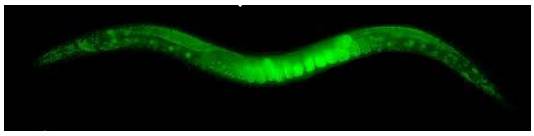
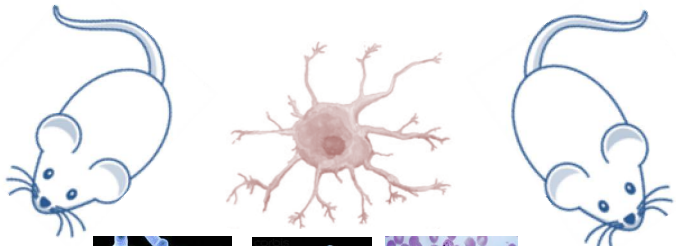
11th Symposium on Frontiers in Biomedical Research

Challenges in human health: Prevention, Diagnosis and Cure





Organized by

Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi

19th - 21st February, 2018
At
Conference Center, University of Delhi
(North Campus), Delhi-110007,

Professor Yogesh K Tyagi, Vice Chancellor University of Delhi

UNIVERSITY OF DELHI
दिल्ली विश्वविद्यालय

Professor Yogesh Tyagi
Vice Chancellor

Message

I am pleased to know that Dr. B.R. Ambedkar Center for Biomedical Research (ACBR), University of Delhi is organizing a symposium on "Frontier in Biomedical Research" during 19-21 February 2018, with a focus on the theme entitled "Challenges in Human Health, Prevention, Diagnosis and Cure." This theme is contemporary and quite relevant in the present context. Health issues need careful consideration in our country of more than One billion.

I am sure that the deliberations at the Symposium will not only enrich the knowledge of the participants but also set the path for future research and development in the area of human health.

I extend my best wishes for the Success of the Symposium.

Y. K. Tyagi

Yogesh K. Tyagi

University Road, Delhi-110 007, India, Phones : +91-11-27667011, 27667190 Fax : +91-11-27667049
Email : vc@du.ac.in

Professor Devesh K Sinha
Dean of Colleges

Message

I have great pleasure in congratulating the faculty of Dr. B.R. Ambedkar Center for Biomedical Research for organizing 11th Symposium on "Frontiers in Biomedical Research", at University of Delhi during 19th to 21st February 2018. I am sure this will be a wonderful opportunity for the scientists carrying out work in diverse fields of Biomedical Research to discuss their ideas, approach and findings with students, peers and faculty of ACBR at Delhi University. I am sure that some very important issues of societal relevance like auto-immune diseases including cancer will find place in discussion amongst experts. I wish the conference a great success.

Devesh K Sinha

Professor Daman Saluja
Director, ACBR

Message

It is my pleasure to invite all the eminent scientists, academicians, young researchers and students to **11th Frontiers in Biomedical Research 2018 symposium**. The conference aims to share an insight into the recent research and cutting-edge technologies in the field of Biomedical sciences.

Dr. B R Ambedkar Center has a distinguished record in both teaching and research. In a short span of two decades, ACBR has made a mark in the country and is recognized as a premium institute in the country. Faculty members have excellent academic credentials and are highly regarded. They have been conferred with many prestigious awards at national and international levels.

The primary goal of the conference is to bring together a multi-disciplinary group of scientists to present and exchange break-through ideas related to the human health and to promote discussions on recent trends in these areas. This shall not only stimulate the young minds but will further strengthen the research in the Center through collaborations.

We're looking forward to an excellent meeting with great scientists from different Institutes to share their research and enlighten us through their presentations.

Daman Saluja

Dr. Ajay K. Yadav
Organizing Secretary

Message

It's give me great pleasure to heart-warm welcome all the distinguished speakers and participants to the Annually organized 11th Symposia on Frontiers in Biomedical Research, University of Delhi, February (19- 21) 2018 in Conference center of University of Delhi (North campus). This been a honorable moment for us to collegiate the event with distinguished fraternity, to discuss more about challenges in human health care.

The theme dedicated for FBR-2018 symposia "*Challenges In Human Health:* Prevention, Diagnosis and Cure" was chosen reflecting the amalgamation in biomedical sciences across the major science disciplines. As our center that started the interdisciplinary course in Biomedical sciences, keeping the soul structure comprehended in a form of Scientific sessions: Infectious Disease: Modulating Genes for Survival, Innovative Technology Towards Disease Diagnosis, Challenges in Translational oncology, Life Style Diseases: Challenges and Directions, Circumventing Neurobiological Diseases, Confluence of Traditional with Modern Therapies, Mining for lead molecules: Novel approaches to drug discovery; were widely been undertaken with exemplary show case of strategically data to counterfeit the challenging complex diseases.

We are proud that several of our M.Sc or PhDs students from Dr. B. R Ambedkar Center for Biomedical Research, taught by our fraternity were established teachers, scientist and mentors. Keeping this rhythm and rigor for academic progress, we continue to do the annual symposia for open scientific interactions with enthusiastic approach. We hope that all participants will have meaningful outcome, with a drive to counter health challenges.

On behalf of all the members of ACBR, once again welcome you all and thank you for your participation.

Thanking You,

Ajay K. Yadav

PROGRAM COMMITTEES

Chairperson
Prof. Daman Saluja
Director, ACBR

Organizing Secretary
Dr. Ajay K. Yadav

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We are thankful to

Research Council, University of Delhi
Special Assistance Program UGC
Xcelris Labs Ltd, NuLife

For their generous support to FBR 2018

Scientific Program

Day 1: Monday, 19 February 2018

Registration: **9:00 A.M. – 10:30 A.M.**

Inauguration

Welcome by Director **10:30 A.M.**

Opening Remarks by Organizing Secretary **10:40 A.M.**

Introduction of Keynote Speaker by **10:50 A.M.**
Prof. Daman Saluja

Keynote Address

Prof. Seyed E. Hasnain

Vice-Chancellor, Jamia Hamdard and
Professor at Kusuma School of Biological Sciences, Indian Institute of Technology, New Delhi

"Tackling a super intelligent TB bacterium that takes one life every 15 seconds globally:

Challenges Ahead"

Vote of Thanks by Dr. Ajay K. Yadav **11:45: - 11:55**

High Tea **11.55 A.M. - 12.15 P.M.**

Inaugural Lecture

Tackling a super intelligent TB bacterium that takes one life every 15 seconds globally: Challenges Ahead

Prof. Seyed E. Hasnain

Jamia Hamdard-Institute of Molecular Medicine, Jamia Hamdard, Hamdard Nagar, New Delhi, 110062, India and Kusuma School of Biological Sciences, Indian Institute of Technology, New Delhi 110016; DRILS, UoH Campus, Hyderabad 500009
(www.seyedehasnain.org)

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M. tb*), takes one human life every 15 seconds globally and remains the largest cause of world population, there has been no new drug in the public domain, against tuberculosis during the last >50 years, no new vaccine in the last 75 years ago or new diagnostics after tuberculosis skin test (discovered >125 years ago). While it was hoped that with the availability of *M. tb* genome sequence new interventions against TB would emerge, we only have a slightly improved understanding of the smart strategies adopted by this very intelligent, smart and cunning pathogen.

My presentation will describe efforts in our group combining computational, functional genomics, molecular epidemiology, infection biology and clinical approaches to understand the extraordinarily clever strategies adopted by this bacterium, particularly the discovery of molecular mimicry involving intrinsically disordered regions within ORFs, including those belonging to the exclusive PE/PPE family, immune quorum sensing and strategic host pathogen cross-talks. I will also flag some of our recently initiated diagnostic efforts.

I will also focus on TB as a Grand Challenge that not only continues to baffle scientists, but is forcing us to relook at our national and trans-national political, social and economic commitments to eradicate this disease by 2050.

Session I: Infectious Disease: Modulating genes for survival

Chair: Yogendra Singh, *Dept. of Zoology, DU*		
IL-1	**Pawan Malhotra**, *ICGEB: Newer targets for drug development against malaria parasite and Hepatitis B Virus*	12:15 pm - 12:40 pm
IL-2	**Kailash C. Pandey**, *NIMR-ICMR: Role of proteases in Drug Discovery against Malaria*	12:40 pm - 1:05 pm
IL-3	**Jayantha Bhattacharya**, *THSTI: Characterizing circulating HIV-1 obtained from individuals who mount strong humoral immunity – translational insights*	1:05 pm - 1:30 pm
OP-1	**Brijendra Kumar Tiwari,** *ACBR DU: Mycobacterium tuberculosis subverts Ca^{+} signaling by inducing miR-30e expression in human dendritic cells*	1:30 pm - 1:45pm
OP-2	**Upasana Bandyopadhyay** *ACBR DU: Suppression of Toll Like Receptor 2 Mediated Pro-Inflammatory Responses by Mycobacterium tuberculosis Protein Rv3529c*	1:45 pm - 2:00 pm

Lunch: 2:00 P.M. – 2:45 P.M.

Poster Session 2:45 P.M. - 3:55 P.M. (Ends with Tea Break)

Session II: Innovative technology towards disease diagnosis

Chair: Seema Sood, *Dept. of Microbiology, AIIMS*		
IL-4	**Sunil K. Verma** *CSIR Centre for Cellular and Molecular Biology: Understanding of Basic Signalling Pathways in Cancer: Towards Novel Diagnostics and Therapeutics*	3:55 pm - 4:20 pm
IL-5	**M. Zahid Ashraf,** *Jamia-Millia Islamia: The NLRP3 Inflammasome: A Sensor for Vascular Perturbance?*	4:20 pm - 4:45 pm
IL-6	**Vinay Gupta**, *Dept. of Physics and Astrophysics DU: Development of flexible biosensors as a point-of-care diagnostic system*	4:45 pm - 5:10 pm
OP-3	**Alka Pawar**, *ACBR DU: Targeting Glutamate racemase of Mycobacterium tuberculosis: Experimenting new tricks over old enzyme to tackle antibiotic resistance menace*	5:10 pm - 5:25 pm
OP-4	**Deepali Joon** *ACBR DU: Evaluation of loop mediated isothermal amplification assay with GeneXpert MTB/RIF assay for diagnosis of tuberculosis*	5:25 pm - 5:40 pm
OP-5	**Kaushik Bhhatacharya**, *ACBR DU: Analysis of genome Variation and its functional implication in Clinical isolates of M. tuberculosis*	5:40 pm - 5:55 pm

Day II: Tuesday, 20th Feb 2018

Session III: Challenges in Translational Oncology

Chair: M. M. Chaturvedi, *Dept. of Zoology, DU*		
IL-7	**Alo Nag**, *Dept. of Biochemistry DU South Campus*: *Understanding the complexities of HPV oncogenesis to devise new treatment strategies*	9:15 am - 9:40 am
IL-8	**Rohini Muthuswami** *SLS JNU: Transcriptional regulation of the DNA damage response pathway by SMARCAL1 and BRG1*	9:40 am - 10:05 am
IL-9	**Paban Agarwala**, *INMAS: a novel approach towards medical radiation countermeasure*	10:05 am - 10:30 am
OP-6	**Parveen Kumar**, *Dayal Singh College DU*: *Co-delivery of Vorinostat and Etoposide via Disulfide Cross-Linked Biodegradable Polymeric Nanogels: Synthesis, Characterization, Biodegradation, and Anticancer Activity*	10:30 am - 10:45 am
OP-7	**Manasi Mittal**, *ACBR DU: Profiling of Sin3B mRNA alternate splicing in oral squamous cell carcinoma (OSCC)*	10:45 am - 11:00 am

Tea Break **11:00 A.M. – 11:30 A.M.**

Session IV: Life style diseases: Challenges and Directions

Chair: Anurag Agrawal, *CSIR-IGIB*		
IL-10	**Govind Makharia,** *Gastroenterology and Hepatology, AIIMS: Discovery of biomarkers for assessment of enteropathy in patients with celiac disease*	11:30 am-11:55 am
IL-11	**Rajiv Narang**, *Cardiology AIIMS: Lifestyle related cardiovascular diseases: Challenges in India*	11:55 am-12:20 pm
IL-12	**Seema Sehrawat**, *Shiv Nadar University: Combination Therapy Inspired anti-Angiogenic in vitro approach for Triple Negative Breast Cancer Treatment*	12:20 pm-12:45 pm
IL-13	**Sanjeev Sengupta** *Army Hospital Kolkata:* Obesity-the pandemonium and the pandemic	12:45 – 1:05 pm
OP-8	**Uma Dhawan**, *Bhaskaracharya College of Applied Sciences DU: Screening of environmental toxicants as risk factors for developing ALS*	1:05 pm-1:20 pm
OP-9	**Akanksha,** *ACBR DU: Role of stress inducible non-coding gene hsrω in development and characterization of its interactor DNApol-ε^{pl10R} in Drosophila melanogaster*	1:20 pm - 1:35 pm

Lunch: 1:35 P.M. – 2:30 P.M.

Poster Session 2:30 P.M. - 3:55 P.M. (Ends with Tea Break)

Session V: Circumventing Neurobiological diseases

Chair: Shashi Bala Singh, *DIPAS*		
IL-14	**Manjari Tripathi**, Neurology AIIMS: *Clinical research in epilepsy: What matters*	3:55 pm-4:20 pm
IL-15	**P.N. Yadav**, *CDRI*: *Kappa opioid receptor (KOR): Molecular target for Depression and Pain*	4:20 pm-4:45 pm
IL-16	**Simantini Ghosh**, *Ashoka University: Inflammosomes are Closely Associated with Neuroinflammation in Mouse Models of Chronic Stress*	4:45 pm-5:10 pm
IL-17	**Aparna Dixit**, *ACBR, NBRI: Understanding the molecular mechanisms underlying epileptogenesis and/or drug-resistance in patients with Mesial temporal lobe epilepsy with Hippocampal sclerosis (MTLE-HS)*	5:10 pm-5:35 pm
OP-10	**Shikha Kumari**, *ACBR DU*: *Discovery of Novel Methylsulfonyl Phenyl Derivatives as Potent Human Cyclooxygenase-2 Inhibitors with Effective Anticonvulsant Action*	5:35 pm - 5:50 pm
OP-11	**Daya Shankar Lal Srivastava**, *PGIMS Rohtak*: *Glutathione S-Transferase M1 and T1 Gene Polymorphisms in Patients with Acne Vulgaris: A Case-Control Study*	5:50 pm - 6:05 pm
OP-12	**Avadh K. Shah**, *Bussiness Development Division, Xcelris Labs Ltd., Ahmedabad, Gujarat: Interpretation of Human exome sequence data for genetic diseases and disorders*	6:05 pm - 6:20 pm

Tea Break **6:20 P.M. – 6:35 P.M.**

Tuesday, February 20 2018

Public lecture 6:35 P.M. - 7:35 P.M.

Chair: **Yogendra Singh**, *Dept. of Zoology DU*

Prof. Samir K. Brahmachari

FNA, FASc, FNASc, FNAE, FTWAS, FESPM

Innovation in Healthcare: What it takes to bring ideas to market place!

Banquet Dinner 7:45 P.M. onwards

Venue: University Guest house

Day III: Wednesday, 21st Feb 2018

Session VI: Confluence of Traditional with Modern therapies

Chair: Shive M. S. Chauhan, *Dept. of Chemistry, DU*		
IL-18	**Anil K. Mishra**, *INMAS*: *Conventional vs Receptor Directed Therapies: Track and Treat*	9:15 am - 9:40 am
IL-19	**Mitali Mukerji**, *CSIR-IGIB: Medicine for affordable health care in Indian population: the need for innovation*	9:40 am - 10:05 am
IL-20	**Madhu Chopra**, *ACBR DU: Mechanism Based Rational Design and Development of Drugs*	10:05 am- 10:30 am
OP-13	**Deepika Yadav**, *Shivaji College DU: Zoo therapeutics: A traditional and modern interface*	10:30 am - 10:45 am
OP-14	**Diksha Awadesh Verma**, *ACBR DU: Structure based Virtual Screening of Natural Compounds against Epithelial to Mesenchymal transition (EMT) Receptors in Cancer*	10:45 am - 11:00 am

Tea Break **11:00 A.M. – 11:30 AM.**

Session VII: Mining for lead molecules: Novel approaches to drug discovery

Chair: Vani Brahmachari *ACBR DU*		
IL-21	**Prasad V. Bharatam,** *Department of Medicinal Chemistry NIPER: Design and synthesis of GSK-3β inhibitors as anti-diabetic agents*	11:30 am - 11:55 am
IL-22	**B. Jayaram,** *IIT-Delhi: Genomes to Hit Molecules In Silico - An Update Integrating Chemistry with Biology & IT: Towards a Disease-Free Planet*	11:55 am - 12:20 pm
IL-23	**S. Gourinath**, *SLS JNU: Structural and functional studies, inhibitor development against cysteine biosynthetic pathway enzymes of E. histolytica*	12:20 pm - 12:45 pm
IL-24	**Agam P. Singh**, *NII*: *Vaccines for malaria pre-erythrocytic stage parasites*	12:45 pm - 1:10 pm
OP-15	**Amresh Prakash**, *SCIS JNU: Multistage Unfolding Dynamics of TDP-43 Involve in Amyotrophic Lateral Sclerosis*	1:10 pm - 1:25 pm
OP-16	**Saurabh Aagrawal**, *ACBR: Synthesis of Novel and Selective N-(benzo[d]thiazol-2-ylmethyl)-4-substituted-piperazine-1-carbothioamides and evaluate their NOS inhibiting potential in HEK cells transfected with human nNOS and eNOS*	1:25 pm - 1:40 pm
OP-17	**Rimpy Kaur Chowhan** *ACBR: Peroxiredoxin 6, a cytosolic antioxidant protein has high aggregation propensity at physiological conditions*	1:40 pm - 1:55 pm

Lunch: 2:00 P.M. – 3:00 P.M.

Valedictory Function

Chair: Dr. S.K Gupta, *NII New Delhi*

Welcome **3:45 P.M- 4:00 P.M.**

Valedictory Address: **4:00 P.M – 4:45 PM.**

Prof. Thomas Rudel

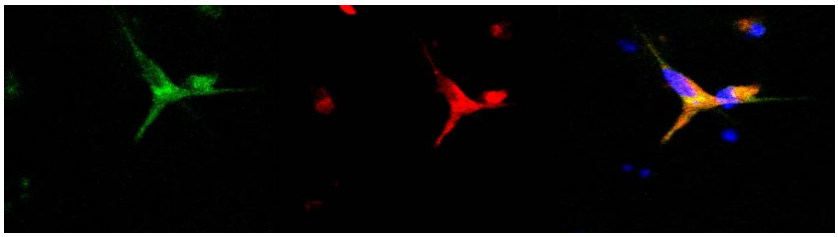
Biocentre, University of Würzburg, Germany

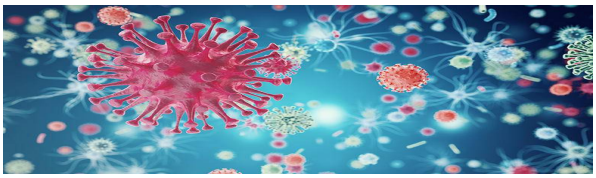
New approaches to target obligate intracellular pathogenic bacteria

Poster Prize Distribution **4:45 P.M. - 5:15 P.M.**

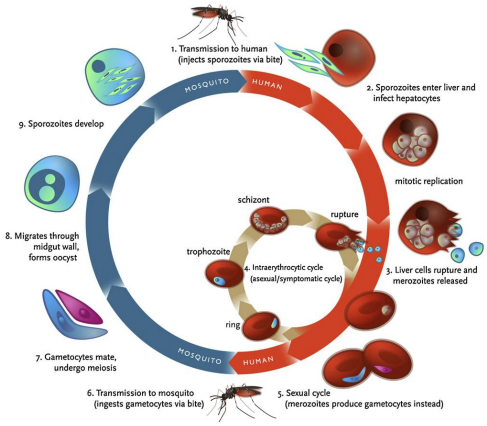
Vote of thanks **5:15 P.M. – 5:30 P.M.**

High Tea **5:30 P.M.**





Infectious Disease: Modulating Genes for Survival



INVITED LECTURE-1

Newer targets for drug development against malaria parasite and Hepatitis B Virus

Priya Gupta, Subhanita Ghosh, Rajan Pandey, Abhinav Kaushik, Avishek Kumar Singh, Dinesh Gupta, Asif Mohmmed, Shiv Kumar Sarin, Sunil K Mukherjee, Raj K, Bhatnagar and Pawan Malhotra

International Centre for Genetic Engineering & Biotechnology, New Delhi-110067
Institute of Liver and Biliary Sciences, Vasant Kunj. New Delhi-110070

Modern genomic and proteomic approaches have given useful information by linking genes (proteins) with diseases and have thus provided novel putative targets for drug discovery. Therefore, the target oriented drug discovery programs involving large scale screening of chemical compound libraries on different targets are one of the most popular modern drug discovery approaches. Here we applied targets oriented approaches to search for new antimalarial and to identify small molecule inhibitors of hepatitis B virus replication. Hemoglobin degradation and hemozoin formation are essential steps in the malaria parasite life cycle and two existing antimalarial; chloroquine and artemisinin have been suggested to act on these pathways. We have recently identified and characterized a large ~200kDa hemoglobin degradation/ Hz formation complex in the *P. falciparum* and developed an *in vitro* hemozoin formation assay. Using *in silico* and biochemical approaches, we next screened a chemical library; Maybridge Screening Collection targeting a component of hemoglobin degradation/ Hz formation complex referred as Heme Detoxification Protein, HDP. Similar way, we have targeted the hepatitis B virus X protein (HBx) that plays a critical role countering host defenses. These screening assays have allowed us to identify novel small molecule inhibitors against malaria parasite as well as against Hepatitis B virus. These results thus potentiate the development of next-generation antimalarial and RNAi based therapeutics against human viruses.

INVITED LECTURE-2

Role of proteases in Drug Discovery against Malaria

Pant A[1], Vandana [1], Kumar R[2], Wani NA[3], Singh AP[4], Verma S[1,5] ,Rai R[3], Dixit R[1], Pande V[6], Katyal A[7], Pandey KC[1,7]

[1]National Institute of Malaria Research, ICMR, New Delhi, [2]Integrated Science Lab, Umeå University, Sweden, [3]Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu, [4]National Institute of Immunology, New Delhi, [5]University of Bern, Switzerland, [6]Department of Biotechnology, Kumaun University, Nainital, [7]Dr. B. R. Ambedkar Centre for Biomedical Research, Delhi University, New Delhi, [8]National Institute for Research in Environmental Health, Bhopal.

Malarial cysteine proteases are among the critical enzymes required for parasite machinery. Structural and functional analysis of these enzymes showed that they have unique domains for refolding, inhibition and hemoglobin binding. Malarial cysteine proteases are synthesized as inactive zymogens, and hot-spots interactions are required for auto activation. The activities of malarial cysteine proteases are regulated by a new class of endogenous inhibitors of cysteine proteases. Our group is looking for new strategies to develop anti-malarial agents based on hot-spot interactions involved in activation of enzymes. Targeting protein–protein interactions is a new field to explore in malaria, which might be better tool to combat drug resistance. We have designed small molecules that interfere at the hot-spots residues involved in protein–proteins interactions. Our study also focusing unusual cysteine proteases as potential targets which are absent in human and act as potential modulator of programme cell death in *P. falciparum*.

