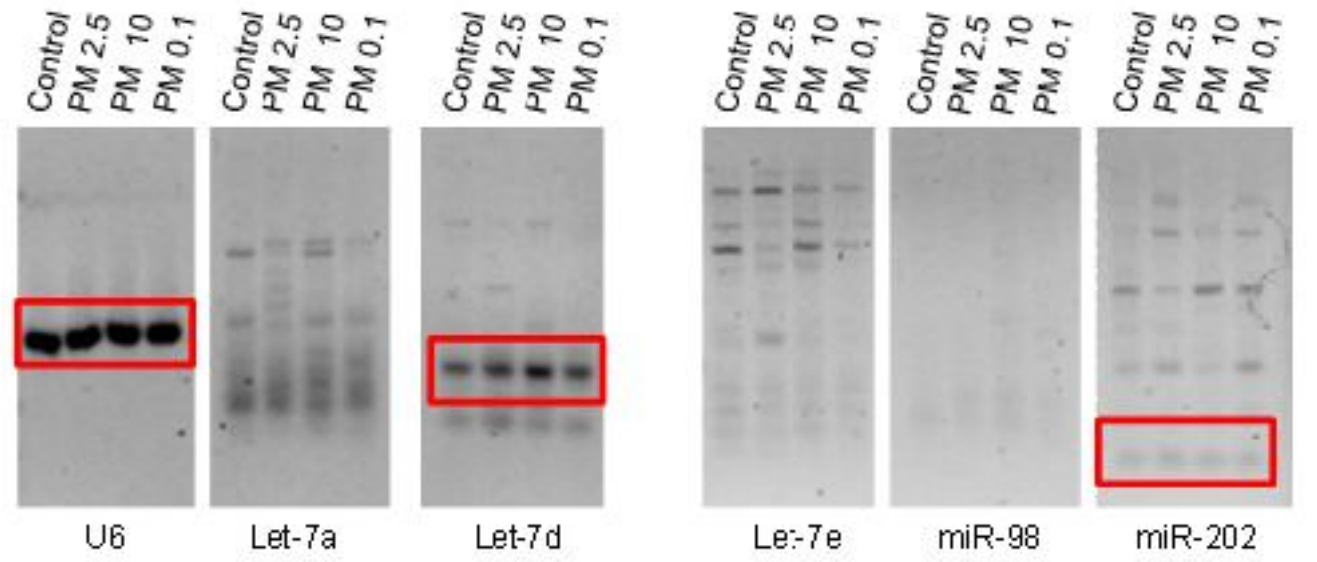


Fig-24: Cellular miRNA profiling in PM-treated lymphocytes through conventional PCR method. The enblocked bands represent the specific miRNA positioning

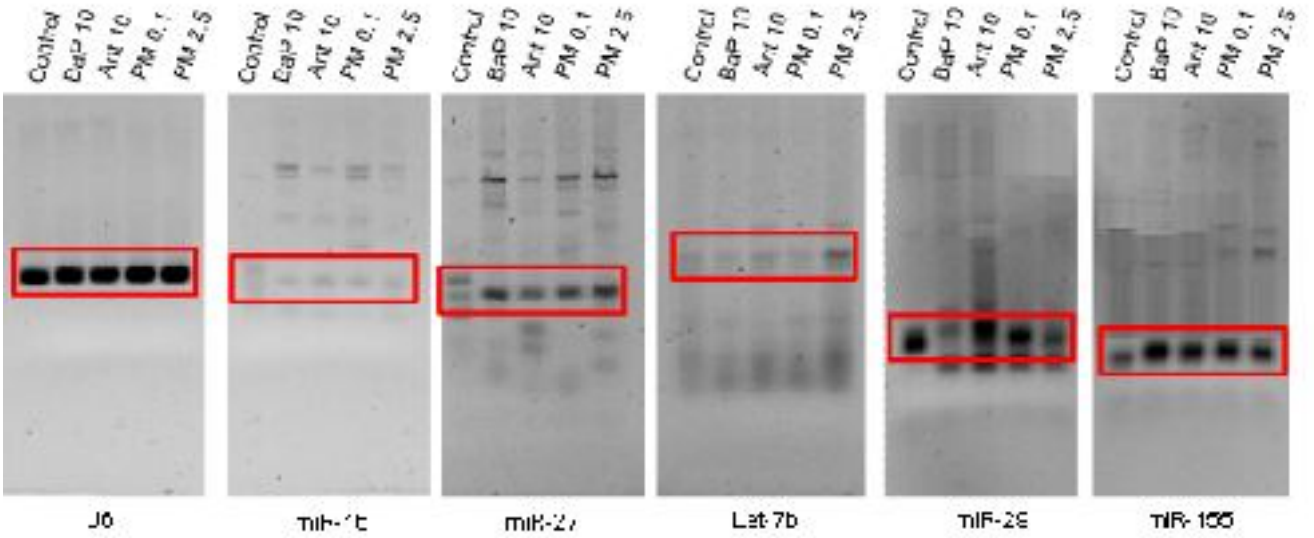


Fig-25: Cellular miRNA profiling in lymphocytes through conventional PCR method following B[a]P, ANT and PM treatment. The enblocked bands represent the specific miRNA positioning

suppressor miRNAs and are involved in the regulation of EMT signalling pathways. This altered expression suggested a direct relationship with the regulation of apoptotic pathway, cell proliferation, migration and invasion. Studies are in progress.

PROJECT 8

Biochemical basis of pathogenesis of chronic obstructive pulmonary disease

Investigators : Dr. K.C. Pandey (PI), Dr. Sajal De, Dr. R. Galgalekar, Dr. P. K. Mishra, Dr. Y. D. Sabde (NIREH, Bhopal); Prof. A. K. Saxena (JNU, Delhi)

Duration : 3 Years (December 2016 - November 2019)

Funding : ICMR (IM)

Chronic obstructive pulmonary disease (COPD) is enhanced inflammatory response of airways as well as lung parenchyma to harmful particles or gases. It is generally associated with progressive destruction of airways and lung parenchyma. The inflammation causes structural damage, narrowing of airways, and the destruction of lung parenchyma (emphysema). The airflow obstruction in COPD is not fully reversible and usually progressive. COPD broadly encompasses two pathologic entities i.e., emphysema and chronic bronchitis. Various factors play an important role in the development and progression of COPD, like imbalance of proteases, environmental and genetic factors and oxidative stress. In this study we are aiming at identifying unusual proteases and analyzing differential protein expression in stable COPD patients vis-a-vis healthy individuals.

Blood samples (3 ml) were collected from 30 stable COPD patients and 15 healthy persons under aseptic conditions. After serum seperation, Indirect Enzyme-Linked Immunosorbent Assays were performed for estimating levels of serum proteases/biomarkers. Obtained values were plotted and analyzed using PRIZM software. All estimations were carried out in duplicates including controls. Average values were used for statistical graphical presentation.

8.1 Identification of unusual proteases

For this objective, samples from 2 chronic kidney disease (CKD) patients were also included (as negative control) in addition to samples from 30 stable COPD patients and 15 healthy persons as mentioned above.The expression level of caspases-3, a cysteine protease enzyme, was found uniformly distributed in patients and healthy individuals (Fig-26)

We estimated the concentration of the enzyme Serum Dipeptidyl Peptidase IV (DPP IV), a serine exopeptidase that catalyses the release of the N-terminal dipeptide, in COPD patients. We did the quantitative analysis of DPP IV, using specific detection kit. The estimation of secreted DPP IV was done using a standard curve (Fig-27). The concentrations of DPP IV was found in the range of 1200-1800 ng/ml in healthy person. However, in 9 COPD patients the concentrations were in between 1200-1500 ng/ ml, and in 11 patients the concentration ranged from 900-1100 ng/ml.

We further estimated the concentration of Matrix Metallo Protease 9 (MMP-9), using specific antibody against this enzyme.The levels of this enzyme was high in only three COPD patients as compared to healthy subjects (Fig-28).

We found the concentrations of MMP-2 (Fig-29A) and Neutrophil Elastase, a serine protease, (Fig-29B) higher in COPD patients compared to healthy subjects.

We also investigated the protease activity by qualitative zymography in limited number of COPD

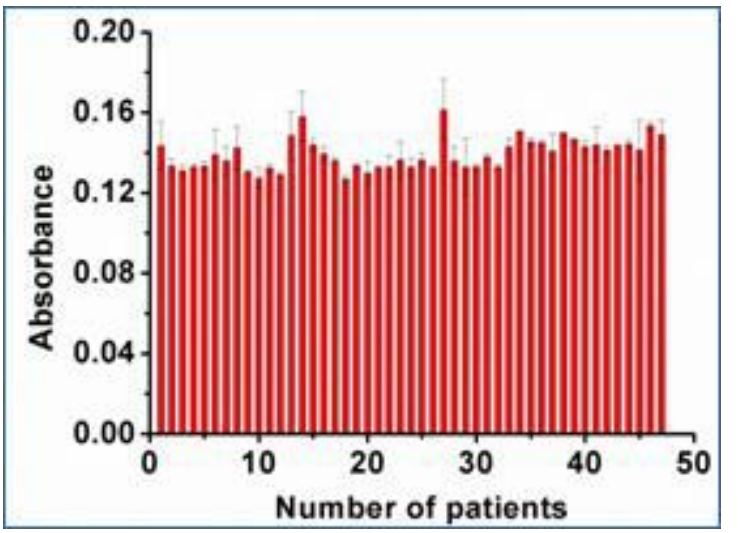


Fig-26:A bar graph showing the expression profile of caspase-3 in healthy persons (bar 1 to 15), stable COPD patients (bar 16 to 45) and CKD patients as negative control (bar 46 and 47)

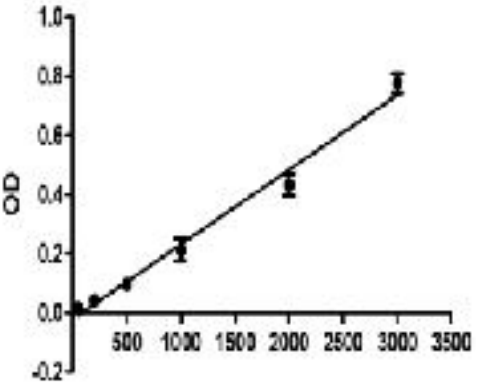


Fig-27: Standard curve showing the conc. of DPP IV in ng/ ml (x axis) and OD values (y axis)

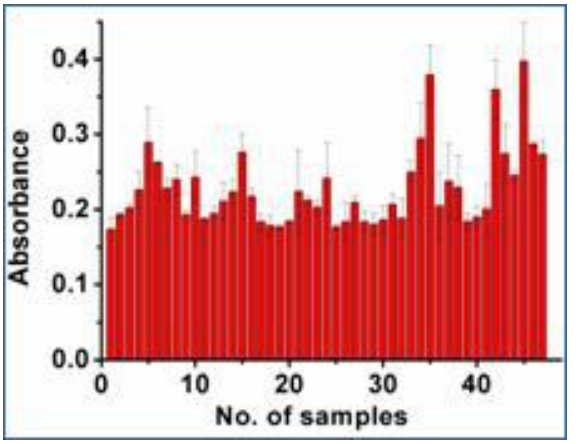


Fig-28: A bar graph showing the expression profile of MMP-9 in healthy persons (bar 1 to 15), stable COPD patients (bar 16 to 45) and CKD patients as negative control (bar 46 and 47)

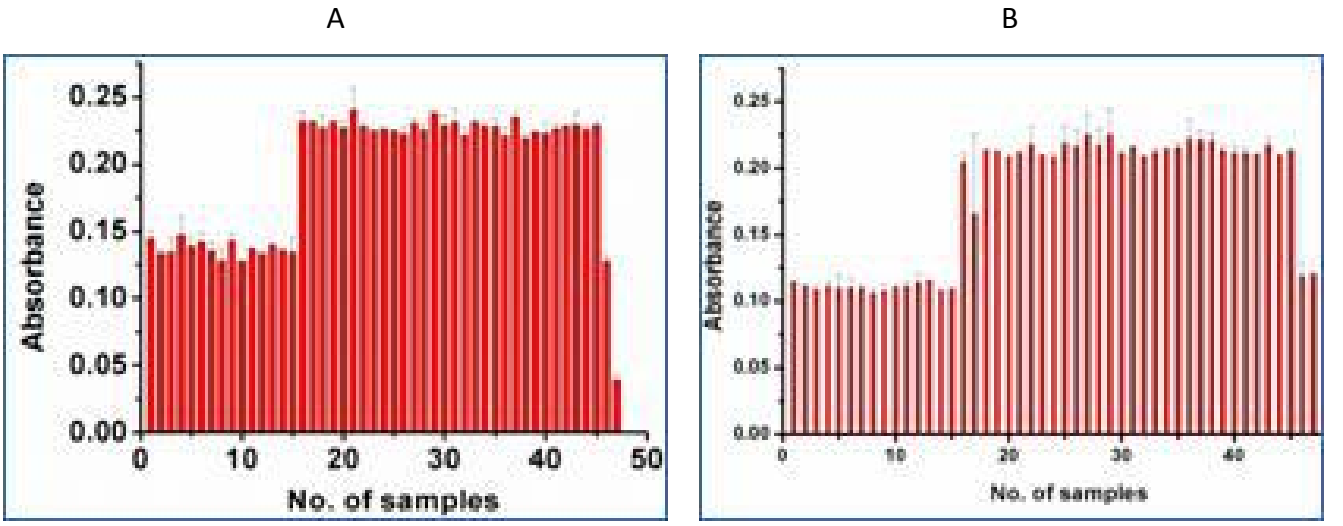


Fig -29:Bar graphs showing the expression profiles of MMP-2 (A) and neutrophil elastase (B) in healthy persons (bar 1 to 15), stable COPD patients (bar 16 to 45) and CKD patients as negative control (bar 46 and 47)

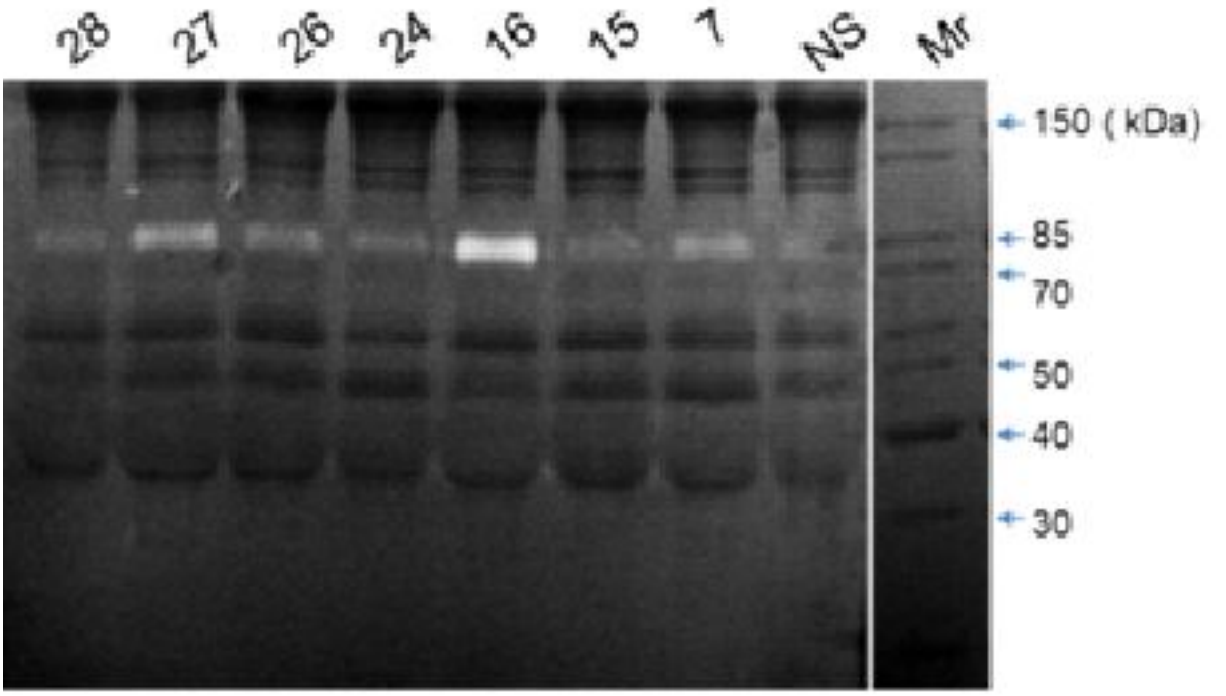


Fig- 30: Zymography analysis showinghigher expression of matrix mettloprotease-2 (MM-2, 82 Kda) in COPD sample nos. 16, 27 as compared to normal serum

patients' and foundhigher MMP-2 activity in sample no. 27 and sample no. 16 (Fig-30). To confirm that 82 Kda band is MM-2, we processed the sample for mass spectrophotometry.

8.2 Differential protein expression

Serum of limited number of COPD patients was analyzed for differential protein expression analysis. Large SDS page gel electrophoresis was run to get better resolution of serum samples (Fig-31). Different spots appeared as higher expression compared to healthy serum samples were processed for Mass-Spectrophotometry in Delhi University for detail characterization of proteins. Detail analysis of proteins is under progress.