INVITED LECTURE-3

Characterizing circulating HIV-1 obtained from individuals who mount strong humoral immunity – translational insights

Jayanta Bhattacharya

HIV Vaccine Translational Research Laboratory, Translational Health Science & Technology Institute, NCR Biotech Science Cluster, Faridabad, Haryana.

HIV-1 is notorious in evading the antiviral immunity elicited in infected patients. It evolves exponentially in the natural disease course and contributes in gradual decline in CD4-T cells thereby promoting gradual progression to AIDS. Some rare individuals infected with HIV-1 were found to significantly withstand to a greater extent the typical clinical progression by virtue of presence of highly potent broadly cross neutralizing antibodies in them. We have examined viral envelope proteins isolated from such patients that are target of neutralizing antibodies and found unique properties that provided avenues in designing prevention strategies.

ORAL PRESENTATION-1

Mycobacterium tuberculosis subverts Ca^{+} signaling by inducing miR-30e expression in human dendritic cells

Brijendra K. Tiwari[1,2], Yogedra Singh[1,3], Krishnamurthy Natarajan[1]

[1]Infectious Disease Immunology Laboratory, Dr. BR Ambedkar Centre for Biomedical Research University of Delhi, Delhi, India; [2]Allergy and Infectious Diseases Laboratory, Institute of Genomics and Integrative Biology, Council of Scientific and Industrial Research, Mall Road, Delhi 110007, India; [3]Department of Zoology, University of Delhi, Delhi, India.

The adequate regulation of innate immune responses is central aspect of host defences in contradiction of mycobacteria. MicroRNAs (miRNAs) play indispensible roles in regulating multiple biological pathways comprising innate host fortifications against various infections. MiRNAs have materialized as important post-transcriptional "fine-tuners" of gene expression in retort to pathophysiological stimuli. A given miRNA can consecutively regulate multiple target genes, frequently with linked functions, resulting in potent cumulative effects on gene networks. MiR-30 family of miRNAs are up regulated in case of tuberculosis infection.

By H37Rv infected human Monocytes derived dendritic cells (MDDCs); we establish that miR-30e expression was increased after a *Mycobacterium tuberculosis* (*M. tb*) challenge in a time and dose-dependent manner. The same tendency was also observed after BCG and H37Ra challenges.

To determine the role of miR-30e during *M. tb* infection, we observed bacterial survival using the colony-forming unit (CFU) assay. MDDCs were transiently transfected with a miR-30e mimic or inhibitor and then challenged with H37Rv at various MOI. Our results showed that the treatment with miR-30e increased the endurance of intracellular *Mtb* compared to the endurance in the control group in a time-dependent manner. Furthermore, the transfection with a miR-30e inhibitor led to the opposite outcome. Insilco we predicted that Toll-like receptor signaling, Ca2+ associated signaling, autophagy, autophagolysosomal and cytokine signaling pathways are affected by miR-30e during *M. tuberculosis* infection in human DCs.

The Ca^{2+} associated genes including calcium channel component *TRPC6* of the TRPC family and downstream effector *NFATC3* of the NFATC family have potential matches as target for miR30e. The q-PCR loss of function experiment of the targets of miR-30e further confirms our finding. Remarkably, these genes have role at various steps of this signaling pathway, from Ca2+ admittance to downstream signaling, suggesting that miR-30e might strongly constrain calcium signaling. These results indicated that miR-30e could suppress the ability of host cells to kill intracellular *M. tb.*

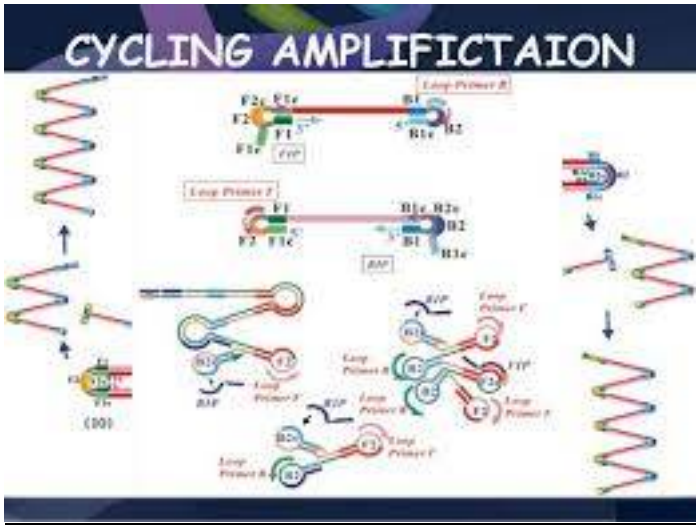
ORAL PRESENTATION-2

Suppression of Toll Like Receptor 2 Mediated Pro-Inflammatory Responses by *Mycobacterium tuberculosis* Protein Rv3529c

Upasana Bandyopadhyay[1,2], Attinder Chadha[1], Priya Gupta[7], Brijendra Tiwari[1], Kausik Bhattacharyya[3], Sonam Popli[4], Rajagopal Raman[4], Vani Brahmachari[3], Yogendra Singh[5,6], Pawan Malhotra[7] and Krishnamurthy Natarajan[1,2]

[1]From the Infectious Disease Immunology Lab, Dr. B R Ambedkar Centre for Biomedical Research, University of Delhi, Delhi 110007, India and [3]Epigenetics and developmental biology lab, Dr. B R Ambedkar Centre for Biomedical Research, University of Delhi, Delhi 110007, India, [4]Gut Biology Lab, Department of Zoology, University of Delhi, Delhi 110007, India, [5]Department of Zoology, University of Delhi, Delhi 110007, India, [6]Allergy and Infectious Diseases Lab, Institute of Genomics and Integrative Biology, Council of Scientific and Industrial Research, Mall Road, Delhi 110007, India, [7]International Centre for Genetic Engineering and Biotechnology, Aruna Asaf Ali Marg, New Delhi 110067, India.

Microorganisms are known to devise various strategies to thwart protective responses by the host. One such strategy is to incorporate sequences and domains in their genes/proteins that have similarity to various domains of the host proteins. In this study we report that *M. tb* protein Rv3529c exhibits significant similarity to the death domain of Toll Like Receptor (TLR) pathway adaptor protein MyD88. Incubation of macrophages with Rv3529c specifically inhibited TLR2 mediated pro-inflammatory responses. This included attenuated oxidative burst, reduced phosphorylation of MAPK-ERK, reduced activation of transcription factor NF-kB and reduced secretion of pro-inflammatory cytokines IFN-γ, IL-6 and IL-17A with a concomitant increased secretion of suppressor cytokines IL-10 and TGF-b. Importantly, Rv3529c significantly inhibited TLR2 induced association of MyD88 with IRAK1 by competitively binding with IRAK1. Further, Rv3529c mediated inhibition of apoptosis and phagosome-lysosome fusion. Lastly, incubation of macrophages with Rv3529c increased bacterial burden inside macrophages. The data presented here shows another strategy evolved by *M. tb* towards immune evasion that centers on incorporating sequences in proteins that are similar to crucial proteins in the innate immune system of the host.



Innovative Technology Towards Disease Diagnosis

INVITED LECTURE -4

Understanding of Basic Signalling Pathways in Cancer: Towards Novel Diagnostics and Therapeutics

Sunil Kumar Verma, *CSIR Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad 500 007, India*

In the year 2001, first cDNA microarray facility of India was established in the Centre for Cellular and Molecular Biology (CCMB) in Hyderabad. During 2001-2003, we studied the microarray gene expression profiles of Indian patients with HNSCC and identified a total of 274 genes with significant differential expression in HNSCC tissues. Of these 274 genes, the gene named **S**ecreted **P**rotein **A**cidic **R**ich in **C**ysteine (SPARC), also known as Osteonectin or BM40 was found significantly up-regulated and **Cry**stallin, **a**lpha **B** (CRYAB) as significantly down-regulated in Head and Neck Squamous Cell Carcinoma (HNSCC). Our findings were later confirmed by various independent studies suggesting these two markers may serve as independent prognostic marker for disease-free interval (DFI) and overall survival in HNSCC.

Furthermore, these findings later led to the discovery of Abraxane® an albumin bound form of paclitaxel for the treatment of several metastatic cancers including breast cancer where SPARC is over expressed in pathological conditions. Abraxane® has indeed received an approval in 34 countries including the USA, Canada and more recently in India.

More recently, we have discovered a novel PKC based regulation of the activities of tumour suppressor Ras association domain family 1 (RASSF1), which is epigenetically inactivated in many human solid tumours; resulting in loss of expression of RASSF1A Transcript in 80 to 100% of small cell lung carcinoma (SCLC) cell lines and tumours, 63% of non small cell lung carcinoma (NSCLC) cell lines and tumours, 49% of primary breast tumours and 64% of breast cancer lines, 70% of primary nasopharyngeal cancers (NPCs), 91% of primary renal cell carcinomas (RCCs), and 100% of RCC lines. The implication of our findings was that this PKC mediated regulation of RASSF1A may contribute to the repertoire of mechanisms engaged to inactivate RASSF1A in tumourigenesis.

Further understanding of these pathways and underlying molecular mechanisms offers the discovery of novel diagnostics and therapeutic targets for various solid tumours where RASSF1A is not epigenetically inactivated. These findings will be presented in detail.

INVITED LECTURE -5

The NLRP3 Inflammasome: A Sensor for Vascular Perturbance?

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Inflammasomes are a multiprotein complex that triggers the activation of caspases-1, leading to the processing and secretion of the pro-inflammatory cytokines interleukin-1β (IL-1β) and IL-18. The best characterized, nucleotide binding domain, leucine rich containing family, pyrin domain containing protein 3 (NLRP3) inflammasome plays a critical role in modulating inflammatory and innate immunity responses. The NLRP3 inflammasome is activated by a wide range of danger signals that derive not only from microorganisms but also from sterile inflammation. We have shown the activation of the NLRP3 inflammasome complexes augments vascular diseases especially thrombosis in response to hypoxia. Utilizing an animal model for hypoxia induced thrombosis, we demonstrated that hypoxia accelerates coagulation and *in vivo* siRNA-mediated inhibition of NLRP3 inflammasome-caspase- 1-IL- Iβ, axis resulted in decreased clot formation due to hypoxic conditions. The study suggested that thrombosis under hypoxia is centrally regulated by a complex network of coagulatory and inflammatory processes, critically linked through hypoxia inducible factor-1 α (HIF-1α).

The translational implication of this novel finding was evident by activation of NLRP3 inflammasome components in human patients, who developed thrombosis while staying under hypoxic environment. The results also suggest that the activation of this complex is likely to be an early response to hypoxia, which precedes coagulation and hence the onset of thrombosis. Thus the NLRP3 inflammasome could be a potential sensor for vascular perturbance and inhibition of NLRP3- IL-1β, axis could prevent thrombotic events and has potential implications for developing therapeutics.

INVITED LECTURE -6

Development of flexible biosensors as a point-of-care diagnostic system

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Biosensors have lead to a revolution in diagnostics with the highly sensitive devices detecting biological analytes in ultra-low concentrations. However, the goal is to further develop these technologies so that the systems become user friendly, miniaturized, portable and wearable. Flexible sensors provide a step forward towards these technologies. A flexible biosensor based on carbon nanofibers has been developed and utilized for electrochemical detection of cholesterol whilst demonstrating its flexibility (in collaboration with Korea Institute of Technology). An integrated electrode biosensor has been developed by miniaturizing the conventional three-electrode system. To reduce reagent volume and enable continuous real time measurements, polydimethylsiloxane (PDMS) microchannels of cross sectional area 300 μm x 40 μm have been fabricated. However, it becomes increasingly important to develop these devices in a low cost and disposable format. Thus, a filter paper based low cost microfluidic biosensor has been developed for cholesterol quantification.

ORAL PRESENTATION-3

Targeting Glutamate racemase of *Mycobacterium tuberculosis*: Experimenting new tricks over old enzyme to tackle antibiotic resistance menace

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Abstract

There is an urgent need to identify novel drug targets and discover new antimicrobial inhibitors given the ever-evolving rate of drug resistance against currently used antimicrobial agents. *Mycobacterium tuberculosis*, the causative agent of infectious disease tuberculosis, has also developed drug resistance against various antibiotics that are used to treat patients. Moreover, multiple drug resistance (MDR) and extensively drug resistance (XDR) strains of *M. tuberculosis* are also reported in literature. System biology approaches offer an important platform that facilitates identification of potential drug targets to circumvent the problem of ever increasing drug resistance. Proteins exhibiting high level of conservation among various species could be considered and reported inhibitors against these homologous proteins may be used for targeting *Mycobacterium tuberculosis*. In the present study, we have analyzed possible mechanism of action of compounds targeting one such protein Glutamate racemase of *M. tuberculosis* (MTB-GR), an enzyme that is involved in the early phases of peptidoglycan biosynthesis. MTB-GR is called as a Moonlighting protein because this protein has two distinct functions. We analyzed various known natural compounds (inhibitors) having reported antimicrobial activities and observed that flavonoid compounds, namely quercetin and naringenin gave the best results. Importantly, both these compounds showed negligible cytotoxic effect on THP-1 human monocyte macrophage cell line as revealed by MTT assay. Both quercetin and naringenin were docked onto the crystal structure active site of the MTB-GR. A UV-CD spectroscopy studies suggest thermodynamic changes at the secondary and tertiary structure level of the protein in the presence of inhibitors. The conversion of L to D-glutamate in the presence and absence of inhibitors was also compared via racemization activity followed by enzyme kinetics to decipher the best inhibitor. In conclusion, our study suggests the role of moonlighting proteins as potential therapeutic targets to design novel drugs to combat MDR tuberculosis.

Keywords: Mycobacterium tuberculosis, Glutamate racemase, Drug resistance

ORAL PRESENTATION-4

Evaluation of loop mediated isothermal amplification assay with GeneXpert MTB/RIF assay for diagnosis of tuberculosis

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Background: Tuberculosis (TB) is a public health problem worldwide. For diagnosis of tuberculosis, smear microscopy is less sensitive, while culture method is time consuming. Automated real-time PCR based Xpert MTB/RIF assay has been endorsed by WHO for detecting the presence of *Mycobacterium tuberculosis*. There is need for sensitive diagnostic test with minimal infrastructure, cost and training. Therefore, present study was carried out to evaluate the diagnostic performance of Loop-mediated isothermal amplification (LAMP) assay with culture and GeneXpert MTB assay in clinical specimens.
Methods: A cross-sectional study was conducted and sputum specimens were collected from patients visiting Vallabhbhai Patel Chest Institute, Delhi during September 2015 to August 2016. Pulmonary TB diagnosis using sputum smear microscopy, culture, GeneXpert MTB assay and *sdaA* LAMP assay was carried out. Demographic characteristics of the study participants were also determined. Analysis of sensitivity and specificity for *sdaA* LAMP assay compared with culture and GeneXpert as a reference standard was performed. Response to antitubercular treatment was also taken into consideration. Cohen's kappa coefficient was calculated as measure of agreement between the tests.
Results: A total of 125 pulmonary presumptive TB patients sputum sample were analyzed. The sensitivity of LAMP was 100% in culture positive specimens. In smear negative and culture negative specimens, LAMP results were compared with GeneXpert MTB assay and response to antitubercular treatment. LAMP assay showed high concordance with GeneXpert MTB assay results in these specimens.
Conclusion: A low cost yet accurate and robust platform is needed to replace smear microscopy for diagnosis of pulmonary TB. In the present study, *sdaA* LAMP assay showed high sensitivity and specificity in comparison with culture and GeneXpert MTB assay. Owing to its low cost, speed, simplicity, sensitivity and specificity, *sdaA* LAMP assay is a potential diagnostic test for diagnosis of tuberculosis especially in resource limited settings.

ORAL PRESENTATION-5

Analysis of genome Variation and its functional implication in Clinical isolates of *M. tuberculosis*

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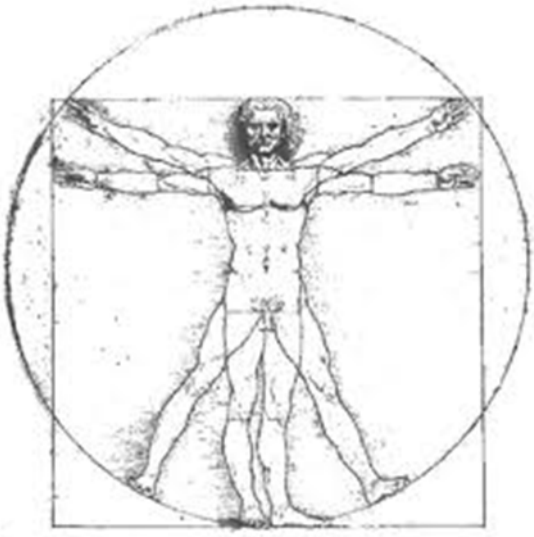
Tuberculosis though preventable and a completely curable disease, there were about 0.7 million deaths due to tuberculosis in 2015 and about 0.2M people got affected with Drug-Resistant tuberculosis in the same year (WHO 2017). We have analysed genetic variation among clinical isolates, including a multidrug resistant clinical isolate VPCI591 of *M.tuberculosis* in a comparative genomics analysis with the reference strain, *M.tuberculosis, H37Rv*. Almost all the data is from Next generation sequencing. One of the variations occurs in the protein, Rv0981, MprA an important Response Regulator of two component system of *M.tuberculosis*. In addition, mprA(Rv0981) is also identified as a late antigen (Deepti *et al,* J Immunol 2010; 184:5444-5455). The variation (208G>A) leading to replacement of glycine by serine (G70>S) has been detected in ~13% of global clinical isolates (tbvar Joshi,K.R. *et. al*. Database 2003). In the light of the functional implication of MprA, we examined the biological implication of this variation if any, in THP-1 cell. Interestingly, we observe the total nuclear localization of the cloned proteins and also its effect on the levels of interleukins. Further we observe variation in the effect on interleukin levels by the reference protein MprA and its variant in THP-1 derived macrophages. In an attempt to investigate if there is any structural implication of this variation, we have carried out molecular dynamic simulation.



Challenges in Oncomedicine

INVITED LECTURE -7

Understanding the complexities of HPV oncogenesis to devise new treatment strategies

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High risk HPV is acclaimed to be the major causative agent of cervical cancer, a devastating disease with significant morbidity. Therefore, understanding the molecular pathway that contributes to HPV oncogenesis constitutes an important area of research. In India, cervical cancer remains the major cause of cancer mortality among women. Till date, there exists no specific treatment for curing HPV infections. Lack of mechanism-based treatment strategies due to poor understanding of the HPV-induced malignant transformation machinery is a matter of great concern and utmost importance. Our study aims at catering to the need of the time by revealing some of the key molecular mechanisms that contributes to HPV oncogenesis that can be utilized to discover promising anti-cancer molecules. We explored some of the novel targets of E6 and E7 and delineated the oncogenic connections. Our study proposes a possible mechanistic basis for HPV pathogenesis by identifying HPV16E6 mediated SUMOylation of hADA3 (a transcriptional coactivator) as the most likely cause of its downregulation in cervical cancer cells and thus, leading to oncogenesis.

In another study, we investigated the mechanism for aberrant expression of the oncogenic transcription factor, FoxM1 cervical cancer. In this work, we report that SUMOylation contributes to destabilization and nucleocytoplasmic shuttling of FOXM1b protein. We highlighted the biochemical mechanism that HPV employs to induce malignancy. Our work also shows how HPV oncoproteins attack the cellular SUMO machinery and wins the battle by manipulating key enzymes. Altogether, these studies shed light on mechanistic aspects of HPV pathogenesis and are important for development of more rationalized anti-cancer modalities.

INVITED LECTURE -8

Transcriptional regulation of the DNA damage response pathway by SMARCAL1 and BRG1

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Abstract: The DNA damage response pathway is modulated by sensors, transducers and effectors. ATM and ATR kinases are the transducers of the DNA damage signal that is detected by gH2AX. These two kinases phosphorylate downstream effector molecules to effect DNA repair. In addition, the DNA damage response also requires chromatin remodeling and non-coding RNA synthesized by DROSHA, DGCR8 and DICER for effecting the repair.

SMARCAL1 and BRG1 are two ATP-dependent chromatin remodeling proteins that play a role in DNA damage repair. Mutations in SMARCAL1 cause Schimke Immuno-osseous dysplasia (SIOD) and mutations in BRG1 cause Coffin-Siris Syndrome (CSS).

SMARCAL1 and BRG1 mutually co-regulate each other and their expression is upregulated when double-strand breaks are induced. This upregulation is needed for co-regulating genes encoding for *ATM*, *ATR*, *DROSHA*, *DGCR8*, and *DICER* so that appropriate DNA damage response could be mounted. This transcriptional loop is feedback regulated by phosphorylated ATM and ATR. Overexpression of PP2A and WIP1 phosphatases that are involved in dephosphorylation of ATM and ATR leads to cessation of the DNA damage response by switching off the transcriptional loop.

Thus, our results indicate that DNA damage response is regulated by an ON/OFF transcriptional switch operated by SMARCAL1 and BRG1 and feedback regulated by phospho-ATM and phospho-ATR. Downregulation of SMARCAL1/BRG1 results in abrogation of the DNA damage response resulting in mitotic abnormalities. In addition, mutations either in SMARCAL1 or BRG1 that impair their ATPase activity also result in impaired DNA damage response, possibly contributing to the pathology of SIOD and CSS.

INVITED LECTURE -9

A NOVEL APPROACH TOWARDS MEDICAL RADIATION COUNTERMEASURE

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Institute of Nuclear Medicine and Allied Sciences, Delhi

Though the need of medical countermeasures against radiation was felt soon after the discovery of X-rays, it became of prime importance immediately after the Hiroshima and Nagasaki nuclear devastation during the world war-II. At initial days it observed little progress since it was being considered important for military. The Walter Reed Army Institute by screening more than 10000 molecules over a period of about five decades could arrive to only one molecule with radioprotective efficacy for human applications under restricted conditions. With better understanding of radiation injury subsequently several free radical scavengers. Vitamins, growth factors, cytokines and also herbal etc have been studied extensively to achieve radioprotection. However, only a little success has been achieved so far worldwide.

Recently, our laboratory has been exploiting HDAC inhibitors for use as radiomitigators or post-irradiation radioprotector with some novel hypothesis. Many HDAC inhibitor molecules have been studied for their radiosensitization and anticancer ability and recently US FDA have granted permission for some HDAC inhibitors for use as chemotherapeutics. The talk will cover the genesis of the hypothesis and few initial results proving HDAC inhibitors as radiomitigators.

ORAL PRESENTATION-6

Co-delivery of Vorinostat and Etoposide via Disulfide Cross-Linked Biodegradable Polymeric Nanogels: Synthesis, Characterization, Biodegradation, and Anticancer Activity

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Treatment regimens for cancer patients using single chemotherapeutic agents often lead to undesirable toxicity, drug resistance, reduced uptake etc. Combination of two or more drugs is therefore becoming an imperative strategy to overcome these limitations. A step forward can be taken through delivery of the drugs used in combination via nanoparticles. Co-administration of chemotherapeutic drugs encapsulated in nanoparticles has been shown to result in synergistic effects and enhanced therapeutic efficacy. In this study, we explored the combination treatment of histone deacetylase inhibitor vorinostat (VOR) and topoisomerase II inhibitor etoposide (ETOP). The concurrent combination treatment of VOR and ETOP resulted in synergistic effect on human cervical HeLa cancer cells. VOR and ETOP were encapsulated into poly(ethylene glycol) monomethacrylate (POEOMA)-based disulfide cross-linked nanogels. The nanogels were synthesized using atom transfer radical polymerization (ATRP) via cyclohexane/water inverse mini-emulsion and were degradable in presence of intracellular glutathione (GSH) concentration. Both the drugs were loaded into the nanogels by physical encapsulation method and characterized by Fourier transform infrared spectroscopy (FTIR), transmission electron microscopy (TEM), X-ray diffraction (XRD), dynamic light scattering (DLS), and differential scanning calorimetry (DSC). Both VOR- and ETOP-loaded nanogels showed sustained release profile. Furthermore, combination treatment drugs encapsulated POEOMA nanogels demonstrated enhanced synergistic cytotoxic effect compared with combination of free drugs. Enhanced synergistic cell killing efficiency of drug-loaded POEOMA nanogels was due to increased apoptosis via caspase 3/7 activation. Therefore, combination of VOR- and ETOP- loaded PEG-based biodegradable nanogels may provide a promising therapy with enhanced anticancer effect.

ORAL PRESENTATION-7

Profiling of Sin3B mRNA alternate splicing in oral squamous cell carcinoma (OSCC)

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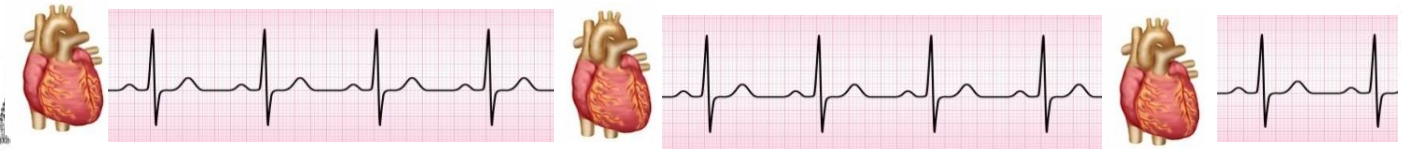
Sin3B is a transcriptional co-repressor that forms a complex with Histone Deacetylases and brings about chromatin modifications that eventually lead to transcriptional repression of the target gene. Sin3 isoforms are capable of undergoing alternative splicing at their mRNA level, which has not been elucidated much, both nationally and internationally. Oral cancer affects a large fraction of Indian population with a poor five-year survival rate connoting the need for its early diagnosis and better prognosis. Therefore, we investigated the importance of splicing of Sin3B mRNA in OSCC disease progression.

The expression of the Sin3B (wild and spliced variant) gene was checked in mRNA isolated from adult tissues, fetal tissues and several mammalian cells lines. mRNA was also isolated from biopsy samples (both malignant and pre-malignant area) of OSCC patients as well as a few normal oral mucosal swabs. The expression of spliced form of Sin3B gene along with wild type was evaluated in these tissue samples by TaqMan assays based real time PCR.

The wild type variant of Sin3B gene gives a band of 800bp where as the spliced variant furnishes a 900bp amplicon after cDNA amplification. The spliced m-RNA was mapped on the Sin3B gene using bioinformatic tools and was found to have an in-frame insertion of 96bps (32 amino acids) at the 3'end of 9^{th}exon. The wild type variant of Sin3B was ubiquitously expressed in all adult tissues examined but the spliced variant was found only in lung, placenta, skeletal muscle and liver tissue. Additionally, the spliced variant along with the wild type variant of Sin3B gene was observed in several mammalian cell lines but no expression of the spliced variant was found in the fetal tissue samples. Furthermore, the expression of spliced form of Sin3B was more in oral
cancer patients as compared to the pre-malignant and the healthy counterparts connoting the importance of Sin3B gene splicing in tumorigenesis.

Life Style Diseases: Challenges and Directions



INVITED LECTURE -10

Discovery of biomarkers for assessment of enteropathy in patients with celiac disease

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Celiac disease (CeD) is a global disease and approximately 0.7% of the global population is estimated to have CeD. While villous atrophy is the hallmark of CeD, there are many other non-celiac enteropathy (NCE), including tropical sprue, parasitosis, immunodeficiency states, Crohn's disease, and drugs (Olmesartan). While demonstration of presence of villous atrophy is essential for the initial diagnosis of CeD, demonstration of mucosal healing is also now being considered as a desirable outcome. Getting access to good intestinal mucosal biopsies is not only invasive and expensive but also necessitate well-oriented high-quality biopsy specimens and experienced pathologist for reading them. In fact, an active debate is going on amongst celiac disease scientific community, whether to do biopsies or skip biopsies in making of a diagnosis of CeD. A relevant question is "can we demonstrate/predict villous atrophy by non-invasive means. Furthermore, many targeted treatment for CeD are evolving. In order to test their efficacy in the clinical trials, these biomarkers can come handy in the assessment of histological responses and may provide options for avoiding repeated or periodic biopsies.

INVITED LECTURE -11

Lifestyle related cardiovascular diseases: Challenges in India

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Lifestyle-related cardiovascular diseases have become a major public health problem in India. These include hypertension, hyperlipidemia and atherosclerotic vascular disease in addition to closely related diabetes and obesity. Hypertension or high blood pressure can, in turn, lead to atherosclerotic vascular disease, heart failure, renal dysfunction etc. Atherosclerotic vascular disease, i.e. development of atheromatous plaques in the arterial tree, can lead to different clinical syndromes depending on the location of these plaques. Atherosclerotic disease in coronary circulation of heart leads to angina pectoris, unstable angina, myocardial infarction, cardiac arrhythmias, heart failure and even sudden cardiac death. Plaques in the cerebral circulation can lead to transient ischemic attacks or stroke which can cause permanent disability. Atherosclerosis in renal arteries can lead to hypertension which can be severe and resistant to drugs and may even lead to acute heart failure with pulmonary edema. Atherosclerotic plaques leading to obstruction of arteries to limbs can lead to acute or chronic limb ischemia and even gangrene which may require amputation. Considering the severe consequences of lifestyle-related heart disease, emphasis has to be placed on prevention and management of these disorders. Lifestyle factors such as smoking, high-calorie high-fat diet, prolonged sitting, lack of physical exercise, psychosocial stress etc need to be avoided. Indians develop lifestyle-related heart diseases at an earlier age than western population. This may be due to genetic factors, various aspects of which also need to be studied.

INVITED LECTURE -12

Combination Therapy Inspired anti-Angiogenic *in vitro* approach for Triple Negative Breast Cancer Treatment

Seema Sehrawat, Naveen Kumar and Peeyush Prasad

Brain Metastasis and NeuroVascular Disease Modeling Lab, Dept. of Life Sciences, School of Natural Sciences, Shiv Nadar University, India and Professor Visiting, Harvard Medical School, Boston,MA, USA

Triple negative breast cancer is one of the subtype of breast cancer which contributes to 12% of the clinical cases and is associated with high mortality among women. Ability of cancer cells to migrate to distant sites and thereby establishing a new niche for proliferation is one of the less understood processes. For migration and growth cancer cells make new angiogenic tube in hypoxic tumor microenvironment. Hypoxia–adenosine in the tumor microenvironment generate a niche and are a potent target for therapeutic intervention. Adenosine and its target receptors modulate the tumor microenvironment and are involved in several processes such as immune response and cellular metabolism. Anti-angiogenic therapy in combination with targeting cancer cells can be effective approach for treating cancer. Blocking the microvessels can stop the nutrient and oxygen supply from endothelial cells to the cancerous cells resulting in decreased tumor growth. We have utilized anti-angiogenic blockers to evaluate the performance of combinational therapy approach in a MDA-MB-231 and HUVEC cell coculture system. We observed that the combinational therapy using inhibitor of adenosine receptor in combination with an FDA approved drug efficiently inhibited the tumor-induced angiogenesis as compared to individual drugs. Our work opens new avenues for breast cancer therapy.

INVITED LECTURE -13

Obesity-the pandemonium and the pandemic

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Army Hospital Kolkata

While the world was dominated with Infectious diseases and Malnutrition till the late 19th century, the last century has seen the emergence of Non-Infectious diseases as the new Captains of Death. Morbidity and mortality in the new emerging industrialised world is now being driven by non-infectious diseases like hypertension, diabetes, dyslipidaemia and Obesity. The following paper attempts to chart the conundrum that Obesity presents in the emerging world with a brief on genetics, the lethality of it and therapeutics.

ORAL PRESENTATION-8

Screening of environmental toxicants as risk factors for developing ALS

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder characterized by progressive loss of motor neurons. The majority (~90%) of the ALS cases are sporadic strongly suggesting a role for environmental factors in the etiology of the disease. The hallmark pathology of ALS is cytoplasmic aggregates composed of TAR DNA binding protein (TDP-43).

This study sought to identify environmental toxicants that increase aggregation of TDP-43. The assay involved the screening of 91 compounds (NTP HTS NeuroTox 91 panel) in rat PC12 cells stably expressing TDP-43::EGFP. Cells were treated with four different doses of each of these toxicants for 18-20 hours and then TDP-43::EGFP distribution was quantified using the In Cell analyzer 2000 (GE Healthcare). The fraction of cells with TDP-43 puncta, the expression level of TDP-43 and cell viability were quantified.

We observed that cells treated with four toxicants (Lead (II) acetate trihydrate, Methyl mercuric (II) chloride, Bis(tributyltin)oxide, and Colchicine) have increased TDP-43 aggregates. In a follow up study, we are testing these compounds in cultured primary neurons.

The preliminary results from this screen indicate that some environment toxicants can induce TDP-43 aggregation similar to that observed in ALS. These results raise the possibility that these toxicants could be risk factors for developing ALS or other related neurodegenerative diseases. Epidemiological studies provide support for the putative role of these compounds as risk factors for ALS. This work also suggests that high throughput screens can successfully identify environmental toxicants that are putative risk factors for ALS.

ORAL PRESENTATION-9

Role of stress inducible non-coding gene *hsrω* in development and characterization of its interactor *DNApol-ε^{pl10R}* in *Drosophila melanogaster*

Akanksha[1] and S. C. Lakhotia[2]

[1]*Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi,* [2]*Banaras Hindu University, Varanasi*

The *hsr-omega* (*hsrω*) gene is a non-coding gene with multiple transcription products. It produces two distinctive primary transcripts, viz., >10 kb long hsrω-n1 and ~1.9 kb long hsrω-pre-c. These are spliced to generate a nuclear hsrω-n2 and a 1.2 kb cytoplasmic hsrω-c transcript, respectively. A small ORF (ORFω), present in the exon1 of the 1.2 kb transcript and encoding 27 amino acid long polypeptide is translatable but the product is not detectable. Extensive studies on the hsrω-n1 and hsrω-n2 nuclear transcripts have suggested their roles in the regulation of certain RNA binding proteins but the functional significance of hsrω-c and the ORFω remains unexplored. The present study was undertaken to study the function and regulation of *hsrω* gene and to characterize one of its novel interactor *DNApol-ε^{pl10R}*.

To study the role of cytoplasmic transcript (hsrω-c) of hsrω and to check if the ORFω (a small ORF present in *hsrω* gene) has any role in fly development, we generated several transgenic lines to overexpress the complete gene or only hsrω-pre-c with or without mutation at the initiation codon of ORFω. It was found that the mutation in the ORFω leads to developmental arrest at larval stage and enhanced thermo-sensitivity. This is the first evidence showing the functional significance of the translation of ORF-ω.

Along with this we found that only 124bp proximal promoter region is sufficient for its developmental expression and also allows heat shock (HS) induction of the gene, although at a lower level compared to wild type resulting in delayed larval lethality. It was found that this altered HS inducibility of *hsrω* affects the hnRNPs redistribution on polytene chromosomes during recovery from HS that would adversely affect restoration of normal cellular activity. One of the genetic and molecular interactor of *hsrω* gene, *DNApol-ε^{pl10R}*, was also characterized by using various genetic and molecular approaches. The *DNApol-ε^{pl10R}* carries mutations in the exon1 of *DNApol-ε* leading to its reduced expression resulting in phenotypic anomalies.

Circumventing Neurobiological Diseases

INVITED LECTURE - 14

Clinical research in epilepsy: What matters

Manjari Tripathi

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Episodic neurological events are paroxysmal neurological dysfunction which are transient, recurrent, and often stereotyped. Proper diagnosis and effective management of episodic events presents one of the biggest challenges in neurological practice for the following reasons. Firstly, diagnosis of the episodic events depends on the accurate history and precise description of the event by an eye-witness. However, often the event may not be witnessed at all or may be witnessed by the strangers. The people witnessing the events become so frightened that they tend to miss the salient features. Secondly, the diagnosis of these events requires careful and meticulous history which is quite labor intensive and time consuming. Most of the busy neurologists often lack the patience and time to undertake such an effort. To compound the problem, majority of these patients do not have any objective findings on clinical examination. Lastly, there are no confirmatory tests to positively diagnose all the episodic events and the available tests including EEG have important limitations. On the brighter side, advent of mobile phones with facility of video recording has simplified the approach to the diagnosis of the events. Once the diagnosis is made begins the journey of classifying the seizure and finding the etiology and treating it. Recent developments in these areas will be discussed.

INVITED LECTURE - 15

Kappa opioid receptor (KOR): Molecular target for Depression and Pain

Shalini Dogra, Poonam Kumari and Prem N. Yadav

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Decades if scientific evidence shows significant role of opioid dysregulation in various psychiatric conditions, and the therapeutic potential of opioid modulation. Psychotomimetic and prodepressive effect by kappa opioid receptor activation in rodents and human has also been shown. Our recent works reveal the molecular determinant of KOR mediated depression and antidepressant response of KOR antagonist. We observed that chronic KOR activation significantly increased depression like symptoms (behavioral despair, anhedonia and sociability) in C57BL/6J mice, which are resistant to SSRIs. Further molecular studies revealed a cross talk between KOR and NR2B-NMDA in hippocampus of the depressed mice, which acts as a molecular determinant of treatment resistant depression like conditions. We have also evaluated another facet of KOR signaling, which is induction of analgesia. Since KOR activation leads to hallucination, dysphoria and sedation in humans as well as humans, several clinical trials with KOR agonists for pain treatment were terminated. However, biased agonist of KOR has never been evaluated for their effect on pain or psychotomimetic effects. Interestingly, using high throughput screening of our chemical libraries, we discovered novel , highly selective baised KOR agonist. In vivo evaluation of our novel biased agonist revealed that such ligand could be potent analgesics without having adverse effect profile of sedation, hallucination and dysphoria. Thus, our studies revealed that a selective KOR antagonist could be used to treat refractory depression, while G-protein biased KOR agonist could be used for the treatment of pain disorders.

INVITED LECTURE - 16

Inflammosomes are Closely Associated with Neuroinflammation in Mouse Models of Chronic Stress

Simantini Ghosh, *Ashoka University, India*

Posttraumatic stress disorder (PTSD) is characterized by an impaired stress response comorbid with severe anxiety. PTSD is a common finding after exposure to occupational and personal traumatic events leading to immense health and socioeconomic ramifications. Present therapies fall short of effectively treating PTSD and preventing relapse, and the neurobiological mechanisms are incompletely understood. In rodents, PTSD is associated with a chronic pro-inflammatory state, characterized by elevated levels of IL1beta, IL-6, TNF-alpha, and other inflammatory mediators in the blood and brain. We investigated neuroinflammation and underlying signaling mechanisms in mouse models of PTSD. We utilized psychological stress and physical stress models of PTSD. Psychological stress was based on exposing mice to predator odor, and concurrent restraining and underwater trauma induced physical stress. Post-stress, mice from both models showed heightened anxious behavior. We observed an increase in pro-inflammatory mediators IL-1beta and IL-6 in the brain at 24 hours following the last stress episode. The molecular steps leading to the maturation of IL-1beta, the master pro-inflammatory cytokine, involve activation of a protein complex called the inflammosome. However, the precise role of inflammosomes in PTSD is unknown. We investigated various inflammosomes in the brains of animal models of PTSD. We observed a significant increase in NLRP3 inflammosomes in the brains of mice at 24 hours post-stress. NLRP3 modulates neuron-microglia interaction and plays an important role in several neurodegenerative diseases. Our data suggest that they could be also crucial in PTSD pathophysiology. Our current studies are directed toward exploring the potential of targeting inflammosomes in PTSD therapy.

INVITED LECTURE - 17

Understanding the molecular mechanisms underlying epileptogenesis and/or drug-resistance in patients with Mesial temporal lobe epilepsy with Hippocampal sclerosis (MTLE-HS)

Aparna Dixit

Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi

MTLE-HS, the most common subset of drug-resistant epilepsy (DRE) associated with large-scale network abnormalities, lacks effective therapies due to lack of understanding of the cellular and molecular mechanisms that leads to aberrant neuronal network formations during the course of epileptogenesis. Array-based profiling studies have shown implication of aberrant gene expression patterns in epileptogenesis. We have performed trancriptome analysis of hippocampal tissues resected from patients with MTLE-HS using RNAseq approach. Healthy tissues from tumour margins obtained during tumour surgeries were used as non-epileptic controls. RNA sequencing was performed using standard protocols on Illumina HiSeq 2500 platform. Differential gene expression analysis of the RNAseq data revealed 56 significantly regulated genes in MTLE patients. Gene cluster analysis identified 3 important hubs of genes mostly linked to, neuroinflammation and innate immunity, synaptic transmission and neuronal network modulation which are supportive of intrinsic severity hypothesis of drug resistance. This study identified various candidate genes like *FN1* which is central in our analysis, *NEUROD6*, *RELN*, *TGFβR2*, *NLRP1*, *SCRT1*, *CSNK2B*, *SCN1B*, *CABP1*, *KIF5A* and antisense RNAs like AQP4-AS1 and KIRREL3-AS2 with potential as diagnostic/prognostic biomarkers of MTLE-HS. We have also studied the excitatory postsynaptic currents (EPSCs) recorded from pyramidal neurons in resected samples under resting conditions from the hippocampal and anterior temporal lobe (ATL) obtained from MTLE-HS patients undergoing resective surgery. We observed higher frequency and amplitude of spontaneous EPSCs in both the samples compared to non-seizure control samples. The magnitude of the change in the expression of the NR2A subunit of the NMDA receptors also varied in these two regions. Thus, we proposed that the mechanism of hyperexcitabilty mediated by glutamatergic network reorganization in the hippocampal region is different from that in the ATL region of patients with HS, suggesting two independent resting-state networks at the cellular level. Taken together, these studies provide novel insights in the understanding of the pathophysiology and the genomic basis of MTLE and a better understanding of the broadly distributed resting-state networks in HS. We propose that novel therapeutic interventions affecting at network level and not just restricted to one or two targets and treatments devised to reverse severity mechanisms might hold promise for the treatment of DREs like MTLE-HS.

ORAL PRESENTATION-10

Discovery of Novel Methylsulfonyl Phenyl Derivatives as Potent Human Cyclooxygenase-2 Inhibitors with Effective Anticonvulsant Action

Shikha Kumari*, Chandra Bhushan Mishra, Manisha Tiwari

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A novel series of methylsulfonyl benzene derivatives has been designed and synthesized to evaluate their COX-2 inhibitory activity along with anti-convulsant potential. In-vitro evaluation revealed that two compounds MTL-1 and MTL-2 appeared as most potent and selective COX-2 inhibitors in entire series. Anti-convulsant potential of both potent COX-2 inhibitors was assessed in sc-PTZ induced seizure test and MTL-1 excellently protected animals from PTZ induced seizure at the dose of 30 mg/kg. MTL-1 also indicates long duration of action in time course studies and displayed significant seizure protection up to 6h of drug administration. Further, the anti-epileptogenic effect of MTL-1 has been examined in PTZ induced chronic model of epilepsy. The results indicated that MTL-1 had a significant anti-epileptogenic effect in PTZ kindled rats as compared to Etoricoxib (ETX) and PTZ alone treated group. Additionally, MTL-1 successfully improved cognition deficit in PTZ kindled rat which was confirmed by Social recognition, Object recognition and Dark-light chamber tests. Moreover, molecular docking and molecular simulation (MD simulation) studies were also performed to elucidated interaction of MTL-1 with the active site of COX-2 and results showed that MTL-1 suitably binds within active site of COX-2. To investigate the safety profile of MTL-1, a sub-acute toxicity study was also performed and MTL-1 emerged as a non-toxic chemical entity. Thus, the present investigation bestowed a potent and safe COX-2 inhibitor which was endowed with an effective anti-epileptic action.

ORAL PRESENTATION-11

Glutathione S-Transferase M1 and T1 Gene Polymorphisms in Patients with Acne Vulgaris: A Case-Control Study

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Background: Acne vulgaris is a complex, multifactorial skin disorder and is not well understood. Inflammatory, oxidative damage, genetic and environmental aspects have been implicated in pathogenesis of the several dermatological diseases including the acne vulgaris. Glutathione S-transferases (GSTs) are a multi-gene family of enzymes that are important in protection against oxidative stress, inflammation, mutagenicity and genotoxicity. Polymorphism of specific subtypes of GST enzymes (GSTT1 and GSTM1 genes) may lead to an imbalance in pro-oxidant and antioxidant systems ensuing increased production of reactive oxygen species that may influence the pathogenesis of acne in North Indian population.

Objects: This case-control study was aimed to elucidate whether the association between GSTM1/GSTT1 gene polymorphism in patients with acne vulgaris could be a susceptibility factor for disease development.

Patients and Methods: In this case-control study, we assessed 109 patients with acne vulgaris and 140 healthy individuals as a control, all from North India. Genomic DNA was extracted from human peripheral blood using phenol chloroform method. The GSTT1 and GSTM1 null genotypes were identified by multiplex polymerase chain reaction (PCR) and data analysis was done by SPSS 20.0 software.

Results: In patients, frequency distribution of null genotype of GSTM1 and GSTT1 was 42.2% and 11.9%. However, in 140 control samples, frequency of null genotype of GSTM1 and GSTT1 was 34.2% and 12.8% respectively. In statistical analysis, we observed non-significant association either in null alleles of the GSTM1 (OR = 1.39, 95% CI = 0.835–2.345, P = 0.202) or GSTT1 (OR = 0.918, 95% CI = 0.428–1.966, P = 0.825) for the susceptibility of acne disease.

Conclusion: In this case-control study, neither GSTT1 nor GSTM1 polymorphism was associated with susceptibility of acne disease. Due to small sample size, further studies with larger sample size and a wider range of GSTs gene polymorphism are warranted to conclude the acne disease susceptibility in North Indian.

ORAL PRESENTATION-12

Interpretation of Human exome sequence data for genetic diseases and disorders

Avadh K. Shah, *Bussiness Development Division, Xcelris Labs Ltd., Ahmedabad, Gujarat*

Next generation sequencing (NGS) technology is one of the rapid growing technology in medicine. Whole-genome sequencing (WGS) and whole-exome sequencing (WES) methods are charming their way in medical research, clinical diagnostic and healthcare settings, due to increased clinical utility and reduced sequencing cost per genome/exome. Although, only, 85% of the disease-causing mutations are located in exonic regions, exome (EXons of genOME) sequencing analysis has great potential to decipher the underlying causes of rare and monogenic genetic disorders as well as pathogenic variants. Every normal individual carries on an average 50–100 mutations in the heterozygous state, which cause recessive Mendelian disorders in homozygous state. WES could identify functional variants including insertions, deletions, nonsense variants, splice variants and copy-number variations, which are suspected to cause a disease.