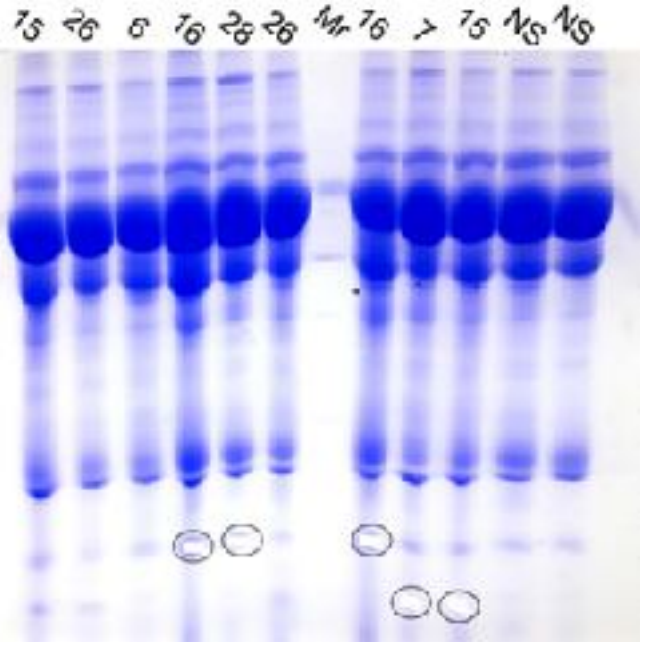


Fig-31: A SDS gel picture with COPD patients samples (samples no. 6,7,15,16,26,28) for differential protein expression compared to normal sera

PROJECT 9

Characterization of prevailing chronic respiratory morbidities among severely gas exposed population

Investigators : Dr. Sajal De (PI), Dr. Anil Prakash, Dr. N. Banerjee, Dr. R. Galgalekar, Dr. K. K. Soni

Duration : 2 Years (February 2018 - January 2020)

Funding : ICMR (IM)

Respiratory morbidities have been reported to be the most common health problem among survivors of the Bhopal gas disaster. However, the prevalence of various respiratory disorders such as bronchial asthma, chronic bronchitis etc., and the lung function of gas exposed survivors has not been systematically evaluated for the last two decades. The present study is aiming at characterizing the prevailing respiratory morbidities among severely exposed cohort of the ongoing Long term population based epidemiological study of NIREH using validated INSEARCH questionnaire, and thereafter evaluating the lung function by spirometry and Forced Oscillation Technique. It is expected that this study will bring out the prevalence and pattern of lung function abnormalities, especially small airway functions, among severely gas exposed survivors to guide appropriate management.

It is proposed to include approximately 4,000 severely exposed individuals who were covered under 54th round of survey (2017) of the Long term population based epidemiological study of NIREH. The recruitment has been initiated and so far 128 individuals have been enrolled.

Post-graduate students' dissertation and summer training programme

ICMR-NIREH continued the Post-graduate students' dissertation and short-term summer training programme in Environmental Biotechnology as part of the human resources development initiative of the institute. Five students completed the 6-months dissertation course (January to June, 2017).

DISSERTATIONS

1. Epigenetic dimension of oxygen radical injury following exposure to airborne particulate matter : an *in vitro* study

Student: Ms. Anushi Shukla, M.Sc. (Applied Microbiology and Biotechnology), Banasthali Vidyapith, Rajasthan

Supervisor: Dr. P. K. Mishra, Sc E

Air pollution is a grievous threat to the human population. Long term exposure to air pollution triggers premature death and diverse health problems. Indisputably anthropogenic activities deteriorate and negatively impact the air quality. Air pollutants such as particulate matter (PM) are hazardous to human health as they possess the potential to invade into the human airway and lungs, thus, resulting in inflammation and onset of various diseases such as cancer, lung ailments and cardiac afflictions. PM has been categorised as a Group 1 carcinogen by IARC (International Agency for Research on Cancer). The size and composition of PM are incriminating attributes for analyzing their biological effects. The ability of PM to induce various toxicogenomic effects are attributed to their pro-oxidant nature which is contributed by the presence of organic fraction of compounds such as Polycyclic Aromatic Hydrocarbons (PAHs), quinones along with the water soluble fraction of metals. These components of PM possess the capability to cause damage by means of generating free radical species (ROS). The over expression of ROS in any system to levels much higher than the system's limit results in a condition of oxidative stress where the system is unable to neutralize or eliminate these elevated ROS levels.

Excessive generation of oxidative stress leads to proteins and lipids oxidation, along with other variations in their structure and functions while the major impact is exhibited on the DNA which undergoes alteration resulting in sporadic mutation. The profusion of ROS triggers activation of various redox-sensitive mechanisms, thus, generating responses which might prove fatal to the cells. PM fosters a condition of redox imbalance consequentially leading to oxidative burst that further alters molecular mechanisms of cellular metabolism and cell functioning besides inducing genetic variations. Apart from these alterations the conjured redox imbalance might also introduce epigenetic variations. These generated ROS effectuates various alterations in the epigenomics such as hypomethylation or hypermethylation of CpG sites of DNA causing transfiguration in the DNA methylation patterns, modifications occurring in the histone proteins, deregulation of miRNA expression and alterations occurring in the nucleosomal positioning on exposure to PM. The reactive oxygen species generated

through PM exposure leads to impairments such as DNA damage due to oxidative stress, nucleosomal release corresponding with cell death along with imparting noxious aberrations in the mitochondria that are mediated by enzymes such as caspase 3 or through membrane depolarization ultimately leading to the apoptotic fate of the affected cell. This study comprehends the repercussions of PM induced oxygen radical injury and aims to determine the mechanistic attributed for instigating various epigenetic modifications and mitochondria associated cytotoxic impairments.

In this study PM were analyzed using an array of techniques incorporating isolation and quantification of DNA, RNA and protein from the cultured lymphocyte cells and semi quantitative methods adapted for analysis. The experimental design included analysis of parameters which determine the impact of ROS generated as a consequence of PM exposure. To study epigenetic modifications DNA methylation, miRNA profiling along with DNMT expression analysis were done. The variations were further examined under two fields which included alteration in the mitochondrial integrity and inflammation which were occurring due to PM exposure, thus, resulting in apoptosis or cell death. The PM samples were categorised on the basis of their aerodynamic diameter into PM 0.1 (ultrafine particulate matter), PM 2.5 (fine particulate matter) and PM 10 (coarse particulate matter).

The study demonstrated (Fig 32-37) higher generation of ROS and higher DNA damage within the cells when cells were exposed to PM 0.1 as compared to PM 10 thus, proving that PM 0.1 is more genotoxic in nature. The deregulation of miRNA expression and higher levels of DNA methylation confirmed the ability of PM 0.1 in inducing epigenetic alterations as well. The flow cytometric analysis also demonstrated the distinctive ability of PM 0.1 to induce mitochondrial damage and cell apoptosis along with a decrease in mitochondrial copy number. Thus, conclusively PM 0.1 is the most harmful of the three classes selected for analysis as it inherently procures a smaller size and larger surface area allowing it to penetrate deeper into the cells closely followed by PM 2.5 whereas PM 10 subsists as a larger particle and prevail at the superficial levels thus, getting eliminated or restrained from causing various ill effects.

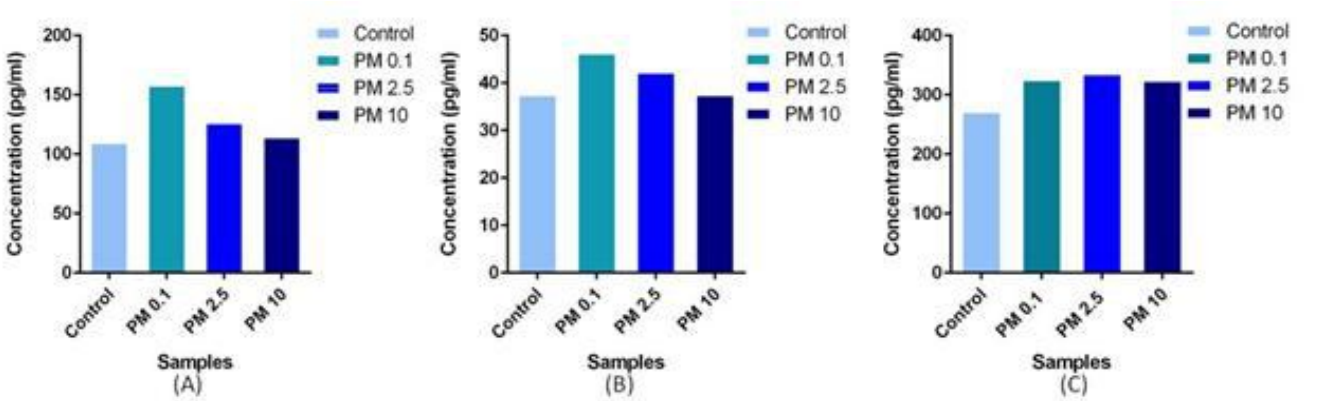


Fig-32: Inflammatory cytokines release on PM exposure (A) TNF-a (B) IFN-g (C) IL-6

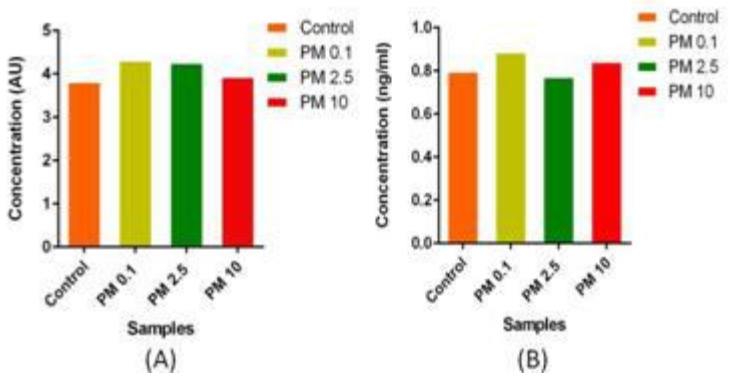


Fig-33: Cytotoxicity and genotoxicity of PM (A) Cell death (B) Oxidative DNA damage

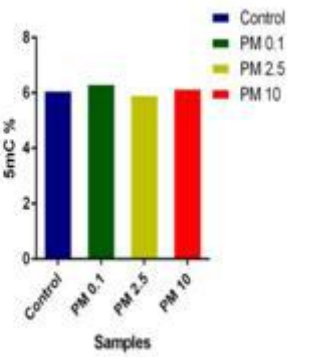


Fig-34: DNA methylation alteration amidst PM exposure

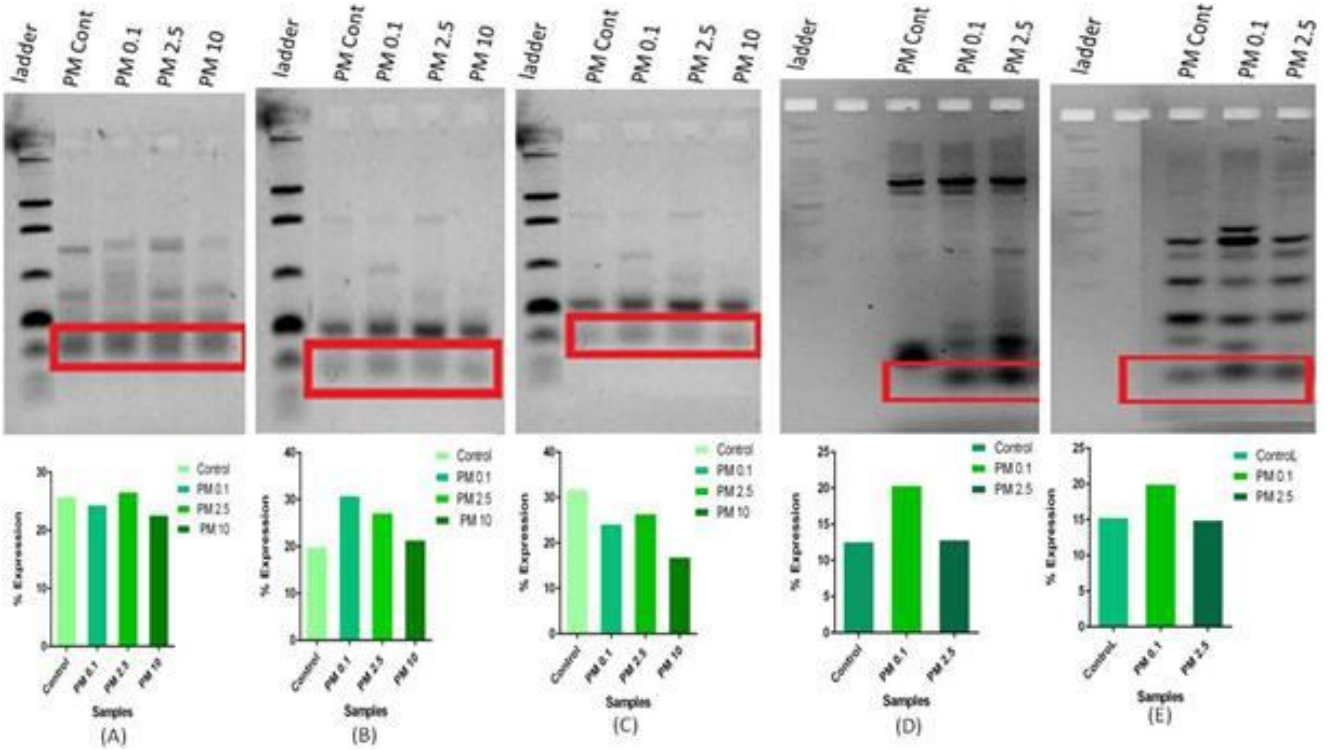


Fig-35: miRNA expression profiling (A) miR let7a (B) miR let 7D (C) miR let 7e (D) miR 29a (E) mir 155

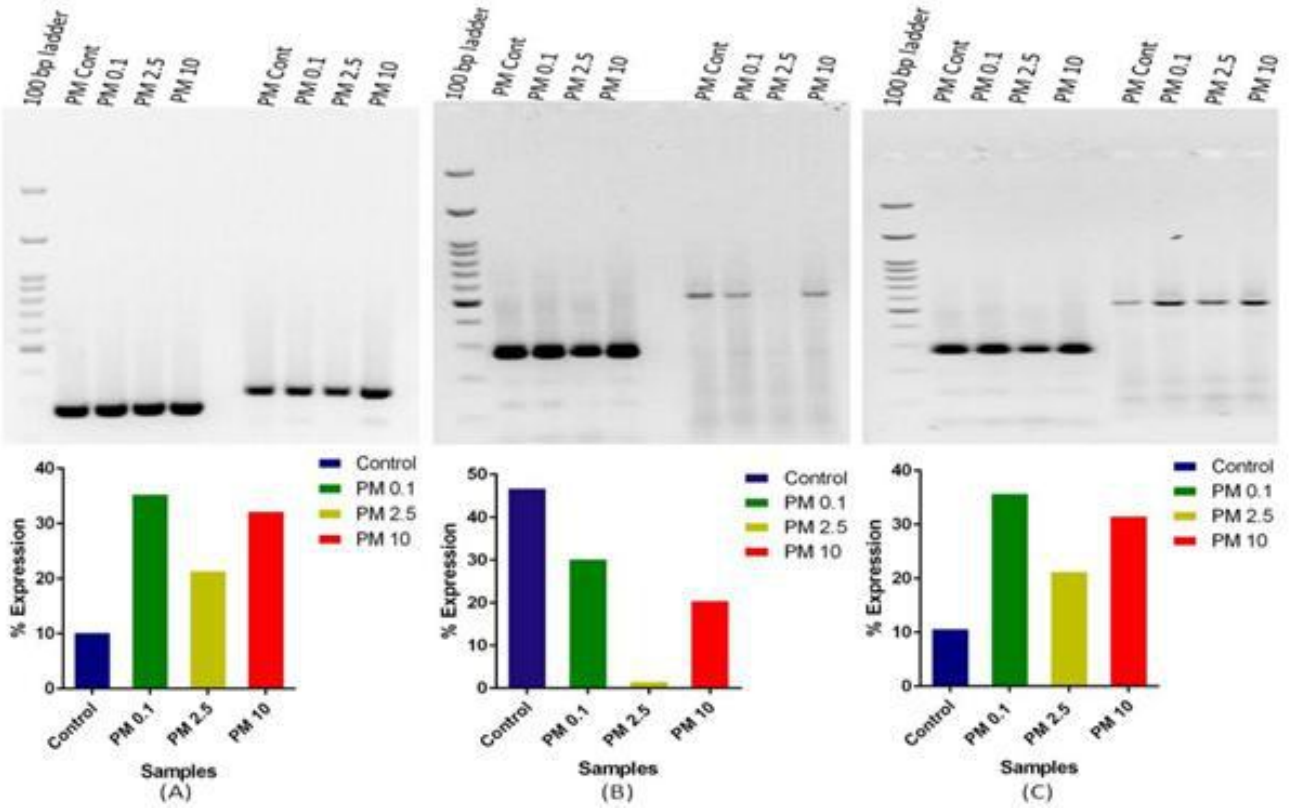


Fig-36: Analysis of DNMT expression against internal control (U6) after PM exposure (A) DNMT 1 (B) DNMT 3a (C) DNMT 3b