WES has been applied in different areas of research and diagnostics, including diagnosis (prenatal diagnosis (PND), pre-implementation genetic diagnosis (PGD), carrier/mutation detection of the heterogeneous disorders such as hearing loss with many causal genes), prognosis of pre-clinical individuals, newborn screening procedures and treatment. WES provides insights into genetic diagnosis of the challenging cases by doctors, such as diagnosis of lethal fetal disorders are the presence of large number of potentially associated genes, phenotypic variabilities linked with known genetic predisposition factors and difficulties in defining pathology of mid-gestation fetus. WES of the genes made the diagnosis easier, for example, a phenotypically and genetically heterogeneous disorder named neuroacanthocytosis (NA) syndrome includes chorea-acanthocytosis (ChAc), X-linked McLeod syndrome (MLS), Huntington's disease-like 2 (HDL2) and pantothenate kinase-associated neurodegeneration (PKAN).

WES has a useful application in treatment and management of patients, screening and prenatal diagnosis, gene discovery, risk assessment, SNP detection for therapeutic selection, drug discovery, leading to the recommendation of personalized treatment for better outcomes. We will focus on few limitations of this technology along with battery of services and case histories from Xcelris Labs.

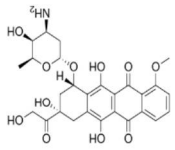
Public Lecture

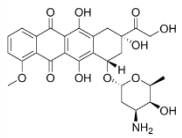
By

Prof. Samir K. Brahmachari

Innovation in Healthcare: What it takes to bring ideas to market place!

Confluence of Traditional with Modern Techniques





INVITED LECTURE – 18

Conventional vs Receptor Directed Therapies: Track and Treat

Anil Kumar Mishra

MIRC, Institute of Nuclear Medicine and Allied Sciences. Email: akmishra63@gmail.com

Many diseases are leading cause of mortality worldwide and smart specific and life changing drugs conjugate are the need of hours.

In my opinion, targeted therapies affords viable option with multidisciplinary approach keeping in view of Magic Bullet of Paul Ehrlich's century old concept is the reality of today therapeutic regimens.

Receptors of many regulatory peptides can be highly expressed in tumors thus opening an avenue of specific molecular imaging with radioligands to see where it is located and can be quantified specifically. Appropriate pharmacological properties, excellent labeling approaches with suitable isotopes offers both diagnostic and therapeutic window if exploited intelligently. The success encountered with many radiolabeled peptides for imaging and targeted therapy of tumors is endocrine tumors is one of them which are being realized at many centres in the country. Knowledge of receptor distribution in healthy organs and tumoral tissues is a fundamental pre-requisite for successful clinical applications.

INVITED LECTURE – 19

Medicine for affordable health care in Indian population: the need for innovation

Mitali Mukerji

CSIR-Institute of Genomics and Integrative Biology and CSIR's Ayurgenomics Unit-TRISUTRA, Sukhdev Vihar, Mathura Road, New Delhi, India mitali@igib.res.in

Despite major advancements in medicine, common and complex diseases such as heart disease, diabetes, obesity and cancer still remain the leading cause of morbidity and mortality across all world populations. Even the combined prevalence of rare monogenic disorders is nearly 1 to 5 % in any population. The life time prevalence of these diseases and increase in average life expectancy further lead to secondary complications due to natural progression of the disease as well as drug side effects. The need of the hour is in developing affordable solutions that would help prevent disease or maintain quality of life (QOL) in both health and disease. It is well acknowledged that there is an immense inter-individual variability in susceptibility to diseases as well as response to environment and medications. The primary aim of precision medicine is to personalize therapies that are tailored to an individual's genetic make up as well as biological state. With the advent of genomics and NGS technologies, there has been an unprecedented increase in the catalog of human genome variations not only from population but from an individual perspective. Comprehending these variations and predicting their cumulative phenotypic outcome in an individualized manner has now become a challenge. This not only involves comprehending the effect of these variations at each functional hierarchy but also threading the different hierarchy from the cellular to the system's level.

Precision medicine has been in practice for over 5000 years in Ayurveda, a system of predictive, preventive and personalized medicine. The basic tenets of the practice relies on the understanding of an individual's constitution that is important for predicting the individuals responsiveness, susceptibility and treatment. The treatment is also personalized depending on the constitution type, the state of the disease and the diseased individual. Individuals in a population are stratified into seven broad groups of constitution types that differ with respect to a large number of systemic attributes viz. anatomical features, physiological and psychological attributes and are also described to be differently susceptible to diseases and responsive to environment and treatment.

We hypothesized that phenotypic stratification of individuals using Prakriti methods might help identify homogeneous groups of individuals who are likely to display different health trajectories as well as respond to specific therapeutic interventions. Using a novel integrative approach of Ayurgenomics, we have integrated phenotypic stratification methods of Ayurveda along with objective methods for phenotype assessments, high throughput multio-mics and machine learning approaches to dissect inter-individual variability within genetically homogeneous populations. This framework has enabled us to discover Prakriti associated markers that are predictive for high altitude adaptation and susceptibility to HAPE as well as differences in response to drug and therapy. The potential of this approach for risk stratification and increasing affordability of precision medicine would be highlighted.

INVITED LECTURE – 20

Mechanism Based Rational Design and Development of Drugs

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Drug Discovery and development is a challenging multidimensional problem involving design, synthesis and optimization of compounds. Rational drug design using computational tools is used by pharmaceutical companies, research laboratories across the world at several stages of the drug discovery process. The pharmacophores may be used in several ways, for example, as a 3D query in searching 3D databases containing "drug-like" small organic molecules to identify active and specific inhibitors or in evaluating a new compound for mapping on a known pharmacophore. A drug discovery cycle, to identify, optimize, and eventually take a compound to the market, is generally a long process (approximately 12-15 years) and is very expensive (approximately $800 million R&D expense). Therefore, there is a pressing need to reduce the cost of drug discovery steps. Pharmaceutical companies are taking more rational approaches than trial and error to identify new chemical entities. We reported first model developed for Cholecystokinin receptor antagonists based on hypogen. We used quinazolinone ring system as a template for the synthesis of two series of CCK-BR antagonists. The study resulted in the development of potent CCK-BR antagonists. All the compounds were predicted for activities using pharmacophore mapping exercises and a good correlation was found between the experimentally determined and predicted antagonistic activities. The compounds showed favorable interactions within the binding site of the homology modeled CCK-BR structure. The two best compounds 3c and 4a exhibited remarkable antagonistic activities of 0.2 nM and 17.36 nM, respectively. The compounds also showed promising results in a functional gastric acid secretion assay using a lumen-perfused isolated mouse stomach and inhibited the growth of pancreatic cancer cells (MiaPaca-2) exhibiting good cytotoxicity with compounds 3f (hydrazinecarbothioamide linker) and 4b (hydrazine linker, indanone series) as the most active compounds. Compound 3f, being the best overall compound, exhibited good receptor binding affinity and cytotoxicity activity. Thus the optimized compounds in this study can be taken further for pre-clinical evaluation in drug discovery processes to develop anticancer compounds against pancreatic cancer. The predictive 3D pharmacophore model was also developed and validated for a set of inhibitors against COX-2 enzyme. The model can be used as a 3D query tool in the virtual screening of drug like molecules to retrieve new chemical entities as potent COX-2 inhibitors. Another study resulted in the identification of two novel lead compounds with potent inhibitory effect on ADAMTS-4 activity in the sub-micromolar range (IC_{50} of 0.042 µM and 0.028 µM). These results provide a guideline to the pharmacophoric requirements for the development of more potent ADAMTS-4 inhibitors. Same strategy has been applied to produce hit compounds against Histone deacetylase inhibitors and work will be published subsequently.

ORAL PRESENTATION-13

Zoo therapeutics : A traditional and modern interface

Deepika Yadav[1] and Khushi Jain[2]

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Since time immemorial, zootherapy prevalence in global traditional medical practices and pharmacopoeias along with its importance as bio- prospection for novel pharmaceutical compounds in modern times is significant. The treatment of myriad ailments with animals and their products is known as zootherapy. Of the 252 essential chemicals, selected by the World Health Organization (WHO), 8.7% comes from animals. Invertebrate and vertebrate presence has been ubiquitously chronicled in the zootherapeutics armamentarium to treat various dermatological, gastrointestinal, respiratory,cardiovascular, musculoskeletal, gynecological, neurological, urinary and hepatic diseases along with the veterinary ones. Amongst the invertebrates earthworm possess anti-pyretic, anti-spasmodic, anti-hypertensive, anti-allergic, anti- asthmatic, diuretic, de-toxic and spermatocidal effects. Whereas the sponge products act as immunosuppressive, antimicrobial, anticancer and antitumor agents. Leeches are traditionally used to cure abnormal swellings, piles, inflammatory abscess, skin diseases, rheumatoid arthritis, eye diseases, poisonous bites etc. *Hirudo medicinalis* saliva acts as an anticoagulant, local anesthetic, vasodilator and antibiotic. A synthetic congener of leech saliva's Hirudin, Bivalirudin acts as a specific and reversible direct thrombin inhibitor (DTI). Insects have anticoagulant, analgesic, antibacterial, diuretic, anesthetic, anti-inflammatory and anti rheumatic properties. Immunosuppressant margatoxin, from the scorpion *Centruroides margaritatus* venom blocks lymphocyte activation and the production of interleukin-2 (IL-2), thus is useful in the treatment of autoimmune diseases and organ transplantations.

Vertebrate fish compounds are used in the traditional and modern medical cannon as anticancer, antiviral, cardiac stimulatory, anti-arthritic, narcotic and analgesic aid.

Amphibian compounds have vaso-constrictive, hypotensive, hallucinogenic, anti-cancer, anti-viral and anti-microbial effects. Dermmophin, a novel opioid hepta-peptide produced in the skin of *Phyllome dusa*, has greater effect than morphine hence used in the treatment of depression, stroke, seizures and cognitive loss in ailments like Alzheimer's disease. Drug development from snake venom (*Bothrops jararaca)* inhibits angiotensin-converting enzyme (ACE) which reduces blood pressure (B.P.) subsequently. ACE inhibitors are amongst the best selling medicines in the modern times. Birds and mammals also have a great amount of contribution in terms of zoo therapeutics.

Zoonotic disease transmission potentials and biodiversity sustainability threats clearly illustrate the need to further explore possibilities that would foster successful integration of these traditional medicines into the modern public health framework as a potent drug store.

ORAL PRESENTATION-14

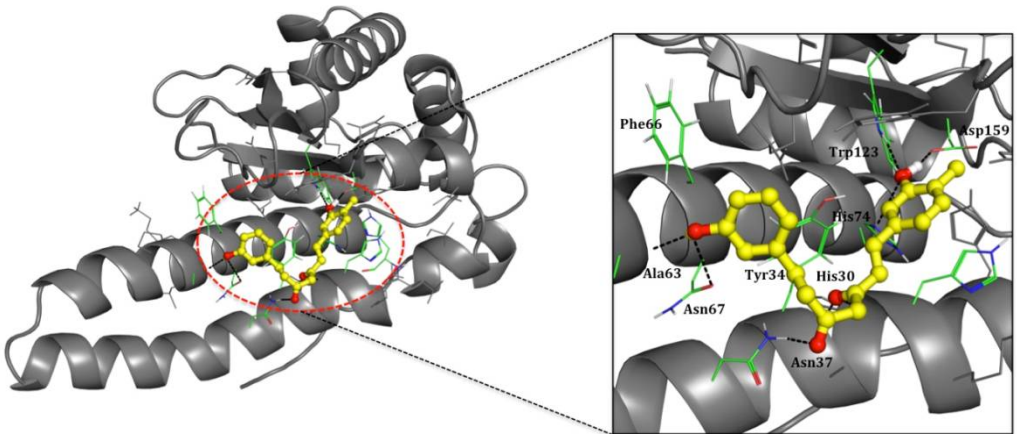
Structure based Virtual Screening of Natural Compounds against Epithelial to Mesenchymal transition (EMT) Receptors in Cancer

Diksha Varma, Simran Vinaik, Neha Dinesh, Manisha Tiwari.

Bioorganic Chemistry Laboratory, Dr. B. R Ambedkar Center for Biomedical Research, University of Delhi- 110007.

Medicinal natural products like taxol, vinblastine, Camptothecin, triterpenes, etc and their analogs have been the major sources of chemical diversity for driving pharmaceutical discovery of anti-cancerous medicines over the past century. The World Health Organization (WHO) estimated that as much as 80 % of the world's population relies on traditional medicinal plants to cure their chronic ailments like diabetes , cardiac ailments and cancer. Cancer is the second leading cause of death globally, accounting for 8.8 million deaths reported in 2015. Cancer progression and metastasis is marked by hyper-activation of proto-oncogenes like one that encodes for receptor tyrosine kinases (RTK) such as EGFR, VEGFR and c-MET whose activation and crosstalk signaling activates downstream signaling pathways including MAPK/RAS, PI3K/AKT, and phospholipase Cγ (PLCγ), NOTCH, STAT/Wnt signaling pathways in variety of cancer types including lung, gastric, colon cancer. In order to understand the potential role of natural compounds as anticancer molecules, these targets can be approached through combination of emerging structural biology, rational drug design, and virtual screening approach to increase the efficacy of the molecule towards the target.

In the present work, we have used the structure based virtual screening approach to mine the active natural lead molecules against EGFR, VEGFR and c-MET to target and prevent metastasis in cancer. For this, the essential pharmacophore features of the target were determined using Discovery Studio 2.5 that comprises of 4 H-donors, 1 hydrophobe, 1 ring aromatic (VEGFR-2); 2H-acceptors, 2 H-donors, ring aromatic (c-MET); 2 H-acceptors, 2 H-donors, 1 hydrophobe, ring aromatic (EGFR) that are important for the receptor-ligand interactions and activity. These pharmacophore features was then used to screen the library of natural compounds with the best fit value ≥0.95. These hits were further filtered using ADMET and TOPKAT modeler to satisfy all the drug-like properties. Screened molecules were further validated by docking with the targets using Discovery Studio 2.5 and Autodock 4.



Mining for lead molecules: Novel approaches to drug discovery

INVITED LECTURE – 21

Design and synthesis of GSK-3β inhibitors as anti-diabetic agents

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Glycogen Synthase Kinase-3 (GSK-3) is one of the validated target for the development of small molecules with the potential of therapeutic effect against Type-II diabetes, Alzheimer's disease and cancer. Currently Tideglusib, a GSK-3β inhibitor is preparing for the Phase-III of the clinical trials. GSK-3 is an enzyme which is active under normal circumstances however, under diabetes conditions the expression and activity of the enzyme increases several folds and thus leads to the related pathologies. Hence it can be envisaged that targets such as GSK-3, which has implications in various pathological conditions can be targeted for the development of the drug like molecules with the potential of curing the patients suffering from multiple diseases. The theory further gains strength from the reports published in the reputed journals, where cell based assays were taken up to prove the role of GSK-3 in Type-II diabetes, cancer and Alzheimer's diseases.

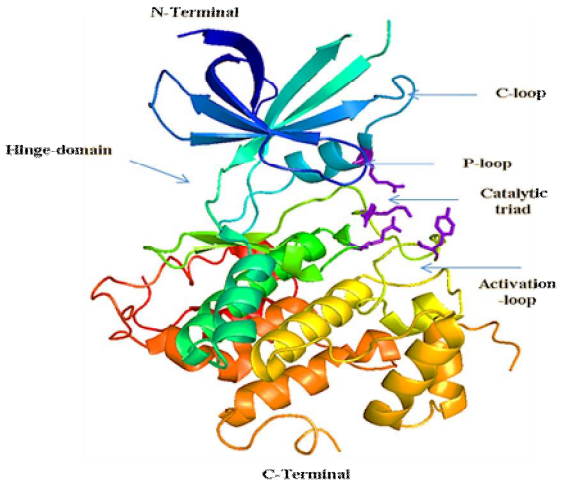

Figure. Structure of GSK-3β (PDB ID -1Q4L).

INVITED LECTURE – 22

Genomes to Hit Molecules *In Silico* - An Update Integrating Chemistry with Biology & IT: Towards a Disease-Free Planet

B. Jayaram

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The advent of information rich era grants us the opportunity to sketch a pathway from Genome àGene àProtein àDrug to develop personalized medicine almost in an automated way. Currently however, without the help of any database, an inspection of a DNA sequence does not tell us whether it is likely to be a gene and if it is a gene for mRNA, what the likely three dimensional structure of its protein product is. Also drug design softwares fall short of expectations even if the structures of drug targets are known.
Addressing these issues from a *physico-chemical perspective*, we have developed all atom energy based methodologies for whole genome analysis (1) (*ChemGenome*), tertiary structure prediction of proteins (2) (*Bhageerath and Bhageerath*-H) and protein/DNA targeted lead molecule design (3) (*Sanjeevini*). During the process, we discovered that physico-chemical properties such as hydrogen bonding, stacking and solvation energies convey the functional destiny of DNA sequences. *Bhageerath-H* is rated among the leading servers gloablly for predicting tertiary structures of soluble proteins to medium resolution. *Sanjeevini* in collaboration with experimental groups delivered low micromolar compounds against breast cancer, Alzheimer's, HAV & HBV infections and nanomolar compounds against malaria. These software suites are configured into (*Dhanvantari*) an assembly line to deliver hit molecules from genomic/proteomic information with entry at any point along the pipeline.

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INVITED LECTURE – 23

Structural and functional studies, inhibitor development against cysteine biosynthetic pathway enzymes of *E. histolytica*

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Gastric infections are the most common diseases in developing and underdeveloped countries, due to unhygienic conditions, and these infections are generally caused by *Helicobactor pylori* and *Entamoeba histolytica*. Sulfur is an essential nutrient for the growth and development of these pathogens (as well as all other organisms like *M. tuberculosis*), and enzymes involved in the metabolism of the cysteine biosynthetic pathway have been reported as promising targets for drug design. Our lab has reported the structures of most of serine/cysteine biosynthetic pathway enzymes from *E. histolytica* (Proteins, 2008; JBC, 2011; BBA, 2013, FEBS J, 2014), as well as the structures of some of their homologues from other organisms for comparative studies (Acta D, 2012; BBA, 2014; Biochem J, 2017; FEBS J 2017). We also deciphering the structures of enzymes of the sulfate activation pathway (Acta D, 2014), which are needed for cysteine biosynthesis and sulfonation of lipids and other biological molecules, and are hence essential for the survival of *E. histolytica*. Recently we have also reported initial inhibitor development (lead like molecules) against the one of the enzyme (OASS) from *E. histolytica* (PLoS One, 2011) and been involved in inhibitor screening for other enzymes. The high affinity inhibitors could be potential drug molecules against the *E. histolytica* or related organism infections. This pathway is quite different in *E. histolytica* compared to humans; holding out promise for a treatment with expected no side effects for the host

INVITED LECTURE – 24

Vaccines for malaria pre-erythrocytic stage parasites

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Plasmodium sporozoites are introduced in the vertebrate host by the infectious mosquito bite. In the vertebrate host invasion of the hepatocytes is the first step towards developing the malaria disease. Sporozoites invade hepatocyte and transform into exo-erythrocytic forms that reside in a parasitophorous vacuole. Malaria disease symptoms are caused by the blood stage infection. Reports suggest resistance to most of the drugs in use against the malaria. Currently there is only one and partially effective malaria vaccine available. We need to address the malaria vaccine from an angle of better efficacy. Presentation will focus on various strategies used for malaria vaccines. I'll also talk about antigens that we have identified and their features.

Mosquirix, the RTS'S/ASO1 based 1st generation vaccine although partially effective, it gives hope for development of 2nd generation subunit vaccine with better efficacy, which is acceptable by WHO standards. RTSS is based on the sporozoite surface protein known as Circumsporozite or CS. I'll discuss why CS is highly immunogenic and protective antigen as well as its role in liver parasite development. Recently we have identified two liver stage antigens, which are protective and share similar features with that of CS protein. I'll describe the characteristics and protective immune response of these antigens.

ORAL PRESENTATION-15

Multistage Unfolding Dynamics of TDP-43 Involve in Amyotrophic Lateral Sclerosis

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The thermodynamic stable conformation of a protein is of paramount importance to perform the biological function. However, the capability of adapting the different dynamic behaviour due to physio-chemical modulation in native structure, display the distinct functional properties. Various and efficient computational methods have been evolved to capture dynamic behaviours of proteins in different physiological condition. Here, we determined the biophysical properties of TDP-43 (TAR DNA-binding protein), normally involved in mRNA splicing, translational regulation, and transport. However, mutants of human TDP-43 are known to be associated cytoplasmic aggregation, lead to the pathological condition to amyotrophic lateral sclerosis (ALS). We employed the long range (2μs) all-atoms molecular dynamic simulations to investigate the aggregation propensity of RRM1 domain of TDP-43 wide-type (WT) and mutant. Results from free-energy landscape (FEL) and time independent component analysis (tICA) showed the existence of multiple transition states ensemble as an intermediate and metastable states in mutant as compared to WT. This results suggested that the characterisation of intermediate ensemble is an essential for the better understanding of pathogenic condition for ALS.
Keywords: TDP-43; protein dynamics; free-energy landscape; time independent component analysis.

ORAL PRESENTATION-16

Synthesis of Novel and Selective N-(benzo[d]thiazol-2-ylmethyl)-4-substituted-piperazine-1-carbothioamides and evaluate their NOS inhibiting potential in HEK cells transfected with human nNOS and eNOS.

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Nitric oxide synthase is involved in various signalling mechanisms in the human body and consists of three isoforms-inducible nitric oxide synthase (iNOS) controlling inflammatory diseases and septic shock; endothelial nitric oxide synthase (eNOS) contributing to blood vessels dilation, blood pressure, and numerous other vasoprotective and anti-atherosclerotic effects and neuronal nitric oxide synthase (nNOS) involved in regulation of synaptic plasticity in the central nervous system (CNS), central regulation of blood pressure, smooth muscle relaxation, and vasodilatation via peripheral nitrergic nerves. The study involves the targeting of nNOS to ameliorate the treatment of neurodegenerative disorder/s. In the present work, we designed a series of N-(benzo[d]thiazol-2-ylmethyl)-4-substituted-piperazine-1-carbothioamides (28 compounds) as nNOS inhibitors anticipating selectivity over eNOS isoform. The compounds were evaluated for toxicity in HEK cells using MTT assay. The compounds possessing $\geq$ 90% cell viability were screened for NOS inhibition activity using transfected HEK cells with human nNOS and eNOS. NOS inhibition was measured as the % of release of NO in the cell in the presence of compound using DAF-FM dye. Among the series of N-(benzo[d]thiazol-2-ylmethyl)-4-substituted-piperazine-1-carbothioamides, the most active and selective compound was the N-(benzo[d]thiazol-2-ylmethyl)-4-methylpiperazine-1-carbothioamide (nNOS=33%; e-NOS=10%) and was comparable to the nNOS standard drug 7-NI (nNOS=35%; eNOS=7%). Precisely, the results demonstrated that the N-(benzo[d]thiazol-2-ylmethyl)-4-methylpiperazine-1-carbothioamide possessed the potential nNOS activity.