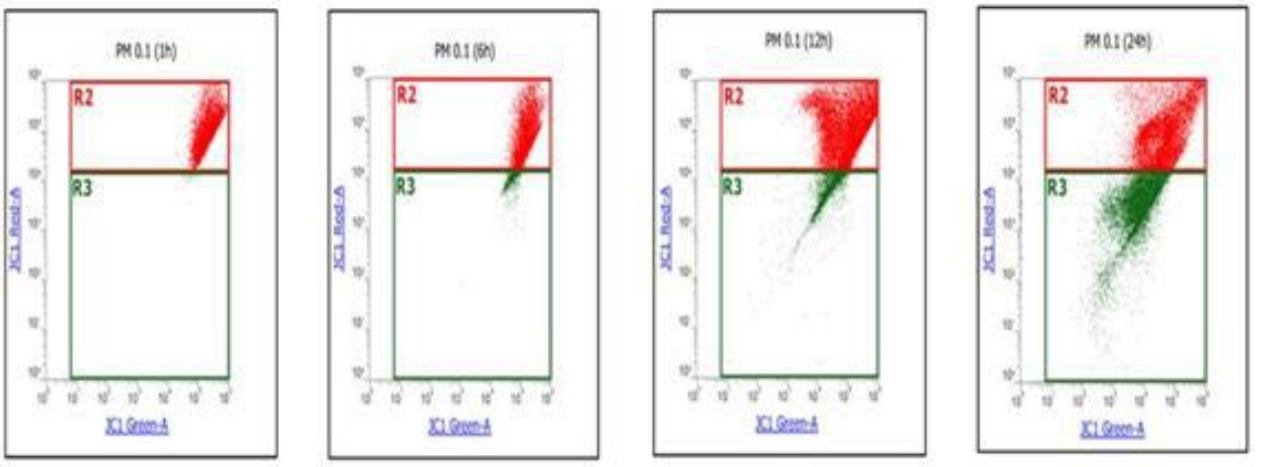


Fig-37: Mitochondrial membrane depolarization induced by PM 0.1

2. Amelioration of particulate matter-induced impairment of mitochondrial-retrograde signaling by nano-engineered flavonoids

Student: Ms. Janhavi Gawande, M.Sc. (Biochemistry), Devi Ahilya University, Indore

Supervisor: Dr. P. K. Mishra, Sc E

According to World Health Organization, air pollution resulted in approximately 7 million premature deaths worldwide in 2012. Clinical and epidemiological studies have mutually established a close link between air pollutant exposure and different respiratory tract disorders including chronic obstructive pulmonary disease, asthma, and cancer of lungs. The environmental pollution can be natural or anthropogenic, carcinogenic and non-carcinogenic caused by pollutants most commonly as particulate matter, benzo(a)pyren, and anthracene that further lead to development of degenerative diseases as a result of genetic and epigenetic modifications through mitochondrial nuclear cross talk in human lymphocytes. Mitochondria, play a precise role in regulation of different cellular functions. Disturbances in mitochondrial metabolism results in augmented oxidative stress that consequently lead to alteration in the mitochondrial-nuclear crosstalk and causes disturbances in epigenetic machinery to further, initiate the process of carcinogenesis. Importantly, cancer cells possess higher levels of inherent reactive oxygen, which significantly declines their antioxidant capability and makes them more vulnerable to oxidative stress. Since, mitochondria are one of the major cellular sources of ROS this misregulation can be controlled by targeting mitochondria through redox active compounds capable of limiting excessive ROS generation.

Natural plant metabolites have drawn attention towards designing novel cancer preventive strategies. Flavonoids, the ubiquitous bioactive phytochemicals derived from plant secondary metabolites through phenyl propanoid pathway, possess the ability to interact with different biological macromolecules. This property of flavonoids has been widely explored for clinical benefits against several environmental and age-associated degenerative pathologies including cancer. Earlier studies have shown that flavonoids own the ability to restrict cell growth and provoke apoptotic response against various types of cancers. The anti-carcinogenic property of flavonoids was mainly attributed to their ability to check aberrant cell cycle regulation, maintain anti-oxidant defence and restrict reactive oxygen species (ROS). The active functional groups present in flavonoids counter the elevated oxygen-radicals and chelate transition metal ions to downregulate the redox reactions. Moreover, the maintenance of cellular integrity is tightly regulated by epigenetic mechanisms which underlie cellular differentiation and homeostasis. Interference in any of these activities, due to oxygen-radical injury may trigger the process of oncogenic transformation. It is also suggested that oxidative stress induced disturbances in epigenetic machinery, broadly affects vital transcriptional processes and may result in abnormal cellular homeostasis and uncontrolled proliferation. Importantly, cancer cells are known to possess higher levels of ROS along with a weaken antioxidant defence system and are more vulnerable to oxidative stress. Mitochondrion being the sole source of electron transport chain is considered as a major contributor for this increased oxidative stress. It has been recently shown that mitochondrial oxidative stress induced deregulation of epigenetic machinery initiate the process of carcinogenesis. Thus, designing strategies to actively target mitochondria and modulate ROS levels may certainly help to maintain redox imbalance and their resultant effects. In this regard, utilizing natural bioactive compounds like flavonoids may be an appropriate option. However, the less bioavailability of dietary

flavonoids restricts their broader therapeutic applications. This is mainly because our body recognizes flavonoids as other xenobiotic compounds like drugs and toxins and removes them through involvement of gastrointestinal tract. These compounds are initially metabolized (glucuronidation sulfation and methylation) in small intestine followed by their removal in liver. Therefore, the therapeutic outcome of flavonoids is limited, which is due to reduced bioavailability as a result of limited solubility, poor permeability and pre-systematic metabolic effect. The other mechanisms involved in limiting the application of flavonoids includes metabolism of the administered flavonoids by gut microflora, its absorption across the intestinal wall, active efflux, and also susceptibility to modification by environmental factors such as temperature, pH and light. Thus making a nano-carrier based system for the mitochondrial targeting would offer a suitable strategy. In the present work, the protective ability of mitochondria-induced-epigenetic modification potential of a SLNP encapsulated flavonoid fraction isolated from Selaginella bryopteris (Sanjeevani) was assessed.

We carried out a set of in vitro studies to catalogue the epigenetic protective mechanisms of the encapsulated fraction (NP.SB) through a mitochondrial-targeted therapeutic strategy. The results of this study (Fig 38 - 42) demonstrated that the mito-protective activity of NP.SB is dose-dependent when tested in human lymphocytes following exposure to air-borne particulate matter and polycyclic aromatic hydrocarbons, a known and potential source of environmental carcinogens. Smaller size, rapid internalization, faster mobility and site specific delivery conferred significant cancer protection in cultured cells. Notably, this encapsulated flavonoid supplementation prevented aberrant regulation of miRNA expression profile, DNA methylation and histone modifications following mitochondrial oxidative stress-induced aberrant epigenetic modifications.

The results conclusively demonstrated that flavonoids could be a possible alternative of conventional chemopreventive agents with reduced associated toxicities. Nano engineering of flavonoids significantly increased their bio-availability and reduced the induced toxicity evidencing effective mitochondrial targetability, thereby maintaining the normal mitochondrial function and epigenomic integrity and thus offering attractive opportunities for the effective, safe and targeted delivery of flavonoids in to the mitochondrial framework reshaping the epigenome particularly in case of cancer therapeutics.

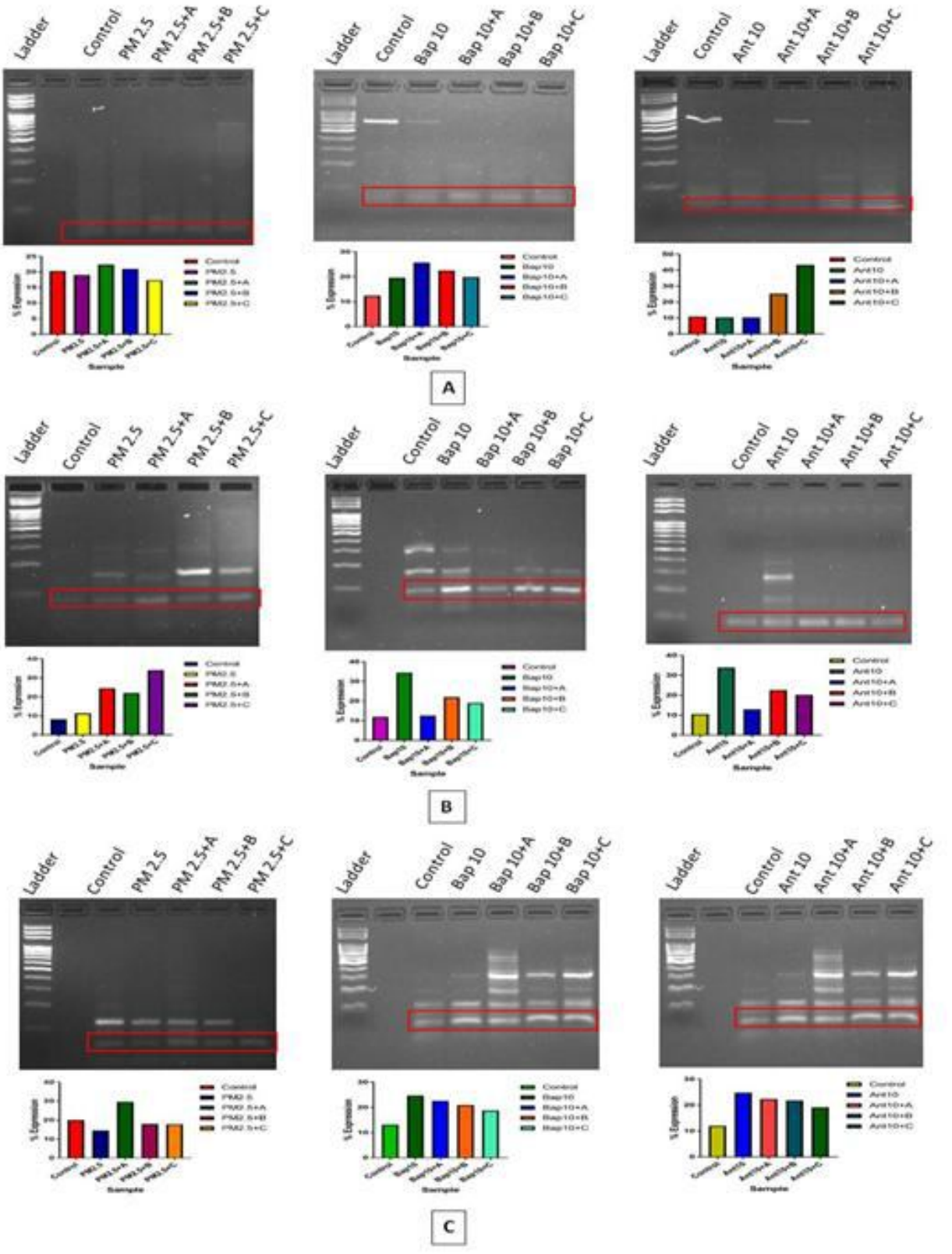


Fig-38: Restoration in miRNA expression profiling in presence of NPSB amid exposure (A) miR 29a (B) miR 155 (C) miR 202

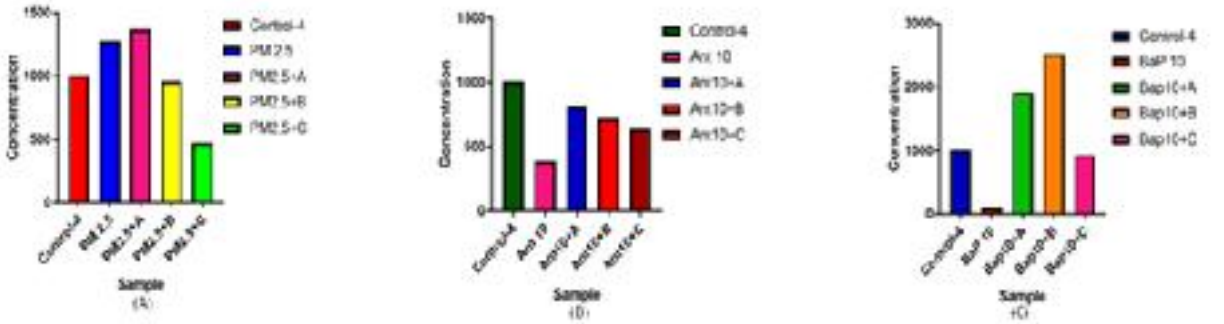


Fig-39: Preventive effects of NP.SB on the mt DNA copy number following exposure of (A)PM 2.5 (B) Ant10 (C) BaP 10

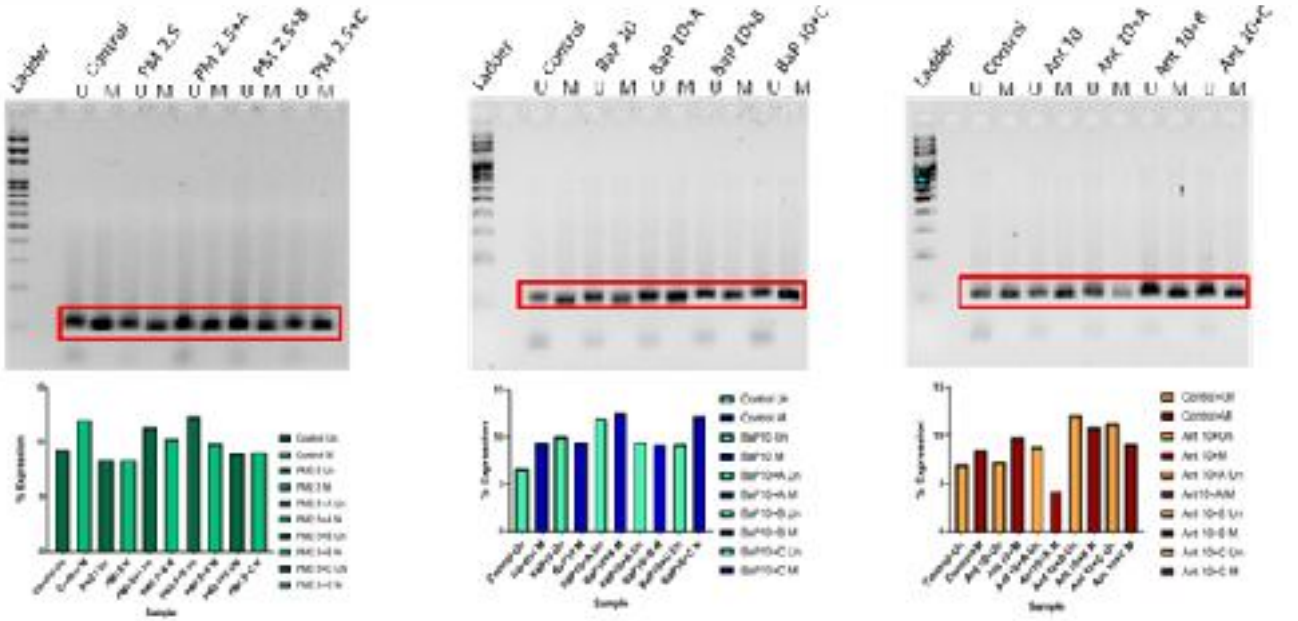


Fig-40: Restoration in methylation patterns in the presence of NP.SB amid exposure (A) PM 2.5 (B) BAP 9C) Ant

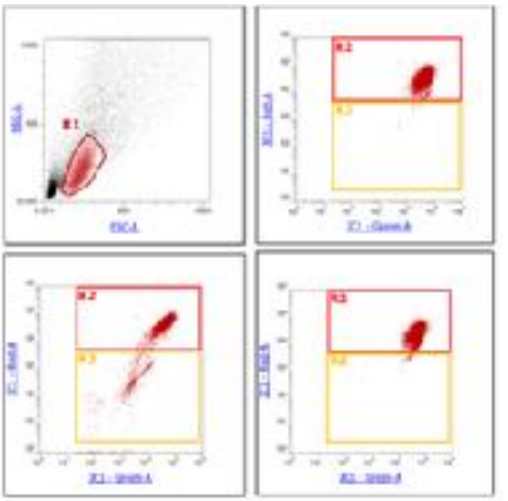


Fig-41: JC-1NP.SB mediated prevention of membrane integrity compromised due toPM 2.5 exposure

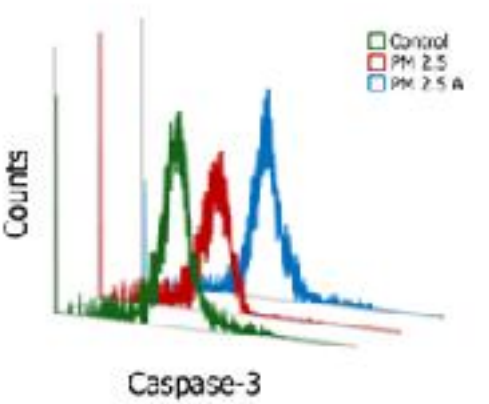


Fig-42: Combating Caspase-3 mediated apoptosis by use of NP.SB

3. An*in vitro* assessment of mitochondrial mediated immunotoxicity by landfill leachate

Student: Ms. Priyal Gupta, M.Sc. (Biotechnology), Institute for Excellence in Higher Education, Bhopal

Supervisor: Dr. P. K. Mishra, Sc E

Generation of municipal solid waste is growing faster than the rate of urbanization which is posing serious threat worldwide. It is estimated that by 2025 there will be a generation of 1.42 kg of waste per person per day by about 4.3 billion urban residents making management of solid waste management a huge problem. Due to ease and economic advantages land filling is the most common strategy for solid waste management in both developing as well as developed countries. Unlined sanitary landfills used for solid waste management in majority of developing countries like India have been responsible for the discharge of extensive amount of dangerous and injurious chemicals to the groundwater and the air, by means of leachate and landfill gases, respectively. Due to its composite configuration (incorporating heavy metals, macro-inorganic compounds, xenobiotic compounds), leachate leads to several mechanisms of toxicity in the cell.