ORAL PRESENTATION-17

Peroxiredoxin 6, a cytosolic antioxidant protein has high aggregation propensity at physiological conditions

Rimpy Kaur Chowhan, Sunaina Hotumalani and Laishram Rajendrakumar Singh

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Peroxiredoxin 6 (Prdx6) is a ubiquitously expressed highly conserved cytosolic antioxidant protein. Apart from reducing H_2O_2 and short-chain hydroperoxides, its ability to directly bind and reduce phospholipid hydroperoxides plays an important role in its antioxidant defence. Its levels are known to exponentially increase in response to high oxidative stress associated with various respiratory, neurological, ophthalmic, metabolic, cardiovascular and neoplastic diseases. Additionally, Prdx6 shows moonlighting function of phospholipase A2, maximal at pH 4.0 (lysosome). There are various reports that suggest heightened Prdx6 associated PLA2 activity to be responsible for enhancing oxidative stress in neurodegeneration and carcinogenesis. In the present study we are reporting for the first time that Prdx6 has a propensity to aggregate at physiological pH (pH 7.0) and temperature (37°C) conditions while being very stable at room temperature (20-25°C). We have observed Prdx6 in neutral pH conditions to be a highly aggregation prone protein with T_{agg} (Temperature at which 50% of the protein aggregates) of 62.5°C and T_o (aggregation onset temperature) of 37°C. Our study indicates that Prdx6 aggregation followed by prolonged overexpression of Prdx6 in degenerative neurons and cancer cells might be the cause for enhanced Prdx6 associated disease aggravation. Buttressing our hypothesis, there is an early study where in PD (Parkinson's disease) and DLB (dementia with Lewy bodies) diseased brains presence of Prdx6 in Lewy bodies has been demonstrated. However, in normal conditions, we believe that cellular milieu might have certain co-solutes or protein interacting partners which stabilize and prevent aggregation of Prdx6 at physiological temperature without affecting its native function. In fact, while screening for such stabilizing cellular co-solutes, we found human polyamines, putrescine, spermidine and spermine to inhibit Prdx6 aggregation at physiological temperature. Moreover, we realized that none of these polyamines displayed any negative effect on Prdx6's peroxidase activity, thereby supporting our above proposed theory.

VALEDICTORY LECTURE

New approaches to target obligate intracellular pathogenic bacteria

Thomas Rudel

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Incidences of sexually transmitted diseases (STI) have increased during the past decades with a concomitant rapid spread of antibiotic resistant bacteria. *Chlamydia trachomatis* is the most frequent cause of bacterial STIs, often in the context of co-infections with other STI-causing bacteria (including multidrug resistant superbugs). These infections often remain asymptomatic and are consequently not diagnosed and treated, resulting in the subsequent development of severe diseases and an enormous economic burden for health systems. As obligate intracellular bacteria, *Chlamydia* depends on metabolites such as nucleotides, which they take up from the infected host cell. Due to their intracellular lifestyle and dependence on the host metabolites, *Chlamydia* protect the infected host cell by actively interfering with infection-induced stress responses like the generation of reactive oxygen species (ROS), damage of host DNA, and nutrient deprivation. In addition, these bacteria have to overcome their destruction by the cell autonomous and innate immune defense in order to propagate themselves in the human host.
The current antibiotics crisis forces researchers to develop new concepts of antibacterial therapy. I will present recent progress in basic research aiming at the understanding of metabolic dependencies of *Chlamydia* and cell autonomous as well as innate immune defense against this pathogen. Detailed understanding of host – pathogen metabolic and immune interactions offer exciting new approaches to defeat diseases connected to obligate intracellular pathogenic bacteria.

Poster Presentations

P01: UPR and Autophagy crosstalk: Potential Antiviral Strategy against Chikungunya Virus

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Chikungunya Virus (ChikV) is an Alphavirus of the Togaviridae family transmitted to humans through arthropods bites (mosquitoes of the Aedes genus). First described during a Tanzanian outbreak in 1952, ChikV has started drawing worldwide attention since its re-emergence in India and Southeast Asia in 2005. Chikungunya virus is a positive ssRNA virus consisting of nine genes encoding for four non-structural polyprotein i.e. nsP1, nsP2, nsP3 and nsP4 proteins and five structural polyprotein i.e. Capsid, E3, 6K, E2 and E1 proteins. Most RNA virus infection lead to induction of various signaling cascades that is associated with pathogenesis of virus. One such pathway is UPR pathway that restore ER homeostasis, however various viruses modulate these pathways and exploit them for their own replication. Viral infections overload the ER lumen by production of viral encoded protein, which may leads to the activation of UPR response. UPR alleviates ER stress by initiating signaling cascade mediated by three ER-resident transmembrane proteins: the IRE1 (kinase and endoribonuclease), PERK kinase and the basic leucine zipper activating transcription factor ATF6. UPR also induces autophagy in an attempt to reduce ER stress from an accumulation of unfolded or misfolded proteins which cannot be degraded by the proteasome. Autophagy is a catabolic process that is important for maintaining cellular homeostasis by removing excess or damaged cellular organelles as well as long-lived and aggregated proteins. In the current study we analyzed the activation of various branches of UPR pathways and autophagy on chikungunya infection. We also report the effect of blocking individual branches of ER stress on Chikungunya replication and autophagic response.

P02: Determining the misuse / overuse of Antibiotic in Non Viral Sexually Transmitted Infections

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Background: The emergence of multi-drug resistant sexually transmitted infections (STIs) is causing treatment crisis across the globe. Syndromic management and indiscriminate use of antibiotics has resulted in development of resistant strains to commonly used antibiotics. Consequently, these resistant strains are becoming a public health problem in a number of countries including India. NAAT based diagnostic methods can help in guiding the treatment and can thus prevent misuse and /or overuse of antibiotics to the patient.

Methods: Identification of the infection causing pathogens (Chlaymydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis) using NAAT based assay was carried out in patients enrolled in the study and recommended syndromic treatment was using NACO-NACP guidelines of 2016.

Results: Validation of antibiotic treatment in 588 syndromically treated women was checked by carrying out NAAT based diagnosis. 46(7.82%) women tested positive whereas 542(92.17%) samples were negative for these three pathogens as determined by PCR based assay. The total estimated percentage of the overuse and misuse of antibiotics in the study were 72.17% and 8.69% respectively. Correct and complete treatment estimated as compared to laboratory measures and NACP was 42/46 (91.30%). The overuse of antibiotics estimated for Azithromycin and Cifiximewas 55.90%, combination of Dixycilin, Cefixime and Metrodizonole (31.18%) and combination of Dixycilin, Cifixime, Metrodizonole, Azithromycin was (13.65%).

Conclusions: Our results clearly demonstrate that the prevalence of infections is still significant among female patients visiting Obstetrics & Gynecology Departments. The study underpins the need to conduct diagnostic assays for identification of causative pathogen before implementing antibiotic treatment to patients with vaginal discharge. It also divulges the need to review the use of syndromic case management for controlling sexually transmitted disease.

P03: Cloning, Expression and Purification of MurI of *Neisseria gonorrhoeae*

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Neisseria gonorrhoeae is a pathogenic organism known to cause various Sexually Transmitted Infections (STIs) in the human biological system. Gonorrhea, also known as "The Clap", remains a frequently reported STI and an important cause of pelvic inflammatory disease (PID) and subsequent infertility. *Neisseria* is transmitted during vaginal, anal or oral sex and the primary infection site is the columnar and transitional epithelium of the urogenital tract, the rectal mucosa, the conjunctiva, and pharynx. Over time, *N. gonorrhoeae* has grown resistant to numerous antibiotics, including the sulfonamides, penicillins, tetracyclines, fluoroquinolones and cephalosporins. Development of antimicrobial resistance (AMR) by various pathogenic bacteria has posed a serious threat to mankind. It has lead to the rampage of superbug gonorrhea and thus the increased complication in gonorrhea treatment worldwide. In this study, we have focused on the MurI gene as the expressed protein serves two distinct and essential functions. Firstly, it functions as a critical enzyme in the biosynthesis of D-glutamic acid, a specific component of the bacterial cell wall peptidoglycan, by helping in the interconversion of D to L-glutamate through racemization. Secondly, it plays an important role in gyrase inhibition. This ability of a protein to serve two different functions is called as moonlighting and therefore MurI is a 'moonlighting enzyme'. Since the MurI gene is specific to the bacterial kingdom, it can be exploited as a potential drug target for the treatment of bacterial diseases particularly gonococcal infections. We have cloned and expressed the MurI gene in an *E. coli* expression vector PQE30Xa and purified it using Ni-NTA beads. The future prospective of the study lies in the elucidation of the structure of the protein and assessment of its biochemical properties as a potential drug target for the treatment of STDs.

Keywords: *Neisseria gonorrhoeae,* Sexually Transmitted Infections, antimicrobial resistance

P04: Inflamed and deregulated T-cells in HIV-infected patients cause Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome (TB-IRIS)

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Tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS) is defined as an inflammatory response in HIV infected patients, which either produces progressive worsening of TB (paradoxical IRIS) or unmasks a previously undiagnosed TB (unmasking IRIS). Tuberculosis (TB) is one of the major causes of IRIS in human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients. The aim of the study was to understand the immune-pathology of TB-IRIS. In this total 560 HIV patients with and without TB at baseline were enrolled in the study. Identified 50 (25 unmasking and 25 paradoxical) TB-IRIS patients and another set of 50 age, gender and body mass index (BMI; kg/m^2) matched HIV/AIDS patients who did not develop IRIS constituted as controls. Flow-cytometry was done for immuno-phenotyping and we found that higher expression of CD4+CD69+ and CD8+CD69+ T cells and lower $CD4^+Ki67^+$ and $CD8^+Ki67^+$ T cells TB-IRIS patients. Similar, activation and proliferation profile was observed in $CD161^+$ T cell compartment. As well as pro-inflammatory cells; IL-17A and cytokines; IFN-γ, IP-10 and MIG, were elevated and lower expression of anti-inflammatory cytokines; IL-10 and TGF-β in TB-IRIS patients. With the help of these results, we observed that in TB-IRIS patient's immune system were pre-dominantly tilted toward the pro-inflammatory environment and anti-inflammatory cells and cytokines are unable to limit the inflammation in HIV and HIV-TB patients.

P05: Ligand based pharmacophore modeling and virtual screening to identify Mycobacterium tuberculosis pantothenate kinase (Pank).

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Tuberculosis (TB) still remains an enormous public health challenge worldwide. Due to lack of potent vaccines and emergence of drug resistance in parasites, development of leads with novel mechanism and few side effects are imperative. Coenzyme A (CoA) is an important cofactor used by many proteins in a network and a part of metabolism of many organism. CoA synthesized from pantothenic acid in most of bacteria in five steps. The phosphorylation of pantothenate by pantothenate kinase (Pank) is first step in which Pank serve as phosphate donor. There are three types of Pank and type III Pank have wider phylogenetic distribution than other Panks. Mtb also contain Pank III which shares low sequence homology with other Panks. These findings indicate that Pank would be essential target for the development of antimicrobial with novel mechanism of action. The present study aimed to describe the development of pharmacophore model from structurally diverse series of Pank inhibitors. A total of 25 well defined training set molecules were selected for hypothesis generation using Discovery Studio v4.0. The best pharmacophore model (Hypothesis 1) consists of 4 features, namely, two hydrogen bond acceptor (HBA) and two hydrophobic (HY) features, had a correlation (r) of 0.976, a RMS of 0.723, and the cost difference between the best hypo and null hypothesis was 93.131 bits. This model was validated on a set of 20 compounds and finally utilized as a 3D query for virtual screening to validate against Maybridge database and the hits further screened for ADMET properties and Lipinski's rule of 5. Finally, 47 best fit hits were selected for docking into active site of Pank enzyme to study specificity and selectivity of hit compounds. The present pharmacophore model can thus be helpful for the identification, development and design of potent Pank inhibitors which can be potential lead compounds for development of anti- tuberculosis therapeutic agents.

P06: Delineating the role of Apoptosis in Dendritic cells during *Mycobacterium tuberculosis* infection.

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Mycobacterium tuberculosis (*M. tb*), the causative organism of TB and its evolution in the host has motivated researchers to understand host-pathogen interactions with the view to better manage the disease. However, with the emergence of drug resistance in the pathogen, a deeper understanding of immune responses is the need of the hour. *M. tb* employs multiple mechanisms to evade immune responses. The pathogen remains undetected within the host by modulating cell survival of different cell types for its own advantages by altering pathways that are responsible for recognition and elimination of the pathogen. We showed that *M. tb* on its own as well as in conjunction with HIV inhibits macrophage apoptosis. This inhibition involves the TLR2 pathway and the route of calcium influx into cells that play complementing and contrasting roles in regulating apoptosis. To extend these observations we wished to delineate the role of apoptosis during *M. tb* infection in dendritic cells (DCs), which are the primary drivers for T cell response. To gain insights into the activation and functional status of DCs upon inhibiting apoptosis we investigated host defence responses such as expression of co-stimulatory molecules cytokine receptors and cytokines profiles, oxidative burst etc. Our results indicate that Rv3416 induces apoptosis of DCs. Inhibiting apoptosis prior to antigenic stimulation leads to increased expression of costimulatory molecules, ROS responses and induction of pro-inflammatory cytokine expression. Co-culture of these DCs with antigen primed T cells increased their proliferation and activation. Further, there was a propensity to increased effector memory responses. These data indicate the role of apoptosis in enhancing host-defense responses to combat the infection.

P07: Regulation of SUMOylation in Dendritic cells upon *Mycobacterium tuberculosis* infection

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M. tb has evolved several strategies that contribute to its successful establishment in the host. The role of SUMOylation during *M. tb* infection has not been studied in detail. Among the antigen presenting cells (APCs) of the immune system, dendritic cells (DCs) are the most potent and act as a bridge between the innate and the acquired arm of the immune system. Our previous work identified Rv3416 as an antigen expressed inside infected macrophages as a function of time. Characterization of Rv3416 showed that it suppresses host response to *M. tb* from DCs as well as macrophages Therefore, we hypothesize that Rv3416 might have a role in regulating SUMOylation during *M. tb* infection. We used mouse-derived DCs for our study to decipher the role of SUMOylation. Our data shows that inhibiting SUMOylation in bone marrow-derived mouse DCs increases ROS production, pro-inflammatory cytokines and expression of cytokine receptors and increased expression of surface co-stimulatory molecule CD40. These results indicated that *M.tb* modulates SUMOylation during *M. tb* infection. In addition inhibiting SUMOylation increased the activation of NF-kB, phospho p38, p-CREB, p-STAT1, pERK indicating enhancement in the pro-inflammatory responses. These results point towards a determinant role of SUMOylation exploited by the pathogen to thwart host immune responses.

P08: Investigating the plant extracts and alkaloids of *Justicia adhatoda,* for anti-mycobacterial activity.

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Tuberculosis, being an infectious disease, is a global threat for humans. According to WHO Global TB report, total 9.4 million new TB cases occur annually worldwide, in which around 2 million cases come from India. In spite having numerous drug regimens for treatment, disease spreads all over the world. This is due to the fact that the course of TB medication is very long and taxing, causing the patients to leave the course in between, as soon as they feel ameliorated. And the continuous resistance development by bacteria against the drugs due to their long term exposure on them, leading to the severity of disease in patients, emerging as MDR-TB, XDR-TB and TDR-TB. Moreover, the medicines which are used for treatment are so potent, they cause severe side effects and kill gut microbiota, making patients more vulnerable for other opportunistic infections. Ancient traditional medicines are basically developed from medicinal plants, which are abundant in our country. Today people are approaching to these medications, which are proving themselves very much beneficial as compared to the synthetic one. But the efficacy and specificity of these medicines are questionable. Although the traditional medication and therapies were successful to treat different chronic maladies, yet much research is needed where TB disease treatment is concerned. It is important to specify these traditional plant medicines by using modern techniques. In our work, *Justicia adhatoda*, a medicinal herb, is undertaken for searching the bioactive component against Mycobacterial activity.The plant in question has been described and proven to have anti-mycobacterial properties, by ancient texts as well as different research conducts. The phytochemical profiling of different extracts of *J.adhatoda* leaf was done. All leaf extracts have been screened against *Mycobacterium smegmatis* and *Mycobacterium bovis.* Ethanol extract scored as the best growth inhibitor against both strains and have been further extracted to obtain alkaloids. The alkaloids have again screened against the bacterium and found to be the potent inhibitor. Bioactive guided frationation of alkaloids was done and the compounds were further subjected for NMR analysis and cytotoxic effect study via MTT/XTT assays on THP1 and A549 cell lines.The tested compounds showed very less cytotoxic effects on the cell lines, hence promising compounds for TB drug development.

P09: Targeting Glutamate racemase of *Mycobacterium tuberculosis*: Experimenting new tricks over old enzyme to tackle antibiotic resistance menace

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Abstract

There is an urgent need to identify novel drug targets and discover new antimicrobial inhibitors given the ever-evolving rate of drug resistance against currently used antimicrobial agents. *Mycobacterium tuberculosis*, the causative agent of infectious disease tuberculosis, has also developed drug resistance against various antibiotics that are used to treat patients. Moreover, multiple drug resistance (MDR) and extensively drug resistance (XDR) strains of *M. tuberculosis* are also reported in literature. System biology approaches offer an important platform that facilitates identification of potential drug targets to circumvent the problem of ever increasing drug resistance. Proteins exhibiting high level of conservation among various species could be considered and reported inhibitors against these homologous proteins may be used for targeting *Mycobacterium tuberculosis*. In the present study, we have analyzed possible mechanism of action of compounds targeting one such protein Glutamate racemase of *M. tuberculosis* (MTB-GR), an enzyme that is involved in the early phases of peptidoglycan biosynthesis. MTB-GR is called as a Moonlighting protein because this protein has two distinct functions. We analyzed various known natural compounds (inhibitors) having reported antimicrobial activities and observed that flavonoid compounds, namely quercetin and naringenin gave the best results. Importantly, both these compounds showed negligible cytotoxic effect on THP-1 human monocyte macrophage cell line as revealed by MTT assay. Both quercetin and naringenin were docked onto the crystal structure active site of the MTB-GR. A UV-CD spectroscopy studies suggest thermodynamic changes at the secondary and tertiary structure level of the protein in the presence of inhibitors. The conversion of L to D-glutamate in the presence and absence of inhibitors was also compared via racemization activity followed by enzyme kinetics to decipher the best inhibitor. In conclusion, our study suggests the role of moonlighting proteins as potential therapeutic targets to design novel drugs to combat MDR tuberculosis.

Keywords: Mycobacterium tuberculosis, Glutamate racemase, Drug resistance

P10: STUDY OF CO-INFECTION OF NEISSERIA GONORRHOEA, CHLAMYDIA TRACHOMATIS AND TRICHOMONAS VAGINALIS IN PATIENTS VISITING SAFDURJUNG HOSPITAL, NEW DELHI

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Gonorrhoea, chlamydia and trichomoniasis are among the major Sexually Transmitted Infections (STIs) seeking global health priority due to their devastating effects on infants, men and women of all ages. They lack conspicuous symptoms and are often misdiagnosed. Consequently, if left untreated, they result into serious long-term complications which include Pelvic Inflammatory Disease (PID), ectopic pregnancy, infertility and birth defects. Also, their co-occurrence with each other in Indian sub-population is alarming and impels to look for desperate measures. Patients visiting Department of Obstetrics & Gynaecology, Safdarjung Hospital, complaining vaginal discharge, cervical discharge, cervical vaginal syndrome and PID were enrolled in the study to check for the frequency of co-infection caused by *Neisseria gonorrhoea* (NG), *Chlamydia trachomatis* (CT) *and Trichomonas vaginalis* (TV). Genomic DNA was extracted and tested by in-house developed PCR assays using *PFO B, PHA* and *ORF-1* gene specific primers for diagnosis of *TV, CT and NG* respectively. Out of 314 patients enrolled in the study, 287 (91.4%) were infected with at least one of the three concerned STIs and 27 (8.6%) were negative for them. Among infected patients, 31.01% (21.25% NG, 5.22% CT and 4.53% TV) were found positive for one of the three infections and68.99% patients were co-infected with at least two. Percentages of co-infection caused by *NG+CT, CT+ TV, TV+ NG* are 55.4%, 23.3% and 24% respectively. 18.47% of patients were co-infected with all three pathogens. Based on our study, this high degree of co-infection impinges towards the understanding that infection caused by one micro-organism increases the risk of co-infection. Since, all three infections result into similar symptoms, there are chances that one or more infections might remain unnoticed in case of co-infection. Hence, the need of clinical diagnosis over WHO/NACO/NACP based syndromic case management is recommended.

P11: Toll-Like receptor 5 and its signaling mechanisms of *T. vaginalis* isolates from symptomatic and asymptomatic infected women

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Introduction: *Trichomonas vaginalis* is a parasitic protozoan that causes 'Trichomoniasis' sexually transmitted diseases in developing countries. In men it remains asymptomatic while women shows symptoms like vaginal discharge, itching, pruritis, dysuria, dyspareunia and abdominal pain. It can lead to Preterm delivery, low birth weight, and increased mortality as well as predisposing to HIV infection and cervical cancer. Here, trophozoite stage leads to direct transmission of infection and infects squamous epithelial cells in the genital tract, which results in cytokines secretion. The aim of this study was to investigate the establishment of infection and estimates expression of TLR5 in the mice model infected with symptomatic and asymptomatic strain of *T. vaginalis*. **Material and Methods**: For this study, Balb/C mice were infected with both the strains of *T. vaginalis* at different time points. Further, the symptoms and infection was observed via H&E and expression of TLR5 receptor was investigated by immunohistochemistry.
Results & Discussion: Overall, during the experiment it was clearly observed that in Balb/C mice infected with Symptomatic isolates, desquamation and neutrophils infiltration was present on 2^{nd} day post infection (PI) group and reached highest at 8^{th} day post infection group. Whereas, after 8^{th} day of post-infection severity of infection was dramatically decreased.On the contrary,in mice infected with Asymptomatic isolates,2^{nd} day of post-infection showed focal desquamation which became severe on 6^{th}day and abundant filtration of neutrophils was observed. Complete desquamation and abundant infiltration of neutrophils and leucocytes was seen on 14^{th} day of post infection. TLR5 expression was highest on day 2and day 4 after infection in vagina and cervix respectively, while expression was lowest on 14^{th} day of post-infection in both vagina and cervix in symptomatic trichomonas isolates. Whereas, in case of asymptomatic isolates TLR5 expression increased in mice vagina and cervix after 2^{nd} day post infection and reached highest on the 14^{th} day post infection group. Control group without trichomonas infection showed less or no TLR5 expression in both vagina and cervix of mice. Therefore from these results we concluded that the infection of symptomatic *T. vaginalis* isolates showed early immune response whereas, asymptomatic isolates showed delayed type immune response.

P12: ROLE OF INFLAMMASOMES IN INNATE IMMUNITY OF SEXUALLY TRANSMITTED INFECTIONS

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Inflammasomes are cytosolic multiprotein complexes which gets activated in response to pathogen induced infections and play an important role in host innate immune system. Activation of inflammasomes results in release of cytokines, which aim at the removal of pathogens and thus restoring normal tissue function. Sexually transmitted Infections (STIs) has been a serious medical issue around the world, yet very few studies have unveiled the mechanisms involving inflammasome activation in STIs. Understanding how inflammasomes impact the result of STIs may prompt the advancement of novel therapeutics to control the infections. Here we talk about and highlight the current research in this field which may help to reduce economic losses due to these infections.