Mitochondria are regarded as the primary focus of several toxicants which can affect its functionality leading to alterations in the cellular homeostasis. These environmental stressors can lead to the generation of reactive oxygen species (ROS) in the mitochondria by distorting the electron transport chain. Accumulation of this ROS with time and inability of anti-oxidant system to manage it leads to the oxidative burst. This superoxide anion poses serious threat to several lipids, proteins and DNA within mitochondria itself. mtDNA is highly susceptible to this oxidative stress as it lacks protective histones leading to deregulated coding of several ETC proteins, reduced OXPHOS capacity and increased ROS. However, mitochondria undergo several quality control mechanisms like fusion, fission in order to maintain mitochondrial homeostasis. These alterations also induce a retrograde signaling pathway mediated through mitochondrial ROS as an adaptive response. Accumulated oxidative stress triggers mitochondria to initiate the cell demise mainly in the form of apoptosis. Dysfunctional mitochondria are largely associated with several metabolic disorder, neurodegenerative and cardiovascular diseases. It has also been speculated that mitochondrial constituents may function as damage associated molecular patterns (DAMPs) that could trigger innate immune reactions during pathological conditions. Variety of stress signals like metabolic dysregulation can lead to mtROS, mtDNA release which can alter several NF-κB, MAPKs, and IRF signaling pathways ultimately regulating the expression of several pro-inflammatory cytokines (such as TNF, IL-1β/IL-18), type I interferons (IFNs), chemokines. The main objective of this study was to evaluate the mechanistic role of mitochondria that often triggers the innate immune responses among the cells exposed to landfill leachate generated through municipal landfill sites.

The leachate was prepared from the soil samples collected from the 'Bhanpur khanti', municipal dumping site of Bhopal (Fig- 43). The molecular mechanisms of mitochondrial toxicity induced by the landfill leachate was analysed using several in-vitro experiments which includes several fluorimetric and colorimetric parameters. Studies were conducted to assess both dose-dependent and time-dependent response of the leachate. Results (Fig-44 to 49) indicated the potential of landfill leachate to induce oxidative stress in dose dependent manner which was evaluated using 8-Oxo-2'-deoxyguanosine (8-oxo-

dG), an oxidized derivative of deoxyguanosine used as the potential biomarker of oxidative damage. This oxidative stress poses serious threat to the mitochondria which is clearly demonstrated by the reduction in the mitochondrial DNA copy number. Dysfunctional mitochondria can induce several signalling pathways in order to combat the toxic insults and can trigger cell towards apoptosis which was shown through cell death detection ELISA where landfill leachate induced cell death. This was also substantiated by the parameter incorporating the analysis of the activity of caspase 3 (Fig-48) and mitochondrial membrane depolarization (Fig-49) which showed an increase in the time-dependent manner. Caspase 3 belongs to the cysteinyl aspartate-specific proteases family. Activation of these caspases is largely associated with cell damage. Caspase 3 is an activated death proteases, which is commonly used as the hallmark of apoptosis. Dysfunctional mitochondria are also associated with the release of several inflammatory cytokines which in our study is clearly indicated by the increased release of TNFα, IL-6, IFNϒ on exposure to landfill leachate (Fig-44).

Fig- 43 : Collection of soil samples from Bhanupur landfill area and preparation of leachate in the laboratory

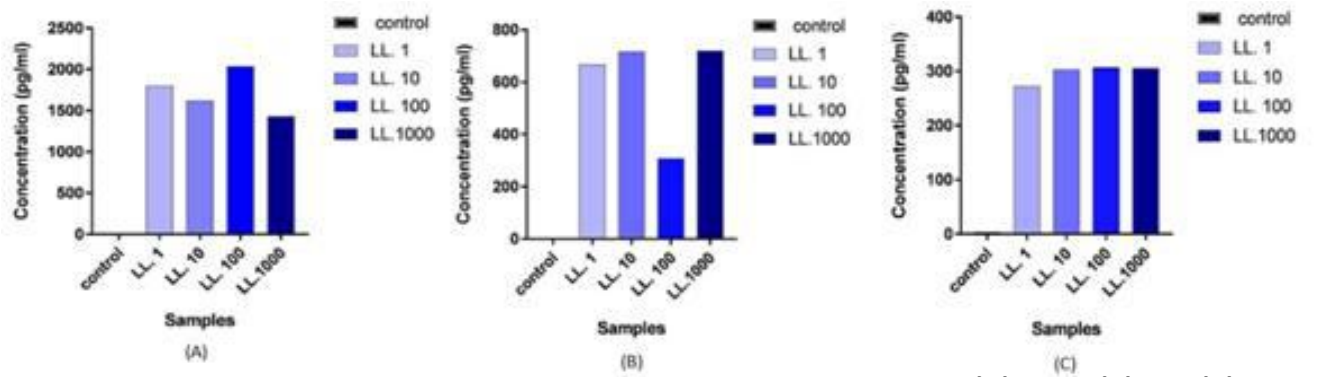
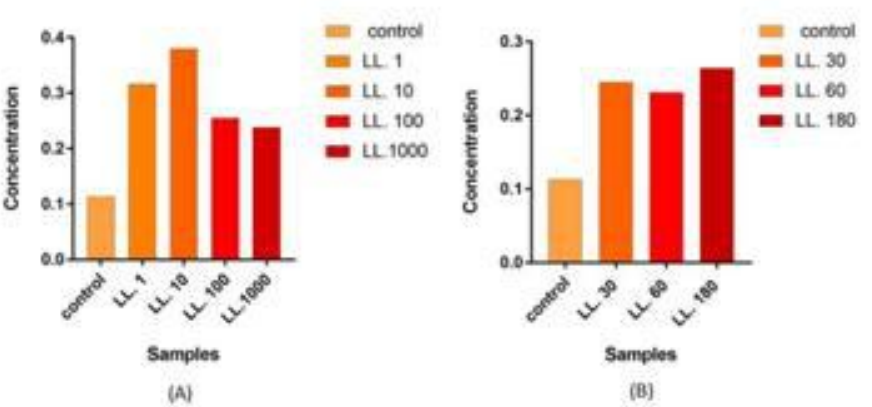


Fig-44: Inflammatory cytokines release during exposure of landfill leachate (A) TNF-a (B) IL-6 (C) IFN-Y



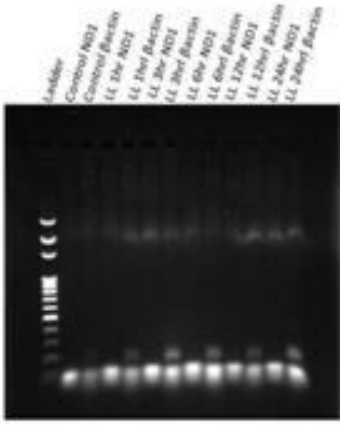


Fig-45:Landfill leachate induced cell death (A) Dose dependent (B) Time dependent

Fig-46: Electrophoresis of ND1 and Beta-Actin for mtDNA damage evaluation

In conclusion the results obtained from the present study provide insights to the comprehension of immunotoxic potential of landfill leachate at the genomic level. The heavy metals, xenobiotic compounds and several organic and inorganic components which makes the constituents of the landfill leachate has the property to get accumulated with time, leading to the extensive damage in cellular machinery. Results demonstrated that mitochondria, the most versatile organelle is highly vulnerable to the landfill leachate leading to the onset of several molecular cascades. Eventually, our results clearly demonstrated that landfill leachate potentially induces oxidative stress via generating enormous amount of ROS, leading to DNA damage, increased level of pro-inflammatory cytokine response via activating several mitochondrial mediated pathways, ultimately leading cell towards relentless cell death. All these evidences suggest that the exposure of landfill leachate via contaminated ground water can severely impact the human health.

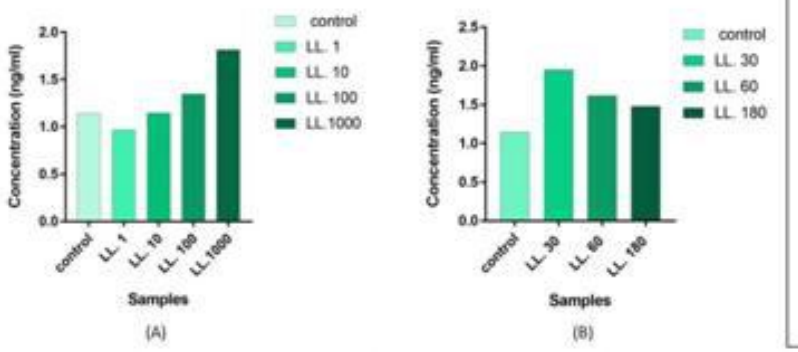


Fig-47: Genotoxic effects of landfill leachate via 8 oxo-dg analysis (A) Dose-dependent (B) time dependent

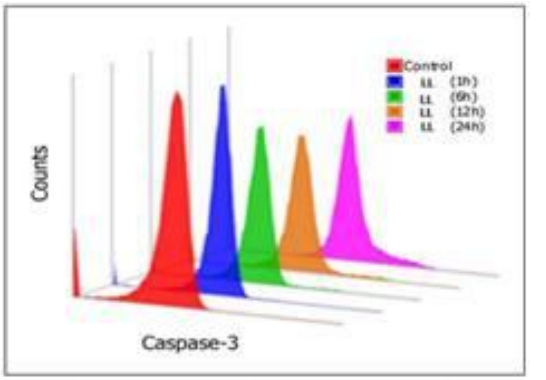


Fig-48: Caspase 3 mediated apoptosis induced by leachate

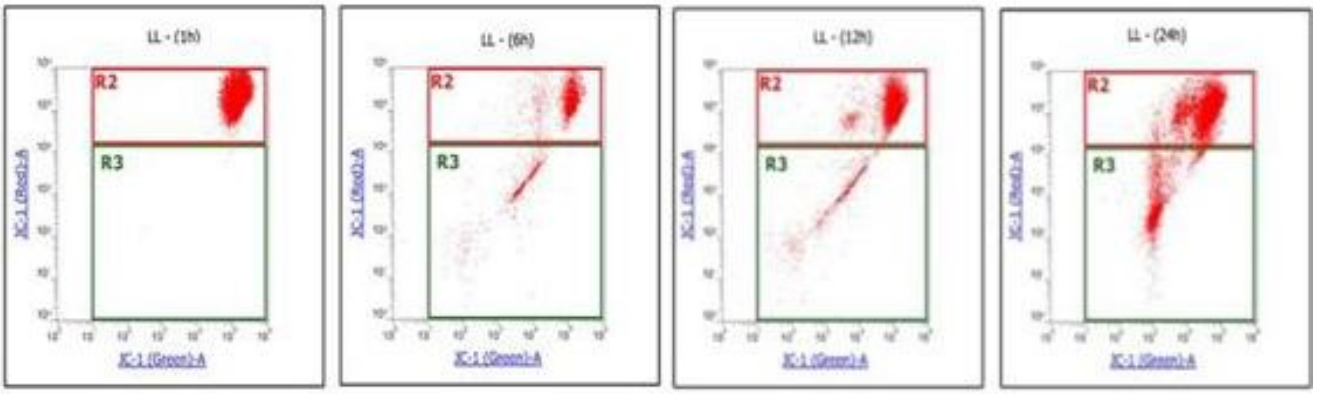


Fig-49: Mitochondrial membrane depolarization by landfill lechate exposure

4. Aberrant regulation of micro RNA expression following exposure to carcinogenic and non carcinogenic polycyclic aromatic hydrocarbons (PAHs)

Student: Mr. Rajat Kumar, M.Sc. (Genetic Engineering), Devi Ahilya University, Indore

Supervisor: Dr. P. K. Mishra, Sc E

Polycyclic Aromatic Hydrocarbons (PAHs), which contribute to majority of air pollution, are a large class of organic compounds that contain carbon and hydrogen with two or more fused aromatic rings. Reports and literatures show that PAHs possess mutagenic, teratogenic and carcinogenic properties. Omnipresent PAHs are known to amend gene expression patterns but the mechanism underlying these alterations are largely unknown. Densely populated country like India is found to have greater levels of PAHs in the environment, mainly in urban areas where vehicular traffic, industrial processes and waste incineration are the major sources. According to the latest reports it has been found that 80% of all registered human health effects are related to roughly 10% of the BaP, DahA, and Flu outflow and an affirmative linear association has been established between these and mortality from malignant tumors, as well as from heart, nervous system, and cerebral vascular diseases. PAHs primarily occur as mixtures of two or more compounds rather than occurring individually in the environment where they are present in both vapor and particle phase. Some PAHs promptly dissipate into the air and tend to last for a considerable length of time as they don't burn easily and travel long distances. The effects of PAHs on human health is difficult to predict as it depends on their intrinsic toxicity and exposure levels.

PAHs are known to trigger three kinds of chemical responses which result in a broad mélange of physical, chemical and toxicological attributes. Inhaling ambient indoor air, drinking water, eating grilled or charred food, soil, dust particles or smoking cigarettes etc. are the routes through which PAHs enter into our body. Skin contact with soil having high levels of PAHs or with heavy oils or other products can lead to the entry of PAH in the body. IQ deficiencies, cognitive developmental deferrals, decreased gestational size, and respiratory effects are connected with in utero PAH exposures. Interaction with hormone system, probable effects on reproduction and potential to depress immune functions are some of the alarming concerns related to PAHs. PAHs also cause oxidative stress by disrupting the antioxidant defense system and disturb cell homeostasis by forming electrophilic metabolites and other reactive oxygen species (ROS) during metabolic activation of PAHs by cytochrome P 450 (CYP) 1A1-catalyzed reactions. Certain PAHs mimic steroid hormones as paradigm of environmental estrogens and endocrine disruption is thought to be a repercussion of human exposure to non-steroidal environmental estrogens. It is speculated that exposure to these contaminants may contribute to exacerbated genetic and epigenetic alterations. MicroRNAs (miRNAs) are key regulators of various genes that play a crucial role in modulating cellular responses towards genetic damages and oxidative stress which are often triggered in presence of these environmental pollutants. The connections between miRNA dysregulation and human ailment have been delineated in virtually all fields of medicine. MiRNAs have a potential to serve as stable non-invasive markers of exposure to environmental pollutants such as PAHs.

The present study investigated the association of PAHs with miRNA in cellular moieties and their potential of being used as an epigenetic marker of exposure. A two stage in vitro study was performed to identify differential expression profiles of cellular miRNAs in cultured human lymphocytes when

exposed to two different classes of PAHs i.e. carcinogenic and non-carcinogenic. The PAHs selected for the study were; Benzo(a)pyrene (BaP) which is a carcinogenic PAH and Anthracene (Ant) which is a non-carcinogenic PAH. MiRNA profiling was done by using pri miRNA specific PCRs and densitometric analysis of their expression levels in various cell populations which were exposed to different concentrations of BaP and Ant. The miRNA panel used in this study were mainly known to be associated with tumor suppressor genes, DNA damage signaling, ROS mediated responses and apoptosis. The miRNAs selected here have previously been reported in many trials conducted for determining potential of miRANs as a biomarker for detection and progression of lung cancer.

Results show (Fig 50 to 58) that when exposed to BaP miRNA expression profile of cultured lymphocytes displayed significant up-regulation of miRNA 155 (Fig-58) which is a known oncomiR while the miRNAs which are tumor suppressors in nature i.e. miR let 7a (Fig-50) & miR let 7e (Fig 52) were significantly downregulated. MiR let 7d (Fig-51) was also upreguated in BaP treated samples due to its highly anti-estrogenic properties. During Ant exposure, miRNAs involved in apoptosis i.e. miR let 7e (Fig-52), miR 16 (Fig-55), miR 27 (Fig-56) and oxidative stress i.e. miR let 7b (Fig-54), miR 29 (Fig-57) were highly upregulated. miR let 7d (Fig-51) was slightly upregulated due to the weak anti-estrogenic nature of Ant. The contrasting nature of miRNAs also helps in testifying a novel mechanism mediating the effects of PAH exposure. Results indicated that Benzo(a)pyrene induced miRNA expression alterations promulgate cells towards a cancerous kismet whereas Anthracene induced miRNA expression alterations doom cells towards an apoptotic fate.