KEYWORDS: Sexually transmitted infection, Inflammosomes, Innate immunity, pathogen

P13: Another reason to go cashless: Currency notes you carry can transmit diseases

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Background: The most common form of currency that is used worldwide is in form of paper currency notes. Each currency note is thus exchanged several times during its life. Paper currency can be contaminated by droplet infection through sneezing, coughing, previously infected hands and by placing over previously contaminated surfaces. Since many communicable microbial infections can spread through fomites paper currency, these may pose a serious risk to public health. If these currency notes are contaminated with pathogenic microorganisms, then there is potential for spread of the same from one person to another. The aim of this study was to investigate the likelihood of microbial contamination of Indian paper currency notes.

Methods: A total sample size of 100 ten rupee notes was collected from individuals near Vallabhbhai Patel Chest Institute, University of Delhi, Delhi. They were collected from vendors on stalls near the area as well as patients with respiratory ailments, who visited the institute. The notes were collected in sterile plastic bags. The notes were washed with sterile solution and total genomic DNA was extracted using Universal sample processing technique. Polymerase Chain Reaction was carried out to detect presence of *Mycobacterium tuberculosis*.

Results: The currency notes were classified according to condition, appearance and degree of dirtiness as new, moderate and torn. Out of 100 samples, 11 were positive for presence of *Mycobacterium tuberculosis*. There was no significant correlation between condition of note and positive status.

Conclusion: Paper currency notes could be one of the most potential vehicles to transmit diseases amongst the people. The findings of the preliminary study suggest that currency notes show presence of pathogenic bacteria which represents risks and public health hazards to the community and individuals handling currency notes.

P14: Radiation Induced Gastrointestinal Syndrome and its modification by HDAC inhibitor (Trichostatin A)

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Background: GI claims to be richest niche of microbes and radiation damage results in development of inflammation and possibilities of bacterial migration to adjacent organs and blood.

Objectives: We focused on

(a) Studying radiation mediated GI tissue damage (villi and crypts damage).

(b) Establishing correlation between changes in TLR 5 expression in GI tract of irradiated mice.

c) Evaluating the efficacy of HDAC inhibitor (Trichostatin A) in mitigating radiation effects on GI and microbial translocation.

Methodology: C57BL/6 male mice were used in 4 different groups (a) Radiation alone (7 Gy whole body γ-irradiation (Co60)) (b) Drug alone (c) Radiation plus drug (TSA) and (d) control. Bacterial isolation was studied from duodenum, jejunum and ileum part of small intestine and adjacent organs (liver, spleen and mesenteric lymph nodes) to check the translocations at different time points. Alterations in TLR 5 expression by western blot technique and histological analysis (villi and crypts damage) were also performed.

Results: A significant reduction in microflora count in GI tract after 24 hrs of radiation exposure was observed which later recovered back to normal count. The damage in villi and crypts were seen. The translocation of bacterial strain was found on 8^{th} day after radiation exposure on liver (33%), spleen (33%) and mysentric lymphatic system (66.66%). TSA was observed to control the translocation of bacteria from GI tract to other organs. Drug (TSA) was also observed to control the TLR 5 expression in irradiated mice.

Conclusion: HDAC inhibitor TSA was observed to have potential to prevent translocation of gut bacteria to other organs. Further, the role of toll like receptors (TLR5) in the small intestine and their interaction with the microbes are being studied to correlate the radiation induced decreased immune status with the disease condition observed after at least 14 days post radiation in our experimental set up.

P15: Functional characterization of a molecular motor (terminase enzyme) purified from a mycobacteriophage (PDRPxv)

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DNA encapsidation is a remarkable process in bacteriophages and during the synthesis of a new virion, it is responsible for translocating the genome into a preformed procapsid. Terminases are the enzymes that are involved in the process and they do so by coupling translocation of DNA to ATP hydrolysis, via the portal protein. Terminases are also referred to as the 'molecular motors' because of their ability to package DNA very densely into the prohead, and are reported to create an internal pressure of about 50 atm which is 10 times higher than found in any living system. This makes them one of the most powerful motors in the biological world.

Conventionally, terminases are oligomeric complex, consisting of a small and a large subunit. The large sub-unit is the primary component of terminase complex that exhibits ATPase and nuclease activities and acts as the packaging motor. The small sub-unit is known to recognize the packaging initiation region known as *cos* and *pac* sites in the phage genome.

Our group is working on bacteriophages infecting *Mycobacterium tuberculosis* and in this study, we have analysed terminases in PDRPxv, a mycobacteriophage isolated from New Delhi. While annotating the genome using computational tools, we noticed an unusual property in the small sub-unit of the enzyme. It was predicted to contain features such as WalkerA motif and p-loop NTPase domain, which are associated with the enzymes exhibiting ATPase activity and are characteristic of the large sub-unit. Thus, to validate the predicted ATPase activity in small subunit, we purified both the sub-units and assayed them for ATP hydrolysis using Malachite green assay (the large sub-unit served as positive control). We found activity in small sub-unit (0.57 nmol Pi/min) was indeed significant though less than what was observed for large sub-unit (1.49 nmol Pi/min). We also created a mutant (K21R) of small sub-unit by site-directed mutagenesis and observed complete loss of enzyme activity on mutation of a key lysine residue in its ATP binding site, which further substantiated our finding.

Why does terminase in mycobacteriophage PDRPxv requires an additional ATPase activity needs to be investigated further but this study highlights the interesting yet unexplored variations found in bacteriophages, which are largely untapped natural resources in our country.

[1]Both the authors contributed equally.

P16: Study of differentially-expressed genes (DEGs) in Argyrin A, an anti-proliferative drug treated samples of intestinal adenomatous polyps using an integrated bioinformatics analysis

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Cell cycle regulation is a result of interplay of cyclin and cyclin dependent kinases (CDKs). One of the cyclin dependent kinase inhibitor, 1B gene (**CDKN1B),** which encodes the protein p27 (Kip1) is shown to play an important role in controlling the cell cycle, growth and division. The p27 normally blocks cells from entering the G1 phase of the cell cycle and induces apoptosis through the inhibition of 20S proteasome, hence a tumor suppressor gene. Argyrin A, a cyclical peptide drug derived from the myxobacterium ***Archangium gephyra*** is useful to prevent the destruction of the p27 protein.

In order to find DEGs in the treated and the control samples of the Argyrin A a microarray dataset, GSE8565, was retrieved from Gene Expression Omnibus (GEO, NCBI). These datasets were analyzed using the GEO2R tool. Gene Ontology (GO) and pathway enrichment analysis for DEGs were performed using the Database for Annotation, Visualization and Integrated Discovery. Protein-protein interaction (PPI) analysis for DEGs was conducted using the Search Tool for the Retrieval of Interacting Genes software and visualized using Cytoscape followed by hub gene identification, biological process and pathway enrichment analysis of the module selected from the PPI network. In this study we identified a total of 121 DEG genes.. A significant interaction module was detected from the PPI network for FGF1, FGFR2, VEGFA, FLT1, ERAP1, LRP1.. These genes were mainly involved in the cytokine-cytokine interaction, vasculature development, angiogenesis, RAS, Rap 1 and PL3K-Akt signalling pathways. The functional studies of candidate genes from these databases may lead to an increased understanding of the genes that are differentially regulated at the time of treatment of the Argyrin A drug. The detailed graphical representations of the analysis and results will be discussed.

P17: Transcription coregulator SIN-3 regulates ROS mediated autophagy and decline in longevity in *Caenorhabditis elegans.*

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Irregularities in cellular homeostasis have direct manifestation on fecundity and lifespan of an organism. Various theories of aging propose that accumulation of deleteriome, ROS and genetic dysfunction are some of the causes of aging. Dysfunction in the synchronised and coordinated regulation of genes and antioxidant machinery is critical for the fitness and longevity of an organism is the hallmark of aging. Sin3 is a transcriptional regulator which serves as a scaffold for various chromatin modifying enzymes comprising of multiprotein complex. Though Sin3 has been implicated in stress tolerance and differentiation, its role in overall longevity is not well explored. Using *Canerhabditis elegans* as a model system, our work provides evidence that elevated ROS and enhanced aging in *C. elegans* is attributable to SIN-3. An augmented level of ROS also leads to increased autophagic flux though it fails to restore the normal lifespan. Supplementation with antioxidant, vitamin C not only restored the lifespan in *sin-3* mutant worms but also brought various metabolic enzymes (such as activity of different SOD enzymes and catalases), metabolites (such as glutathione and NADPH) and aging markers (such as malondialdehyde) near basal levels. Our results demonstrate that the reduction of lifespan and surge in autophagy in *sin-3(tm1279);him-5(e1490)* worms is due to excessive oxidative stress which in turn differentially regulates the antioxidant machinery of the cell. We for the first time, provide evidence of the critical role of SIN-3 in the regulation of oxidative stress and lifespan *in vivo* under normal growth conditions without any environmental or oxidative stress. Our data further points in the direction of validating the deleterious accumulation theory of aging.

P18: Analysis of Long-Range interactions of human *PRE-PIK3C2B* through Chromatin Capture Assay (4C)

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Background: *cis*-regulatory elements such as Polycomb/Trithorax Response Elements (PRE/TRE) and *trans*-factors (Polycomb and Trithorax Group of proteins - PcG/TrxG) comprise the Cellular Memory Modules. The PcG/TrxG members are known to be dysregulated in cancers. We identified a regulatory element, *PRE-PIK3C2B* in the first intron of *PIK3C2B* gene, which shows a dual nature and interacts with both PcG and TrxG members. We observed that knocking down the recruiter of PcG complex (YY1) or members of the Trithorax group (MLL), changes chromatin histone marks associated with *hPRE-PIK3C2B* as well as the expression of the neighboring genes.
Objective: The coordinated changes in expression can be explained; a) first, that all the neighboring genes are under the control of *hPRE-PIK3C2B* i.e. *hPRE-PIK3C2B* exerts a long range effect on the transcription of these genes; b) second, there is a possibility of other PREs controlling the expression of neighboring genes by coordinating with and/or interacting with *hPRE-PIK3C2B*. This prompted us to study the long-range interaction of *hPRE-PIK3C2B*.
Methods: Capturing Circular Chromosome Conformation (4C)-sequencing was performed in order to identify interacting partners for *hPRE-PIK3C2B*.
Results: We detect both intra-and inter-chromosomal interactions. The intra-chromosomal interacting regions are at distance ranging from 10-11kb to 80 Mb. Majority of the DNA interactors identified map to repetitive region, that are often targeted by PRC2 and PRC1 complexes. The LINE elements implicated in heterochromatin organization are enriched among the repetitive sequences. The *hPRE-PIK3C2B* is itself derived from LINE-1 element. The genes associated with the DNA interactor sequences show a coordinated expression in normal tissue as well as cancer cells.
Conclusions: 4C analysis has led to the identification of the long-range interactions of a human PRE. It is yet to be established whether these domains along with *hPRE-PIK3C2B* form a part of the repression hub and further, whether the interactions differ in different cell lines and cancers.

P19: A comparative analysis of the repertoire of histone methyltransferases and demethylases in insects

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The epigenetic regulation of the genome is principally attributed to the post-translational modification of histones and the methylation of DNA. Epigenetic regulation is highly conserved overall, meaning that the modes of epigenetic regulation is largely similar across evolution. One of the largest phyla among animal kingdom is the Insecta. This phyla also offers a wide variety of mechanisms to achieve similar biological outcome; an example of this is the mechanisms of sex determination. It is interesting to note that epigenetic phenomenon of genomic imprinting or parental-origin effect is closely linked to sexual reproduction. In this background and our interest to decipher the epigenetic regulatory mechanism in the mealybugs in which 50% of the genome is sensitive to parental-origin-effect we have carried out a comparative analysis of histone methyltransferases and demethyalses in a selection of insect species. In this study, we retrieved the protein sequences of the histone methyltransferases and the demethylases in the genome of representative dipteran, hymenopteran, lepidopteran and hemipteran insects. We have compared the domain-architecture of the histone methyltransferases and the demethylases. The evolutionary relationship of the different insects has also been studied with reference to the sequence of histone methyltransferases. The results indicate that the insects have varying number of methyltransferases and demethylases. The copy number of the genes also shows variations. Through this analysis we have identified the shared and unique domains, which would be important in the annotation of genome sequences for epigenetic tool-kit.

P20: Nuclease Resistant Chromatin (NRC): a unique chromatin organization in mealybugs as a correlate of Genomic Imprinting.

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Genomic Imprinting or parental-origin-specific effect is a well-known epigenetic phenomenon in most of the organisms. In humans, about 1-2% of the genes are subjected to parental-origin-specific expression, while in mealybugs, (*Maconellicoccus hirsutus*) 50% of the genome is subjected to genomic imprinting. In addition to this, the mealybugs have several other distinctive features, including high resistance to ionizing radiation. To understand its unique biology, our lab completed whole genome sequencing followed by *de novo assembly* of *Maconellicoccus hirsutus*, and the annotation is currently being carried out with a focus on the epigenetic modifiers.

One of the manifestations of genomic imprinting in mealybugs is the differential chromatin organization in male mealybugs. We have earlier shown that approximately 10% of the genome in the male mealybug is highly condensed chromatin and is resistant to nuclease and hence, designated as 'NRC' (**N**uclease **R**esistant **C**hromatin). NRC was shown to be enriched with middle repetitive DNA and is predicted to function as putative centers of inactivation (Khosla et al. 1999, NAR). To decipher the nature of sequences organized as NRC, we have carried out the complete sequence of NRC. We have also identified the differential enrichment of Heterochromatin Protein (HP1) and Polycomb protein in NRC. The histone modification profile is being analysed to examine the differential enrichment in the nuclease resistant versus the sensitive chromatin.

P21: Hydrothermal Synthesis of Magnetite Nanoparticles and their Interaction with DNA

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For past few years, immense interest has been developed in the magnetic nanoparticles due to its numerous applications in the field of hyperthermia, cell isolation, targeted drug delivery, gene therapy, bio sensing, MRI and recently in cancer therapy. Keeping all these applications in mind, a simple and benign hydrothermal route was taken to synthesize iron oxide nanoparticles of 25nm size in the form of magnetite. The purity of phase and size of nanoparticles were determined by X-Ray powder diffraction (XRD) analysis. Nanoparticles were further characterized using UV-Visible spectroscopy, Dynamic Light Scattering (DLS) and Fourier- transform infrared spectroscopy (FTIR) studies. Nanoparticles morphology was studied using scanning electron microscopy (SEM) and Energy Dispersive X-ray (EDX) analysis. Interaction studies of nanoparticles with Calf Thymus (CT) DNA was done using various techniques like UV-Visible spectroscopy, UV-Tm analysis, fluorescence spectroscopy, Circular Dichroism (CD) and agarose gel electrophoresis. Increase in absorption values in UV studies, quenching of fluorescence intensity on addition of nanoparticles and alteration in the conformation of B form of DNA in CD studies clearly show interaction of magnetite nanoparticles with CT-DNA. Based on the present studies, it is suggested that the nanoparticles synthesized are genotoxic in nature and this property can be exploited further in DNA damage of cancer cells during chemotherapy.

P22: Environment friendly Green Synthesis of NiO Nanoparticles: Characterization and Interaction with DNA

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In recent times, engineered nanoparticles have generated lots of interests due to their unique properties, which differ greatly from their bulk forms and utility in various fields, such as medical, environmental, electronics, catalytic, etc. Green synthesis especially is of importance because it attempts to use complex yet benign natural products for synthesis of the nanoparticles from the parent compounds.In this study, Nickel oxide (NiO) was preferred because of its unique characteristics; firstly, it is easier to synthesize and unlike iron, it doesn't exist in multiple oxidation states, which makes it ideal for environmental applications. Secondly, they possess unique magnetic properties,which impart them with an additional mode of detection and manipulation.NiO nanoparticles (Nio-Np) are of special interest because they show genotoxic and cytotoxic properties, which can be useful in developing anti cancer drugs.Keeping these properties in mind, Ni nanoparticles were synthesized via green route from nickel acetate using extract of*C. sativum*(Coriander). The Ni nanoparticles were purified and converted to Nio-Npvia calcination. Nanoparticles were characterized using UV-Vis spectroscopy andX-Ray Powder Diffraction studies were used to determine lattice structure and lattice size.Fourier Transform Infrared Spectroscopy(FTIR) analysis was used to determine functional groups, which act as capping agents. Interactions of Calf Thymus (CT) DNA were studied using agarose gel electrophoresis, UV-Vis spectroscopy, UV-Thermal melting, fluorescence spectroscopy, and Circular Dichroism spectroscopy. Such studies may facilitate our understanding about the mechanism of DNA-Nanoparticle interactions for exploiting their potential for *in vitro* and *in vivo* applications.

References: Ezhilarasi, A.A., et al., (2016), "Green synthesis of NiO nanoparticles using *Moringa oleifera* extract and their biomedical applications: Cytotoxicity effect of nanoparticles against HT-29 cancer cells," Journal of Photochemistry and Photobiology, 164, 352-360.

P23: Sin3 Regulation in presence of Calcium ions

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Sin3, a global transcription regulator, helps to regulate many biological functions including nucleosome remodeling, DNA methylation, cell proliferation and apoptosis. Sin3 does not bind to DNA but is a scaffold protein that helps the transcription of various genes by interacting with different transcription factors, forming Sin3 complex. The core complex of Sin3 consists of eight components in humans: Sin3, SAP18, SAP30, HDAC1, HDAC2, RbAp46, RBaP48 and SDS3. It has been known that divalent cations are involved in the transcription regulation of various genes, Calcium is one such divalent ion. Till date, there is no direct study regarding the Sin3 regulation due to Calcium ions. We discovered that (i) Calcium ion can interact with Sin3 and can regulate its function (ii) Calcium ions do not have any role in steady state level oh HDAC1 (iii) Calcium ions do not play role in nucleo-cytoplasmic migration of HDAC1 (iv) Conformation induced by 15Mm Concentration of $CaCl_2$, is non functional Sin3.

P24: Generation of Native-Like Protein Aggregates Upon Modification By Homocysteine Thiolactone: New Insights Towards Functional Loss Upon N-Homocysteinylation

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Covalent protein modification by cellular metabolite, homocysteine thiolactone (HTL, called N-homocysteinylation) is known to result in functional loss of the target proteins. Conformational alterations as a result of HTL binding have been shown to be the primary cause of functional loss so far. In the present study, effects of HTL on structure and function of RNase-A, Lysozyme and Carbonic anhydrase were investigated. Carbonic anhydrase was found to follow usual pathway for the loss of function, via conformational alterations resulting in amyloid formation as suggested by ThT binding assay and TEM imaging. RNase-A and Lysozyme showed minimal functional alterations upon incubation with HTL for three days, with subsequent functional loss upon prolonged incubation. These were not accompanied by structural loss as suggested by intrinsic fluorescence and CD analyses. However, DLS measurements provided sufficient evidence for substantial oligomerization of these native protein molecules upon N-homocysteinylation. Furthermore, TEM imaging suggests generation of "supramolecular" spherical structures of modified proteins with varying sizes. RNase-A and Lysozyme tend to be resistant towards structural alterations and require longer incubation to get inactivated, which occur via extensive oligomerization that hampers substrate diffusion to the active sites. Our findings suggest two independent mechanisms occurring for protein functional loss upon post-translational modification via N-homocysteinylation.

P25: Why India Needs Vitamin D Supplementation Programme; A one arrow Preventive Approach

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Background & Aim: With a great interest to heighten bone health among populations, we wish to express our concern for the need of vitamin D supplementation programme in a tropical country like India. Several studies have uniformly discussed about the wide range of vitamin D deficiency in Indian population including from children to elderly from urban to rural and from planes to hills with a prevalence rate between 70 to 100% despite having a generous sun exposure. Deficiency of vitamin D not only affects musculoskeletal health but also associated with a wide range of acute and chronic diseases too including risk factor for the development of osteopenia and osteoporosis as well. **Methods:** We have gone through studies using pubmed database including those who have used fortification of vitamin D in milk and edible oil. Since, fortification of food products in India is rare and not everyone can afford such products, we therefore advocate the supplementation of vitamin D.

Results/Observation: Indian studies have shown benefits of vitamin D supplementation in pregnant women with Decrease risk of maternal co morbidities and improved neonatal outcomes, improvement in handgrip strength increased newborn's length in pregnant women. Additionally, vitamin D supplementation helps in delaying diabetes and cancer occurrence, enhances immunity, helps in destruction of infectious agents, handgrip strength, maintaining vascular tone of the body, myocardial function including many more complex diseases.

Conclusion: Needless to say, a wide publicity and advocacy of vitamin D supplementation programme from civil societies with the help of government will be an appreciable step likewise the previous major supplementation programes in India. Primarily, this programme can be initiated as pilot programme in a small metro city for a period of five years to observe benefits. This approach will not only help to optimize the vitamin D deficiency but also help to mitigate the growing burden of communicable and non- communicable diseases as well.

Key Reference: Mithal A and Kalra S, Vitamin D supplementation in pregnancy. Indian J Endocrinol Metab 2014; 18:593–596.

P26: Dissecting the genetic signatures of adaptation in Indian populations in response to geo-climatic factors

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After the exodus of human population from Africa, they inhabited and adapted to different geographies and climatic conditions. Understanding, the genetic basis of climate-mediated selective pressures is one of the major interests in population genomics, and thus, there have been concerted efforts in this direction to find genetic signatures of adaptation using both candidate based and genome-wide approaches. Hancock *et al.* (2011) first devised the Bayesian based approach to detect significant correlations between genomics data and geo-climatic variables by correcting biases owing to underlying genetic structure. This study was conducted with genome-wide SNP and climatic data from 61 worldwide populations. However, this dataset does not have sufficient representation from Indian populations. Enigmatic history of India and unique diversity contributed by socio-cultural, linguistic and geo-climatic factors make it a treasure trove of genetic variations and amenable to population genetic studies. Indian Genome Variation Consortium (IGVC) provided the first major catalogue of variations for diverse ethnic Indian populations. However, how the variations are associated with climatic parameters in the context of Indian populations is still unexplored. Therefore, to detect the genome-wide signatures of geo-climatic adaptation, our group has genotyped and analysed ~7 lakh SNPs from 470 individuals in 25 Indian populations using Illumina Human OmniExpress v12. Climatic data of 10 variables related to humidity, temperature, radiation flux and temperature were obtained from the Centre of Atmospheric and Oceanic Sciences (CAOS), Indian Institute of Sciences (IISc),Bangalore. Also, altitude, latitude and longitude parameters for different Indian populations were retrieved from google. Bayesian approach was used to find 48,540 SNPs significantly correlated with one or more geo-climatic variables. We used this dataset to find geo-climatic variables that are correlated with signatures (SNPs/genes) associated with high altitude adaptation. There are numerous studies that identified genetic signatures of high altitude adaptation using genome-wide as well as candidate based approaches in different world populations. We applied fisher's test to find significant (p-value <=0.01) SNPs between highlanders and lowlanders from Tibeto-Burman ethnic group of Indian populations. There were 13,080 SNPs from 1,937 genes that differ between these groups. We found many known and novel candidate genes that are correlated with different geo-climatic variables. This dataset is a valuable repertoire to mine novel candidates of adaptation in response to different climatic and geographic conditions in Indian populations.