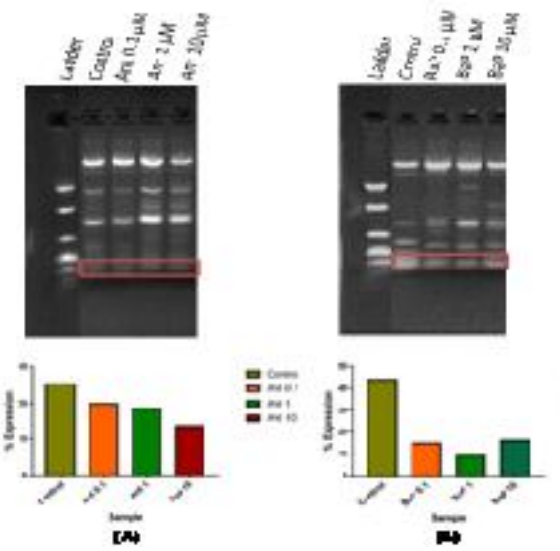


Fig-50: miRlet7a expression (A) Ant exposed cells (B) BaP exposed cells

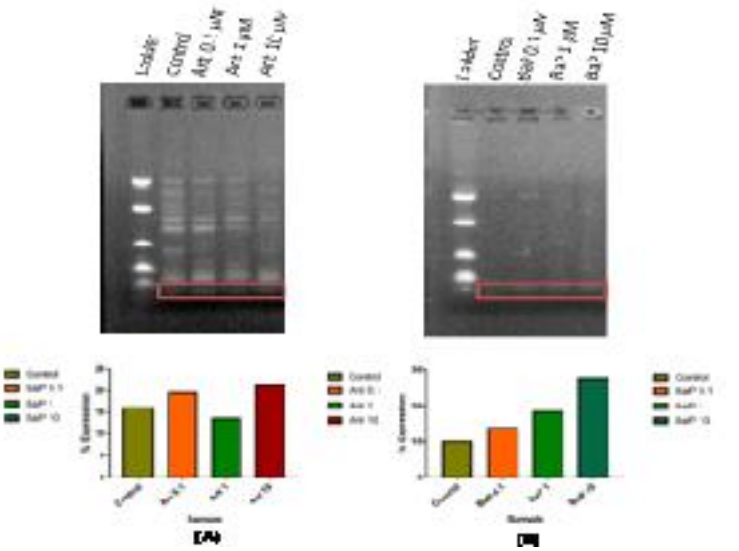


Fig-51: miRlet7d expression (A) Ant exposed cells (B) BaP exposed cells

The present study suggested that miRNAs have a potential to serve as stable non-invasive diagnostic and prognostic biomarker of exposure to environmental pollutants such as PAHs and may help the clinical translation of these epigenetic signatures for early diagnosis, real time monitoring of therapeutic responses and drug resistance. Preparation of biosensors with certain unique physical-chemical-biological interfaces based on these miRNAs can be applied in clinical real samples with high sensitivity and selectivity for assessing effectuation of PAH mediated lung carcinogenesis which can supplement and enhance current procedures for disease recognition and overall survival of patients.

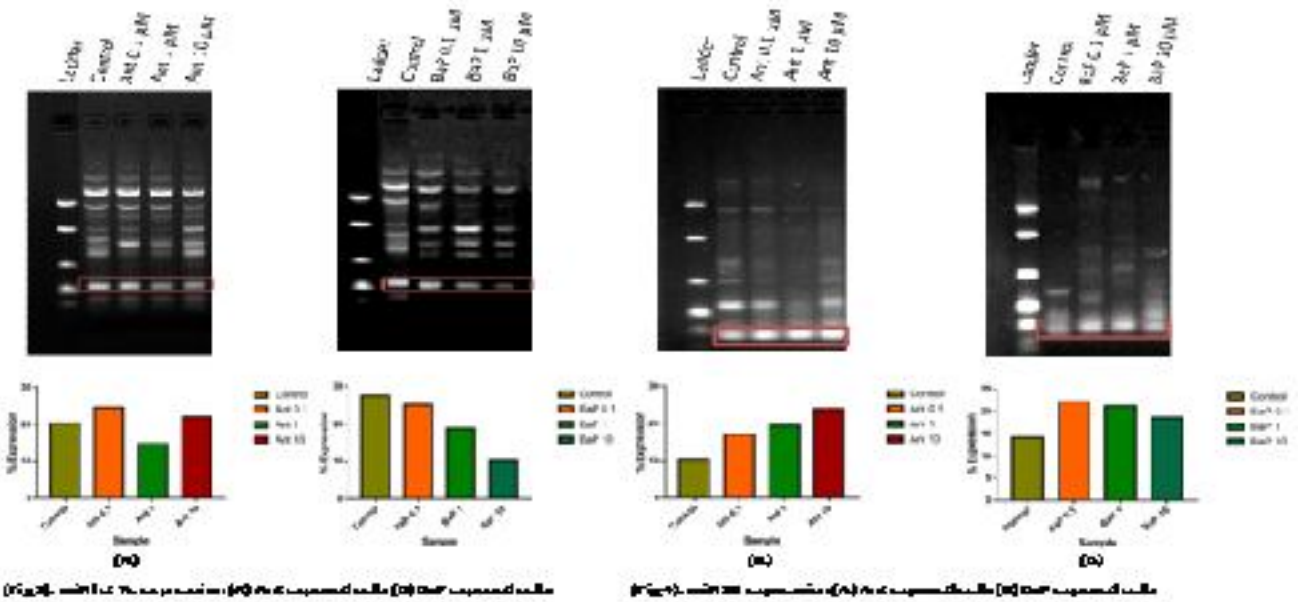


Fig-52: miRlet 7e expression (A) Ant exposed cells (B) BaP exposed cells

Fig-53: miR 98 expression (A) Ant exposed cells (B) BaPosed cells

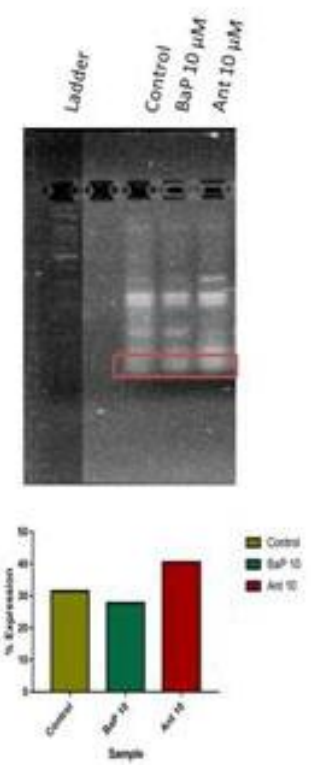


Fig-54: miR let 7b expression in Ant and BaP exposed cells

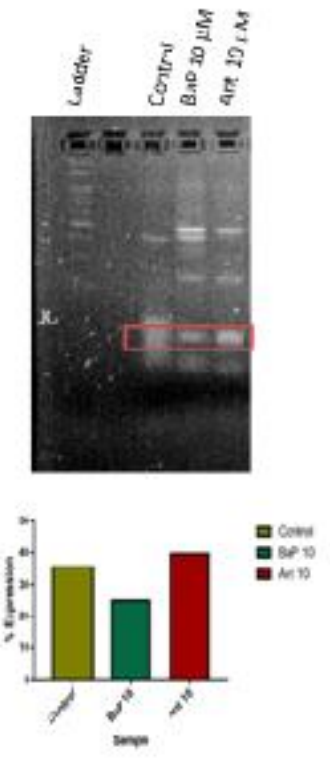


Fig-55: miR 16 expression in Ant and BaP exposed cells

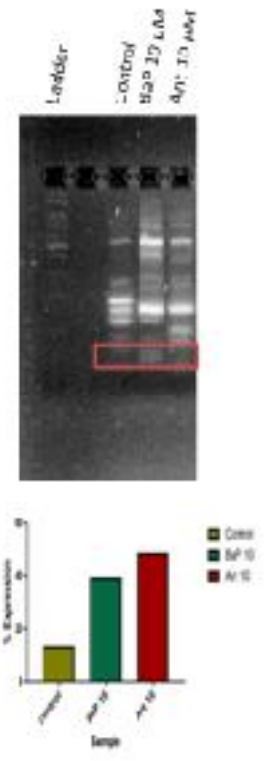


Fig-56: miR 27 expression in Ant and BaP exposed cells

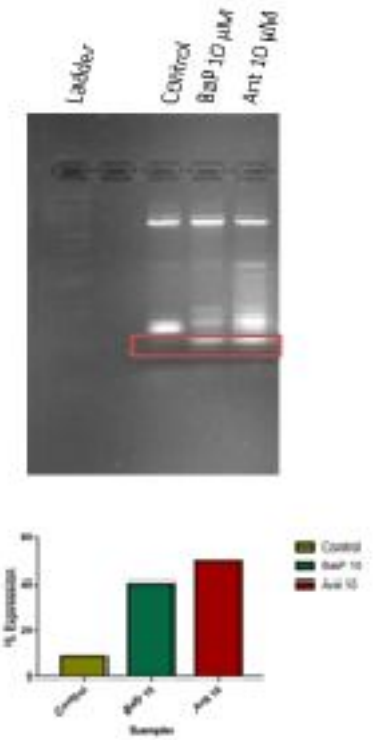


Fig-57:miR 29 expression in Ant and BaP exposed cells

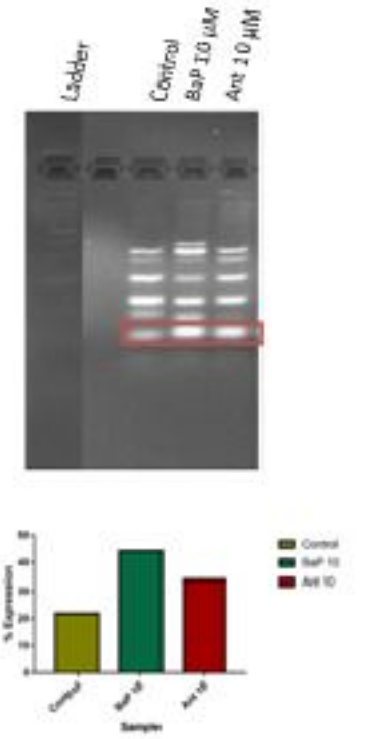


Fig-58: miR 155 expression in Ant and BaP exposed cells

5. To study the cytogenetic damage in chronic kidney patients through micronuclei and chromosomal aberration assay analysis

Student: Ms. Upasna Tomar, M.Sc. (Microbiology), Career College (Affl. BU, Bhopal)

Supervisor: Dr. R. M. Samarth, Asstt Prof, BMHRC

Chronic kidney disease (CKD) is the presence of abnormalityof kidney structure or functionfor >3 months with implications for health. Kidney functions in humans are indicated by Glomerular Filtration Rate (GFR)the value of which should be 120ml/min in a healthy person. According to recent international guidelines CKD is characterized by decreased kidney function(GFR of less than 60 ml/min per 1·73 m^2). Cytogenetic biomarkers are commonly used endpoints in human population studies. Cytogenetic studies have been useful in identifying persistent types of abnormalities related to specific disease. The present study was aimed to study the cytogenetic damage in chronic kidney disease patients through micronuclei and chromosomal aberrations assay analysis.

Peripheral blood (3 ml) was collected from CKD patients (n=10) and normal healthy individuals (n=10) by venepuncture method in a heparin coated vials**.** The standard method was followed for preparation of the chromosomal aberration (CA)assay.Peripheral blood (0.3 ml) was added to 4.5 ml RPMI 1640 medium supplemented with 20% fetal bovine serum and phytohaemagglutinin (PHA) and maintained at 37°C for 72 hrs. The cells were treated with CP (1, 2.5, and 5 µg/ml) for 48 h after initiating the culture. The cells were exposed to colchicine (0.06 µg/mL) 2 h before harvesting. At the end of the incubation, cells were centrifuged at 1200 rpm for 15 min. Then, the cells were treated with 0.075 M KCl (37°C) as the hypotonic solution and methanol: glacial acetic acid (3:1) as the fixative (at room temperature 22°C ± 1°C); fixative treatments were repeated three times. The cells were centrifuged at 1200 rpm for 15 min after each fixative treatment. The staining of the air-dried slides was performed following the standard methods using 5% Giemsa stain for CA. Totally 200 metaphases per individual were evaluatedfor CA and frequency was expressed as percentage (%).

For the analysis of micronuclei (MN) in binucleated lymphocytes, 0.3 mL of fresh whole blood was used to establish the cultures which were incubated for 68 h. To block cytokinesis, cytochalasin-B was added at 44 h of the incubation at a final concentration of 6 µg/mL. After additional 24 h incubation at 37°C, cells were initially harvested by centrifugation at 1200 rpm for 15 min and further processed identically as described for the preparation of CA. The cells were hypotonically treated with 7 ml of cold (4°C) 0.075M KCl to lyse red blood cells and centrifuged immediately 1200 rpm for 8 min. Finally, the slides were stained with 10% Giemsa. In all 5000 binucleated lymphocytes were scored from each concentration for MN frequency, MN frequency expressed as MN/1000 (‰). A total of 1000 cells were scored to calculate the nuclear division index (NDI) using the formula: NDI = ([1 × M1] + [2 × M2] + [3 × M3] + [4 × M4])/N; where M1–M4 represent the number of cells with one to four nuclei and N is the total number of the cells scored.

No significant differencesin mitotic index were observed in CKD and control groups (Table-7).Higher number of chromosomal aberrations such as breaks, fragments, rings and dicentrics were observed in CKD group in comparison to control group. Higher percentage of aberrant cells was observed in CKD group (Table-7; Fig-59). The chromosomal aberrations were significantly higher in CKD males than CKD females. The nuclear division index (NDI) value in CKD group was found to be

2.05±1.39, which was higher than the value of 1.98±1.41 in the control group (Table-8). The values of NDI in males and females of CKD group were higher than the control group. The micronuclei frequency in binucleated cells was significantly higher in CKD group than the control (Table 2; Fig 2) with higher values in females than males in both the groups.

Table-6: Mitotic Index (MI) and Chromosomal aberrations of CKD Vs Control Group

Group	Breaks	Fragments	Rings	Dicentric	Aberrant cells	MI
Control	2.2±0.1	2.4±0.1	-	-	0.42±0.22	5.02±1.93
Male	2.0±1.0	2.1±0.8	-	-	0.50±0.18	5.55±1.27
Female	2.0±0.1	2.0±0.4	-	-	0.40±0.15	4.53±1.35
CKD	5.21±1.3 P<0.001	6.10±1.6 P<0.0001	1.2±0.12 P<0.001	0.8±0.1 P<0.001	7.88±1.6 P<0.001	5.64±1.37
Male	5.10±1.42	6.5±1.92 P<0.001	1.4±0.2 P<0.001	1.0±0.66 P<0.001	7.60±1.84 P<0.001	5.94±2.34
Female	4.70±1.22	5.60±1.86	1.2±0.1	0.08±0.38	6.80±1.64	4.76±1.41

Each value represents Mean ±SE. The student's "t" test was used to make comparison between the groups

Table-7: Nuclear Division Index (NDI) and MN frequency CKD Vs Control Group

GROUP	NDI	MN/1000 (‰)
Control	1.98±1.41	4.21±0.67
Male	1.99±0.12	4.22±0.45
Female	1.88±0.55	4.36±0.68
CKD	2.05±1.39	16.69±2.45 P<0.001
Male	2.08±0.25	14.70±1.64
Female	2.09±0.31	16.62± 1.96

Each value represents Mean ±SE. The student's "t" test was used to make comparison between the groups.

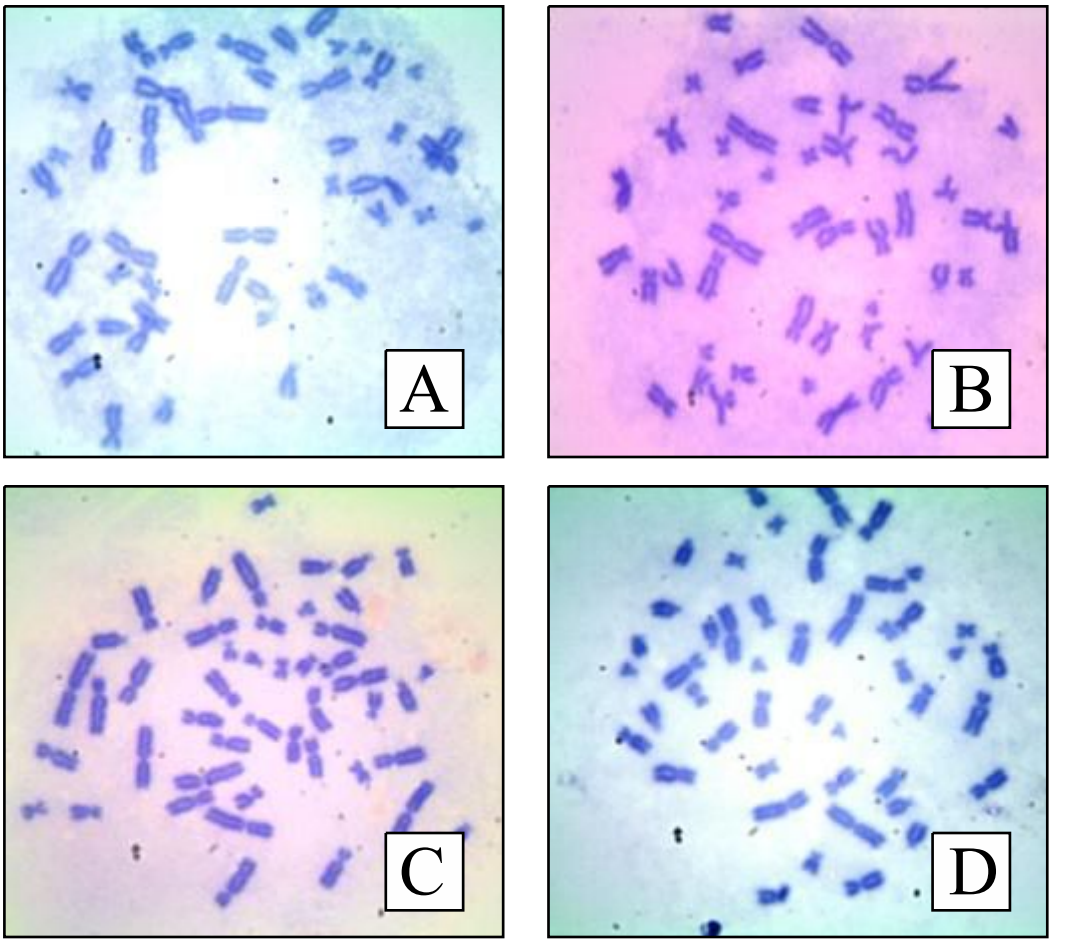


Fig-59 : Representative Metaphase plates showing chromosomal aberrations (A-B CKD Group, C-D in Control group)

Results revealed a remarkable increase in structural chromosomal aberrations, suggestive of genomic instability, and relatively higher cytogenetic damage in CKD patients in comparison to control.

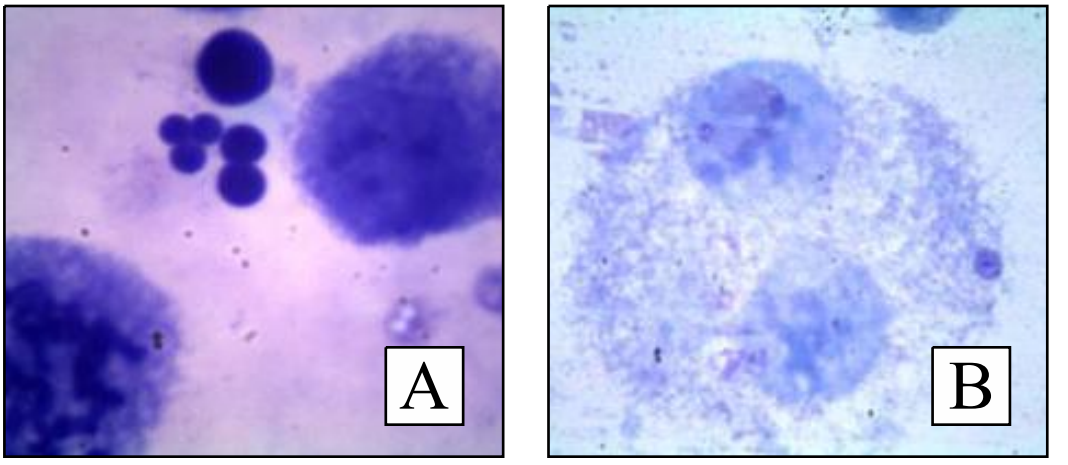


Fig-60: Binucleated lymphocytes (A) without and (B) with micronuclei

SHORTTERM SUMMER TRAINING

A short term summer training Programme (5-17 June, 2017) in Environmental Biotechnology was organized which was attended by 12 students

Name of the student	Affiliation
Mr. Abhijeet Garg	School of Biotechnology, Devi Ahilya Vishwavidyalaya, Indore
Ms. Mrudushi Gupta	School of Biotechnology, Devi Ahilya Vishwavidyalaya, Indore
Ms. Parul Laad	School of Biotechnology, Devi Ahilya Vishwavidyalaya, Indore
Ms. Ealisha Jain	School of Life Sciences, Devi Ahilya Vishwavidyalaya, Indore
Ms. Nikhat Khan	School of Life Sciences, Devi Ahilya Vishwavidyalaya, Indore
Mr. Snehil Waghade	Department of Applied Aqua Culture and Zoology, Barkatullah University, Bhopal
Ms. Sidra Nafees	Department of Biotechnology, Institute for Excellence in Higher Education (IEHE), Bhopal
Mr. Harshit Nanda	School of Biotechnology ,VIT University, Vellore
Ms. Pratiksha Tripathi	Department of Biotechnology, St. Aloysius' College, Jabalpur
Dr. Anagha Puntambekar	Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry
Dr. Neerav Khare	Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry
Dr. Aakash Choudhary	Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry

Other Activities

1. NIREH Respiratory Clinic

Under this programme gas exposed willing subjects having respiratory ailments, identified during the epidemiological surveys, are transported to NIREH pulmonary clinic where they are clinically examined and advised treatment. Their blood investigations and X-ray are done at Kamla Nehru Hospital while ECG and PFT are carried out at NIREH. The existing PFT facility in NIREH was upgraded during the year by installing (i) Forced Oscillation Technique (FOT) System for measuring lung mechanics during normal breathing process. In this technique, small-amplitude pressure oscillations are superimposed on the tidal breath and resultant changes in flow and pressure are calculated to determine lung impedance. The advantage of this technique is noninvasive, versatile, and requires minimal cooperation of the patient. This instrument is very useful to diagnose airways abnormalities especially small airways in disease like COPD, bronchial asthma, and occupational/environmental lung diseases (ii) Portable Forced Exhaled Nitric Oxide measuring instrument (FeNO) to measure non-invasively the level of nitric oxide gas in exhaled air, eosinophilc inflammation of bronchial, alveolar and nasal mucosa. FeNO has clinical, occupational, and epidemiological applications ranging from diagnosing and asthma management to the detection of air pollution related health effects.

Forced Oscillation Technique System

Forced Exhaled Nitric Oxide measuring instrument

During this year 508 new patients attended the NIREH respiratory clinic.

2. Services to Kamla Nehru Gas Rahat Hospital Pulmonary OPD

The Pulmonologist of NIREH started providing OPD services in the Kamla Nehru Gas Rahat Hospital twice a week. During the reporting year a total of 1,371 gas exposed patients having respiratory diseases were examined in the Kamla Nehru OPD and advised treatment.

3. Community based health services

Community based health services being provided by NIREH to the gas exposed people continued during the year. Under this programme on every Friday needy morbid subjects in the severely exposed areas, identified during the epidemiological surveys, are examined by a physician of NIREH at their door steps and, if needed, transported to Bhopal Memorial Hospital and Research Centre (BMHRC) or referred

to other government gas rahat hospitals for investigations and treatment. A total of 166 patients were benefitted during the year by availing this service.

4. Respiratory Physiotherapy Centre

NIREH since its inception had been providing community based pulmonary rehabilitation service at Kenchi Mini Unit of BMHRC. In January 2017 the location of the Centre was shifted to Jawahar Lal Nehru Gas Rahat Hospital due to the space constraint at earlier place and also to provide better access to the patients. Under this activity a qualified full time Physiotherapist, assisted by a field attendant, has been providing pulmonary physiotherapy services on regular basis to the gas exposed COPD patients identified by NIREH physicians at this well equipped centre. A total of 180 patients received respiratory physiotherapy in this centre during the year.

COPD patients receiving respiratory physiotherapy

Important Events

1. WORLD ENVIRONMENT DAY 2017

The World Environment Day was celebrated at ICMR-NIREH, Bhopal on 5th June 2017. On this occasion, the institute organized two invited Lectures and an Essay Competition. The guest speakers for the scientific lectures were Prof. Ramya Sunder Raman from the Department of Earth and Environmental Sciences, Indian Institute of Science Education and Research (IISER), Bhopal and Prof. Rajnish Joshi from Medicine Department, All India Institute of Medical Sciences (AIIMS), Bhopal. At the outset, Dr. R. R. Tiwari, Director NIREH, in his welcome address, explained the need to address the prevailing environmental health concerns and emphasized upon a participatory and proactive approach. He mentioned that environmental literacy which encompasses not only the knowledge but also the changed attitude, skills and habits about environment and environmental hazards, needs to be improved among citizens. He also stressed that conservation of nature requires multi-pronged approach.

Prof. Ramya Sunder Raman, in her talk titled Tiny particles and their influence on the Earth System, discussed the challenges posed by the growing concentration of aerosols in the atmosphere and their impact on the earth system. She highlighted the deleterious effects of aerosols on visibility, climate and human health. Dr. Rajnish Joshi spoke on Changing built environment for healthy life style. He explained the co-relation between various aspects of built environment and the growing prevalence of non-communicable diseases such as obesity, diabetes and cardiovascular diseases. He emphasized upon the need for a shift in environmental health policy from assessment to intervention. Seconding the views expressed by Dr. Tiwari, he emphasized the importance of behavioral change amongst the public at large in addressing the key environmental issues.

On the occasion of World Environmental Day 2017 the Institute had organized an Essay Competition for students on the theme For the Sake of our Future, Nurture Mother Nature. The winners – Mr. Shubham Tiwari, IISER, Bhopal (First Prize), Ms. Tanisha Kasliwal, DAVV, Indore (Second Prize), and Mr. Vivian Lobo, ICMR-NIRRH, Mumbai (Third Prize) were awarded their prizes.

The programme ended with a vote of thanks by Dr. Anil Prakash, Scientist-G. Emphasising upon the importance of living in harmony with Nature, he reminded everyone of their duty to contribute towards conservation of environment and natural resources.

The members of the NIREH family then proceeded to the upcoming campus of the Institute at Bhauri and planted trees in the upcoming campus.

2. INTERNATIONAL YOGA DAY 2017

The International Day of Yoga was observed at the institute on 21st June 2017. On this occasion, two special yoga sessions were conducted. Dr. Anil Prakash, In-charge Director & Scientist-G, while welcoming NIREH family members on International Day of Yoga explained the significance of yoga in maintaining sound physical and mental health and advised everyone to inculcate the habit of practicing yoga on a regular basis.

The first yoga training session was led by Mrs. Seema Khare, Technical Assistant, ICMR-NIREH – a trained yoga teacher, who demonstrated various yogasanas and described the correct way of practicing each asana. NIREH staff members enthusiastically practiced these asanas and got their doubts clarified from her. This was followed by another session by Shri Dilip Dasgupta, a well-known and veteran yoga

Glimpses of World Environment Day-2017 celebrations

expert who delved into the philosophy of yoga – a synthesis of body, mind and soul. Further, he explained the underlying scientific basis of important yogasanas and stressed upon the importance of their health benefits. He advised everyone to consider their strengths and weaknesses while choosing and practicing various asanas. He also took questions from NIREH family members and addressed their queries and concerns related to different yogasanas and their health benefits.

Glimpses of International Yoga Day 2017 at NIREH

3. ORIENTATION TRAINING OF DOCTORS OF GAS RAHAT HOSPITALS ON MENTAL HEALTH CARE MANUAL DEVELOPED BY NIREH

In pursuance of the recommendation of the Hon'ble Supreme Court appointed Advisory Committee during its meeting held on 17/05/2017 an Orientation Training Programme on Manual of Mental Health Care for Medical Officers of Bhopal, developed and released by ICMR-NIREH in 2016, was held on 9th July, 2017 in its Committee Hall for the Superintendents and General Duty Medical Officers of Gas Rahat Hospitals, Bhopal. After 32 years of the Bhopal gas disaster there is a continuing high prevalence of various mental disorders in the general population/survivors of gas disaster in Bhopal whereas the number of expert mental health professionals to provide specialist care in the Bhopal city is limited. As a result a vast majority of the patients with mental disorders are receiving care from the non-specialists - both general practitioners and other medical specialists. Recognizing this fact ICMR-NIREH prepared a self-instructional Mental Health Manual under the guidance of Prof. R. S. Murthy, Retd. Prof. and Head of Psychiatry Department, NIMHANS, Bangalore along with well known Mental Health Experts of the country to share the diagnostic and treatment skills for mental health disorders with non-mental

health doctors of Bhopal so that general duty doctors can provide appropriate primary level of mental health care to the needy Bhopal population.

A total of 18 doctors from Kamla Nehru gas rahat hospital (4), Jawahar Lal Nehru gas rahat hospital (3), Shakir Ali Khan gas rahat hospital (4), Indira Gandhi gas rahat hospital (4) and ICMR-NIREH (3) attended the training.

Dr. R. R. Tiwari, Director, ICMR-NIREH welcomed the participants and enlightened them on the objectives of the training. He gave the background of the preparation of the Mental Health Manual, contents of the Manual and hoped that the training will enable them to diagnose patients with various mental disorders and treat them suitably. Before starting the technical session participants were subjected to pre-training assessment of their knowledge on elementary mental health care.

Dr. J. P. Agrawal, Associate Professor (Psychiatry), Gandhi Medical College, Bhopal apprised the participants about the types and ICD-10 classification of various psychiatric disorders. He discussed in details the assessment of a psychiatric patient, general principles of history taking and techniques of mental status examination. Prof. R. N. Sahu, Head, Department of Psychiatry, Gandhi Medical College, Bhopal spoke on Psychotic Disorders. He explained the mechanism of development of psychosis, various sub-types of psychosis, symptomatology of psychotic disorders, their diagnosis and treatment. With various examples he explained how to differentiate and deal with delusions and hallucinations, pharmacotherapy of the aggressive patients, health monitoring of patients receiving antipsychotic drugs etc. Dr. Rajni Chatterji, Consultant Professor and ex-HOD, Department of Psychiatry, BMHRC, Bhopal deliberated on Mood Disorders. Explaining `Mood' and `Affect' she touched upon epidemiology of mood disorders. She dealt at length with etiology of depression, mania, and bipolar disorders- their symtomatology, management, pharmacological intervention, ECT and psychosocial treatment. Dr. Baibhav Dubey, Associate Professor (Psychiatry), Peoples Medical College, Bhopal discussed Substance Related Disorders. Highlighting various substance use disorders he gave a detailed talk on alcoholism, withdrawal symptoms and management of alcoholic patients. All the lectures during the technical sessions were interactive, largely based on the Mental Health Manual and the faculty shared their day-to-day experiences with the participants in dealing with patients with mental disorders from the general population as well as Bhopal gas survivors. Participants were encouraged to ask queries and clear their doubts.

Participants felt that training has been useful for them but in the absence of availability of common psychotropic drugs in the gas rahat hospitals it will not be possible to treat the patients of common mental disorders. Participants requested to include the common psychotropic drugs in the list of essential drugs in the stores of gas rahat hospitals. Participants also felt that for this type of orientation training younger doctors who have recently joined the gas rahat hospitals should be nominated by the authorities because senior doctors are also involved in various administrative jobs as well. The programme ended with the vote of thanks was by Dr. N. Banerjee, Advisor, ICMR-NIREH to the participants and faculty members.

Glimpses of Orientation training on Mental Health Manual at NIREH

4. MEETING OF BASIC SCIENCES RESEARCH EXPERT GROUP of NIREH

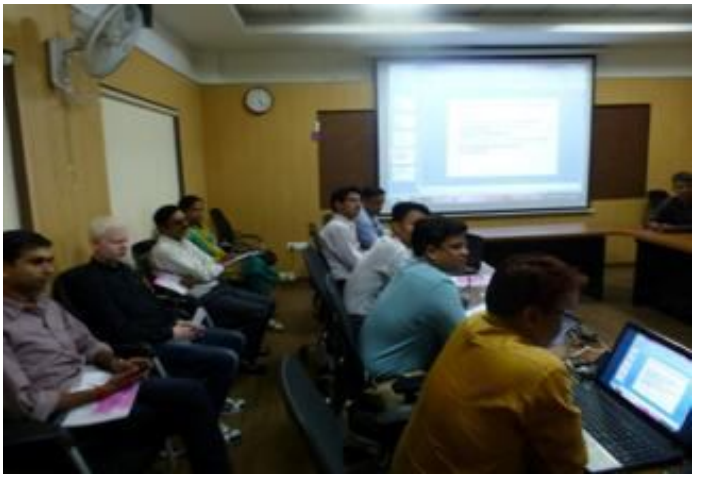
First meeting of the Basic Sciences Research Expert Group of ICMR-NIREH was held on 21st July, 2017 in the Committee Room of ICMR-NIREH, Bhopal. The meeting was chaired by Prof. N. K. Mehra and attended by members- Dr. Mitali Mukerji, IGIB, New Delhi, Dr. Poonam Salotra, NIP, New Delhi, Dr. Rahul Bhattacharya, DRDE, Gwalior, Dr. Tanvir Kaur, ICMR, New Delhi and Dr. R. R. Tiwari.

Glimpses of BSREG meeting at NIREH

The Group reviewed two new projects submitted by the scientists of NIREH related to environmental toxicology and health and also appraised themselves on the ongoing studies related to the field of basic sciences.