P27: Anticancer effect of HDAC 6 specific inhibitor on cervical cancer

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Histone deacetylase inhibitors (HDACi) are promising therapeutic agents which are currently being used in combination with other chemotherapeutic agents for treating different cancers. However number of side effects are associated with the use of Pan HDAC inhibitors so replacement of Pan HDACi with subtype selective HDAC inhibitors has become important for cancer treatment so as to overcome the side effects associated with the use of Pan HDAC inhibitor and obtaining minimal side effects. HDAC6 is overexpressed in variety of tumors including hepatocellular carcinoma, ovarian cancer, breast cancer, multiple myeloma and acute lymphoblastic leukemia. It is an important modulator of many pathways which are involved in oncogenesis like PI3K/Akt, Ras/MAPK/ERK, JAK/STAT and Wnt signaling pathways which makes it important drug target for cancer treatment. It is an important cell survellience factor as it protects cells from cellular stress resulting from accumulation of cytotoxic protein aggregates. Its role in aggresome formation, autophagy, heat shock response and stress granule formation makes it competent for handling cellular stress, hence combination regimen of HDAC6 inhibitor with other chemotherapeutic agents which induce cellular stress would turn out to be synergistic. Also it is functionally and structurally very distinct from other members of HDAC family which reinforces the fact that HDAC6 specific inhibitor would show minimal side effects compared to other HDAC inhibitors. The IC_{50} of the chosen HDAC6 specific inhibitor has been found to be in the range of 2-10 µM in several cancer types such as breast, pancreatic and ovarian cancer. Cytotoxicity of the chosen HDAC 6 specific inhibitor was determined in Hela cells by MTT. The inhibitor was found to be 50% cytotoxic at 25 µM concentration which is too high concentration for an inhibitor to be used as a drug. However further experiments are needed to validate HDAC6 as a target for cervical cancer. Future work will involve screening of HDAC6 specific inhibitor for various other cervical cancer cell lines such as SiHa and also other cancer subtypes to see its effect on solid tumour models alone and in combination with other chemotherapeutic agents.

P28: *In-Silico* Designing and Development of subtype selective HDAC inhibitors as anticancer agents

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In India 0.3 million deaths per year occur due to cancer. Epigenetic alterations are one of many causes of cancer prognosis and development. Histones play a major role in controlling epigenetic modifications. HDACs are enzymes which removes the acetyl group from N-terminal lysine residues of histones resulting in transcriptional repression. HDAC6 is unique among all other 18 HDACs as it contains two catalytic domains and is mainly located in the cytoplasm. HDAC inhibitors (HDACi) have proved to be useful in cancer treatment but the non-specificity of the target is major side effect limiting the use of pan-HDACi. Over expression of HDAC6 is related to tumerogenesis and improved survival. Designing HDAC6 specific inhibitors results in inhibiting HDAC6 functions, promoting the cancerous cells towards apoptosis whereas normal cells are not affected much thereby minimising the side effects of pan inhibitors.

Previous work done in the lab with HDAC6 pharmacophore gave us a list of hit compounds (screened through a database). These compounds were docked with HDAC6 crystal structure. The compounds showing best energy scores and interactions were selected. These selected compounds were screened for their ADMET and TOPKAT properties. Only the best compounds which passed all the screening parameters *in silico* were further modified to provide them specific cap groups enhancing their selectivity for HDAC6. These modified compounds were again screened for their ADMET and TOPKAT properties and also they showed better docking scores and interactions than the unmodified compounds. They provide us a better lead towards the designing of novel HDAC6 specific inhibitors which will be helpful as anticancer agents. Future work is to synthesise these lead compounds and their *in vitro* testing.

P29: Electrochemical Immunosensor for Lung Cancer Detection based on Silver Nanoparticle-Graphene Oxide Nanocomposite

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A label free electrochemical immunosensor was designed to detect lung cancer in serum *via* targeting circulating antibodies against anti-Melanoma Associated Antigen A2 (MAGE A2) in real samples using differential pulse voltammetry method. Detecting circulating antibodies against MAGE A2 antigens during onset or first stage of lung cancer (probably asymptomatic phase) can revolutionalize cancer detection and bring huge fall in mortality rate. This immunosensing system used cysteine (Cys) conjugated silver nanoparticle decorated graphene oxide (GO-Ag/Cys) onto graphite electrode as a sensing platform and MAGEA2 as a sensing probe. The structural and morphological investigations of as prepared immunosensing platform were accomplished at each step of modifications using UV-visible (UV-Vis) spectroscopy, transmission electron microscopy (TEM), scanning electron microscopy (SEM) and electrochemical cyclic voltammetric (CV) studies. MAGEA2/Cys/GO-AgNPs/Graphite immunosensor detected 1 fg mL^{-1} to 500 ng mL^{-1} anti-MAGE A2 in spiked serum using differential pulse voltammetry; exhibited outstanding stability, reproducibility and selectivity towards anti-MAGE antibodies. Furthermore, this immunosensing platform could detect target analyte in lung cancer patient sample showing the realization of commercially viable diagnostics for easy and low cost lung cancer detection in biological fluids.

Key words: Graphene oxide, Immunosensor, Electrochemical, Lung cancer

P30: Myc dependent role of Gsk3alpha in Glioma progression and its development

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Glycogen synthase kinase 3 (GSK3) is a constitutively active regulatory enzyme important in cancer. It has two isoforms GSK3α and GSK3β. Though, GSK3α and GSK3β are known to share a high degree of homology in kinase domains and perform similar functions but some recent studies suggest isoform-specific roles. Earleir many studies, demonstrated that inhibition of GSK3β attenuates the survival signaling cascade, however; the role of GSK3α in Gliomas is sparsely understood. As c-MYC is a proto oncogene and it is highly expressed in cancer so we checked the c-MYC binding site (CACGTG) in GSK3α & GSK3β promoter with the help of RBPmap. Here, we found that GSK3β has c-MYC binding site but there is no c-MYC binding site in GSK3α. We also checked the DNA-Protein interaction with the help of Chromatin immunoprecipitation (CHIP). The role of GSK3 alpha is elucidated using gene knock down approach, where cell viability is increased. Silencing GSK3α elevates hnRNPA1 (splicing factor), Cyclin D1, p-ERK & c-MYC expression in glioma cell lines. So we have concluded that GSK3α knock down helps to migrate glioma cells rapidly than the control cells with the increase of Myc expression. As a conclusion restoration of GSK3α in gliomas could be a best strategy to inhibit progression.

P31: INSIGHTS INTO THE ROLE OF DEUBIQUITINATING ENZYMES IN BREAST CANCER.

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Deubiquitination considered as a Post-translational modification where the proteins to be destined for degradation by Proteosome are modified with the help of Deubiquitinating Enzymes by the removal of Ubiquitin to stabilize the protein. There are several Deubiquitinating enzymes (DUBs) studied so far. In this study we have focused mainly on DUBs such as USP5 and USP8. We have investigated for the synergistic roles of these DUBs in breast cancer,andthe study was carried on using certain inhibitor such as Ubiquitin-aldehyde to inhibit DUBs in breast cancer cell lines. The panel of breast cancer cell lines is classified as ubiquitin dependent protein degradation and as cell viability assay. And has come up with the result that treatment of breast cancer cells with these inhibitors causes dose dependent caspase-3 activation and apoptosis which occurs well after an onset of proteotaxis stress concluding that the apoptosis mediated cell death is a result of unstable level of Ubiquitin-Proteosome System (UPS) stress in breast cancer cells after DUBs inhibition. The treatment has shown that the inhibitors activate the autophagy as a process to escape the unstable levels of UPS stress and such approach can help in leading to further studies in order understand the role of several more DUBs in Breast Cancer.

P32: *In silico* investigation and structure-guided design, synthesis and screening to explore the therapeutic potential of PAD4 inhibitors

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Protein arginine deiminase 4 (PAD4) is an enzyme responsible for citrullination (conversion of peptidyl arginine into peptidyl citrulline). Loss of ionic interactions due to citrullination may destabilize intra- and intermolecular interactions leading to protein unfolding/ disruption of protein complexes. This enzyme is reported to be linked to variety of diseases including inflammation, neurodegeneration and cancer. PAD4 is overexpressed in several tumors as well as linked to diseases involving abnormal levels of neutrophil extracellular traps (NETs) and thus can be attractive targets for design and development of novel cancer therapeutics.

In this study, we aimed to design, synthesize and screen (biochemical and cell-based) novel PAD4 specific inhibitors showing diminished citrullination with no signs of chromatin decondensation and NET formation. Further to understand the mechanism of inhibition, we are working on solving the crystal structure of human PAD4 complexed with these inhibitors and explore their off-target activity against unrelated proteins.

P33: Cancer Diagnosis: Use of Bioprinting and Biosensors

Arpita Bhatt, Bhawana Verma, Mohini

Bioprinting is manipulating the ability of 3-D biomolecules to biomimic the spatial and chemical attributes of native tissues and provide an in vivo-in vitro correlation. This will in turn shed light on its application-Biosensor Fabrication. It is important to harness bioprinting technologies for biosensor applications in order to investigate multiple anylates or biological outcomes with high outcomes with high throughput. Techniques like electro-deposition can be used to print thin films of biomolecules and bacterial cells that can be used as a transducers. In biosensing the delivery of a molecule to the site of destination is done via patterning which allows their direct delivery to the desired locations via Contact Based (touching the substrate such that cell get constrained to specific area) and Non-Contact Based (on transferred material comes in contact with substrate. Due to alarming increase in cancer cases being diagnosed and number of fatalities due to late disease detection, new enabling tools are required to provide extensive molecular profiles in making viable diagnosis and prognosis. Biosensors can play an important role in the early diagnosis of cancer, it helps in detecting multiple cancer biomarkers that exist at low concentrations in biological fluids. Cancer Markers (PSA, CA72-4, hCG, BAT, HA-Hase,MUC-1) are tumor associated antigens present in extracellular fluid and within the tumorous cell. Biosensors are point of care (POC) devices which can bring the capability of analyzing clinical samples in home or at the doctor's surgery. Elements of biosensors are Molecular Recognition Elements (sensing biomarkers of cancer, both monoclonal and polyclonal antibody are used), Transducers (convert recognition signal events into electrical signals), Nanomaterials (signal enhancement and amplification of signals) and Microfludics (hand held biosensing device). For future perspective and challenges: biosensors must be highly specific, quantitative, inexpensive, sensors must be multi-arrayed, prevention from false positive and false negative results.

P34: Comprehensive mapping of HPV infection in human cancers

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Background: Accumulating evidences indicate the incidence of HPV-related cancers (gynaecological, head and neck and other cancers) with varied prevalence in India has been rising. Despite the introduction of HPV vaccines, it is important to know HPV prevalence and type distribution not only in cervical but also in other cancers in order to better management of HPV vaccination program in Indian population.

Methods: Present study included a total of 509 histopathologically confirmed cancer biopsies of cervical (n=30), endometrial (n=31), ovarian (n=30), breast (n=40), oral (85), esophageal (75), gastric (n=50), lung (n=28) and 140 controls for all cancer sites except lung cancer. These samples were employed for analysis of HPV infection and genotypes using PCR and RLB assay. **Results:** The overall HPV prevalence was 80%, 19.7%, 17.65% and 3.2% in cervical, esophageal, oral and endometrial carcinomas respectively whereas no HPV DNA was detected in breast, ovary, stomach and lung carcinomas. Exclusively, HPV16 was found in 100% of almost all HPV^{+ve} cancers except cervical cancers in which HPV6, HPV11, HPV52 and HPV45 were also recorded. Interestingly, in oral cancers, HPV16 infection was found significantly higher in well differentiated tumors whereas in cervical and esophageal cancers, infection rate was higher in poorly differentiated tumors. **Conclusion:** On mapping of HPV-related cancers, HPV16 was found to be most prevalent type in cervical, oral and esophageal cancer suggesting a critical role in tumor progression. In cervical and esophageal cancer, HPV infection was seen mainly in poorly differentiated tumors whereas in oral cancer it leads to well differentiation of tumor with better prognosis.

P35: Altered levels of miR-21 and miR-184 during tongue squamous cell carcinoma

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Background: Tongue squamous cell carcinoma (TSCC) is a most prevalent and lethal cancer in younger age population. Tobacco chewing, alcoholism and high-risk human papillomaviruses (HR-HPVs) infection are considered as principal causative agents for TSCC. miRNAs have been implicated in cancer initiation and progression via their ability to affect expression of genes and proteins that regulate cell proliferation and/or cell death. The present study aimed to investigate altered expression of selective miRNAs (hsa-miR-21 and hsa-miR-184) during tongue carcinogenesis.

Methods: HPV diagnosis and TaqMan qRT-PCR were employed to study HPV infection status and the expression of two selected miRNAs (hsa-miR-21 and hsa-miR-184) in 30 TSCC tumors and ten adjacent normal tissues (n=10). The expression levels of these miRs were correlated with clinicopathological parameters and HPV infection.

Results: Initial HPV diagnosis revealed that HPV16 was the exclusive prevalent type in tumor tissues (30%) from TSCC patients and the majority (72.2%) of whom were well differentiated tumors mainly in an integrated form of DNA in to the host genome. miR-21 and miR-184 were the significantly elevated in tumor tissues of TSCC when compared to adjacent controls ($P < 0.05$). High level of these miRs was associated with HPV DNA integration, tumor progression and differentiation during TSCC patients.

Conclusion: Our findings imply that altered expression of miR-21 and miR-184 is associated with HPV infection and tobacco chewing habits and may represent potential biomarkers for HPV$^-$induced TSCCs.

P36: Phenotypic Microevolution of Progressively Transforming Cells Triggers Onset of Low Dose Hyper-Radiosensitivity and Altered Cell Adhesion Dynamics

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A growing body of evidence suggests that alterations in the adhesion properties of cells contribute in the progression of cancers as well as response to radio/chemotherapeutic agents. Previously, we have shown the role of cell-cell interactions and cellular adhesion proteins in radiosensitivity at low doses. Moreover, low-dose hyper-radiosensitivity is suggested to be more prominent in tumour than normal cells, although this needs to be established more clearly. Based on these reports, we hypothesized that the process of carcinogenesis and cellular microenvironment may influence cellular hyper radio-sensitivity. Present study was conducted on two different *in vitro* transformation models recapitulating the distinct progressive stages of tumour progression, followed by metastatic colonization. Generation of multiple progressive transformants were successfully achieved using physical and chemical transforming agents applied to primary human thyroid cells as well as mouse embryonic fibroblast cell line (NIH3T3). Morphological alterations, growth properties, cell-cell and cell substrate attachment capacity, cell adhesion molecule expressions, anchorage dependency and *in vivo* tumorigenicity in nude mice were taken as early and late stage markers of transformation. The study highlights the possibility that low-dose HRS response might be an inherent feature of progressively transforming cells. Alterations in inherent dynamics as well as radiation-induced responses of certain signalling proteins such as connexin-43 seem to be associated with this altered cellular behaviour, and especially involve radiation-induced Cx43 overexpression and mitochondrial translocation. This study thus provides two distinct cellular models for studying alterations in, as well as important role played by, cell adhesion molecules during neoplastic progression (EMT) or during the MET simulating conditions of micrometastases formation.

P37: DNA topology alteration by Histone deacetylase inhibitor enhances cell survival post-irradiation

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Radiotherapy induced disorders of reproduction and hazards to reproductive health have become a question to think about. DNA damage induced by radiation initiates cell cycle blockage, DNA repair and apoptosis. Many types of DNA lesions are produced in cell by gamma irradiation which can induce defects in male reproductive system and may lead to permanent sterilization. To investigate the mitigative potential of HDAC inhibitors male mice were divided into four groups: (i) control (ii) Irradiation only (iii) Drug only (iv) Irradiation + drug. Mice were exposed to 2 Gray gamma radiations and Drug was administered 2 hrs post-irradiation. Mice were sacrificed at various time points and testes were taken out. DNase accessibility assay was performed to examine the topology of DNA in spermatocytes. Apoptosis was studied by the histological observation of testes section microscopically and studying the expression of apoptotic genes. The drug alone and IR+ drug group showed maximum digestion by DNase I compared to control and IR alone groups indicating more access of the enzyme to DNA as a result of change in topology. Overall the remodeling or opening of chromatin structure as evident from enhanced DNA digestion by DNase I due to HDAC inhibitor could possibly facilitated DNA repair as was observed by reduction in apoptosis.

P38: Deciphering the functional role of p73 in tumor suppression

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p73 is a member of the p53 tumor suppressor family, which transactivates p53-responsive genes and mediates DNA damage response. Similar to p53, p73 is also maintained at a very low level in non-stressed cells but it rapidly gets induced upon genotoxic insults. Genotoxic stress leads to activation of p73. Once activated, it can transactivate the promoters of many p53-target genes, thereby inducing cell cycle arrest, apoptosis, and senescence. Such transcriptional targets include the pro-arrest genes like p21 and GADD45, and the pro-apoptotic genes like BAX and PUMA. Recent evidences suggest that other than pro-arrest and pro-apoptotic roles, p73 also exerts its tumor suppressor function by suppressing metastasis. The objective of our study was to find out novel downstream targets of p73 which have anti-metastatic functions upon DNA damage. For this purpose, we first generated p73 knockout HCT116p53-/- cell line using CRISPR-Cas technology. Our next aim is to perform Real Time PCR assay for several genes having anti-metastatic functions such as P-selectin and E-selectin (Cell Adhesion Molecules), Gelatinase-A and stromelysin-1 (ECM Protease Inhibitors), Mdp-3 and ATIP3 (Microtubule Associated Proteins), etc. using Control and p73 knockout cell line. Our results will delineate the mechanism involved in anti-metastatic function of p73.

P39: Autophagy mediated antitumorogenic effect of statin Simvastatin in breast cancer

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Autophagy, a well-described cellular mechanism for lysosomal degradation of cytoplasmic content, has emerged as a tumour suppression pathway. This is attributed to the ability of autophagy to promote cell survival under conditions of poor nutrient supply, as often faced by solid tumours and metastasising cancer cells. In addition, autophagy is frequently upregulated in tumours as a response to therapy and may protect tumours against therapy-induced apoptosis.Statins, also known as 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, are the most commonly prescribed drugs worldwide. They posses to reduce several clinical trials myocardial infarction, ischemic stroke, and peripheral arterial disease. Beside cholesterol reduction, experimental and clinical data exist that demonstrate various effects of statins in different cancers .In the current set of investigation we have investigated the anticancer effect of Simvastatin in breast cancer. Bif-1 (Bax-interacting factor-1), also known as SH3GLB1 or Endophillin B1, is a member of the endophilin B protein family Induction of BIF1 was found in breast cancer MCF7 Cells along with suppression of p53 and p19. In vivo investigation also showed inhibition in DMBA induced breast cancer by Simvastatin.

P40: Differential modulation of cytokine/chemokine regulatory networks in patients with hippocampal sclerosis (HS) and focal cortical dysplasia (FCD)

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Background: Altered expression of cytokines and chemokines have been demonstrated in experimental models of hippocampal sclerosis (HS) and focal cortical dysplasia (FCD). However, there is limited information regarding the modulation of cytokine/chemokine-regulatory networks, suggesting contribution of miRNAs and downstream transcription factors/receptors in these pathologies. Also, simultaneous quantification of these factors in a comparative manner to deduce the pathology specific differences is still lacking. Hence, we studied the level of inflammatory mediators and its downstream targets and upstream microRNAS in HS and FCD comparatively.

Methods: We measured multiple inflammatory mediators (IL1β, IL1Ra, IL6, IL10, CCL3, CCL4, TNFα and VEGF) in brain tissues resected from HS and FCD patients using multiplex immunoassay. We also investigated simultaneously the transcriptional changes of nine selected miRNA and mRNA expression levels of downstream effectors of significantly altered cytokines using quantitative RT-PCR. A total of twenty six MTLE and twenty six FCD patients, and twenty two non-epileptic controls were included in this study.

Results: Up regulation of IL1β, IL6, CCL3, CCL4, STAT-3, C-JUN and CCR5, and down regulation of IL 10 were observed in both HS and FCD cases ($p < 0.05$). CCR5 was significantly up regulated in FCD as compared to HS ($p < 0.001$). Both, HS and FCD presented decreased miR-223-3p, miR-21-5p, miR-204-5p and let-7a-5p and increased miR-155-5p expression ($p < 0.05$). As compared to HS, miR-204-5p (upstream to CCR5 and IL1β) and miR-195-5p (upstream to CCL4) were significantly decreased in FCD patients ($p < 0.01$).

Conclusion: This is the first comparative study demonstrating deregulated cytokine/chemokine regulatory networks in the HS and FCD. Differential alteration of cytokine/chemokine regulatory networks in HS and FCD provide a rationale for developing pathology specific therapy.

P41: Integrated genome-wide DNA methylation and RNAseq analysis of resected brain tissues identifies aberrant signalling pathways in patients with Focal Cortical Dysplasia

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Objective: Focal Cortical Dysplasia (FCD) is one of the most common pathologies of drug resistant epilepsy (DRE). The pharmacological targets are often inappropriate as the molecular mechanisms underlying FCD remain unclear. Implications of epigenetically modulated aberrantgene expression in disease progressionare reported in DREs other than FCD. This studyinvestigates the role of epigenetically deregulated genes potentially involved in the development/progression of FCD.

Methods: We performed Genome scale CpG-DNA methylation profiling byMethylated DNAimmunoprecipitation microarray (MeDIP-chip) and RNA sequencing using standard protocols on IlluminaHiSeq 2500 platform on cortical tissues resected from FCD type II patients undergoingsugery. Differentially methylated genes were analyzed using gene spring software GX version 13.0. and differential gene expression (DGE) was performed using cuffdiff (version= 2.2.1).Integrative analysis of DNA methyaltion and RNAseq data was carried out using genespring software GX version 13.0. Validation of both MeDIP and RNAseq experiments wasperformed using quantitative PCR on autopsy controls(n=10)and FCD type II patients (n=10).

Results: A total of 19088 genes showed altered DNA methylation in all the CpG islands, 5725 genes with altered CpG methylation in the promoter regions out of which 176 genes were showing inverse correlation with the gene expression patterns. Many of these belong to a cohesive network of physically interacting proteins linked to several cellular functions. Pathwayanalysis revealed significant enrichment of receptor tyrosine kinase (RTK) EGFR, PDGFRA,NTRK3and mTORsignaling pathways.

Significance: We report for the first time, integrated analysis of genomic methylation signature and differential gene expression patterns of tissues resected from FCD type II patients undergoing surgery. We have identified epigenetically modified canonical pathways and candidate genes with potential impact on the pathogenic mechanisms of epileptogenesis in FCDtype II patients.

P42: Activation of Transforming Growth Factor Beta (TGFβ/SMAD3) signalling in Mesial Temporal Lobe Epilepsy (MTLE) patients

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Purpose: Recent studies in rats show that blood brain barrier (BBB) damage and albumin extravasation leads to TGFβ signalling activation and contribution to network excitability in epileptogenesis and excitatory synaptogenesis. (Ivens et al., 2007; Cacheaux et al., 2009; Weissberg et al., 2015). Our previous study on RNAseq analysis of hippocampal tissue resected from MTLE+HS patients revealed TGFβRII as one of the candidate genes showing significant up regulation (Dixit et al., 2015). Based on the evidences from animal models and RNAseq data, we hypothesize that TGFβ signalling is activated in MTLE+HS patients. In the present study we aim to investigate the expression level change of TGFβ1 ligand, TGFβRII receptor and its downstream signalling molecule phosphorylated SMAD3 in MTLE+HS versus non epileptic control patients.