5. TRAINING ON IMPLEMENTATION OF e-OFFICE

A training programme on e-office was organized by the e-Governance cell of ICMR, New Delhi on 16 August, 2017 at ICMR-NIREH, Bhopal. The training programme was attended by 16 participants from 3 institutes of ICMR located in central regions viz. ICMR-NITRH, Jabalpur, ICMR-JALMA Agra and ICMR-NIREH, Bhopal. The programmestarted with the introductory remarks by Dr. Anil Prakash, scientist – G, NIREH. Mr. Sanjeev Kumar, PS (e-Governance), Office of Sr. DDG (A), ICMR, New Delhi deliberated on three modules namely, Introduction to e-File (File management system), e-Leave (Leave management system) and KMS (Knowledge management system). The participants were taught step wise implementations like creation of Email ID and how to check them, steps to register with LDAP Server, how to open e-Office portal, steps to create e-Office users, create Post for the users, e-Leave and updating of leave balance. In the afternoon session participants were provided hands on online experience to practice e-office followed by an interacting session. The programme ended with vote of thanks by Dr. N. Banerjee, Advisor, NIREH.

Glimpses of training on e-office at NIREH

6. THIRD MEETING OF THE INSTITUTIONAL ETHICAL COMMITTEE OF NIREH

The 3rd Institutional Ethics Committee (IEC) meeting of ICMR-NIREH, Bhopal was held on 28 August, 2017 in the Committee Room of NIREH. The meeting was chaired by Dr. P. S. Chauhan and attended by members - Dr. S. C. Dubey, Prof. N. P. Mishra, Prof. Reeni Malik, Dr. Rakha Arya, Dr. Ranjana Shrivastava, Pt A. K. Dwivedi, Dr. R. R. Tiwari and Dr. P. K. Mishra.


Glimpses of IEC meeting at NIREH

7. हिन्दी पखवाड़ा 2017

संस्थान में 01–15 सितम्बर 2017 तक हिन्दी पखवाड़ा आयोजित किया गया। इसके अन्तर्गत निबंध एवं श्रुतलेखन प्रतियोगिताऐं आयोजित की गईं। 14 सितम्बर 2017 को 'हिन्दी दिवस समारोह' का कार्यक्रम संस्था के निदेशक डॉ. आर. आर. तिवारी की अध्यक्षता में सम्पन्न हुआ। कार्यक्रम के मुख्य अतिथि एव वक्ता डॉ. शिवचन्द्र दुबे, पूर्व संयुक्त निदेशक, उच्च सुरक्षा पशुरोग प्रयोगशाला, भोपाल थे।




नीरेह हिन्दी पखवाड़े समारोह की कुछ झलकियाँ

कार्यक्रम का आरम्भ संस्था के वैज्ञानिक सलाहकार डॉ. नालोक बैनर्जी द्वारा कार्यक्रम में उपस्थित समस्त प्रबुद्वजनों एवं मित्रों को हिन्दी दिवस की शुभकामनाएं देने एवं मुख्य अतिथि का परिचय कराने से हुआ। उन्होंने अपने वक्त्चय में कहा कि हिन्दी में जितना अधिक कार्य किया जायगा एवं हिन्दी बोली जावेगीए देश–प्रदेश का उतना ही विकास होगा । हिन्दी में समस्त भाषाओं को साथ लेकर चलने की एक अनूठी विशेषता है । अपने अध्यक्षीय उद्बोधन में डॉ तिवारी ने संस्थान द्वारा हिन्दी में किये जा रहेकार्यकलापों के बारे में अवगत कराया। उन्होंने सभी को हिन्दी के प्रगामी प्रयोग और तकनीकी पारिभाषिक शब्दावली सीखने हेतु प्रेरित किया। लेखन व उच्चारण की शुद्धता बनाये रखने हेतु वर्तनी संबंधी नियमों का पालन ईमानदारी करने एवं अपने परिवेश में हिन्दी का महत्व बढ़ाने हेतु सतत् प्रयास के लिए उनके द्वारा सभी को प्रेरित किया गया।

कार्यक्रम के मुख्य अतिथि डॉ. दुबे द्वारा ''तकनीकी हिन्दी लेखन का विकासशील पक्ष'' विषय पर अपना व्याख्यान प्रस्तुत किया गया। उन्होंने हिन्दी भाषा में वैज्ञानिक शब्दावली का प्रयोग एवं नवीन शब्दों का व्याकरण सम्मत निर्माण करने से संबंधित ज्ञानवर्धक जानकारी दी । ज्ञान विज्ञान की शब्दावली गढ़ने के लिए मानक हिन्दी वर्तनी के नियम, तकनीकी शब्दावली, शब्दकोष, स्नातक एवं स्नातकोत्तर हिन्दी पाठ्यक्रमों का अभाव, हिन्दी के उपेक्षित पहलू, हिन्दी साहित्य में पर्याय का महत्व, रोगों के नाम में एकरूपता कैसे लायी जाये इत्यादि पर महत्वपूर्ण जानकारी उन्होंने दी। साथ ही हिन्दी भाषा में प्रचलित नामों के संक्षिप्त रूप, सार्थक उपसर्ग या प्रत्यय द्वारा पारिभाषिक शब्दों की रचना तथा भाषानुसंधान एवं भाषानुशासन की आवश्यकता पर डॉ. दुबे ने सारगर्भित भाषण के उदाहरण दिये सहित दिया । अंत में निबंध लेखन प्रतियोगिता एवं श्रुतलेखन प्रतियोगिता में विजेता प्रतिभागियों को मुख्य अतिथि द्वारा पुरस्कार वितरित किये गये ।

समारोह के अंत में डॉ. अनिल प्रकाश, वैज्ञानिक–जी द्वारा धन्यवाद ज्ञापन प्रस्तुत किया गया।

8. NIREH FOUNDATION DAY

NIREH observed its 8th Foundation Day on 11th October 2017. Professor Pramod Verma, Vice-Chancellor, Barkatullah University, Bhopal graced the occasion as the Chief Guest and delivered the NIREH-Foundation Day-2017 Oration. Dr. Aparup Das, Director, ICMR-National Institute for Research in Tribal Health, Jabalpur and Dr. Prabha Desikan, Director, Bhopal Memorial Hospital & Research Centre were the Guests of Honour. Dr. Anil Prakash, Scientist G presided over the function. The programme was attended by dignitaries, invitees, eminent personalities from Bhopal, besides ICMR-NIREH fraternity.

In his welcome address, Dr. Prakash greeted the NIREH family on the occasion. He briefly highlighted the ongoing research activities and significant contributions of the institute. On the occasion he urged all members of the NIREH family to take a pledge to create an environmentally sustainable society that meets human needs.

Delivering the Foundation Day Oration lecture on the topic Search of water in space, Professor Verma portrayed the presence of water in extra-terrestrial bodies through a series of laboratory-based evidences. He shared his own experience of working with cutting-edge technologies such as, infra-red and gamma spectrophotometer utilized for exploring the possible existence of life out of planet earth.

Dr. Aparup Das articulated his views on how rising temperatures, changing precipitation patterns, and higher frequency of extreme weather events associated with climate change are expected to alter the geographic and seasonal distributions of existing vectors and vector-borne diseases. Dr. Desikan spoke about the role of potential environmental risk factors and social determinants associated with pulmonary and extra-pulmonary multi-drug resistant tuberculosis.


Glimpses of NIREH Foundation Day 2017


The programme concluded with vote of thanks by Dr. P.K. Mishra, Scientist E.

9. VIGILANCE AWARENESS WEEK

The Vigilance Awareness Week-2017 with the central theme My Vision-Corruption Free India (मेरा लक्ष्य भ्रष्टाचार मुक्त भारत) was observed with enthusiasmin NIREH from 30/10/2017 to 04/11/2017. On 30th October, 2017 Dr. R. R. Tiwari, Director administered the pledge to the staff of NIREH. Speaking on the occasion Dr. Tiwari emphasized the importance of vigilance in research institutions. He stressed on the need of Fairness, Accountability and Transparency (FAT) in any system and observed that being a government servant one must uphold highest standards of honesty and integrity and follow the rule of law in all the official activities.

On 1st November 2017, a talk on the themed topic of My Vision-Corruption Free India was delivered in NIREH by Shri Padamvir Singh, retired IAS and current Director General of Atal Bihari Vajpayee Institute of Good Governance and Policy Analysis, Bhopal. Shri Singh highlighted the current position of India in Corruption Perception Index (CPI) and emphasized that corruption is an output of system problems, complex procedures, and lack of transparency and insufficient delegation of power that has reduced individual values and believes. Mentioning money, power and fame as the root causes of low values and believes in the society, he said that simplifying government procedures, privatization of non-public goods, delegation and decentralization, strengthening institutions like Lokpal, proactive disclosure, right to information, strict and quick action against powerful but corrupt individuals and training and education to raise moral values can help to remediate the corruption problems. Discussing on moral values, he suggested that the ultimate goal of every individual should be a happy life. He

Glimpses of Vigilance Awareness Week at ICMR-NIREH

discussed the PERMA theory of happiness comprising of five elements viz. Positive emotion (feeling good), Engagement (finding flow), Relationship (authentic connections), Meaning (purposeful existence) and Accomplishment that can help people to attain a meaningful life of fulfillment and happiness. Emphasizing on "free will over determination" for a corruption free life, Shri Singh concluded by quoting that "man is nothing than the ensemble of his acts" and motivated the NIREH staff members to develop an inspiring powerful nature to live a happy life. After the lecture vote of thanks was given by Dr. Anil Prakash.

10. SWACCHTA ACTION PLAN

Under Swacch Bharat cleaniness in the office premises and out side the premises by shramdaan was maintained routinely throughout the year. Under Swacchta Action Plan (SAP) a village named Berkheda Bondar, near uncoming permanent campus of NIREH in Bhauri area, was adopted for carrying out various health and hygiene related activities under SAP. The population of the village is about 1,200 in 220 houses This village

Swacchta Awareness meeting in Berkhedi Bondar High School

An interactive meeting to create awareness on cleanliness and health was organized in the High School of Berkheda Bondari village, Bhauri, Bhopal on 27/09/2017. The meeting was attended by about 60 students of class IX and X along with teachers of the school. The importance of maintaining cleanliness

in the individual households, its surroundings and the village to improve the environment and promote health was highlighted during the meeting. Dr. Y. D. Sabde, Scientist E deliberated on water borne diseases and simple tips to prevent them. It was stressed to make use of toilets and avoid open defecation by every one. Dr. Anil Prakash, Scientist G spoke on various mosquito borne diseases and preventive measures to reduce mosquito breeding and biting. Dr. Sandhuprava Rana, Scientist B addressed the issues of personal hygiene and reproductive health with the females students. Two short Hindi animation films on `Cleanliness and Drinking water' and `Cleanliness and waste disposal' were screened during the programme which were highly appreciated by the audience. Students and teachers put up several queries which were answered by ICMR-NIREH scientists. Pamphlets and posters on cleanliness and health promotion were distributed to the students. Further, two big sized plastic dustbins were provided by NIREH to the school under the Swacchta Action Plan.

Glimpses of Swacchta Awareness Meeting in Berkhedi Bondar High School

Swacchta Awareness Meeting in Berkheda Bondar Middle & Primary School

To create awareness and promote concept of general and personal hygiene a joint meeting involving about 100 students and teachers of Middle and Primary Schools in Berkheda Bondari village was organized on 17/10/2017. Students were appraised about the ongoing Swacch Bharat Abhiyan of Govt of India and how can they contribute to this programme was explained by Dr. Sindhuprava Rana. Various water borne diseases and Importance of personal hygiene and safe drinking water to reduce

these diseases was elaborated to the students by Dr. N. Banerjee. Role of mosquitoes in spreading diseases such as Dengue and Malaria and simple doable measures by common person to fight these diseases were detailed by Dr. Anil Prakash. Realizing the felt need of safe drinking water in these schools, 2 plastic tanks of 200 litre capacity each to the middle school and primary school were gifted by NIREH along with 4 dustbins each to the schools for solid waste disposal under Swacchta Action Plan. In addition, short Hindi animation films on `Cleanliness and Drinking water' and `Cleanliness and waste disposal' were screened during the programme which were appreciated by the students.

Glimpses of Swacchta Awareness Meeting in Berkheda Bondar Middle School

Promotion of clean drinking water

An advocacy meeting with the villagers in Berkheda Bonder village to promote clean drinking water was held on 09/03/2018. In this meeting various health problem associated with drinking water were discussed and emphasis was given on inculcating the habit of proper hand washing before taking food and consuming clean drinking water for avoiding water borne diseases. Realizing the felt need of the villagers, 200 non-electric water filters were distributed @ 1 each for every house hold


Advocacy meeting to promote clean drinking water in Berkheda Bonder village

11. SEVENTH SCIENTIFIC ADVISORY COMMITTEE MEETING OF NIREH

The seventh Scientific Advisory Committee (SAC) of ICMR- NIREH, under the Chairmanship of Dr. V. K. Vijayan, Kozikhode met on 21/12/2017 in the guest house of the under-construction NIREH campus at Bhauri, Bhopal. Expert members/nominees including Prof. N. K. Mehra, Prof. J. S. Thakur, Prof. I. S. Thakur, Dr. Manoj Murhekar, Dr. K. Krishnamoorthy, Dr. Rajesh Malik, Dr. Prabha Desikan, Dr. R. R. Tiwari and officials from the Council such as Dr. R. S. Dhaliwal and Dr. Tanvir Kaur attended the meeting. The Committee reviewed a total of 11 ongoing / completed projects and 6 new projects and provided valuable advice on various matters and scientific activities of NIREH.


Glimpses of 7th SAC meeting of NIREH

12. WORKSHOPS ON BASICS OF GEOGRAPHICAL INFORMATION SYSTEM (GIS) APPLICATIONS FOR PUBLIC HEALTH PRACTICENERS

NIREH organized a total of 3 Hands-on-workshops on 13 February, 20 February and 16March 2018 on Basics of Geographic Information System (GIS) applications for Public Health Practitioners. These Workshops were attended by 41 researchers/faculties from medical colleges in Bhopal, Mysuru, Delhi, Jabalpur, Wardha etc. Participants were exposed to basics of GIS application in Public Health research using hands on exercises and case studies.

Glimpses of GIS Workshops

Each Workshop was divided into four broader sections viz. (i) GIS data: Where different types and sources of GIS data were explained (ii) GIS software: Different proprietary and open access GIS software were introduced. As an example set up of QGIS version 2.18.16 was installed in the personal laptops of the participants. Participants were also provided with sample data for hands on practice on GIS tools during the subsequent sections (iii) Hands on practice: The third section included hands on practice of some important procedures in GIS using the installed version of QGIS and sample data. For this five different tasks (small projects) were given to the participants to facilitate learning by doing procedures like, creating layers of feature classes in GIS, coordinate capture, managing layer properties, managing attribute tables, using print composer, geo processing and geo statistical applications. All the participants successfully completed the tasks through an active interaction with the faculty as well as other participants (iv) Case studies: Real life experiments of GIS applications were shared through presentation of different published scientific studies. The studies included GIS applications in infectious diseases, health system research, maternal and child health, emergency transport and critical care access.

LIBRARY

ICMR-NIREH library, currently having a very basic infrastructure due to space constraint, is equipped with a computer along with internet facility to fulfill the need of the researchers,scientists, doctors and students to persue their academic activities. Library is having access to all journals available in e-consortia of ICMR. In addition, the library is also subscribing a couple of international journals related to environmental health. Presently NIREH library is maintaining a core collection of more than 200 books on various areas like Bhoapl Gas Disaster, Biomedical Science, Cytogenetic, Epidemiology, Pathology, Computer science, Bioinformatics, etc.The library will be upgraded in the upcoming permanent campus of NIREH at Bhauri.

A view of the library

NIREH library organized demonstration-cum workshop on ICMR e-Consortia & J Gate Plus for the scientists of NIREH on 15th September 2017. In this workshop a representative of J- Gate Plus provided hands on training to the participants in retrieving full length articles from the data base in order to promote maximum utilization of e- resources among the scientist sof NIREH.

Construction of NIREH Campus at Bhauri

Construction of the core building of the upcoming NIREH campus on a 20.0 acres of plot at Bhauri village on Bhopal-Indore by pass road under the consultancy of Capital Project Administration, Govt. of M.P. continued during the year. For construction purpose the core building, housing main laboratories and administration part, has been divided in to 12 blocks and the civil work in all 12 blocks is in various stages of construction and finishing. The construction work is being monitored regularly by the Building Advisory Committee and Building Construction Monitoring Committee of NIREH. It is expected that by December 2018 the core building will be ready for occupying.




Under construction ICMR-NIREH campus at Bhauri

Phase II Staff Recruitment

A total of 183 permanent posts belonging to Scientific cadre (66), Technical cadre (84), Administrative cadre (26) and Engineering cadre (7) were sanctioned by the Government of India for ICMR-NIREH. Process is on for Phase II recruitment of 57 scientific, administrative, technical and engineeringposts. As per Government directives written tests for 7 scientific, 7 administrative, 12 technical and 1 Engineering post, advertised in Phase II by NIREH, were conducted during the year. Consequently, 5 Scientific cadre (3 Scientist C,2 Scientist B (Medical), 7 Administrative cadre, 5 Technical cadre and 2 Engineering cadre incumbents joined the institute during the year.

Meetings / Trainings / Seminars attended

Dr. R. R. Tiwari, Director

1. Faculty in Training programme for PME doctors of Central Coalfields Limited, Ranchi (3-7 April, 2017) at National Institute of Occupational Health, Ahmedabad
2. Delivered lecture on "Occupational Health" during Student-Expert meeting (PFA) during Global Health Symposium 2017 (23 April, 2017) at Manipal University, Manipal
3. Guest faculty in ICMR-WHO Collaborative Expert Group meeting on Prevention and Management of Lead Poisoning (14-16 June, 2017) at ICMR-NIOH, Ahmedabad. Delivered lecture on "Lead exposure in ship breaking workers"
4. Meeting of the Directors and Division Heads of ICMR Institutes (18 July, 2017) at Indian Council of Medical Research, New Delhi
5. Delivered lectures on occupational health topics (22-23 July; 29-30 July and 19-20 August, 2017) for the students of Masters in Industrial Hygiene and Safety, Sardar Patel University, Anand
6. Participated in Interactive session on Occupational Health (6 August, 2017) for Distance learning Certificate Program on Health, Safety and Environment Management at IIPH, Gandhinagar
7. Workshop on Antimicrobial Resistance (13 November, 2017) at Hotel Palash Residency, Bhopal
8. Workshop on Molecular diagnostics a step towards capacity building in rapid diseases identification and their prognosis (17-19 November, 2017) at AIIMS, Bhopal
9. Media Training Workshop of ICMR-East (5 December, 2017) at ICMR-National Institute of Cholera and Enteric Diseases, Kolkata
10. Resource Person for Silicosis in Rajasthan Conclave 5 (13-16 December, 2017) at ICMR-Desert Medicine Research Centre, Jodhpur
11. Guest of Honour in the Inaugural function of NIMH-DGMS National Workshop on "Detection of Pneumoconioses and Use of ILO Classification 2000" (29 January, 2018) at Hotel Pride, Nagpur. Delivered a lecture on Overview of Pneumoconiosis as the Guest Faculty
12. Deliver lectures to Masters in Public Health (EOH) students (31 January – 4 February, 2018) at Manipal University, Manipal
13. Attended training programme on "Climate change and carbon mitigation" (19-23 February, 2018) at Indian Council for Forest Research and Education, Dehradun
14. Chairperson for Selection Committee meetings for the posts of Senior Residents, Junior Residents and Consultants held from time-to-time at Bhopal Memorial Hospital and Research Centre, Bhopal

Dr. Anil Prakash, Scientist G

1. Selection Committee Meeting as Member for the posts of Scientist B and Scientist C (1 -2 May, 2017) at CRME, Madurai
2. Site Monitoring Committee meeting and visit to Jalna, Maharashtra (23 October, 2017) as a Member of the Committee constituted by Deptt of Biotechnology, GOI for monitoring the large cage study(ies) on

OX513A RIDL strain of Ae. Aegypti under contained conditions being conducted by M/S/ GBIT, Jalna.

3. Selection Committee Meeting as Member for the post of Consultant (Public Relation) at BMHRC (25 October, 2017), Bhopal

4. Workshop on Combating Antimicrobial Resistance (AMR) in Madhya Pradesh : Towards an Agenda for Action (13 November, 2017) organized by Directorate of Health Services, Govt of M.P. at Hotel Palash, Bhopal

5. Media Training Workshop of ICMR-East (5-6 December, 2017) organized at National Institute of Cholera and Enteric Diseases, Kolkata

6. First meeting of the Independent Enquiry Committee (15 January, 2018) as a Member to enquire in to purchase procedure of BMHRC, Bhopal

7. Second Meeting of the Inquiry Committee (24 January, 2018) as a Member to investigate recruitments done after 2010 in BMHRC, Bhopal

8. Second meeting of the Independent Enquiry Committee (7 February, 2018) as a Member to enquire in to purchase procedure of BMHRC, Bhopal

Dr. Kailash C. Pandey, Scientist E

1. Invited speaker in *XIII Molecular Parasitology meeting* (9-14 September, 2017) at Marine Biological Laboratory Woods Hole, Massachusetts, USA

2. Guest speaker in *11th Symposium on Frontiers in Biomedical Research; Challenges in Human Health; Diagnosis, Prevention and Care* (19-21 February, 2018) at Delhi University

3. External Examiner for Ph.D. viva voce (27 Feb, 2018) at Dept. of Life Sciences, School of Natural Sciences, Shiv Nadar University

4. External Examiner for Ph.D. viva voce (19 March, 2018) at Dept. of Biotechnology, Goa University

Dr. P.K. Mishra, Scientist E

1. Plenary talk in *International Conference on Environment, Genes, Health and Disease* (22-24 August, 2017) at Bharathiar University, Coimbatore

2. Invited talk in *National Conference on Environmental Impact on Reproductive Health* (8-9 September, 2017) at Punjab Agricultural University, Ludhiana

3. Invited talk in *Indo-German Workshop on Advances in Cancer Research* (19 September, 2017) held at German Embassy, New Delhi

4. Invited talk in *Workshop on New Horizons in Nanomedicine* (11 November, 2017) at Narsee Moonjee Institute of Management & Studies, Shirpur

5. Invited talk in *World Congress on Reproductive Health* (23– 25 February, 2018) at Indian Institute of Chemical Technology, Hyderabad

6. Invited talk in UGC sponsored *National Workshop on Molecular Biology: Theory & Practice* (26-27 February, 2018) at , Central University, Sagar

7. Invited talk in *33rd Madhya Pradesh State Young Scientist Congress* (15-16 March, 2018, at Rani Durgavati University, Jabalpur

Dr. Sajal De, Scientist E

1. National Conference on Occupational Respiratory Disorders held at Raipur Institute of Medical Sciences on 21-22 April 2018.
2. Attended training on measurement of environmental volatile compounds and particulate matters at Regional Occupational Health Centre, Bangalore on 23-26 May 2017.

Dr. Sushil Singh, Scientist C

1. Orientation programme on SPSS software (22 May, 2017) at NIREH, Bhopal
2. Completed *Online SPSS training program* (9June - 8 Dec, 2017)
3. *Orientation for e-office users* (16 August, 2018) organized by ICMR, New Delhi at NIREH, Bhopal
4. *Public Health Dynamics Workshop* (5-7 March, 2018) held under the aegis of the ICMR -NIMS, New Delhi and University of Pittsburgh -Graduate School of Public Health, USA at New Delhi
5. *Workshop on Simplified secrets of Geographic Information System for beginners* (16 March, 2018) at ICMR-NIREH, Bhopal.

Dr. Manoj Kumar, Scientist C

1. International conference on Antimicrobial Resistance (19-20 January, 2018) organized by the Centre for Research in Infectious Diseases (CRID), School of Chemical and Biotechnology, SASTRA Deemed University at Thanjavur (TN)
2. DST sponsored training programme (29 Jan – 2 Feb, 2018) on *Environment and Natural Resources Management* at Indian Institute of Forest Management (IIFM) Bhopal

Dr. Ruma Galgalekar, Scientist B

1. Orientation programme on SPSS software (22 May, 2017) at NIREH, Bhopal
2. Orientation training to Gas Rahat Hospitals doctors on Mental Health Manual developed by NIREH (9 July, 2017) at NIREH, Bhopal

Dr. Amit Kumar Tripathi, Scientist B

1. *Induction Training Program for ICMR Scientists on Research Methods and Research Administration* (10-14 July, 2017) at ICMR-NIE, Chennai
2. *Short course on Principles of Toxicology* (18-22 September, 2017) conducted by Harvard School of Public Health and Public Health Foundation of India at Gurugram
3. *National Seminar on Aquaculture Production & Biodiversity Conservation and Environmental Toxicology* (30-31 August, 2017) at Dept. of Zoology, Sri Venkateswara University, Tirupati.
4. *Workshop on simplified secrets of Geographic Information System for beginners* (16 March, 2018) at ICMR-NIREH, Bhopal
5. *Public Health Dynamics Workshop* (5-7 March, 2018) held under the aegis of the ICMR -NIMS New Delhi and University of Pittsburgh -Graduate School of Public Health, USA at New Delhi

6. *Hands-on-Workshop on RNA Sequencing* (26-28 March, 2018) at Institute for Bioinformatics and Applied Biology, Bengaluru

Dr. Sindhuprava Rana, Scientist B

1. *Induction Training Program for ICMR Scientists on Research Methods and Research Administration* (3-7 April, 2017) at ICMR-NIE, Chennai
2. *Med-Tech internship in Computer Vision Lab, IIT-KGP* (8 May –2 July, 2017). Worked in the project titled *Computer-aided detection (CAD) and clinical decision support system (CDSS) for radiologists for lung nodules in CT images using content-based image retrieval*
3. *Orientation programme for e- office users* (16 August, 2018) organized by ICMR, New Delhi at ICMR NIREH, Bhopal
4. Completed *Online SPSS training program* (9June – 8 Dec 2017)
5. Participated in *7th Bhopal Vigyan Mela* (9-12 February, 2018) at BHEL ground Bhopal
6. *Workshop on Simplified secrets of Geographic Information System for beginners* (16 March, 2018) at NIREH, Bhopal

Dr. Rajesh Ahirwar, Scientist B

1. *Short course on Environmental Health* (25-29 September, 2017) organized jointly by Indian Institute of Public Health, Gandhinagar (IIPHG) and T.H. Chan School of Public Health, Harvard University at Gandhinagar
2. Participated in 7th Bhopal Vigyan Mela (9-12 Feb 2018) at Bhopal

Mrs. Kamini Arya, TA

1. *Short course on Environmental Health* (25-29 September, 2017) organized jointly by Indian Institute of Public Health, Gandhinagar (IIPHG) and T.H. Chan School of Public Health, Harvard University at Gandhinagar

Mr. Aniket Aglawe, TA

1. *National Training on Host-Pathogen Interaction* (9-13 Jan 2018) at Nagpur Veterinary College, Nagpur

Mr.Dharmender Dharway, Technician

1. *Short course on Environmental Health* (25-29 September, 2017) organized jointly by Indian Institute of Public Health, Gandhinagar (IIPHG) and T.H. Chan School of Public Health, Harvard University at Gandhinagar

Publications

Research papers

1. Ahirwar R, Sharma JG, Nahar P, Kumar S. Immobilization of cellulase on three engineered polymer surfaces. *Biocatalysis and Agricultural Biotechnology* 2017; 11: 248-215 **(Indexed)**

2. Banerjee A, Mansoori IH, Soni KK. Are environmental toxins responsible for biochemical and physiological changes in emphysema? *International Journal of Medical Science and Clinical Invention* 2017; 4: 3274-3280 **(Indexed)**

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Research work abstracted/presented

1. H. Lad, R. R. Tiwari, P. K. Mishra. *Development and validation of a mito-epigenetic carcinogenic risk assessment model for environmental chemical exposures*. In World Congress on Cancer (February 3-5, 2018), organized by Mahatma Gandhi University of Medical Sciences & Technology, Jaipur, India

2. H. Lad, S. Maravi, A.S. Aglawe, P. K. Mishra. *Development and validation of a mitochondrial DNA based approach for rapid identification of environmental chemical exposed victims*. In International Conference on NextGen Genomics, Biology, Bioinformatics and Technologies

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3. N. Bunkar, K Chaudhury, P.K. Mishra. *A pan-India study to isolate and characterize aberrant circulating epigenomic signatures from high-risk, mid-risk and low-risk air pollution zones*. In World Congress on Cancer (February 3-5, 2018), organized by Mahatma Gandhi University of Medical Sciences & Technology, Jaipur, India

4. P.K. Mishra. *A next generation point-of-care nanobiosensor for early diagnosis of environmental associated cancers - from biology to clinical translation*. In International Conference on Environment, Genes, Health and Disease (August 22-24, 2017), organized by Bharathiar University, Coimbatore, India

5. P. K. Mishra. *Air pollution-associated adverse reproductive health outcomes: who is really at risk*? Proceedings of the National Conference on Environmental Impact on Reproductive Health (September 8-9, 2017), organized by Punjab Agricultural University, Ludhiana, India

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7. P.K. Mishra. *Nanoengineered dendritic cells for targeting tumor re-initiating cells (TRICS) in environmental associated cancers: From biological framework to clinical translation*. In National Conference on New Horizons in Nanomedicine (November 11, 2017), organized by Narsee Moonjee Institute of Management & Studies, Shirpur, India

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11. R.M. Samarth, T. Khan, A. Vishwakarma, S. Srivas, P.K. Mishra, RR Tiwari. *Evaluation of cytogenetic damage induced by landfill leachate and Cyclophosphamide in human peripheral blood lymphocytes: an in vitro evaluation of genotoxicity*. In International Conference on Fight Against Cancer (5-7 October, 2017), at CSJM University Kanpur

12. S. Singh, N. Banerjee, K.K. Soni, R. Galgalekar, A. Prakash, R. R. Tiwari. *Morbidity differentials in affected and control area in reference to socio-economic parameters in cohort Population*. Annual conference of Indian Society of Medical Statistics (2-4 November, 2017) at SGPGI, Lucknow

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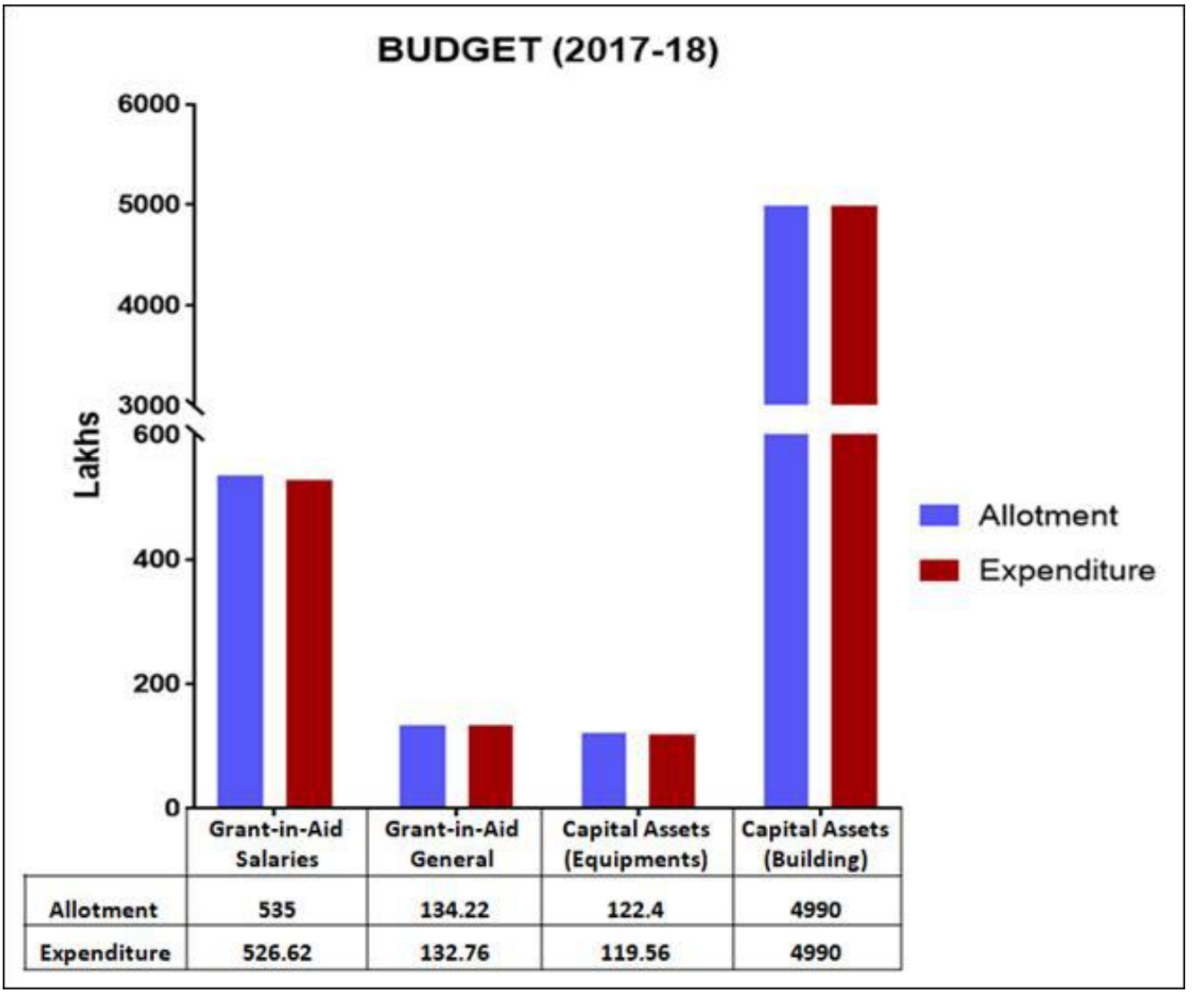
18. Prof, Ramya Sunder Raman, IISER, Bhopal
19. Prof. Rajnish Joshi, AIIMS, Bhopal



	Grant-in-Aid Salaries	Grant-in-Aid General	Capital Assets (Equipments)	Capital Assets (Building)
Allotment	535	134.22	122.4	4990
Expenditure	526.62	132.76	119.56	4990

Director acknowledges the efforts of Dr. Anil Prakash, Scientist G in bringing out this report

NOTE

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