Method: Protein was isolated from the resected hippocampal samples from MTLE patients (n=34) and non epileptic control patients (n=25). Western blot was done with antibodies against TGFβ1, TGFβRII and pSMAD3. Densitometric analysis done by ImageJ software normalised to expression of GAPDH. Statistical analysis was done by Sigma Plot13 software.

Result: TGFβ1 (2.4258±1.4215) and TGFβRII (2.417±1.407) expression is significantly upregulated in MTLE compared to autopsy control (0.6307±0.2636) (0.897±0.419). pSMAD3 expression (2.6010±1.2735) (1.527±0.9425) is significantly upregulated in MTLE in comparison to non epileptic autopsy control(0.5791±0.2679) and tumour periphery control (0.7899±0.3688).

Conclusion: Our study demonstrates that TGFβ signalling is activated in MTLE+HS patients, through the phosphorylation of SMAD3. It is an important aspect of brain inflammation and may be associated with BBB damage and ECM remodelling. These alterations affect excitability of brain and lower the threshold for seizures, enhancing epileptogenesis. Further studies on more number of patients are required to elucidate how this pathway is contributing to epileptogenesis.

P43: Diet and lifestyle – factors modulating the population dynamics of gut microbiota and human health

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The health of an individual is governed by his/her lifestyle and dietary practices. The human body harbours an enormous and diverse number of microbes in the GI tract. This gut microbiota is influenced by our eating habits and lifestyle. Roughly, there are ten times as many microorganisms within the gastro-intestinal (GI) tract of humans as there are somatic cells within the body. The impact of microbiome can be beneficial or detrimental depending on their relative identity and abundance of constituent microbial population. Studies have shown that some bacterial phyla like *Actinobacteria*, *Bacteroidetes*, *Firmicutes*, and *Proteobacteria* are the most populated ones to be influenced by dietary habits and lifestyle. The amount and the type of macromolecule consumption in our diet is the major factor responsible for the diversity of gut microbiota. The non-dietary lifestyle factors like smoking, stress, obesity along with geographical and environmental factors also are known to have a significant impact on the gut microbiota. The interaction of the host with the diverse array of gut microbiota determines the host's immunity standards. The diverse population of beneficial gut bacteria is important to keep harmful bacteria away as they compete for nutrients and sites of colonisation. Here, in this review paper, we summarise the studies performed across the world determining the regional and dietary effects on the population dynamics of microbes in the gut with relevance to human health.

P44: Biological Evaluation of Novel Quinoline Analogues Possessing Amyloid-Beta Disaggregation, Metal Chelation and Antioxidant Properties for the Treatment of Alzheimer's Disease

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In the venture towards the development of potent multitarget ligands for the treatment of Alzheimer's disease, a series of quinoline derivatives were designed, synthesized and characterized by various spectral techniques. In total, seven compounds were synthesized. These derivatives inhibited Aβ self-aggregation as investigated through ThT fluorescence assay and electron microscopy. Specifically, compounds 5g and 5a showed highest inhibitory potential, 53.73% and 53.63% at 50 μM respectively. This was also confirmed by transmission electron microscope (TEM) analysis. Furthermore, compounds 5g and 5a disaggregated Aβ fibrils generated by Cu^{2+}-induced and AchE induced Aβ aggregation respectively. Besides, these compounds also exhibited potential antioxidant activity (1.9488 and 2.7240 trolox equivalent by ORAC assay) and metal chelating property. *In silico* ADMET profiling showed these derivatives to have drug like properties with low toxic effects in the pharmacokinetic study. Overall, these results support our assertion that these compounds could act as templates for developing new multifunctional agents against Alzheimer's disease.

P45: Fighting Against Epilepsy by Employing Brain Carbonic Anhydrases Inhibition Strategy

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Carbonic anhydrases (CAs, EC 4.2.1.1) belong to a super family of metalloenzymes which reversibly catalyze hydration of carbon dioxide to give bicarbonate (HCO_3^-) and a proton (H^+). This reaction controls a wide range of physiological functions which include CO_2/bicarbonate transportation, electrolyte secretion, lipogenesis, respiration, gluoconeogensis, ureagenesis, bone resorption, tumorigenicity and neuronal excitability. In human, there are fifteen different isoforms of CA has been discovered. Seizures are escorted by rapid alterations in ionic composition in brain compartments which include pH shifts and increase in extracellular potassium concentration. It is well studied that alkalosis generally potentiates seizure spreading by increasing neuronal excitability, though acidosis produces just opposite effect. Hence, brain pH has immense role in seizure initiation and progression. The maintenance of suitable pH is mainly direct by CO_2/ HCO_3^- buffer system and CAs actively regulate this equilibrium by catalyzing the inter-conversion of these two components. Thus, CAs are appeared as a fruitful target to control seizure.

Continuing our drug development agenda against epilepsy, we discovered two series of novel benzenesulfonamide derivatives acting as effective carbonic anhydrase (CA, EC 4.2.1.1) inhibitors. The synthesized compounds were tested against human (h) isoforms hCA I, hCA II, hCA VII and hCA XII. The first series of compounds, 4-(3-(2-(4-substitued piperazin-1-yl)ethyl) ureido)benzenesulfonamides, showed low nanomolar inhibitory action against hCA II, being less effective against the other isoforms. The second series, 2-(4-substitued piperazin-1-yl)-N-(4-sulfamoylphenyl)acetamide derivatives, showed low nanomolar inhibitory activity against hCA II and hCA VII, isoforms involved in epileptogenesis. Some of these derivatives were evaluated for their anticonvulsant activity and displayed effective seizure protection against MES and scPTZ induced seizures in Swiss Albino mice. These sulfonamides were also found effective upon their oral administration to Wistar rats and inhibited MES induced seizure episodes in this animal model of the disease. Some of the new compounds showed a long duration of action in the performed time course anticonvulsant studies, being non-toxic in sub acute toxicity studies.

P46: Suppressing TTR amyloidosis: an approach toward therapeutic intervention of senile systemic amyloidosis

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Senile Systemic Amyloidosis (SSA), frequently diagnosed as a restrictive cardiomyopathy, is most commonly reported in men over the age of 60 years and symptoms include congestive heart failure, arrhythmias, and conduction defects. It is caused due to the deposition of wild type transthyretin (TTR) amyloids in the heart. In SSA, though the TTR amyloid deposits accumulate in extracellular compartments of tissues and organs throughout the body, the heart is the predominant site of deposition of the TTR amyloid. The presence of TTR amyloid deposits in the heart disrupts the normal cellular processes and tissue functioning. TTR is present in serum and cerebrospinal fluid. Serum TTR is mainly expressed in the liver, and central Nervous System. The expression of TTR is highest in the choroid plexus, but it also occurs in the retinal and ciliary pigment epithelia of the eye. TTR is a 55 kDa homotetrameric protein responsible for the transport of thyroid hormones and retinol binding protein. Much effort has been made towards identifying strategies for preventing TTR aggregation/amyloidosis. Some small molecule drugs have already been discovered to have the potential to inhibit TTR aggregation. These includes NSAIDS, polyphenols, some herbal drugs etc. However, their use for the therapeutic interventions has been challenged due to high toxicity, low efficacy and practicability to reach target organ. Since, oxidative stress is one of the important causes of amyloid-induced cytoxicity, it is important to look for drugs that have anti-oxidant property and also are capable of suppressing or inhibiting aggregation of proteins. In the light of this, in the present proposal we plan to investigate the effect of naturally occurring low molecular weight compounds, including anti-oxidant chaperons (folic acid, quercetin, ascorbic acid, curcumin) and medicinal plant extracts traditionally used for the treatment of heart ailments (*Crataegus hawthorn*, *Oroxylumindicum*, *Terminaliaarjuna*, *Bombaxceiba*) on the aggregation behavior of TTR.

P47: Fate of HTL on reservoir protein, Hemoglobin

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Homocysteine-thiolactone (HTL) is a toxic reactive thioester formed from homocysteine (Hcy) by methionyl-tRNA synthetase in an error editing reaction. The prime cause of toxicity of HTL is believed to be due to the adduct formation with the lysine residues of the protein (known as 'N-homocysteinylation'). Till date different serum proteins modified by HTL have been identified and their reactivities have been elucidated. Yet there is another class of proteins that remain resistant to alterations upon N-homocysteinylation. Here, using hemoglobin (Hb) as a model protein we have investigated the structural and functional consequences upon N-homocysteinylation by HTL. Interestingly, we found that initial incubation with HTL did not have any significant alterations in the protein's structural conformation; however, with increased concentration of HTL, it tends to form a partially unfolded intermediate structure with subtly distorted secondary structure. The study may provide an insight into the new pathological consequences of Hyperhomocysteinemia.

P48: Glutathione S-Transferase M1 and T1 Gene Polymorphisms in Patients with Acne Vulgaris: A Case-Control Study

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Background: Acne vulgaris is a complex, multifactorial skin disorder and is not well understood. Inflammatory, oxidative damage, genetic and environmental aspects have been implicated in pathogenesis of the several dermatological diseases including the acne vulgaris. Glutathione S-transferases (GSTs) are a multi-gene family of enzymes that are important in protection against oxidative stress, inflammation, mutagenicity and genotoxicity. Polymorphism of specific subtypes of GST enzymes (GSTT1 and GSTM1 genes) may lead to an imbalance in pro-oxidant and antioxidant systems ensuing increased production of reactive oxygen species that may influence the pathogenesis of acne in North Indian population.

Objects: This case-control study was aimed to elucidate whether the association between GSTM1/GSTT1 gene polymorphism in patients with acne vulgaris could be a susceptibility factor for disease development.

Patients and Methods: In this case-control study, we assessed 109 patients with acne vulgaris and 140 healthy individuals as a control, all from North India. Genomic DNA was extracted from human peripheral blood using phenol chloroform method. The GSTT1 and GSTM1 null genotypes were identified by multiplex polymerase chain reaction (PCR) and data analysis was done by SPSS 20.0 software.

Results: In patients, frequency distribution of null genotype of GSTM1 and GSTT1 was 42.2% and 11.9%. However, in 140 control samples, frequency of null genotype of GSTM1 and GSTT1 was 34.2% and 12.8% respectively. In statistical analysis, we observed non-significant association either in null alleles of the GSTM1 (OR = 1.39, 95% CI = 0.835–2.345, P = 0.202) or GSTT1 (OR = 0.918, 95% CI = 0.428–1.966, P = 0.825) for the susceptibility of acne disease.

Conclusion: In this case-control study, neither GSTT1 nor GSTM1 polymorphism was associated with susceptibility of acne disease. Due to small sample size, further studies with larger sample size and a wider range of GSTs gene polymorphism are warranted to conclude the acne disease susceptibility in North Indian.

P49: TMAO have different effects on fast folding and slow folding proteins

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TMAO (Trimethylamine N-oxide), a chemical chaperone, that gets accumulated under stress conditions, is known to have both the stabilizing and destabilizing effect on proteins. Till date the destabilizing effect of TMAO has been confined only to the fast folding proteins. We, therefore, investigated the effect of TMAO on slow folding proteins, Bovine Carbonic Anhydrase and Horseradish Peroxidase. We discovered that TMAO fails to stabilize or refold the proteins. Furthermore, we show that in proteins with high number of proline residues, proline cis-trans isomerisation becomes the rate limiting step in protein folding process, thus resulting into slow folding of proteins. Our results indicate that TMAO might have interfered cis-trans conversion generating a non-native protein species.

P50: Coumarin - Potential compound for inhibition of Candida biofilm

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Microbial resistance to the existing drugs is the major problem in today's world and to overcome this, there is dire need to search for new anti-microbial compounds. One such natural compound is Coumarin (1-benzopyran-2-one), which is fragrant, bitter compound produced by plants as a defense chemical to discourage predation. We have observed potential anti-microbial activity of Coumarin against various pathogenic microbes. However, in this study our main focus is on Candida albicans and its biofilm which causes resistance to the known anti-fungal drugs. The anti-candida activity, measured as Minimum Inhibitory Concentration (MIC_{50}), was observed as 730 □g/ml in biofilm and 500 □g/ml in planktonic cells as assessed by MTT/XTT and microbroth dilution method respectively. Further, our results indicate that treatment of Candida cells with Coumarin causes reduced cell-plate adherence and increased trans-membrane leakage of amino acids as compared to C. albicans control cells. In addition Candida cells grown in hyphae inducing conditions showed significantly reduced hyphae formation. These preliminary results suggest that Coumarin has strong effect on C. albicans cell wall and its interaction with neighboring cells. It is known that the yeast cell wall plays an important role in maintaining cell morphology, cell integrity and response to environmental stresses thus studies are in progress to estimate the effect on cell-cell adhesion, growth on cell wall-perturbing agents and effect on virulence factors for Coumarin treated Candida cells.

P51: Wnt gene perturbations: molecular and phenotypic characterization

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Wnt signaling is evolutionary conserved, developmentally important pathway which has emerged to play crucial role in tumorigenesis through canonical Wnt/β catenin cascade. The genesis of Wnt in cancer, started with discovery of mammary tumors arising in mice infected with Murine Mammary Tumour Virus-1, was traced to the activation of *int-1* gene, which is the homologue of *wingless* gene of the fly and hence, the name *Wnt-1*. Subsequently the protein APC (adenomatous polyposis coli), suppressor of colorectal cancer in human, was identified as a regulator of Wnt/β catenin pathway. Wnt genes regulate myriad of processes during development like cell proliferation, differentiation, polarity, migration, tissue homeostasis and stem cell maintenance Wnt gene family is not only conserved but diverged to function through different receptors and regulators and also to interact with other signaling pathways. This complexity poses a great challenge to understand Wnt pathway and its possible implication in cancer treatment. *Drosophila* serves an excellent model to study Wnt signaling.

Drosophila has a conserved cluster of *DWnt4-wingless(wg)- DWnt6* and *DWnt10* on the left arm of second chromosome. *DWnt4* antagonizes *wg in* patterning of embryonic epidermis while it cooperateswith *wg* during wing imaginal disc development. We report a novel *DWnt4* allele, $DWnt4^{AL7}$ which shows segment polarity defects in embryos. *RNA* interference mediated knockdown of *DWnt4* and UAS-Gal4 mediated gain of function analysis in wild type embryos mimicked segment polarity defects as observed in $DWnt4^{AL7}$. $DWnt4^{AL7}$ exhibits increased *wg* expression and loss of *armadillo* expression. *DWnt6* and *DWnt10* over expression rescues the denticle defects of $DWnt4^{AL7}$ mutant embryos with absence of w*g* expression, however *armadillo (*β catenin) expression isnormal . Thus, DWnt6/10 functions via canonical pathway. Germline clones of $DWnt4^{AL7}$ are lethal at stage 6 of oogenesis. Unlike wg , *DWnt4* has been reported to use a non-canonical Wnt pathway. *DWnt4* maintains stem cell proliferation in ovary niche. Neoplastically transformed somatic clones of tumor suppressor gene (lgl^{-}) in wing discs indicate misregulation of Wnt pathway which is correlated with increase in *DWnt4* expression. Functional characterization of Wnt gene is essential to explore drugability of the Wnt genes for cancer treatment.

P52: Role of Neddylation in regulating immune responses from macrophages during *Mycobacterium tuberculosis* infection.

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Tuberculosis is caused by the bacterium *Mycobacterium tuberculosis*. Being a successful pathogen it has devised various ways to down regulate host immune responses to survive inside host macrophages. We recently reported the role of Neddylation, a pathway, similar to the ubquitination pathway in M. tb infected dendritic cells. In this report we explored the role of Neddylation in mediating macrophage responses during M. tb infection. To that end we used Rv3416 an antigen expressed by *M. tb* inside macrophages that helps the establishment of infection. Rv3416 is a transcription factor expressed during *M. tb* infection causing anti-inflammatory responses like decreasing ROS production and expression of surface markers on the cell. We report that inhibiting Neddylation causes an increase in pro-inflammatory immune responses. This includes an increase in ROS production and upregulation of costimulatory molecules like CD86 and CD54. This points to a negative role of indicating a role in macrophage activation and defense responses. It was further elucidated that levels of calcium along with Neddylation pathway modulates the host immune responses. Inhibiting intracellular calcium release from the ER (using TMB8) along with inhibition of neddylation leads to a decrease CD54 expression and ROS production. In contrast chelating extracellular calcium (using EGTA) along with inhibition of Neddylation leads to increase CD54 expression and ROS production. Neddylation also modulated calcium cytokine responses from macrophages. This point towards a role of Neddylation in regulating immune responses from macrophages in a calcium dependent manner.

P53: Suppression of pro-inflammatory responses in macrophages during *Staphylococcus aureus* infection

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Staphylococcus aureus (*S. aureus)* is a gram positive, round shaped bacteria which causes various infections like respiratory disorders, food poisoning and sinusitis. Earlier studies have shown *Staphylococcus aureus* are able to survive following engulfment by macrophages, and that the intracellular environment of the host cells provide a refuge for *Staphylococcal aureus* survival and dissemination. In our study we report the effect of *Staphylococcus aureus* in modulating immune responses in macrophages. It was observed that *S. aureus* inhibits ROS production in macrophages. However, costimulation of macrophages with TLR2 (and to an extent with TLR4) agonist along with S. aureus infection prevents inhibition of ROS. Interestingly, the route of calcium homeostasis played a significant role in modulating *S. aureus* induced ROS production. Interestingly, either activating or inhibiting L-type Voltage Gated Calcium Channel (VGCC) increased ROS production that were earlier downregulated following *S. aureus* infection. This points to a very tight regulation of ROS production during *S. aureus* infection and points to a very narrow window of thresholds of calcium levels that in turn regulates ROS production. Furthermore, inhibiting calcium release from intracellular stores, increased *S. aureus* inhibited ROS production. The cross-regulation of ROS by calcium homeostasis corrleated very well with the ability of *S. aureus* to survive inside macrophages. *S. aureus* infection also modulated the surface expression of costimualtory markers CD80, CD86 and PDL-1. While the expression of activation markers CD80 and CD86 were marginally increased, the expression of the inhibitory costimulatory molecule PD-L1 showed a significant increase. In addition the expression levels of receptors for IFN-gamma, IL-12 and IL-10 receptor showed a significant decrease. Put together the above data point towards an interesting network of threshold that defines the level of immune responses which tailors the persistence of *S. aureus* in macrophages.

P54: Exploring symbiont-host cooperation in conferring radiation resistance to the mealybugs

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The importance of host-microbiome/host-symbiont cooperation in biology is well illustrated in the Coccid insects, the mealybugs, which are pests of citrus and ornamental plants. They exhibit various biological attributes like extreme sexual dimorphism and nested endosymbionts. Mealybug (*maconellicoccus hirsutus*, insecta; *Hemiptera; coccoidea*) also show high resistance to ionizing radiation (as high as 1100Gy), and even after exposure to such a high dose of radiation, the organism has the ability to survive and produce fertile offsprings. Therefore, it can be used as a model to study response to high doses of ionising radiation. Cytogenetic analysis of the embryos, produced by irradiated parents, show fragmented chromosomes that are capable of metaphase alignment and anaphase segregation. Therefore, it seems obvious that mealybug has very efficient DNA repair machinery that ensures proper healing of double strand breaks induced by ionizing radiation. Homologous recombination and Non-homologous end joining are the two DNA repair processes involved in double strand break repair induced by ionising radiation.
The mealybug *Maconellicoccus hirsutus* has two bacterial endosymbionts namely *Candidatus tremblaya* and *Candidatus moranella endobia*. These bacteria help their host by providing essential amino acids which are scarce in plant sap and are not synthesised *de novo* by the host. With a focus on investigating the mechanism of radiation resistance, we are mining the various DNA repair pathway genes in mealybugs using the whole genome sequence that we have completed. Further, we are examining the role of endosymbionts in cooperating with the host in pathways that would confer radiation resistance to mealybugs.

P55: Meta-analysis of the 4C data for characterization of interactors

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Polycomb proteins were first discovered in *Drosophila* as repressors of homeotic gene expression. They negatively regulate a large number of differentiation and developmental processes by binding to cis-regulatory DNA sequences called Polycomb Response Elements (PRE). A PRE/TRE like sequences in the human genome, hPRE- PIK3C2B has previously been identified in our lab using in silico analysis followed by validation using *Drosophila* as a model organism as well as cell culture models. This PRE was identified in the first intron of PIK3C2B gene and is known to be approximately 1 kb in length with 25 mer repeating unit containing the YY1 binding site repeated 25 times. Further, to analyse long range interactions of hPRE– PIK3C2B in human cells **Circularized *Chromosome Conformation Capture (***4C) followed by sequencing was carried out.

In the present work, meta-analysis of 4C data was done. A number of inter-chromosomal interactions were identified near the hPRE- PIK3C2B which were flanked by Csp6I (G^TAC) sites. Among them 61 interactions were analyzed to characterize them on the basis of their genomic position, associated repetitive sequences, chromatin state, boundary elements and various histone modifications. Recent studies have suggested that Topologically Associating Domains (TADs) are well correlated with chromatin states that were previously defined by epigenetic profiling. The genes involved were also analysed for their molecular function and the pathways in which they participate. These findings provide an understanding of 3D organization of Polycomb bound regions and their functional consequences as deregulation of Polycomb factors is often associated with cancer. The experimental validation of selected interactions will be carried out in the later phase of the project.

P56: Investigating the possible role of INO80 in the transcriptional regulation of intergenic microRNA genes in the human genome.

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INO80, a member of SWI/SNF2 family of chromatin remodellers was first identified in a screen for regulators of inositol biosynthesis. Among its wide array of functions, it has been shown to regulate transcription of various genes. Recruitment of INO80 to promoters of target genes is mediated by Yin Yang 1(YY1) protein in humans. The characterization of a 126 amino acid long DNA binding domain (DBINO), which shows conservation across phyla, led to the hypothesis that INO80 could regulate transcription independently. Subsequently, it was shown to bind to an 11-mer consensus sequence and its DNA binding activity was proved both in vitro and in vivo.

microRNAs are 20-24 nucleotide long non-coding RNAs that fine-tune mRNA expression by diverse silencing mechanisms which are still under investigation. Not much is known about the mechanisms by which the transcription of miRNA genes is regulated because of the difficulty faced in identification of their promoters and different biogenesis pathways involved in the transcription of intergenic and intronic miRNA genes. Earlier, in silico analysis showed the presence of INO80 binding motifs in wide variety of genes including miRNA genes. The binding of INO80 was also detected in ChIP-seq experiments.

In the current project, we have prioritized intergenic miRNA genes to check the effect of INO80 on their transcription. We have used in silico analysis to mine INO80 and YY1 binding motifs in the 2kb upstream of predicted transcription start sites for miRNA genes. Those genes having INO80 binding motif exclusively were selected for further analysis and considered as putative targets of INO80. Finally, for validation, we have selected a sub-set of miRNA genes on the basis of the number of INO80 motifs and their distance from the TSS. The miRNAs whose mRNA targets are already validated were given preferance in our selection criteria. These predictions will be experimentally validated in the subsequent part of the project.

P57: To identify the regulatory effect of dINO80 protein on protein coding genes in *Drosophila melanogaster*

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Chromatin remodelers are ATP dependent proteins that can alter DNA-histone interactions non-covalently to change the accessibility of the DNA as and when required for transcription. INO80 is a member of SWI/SNF2 family of chromatin remodelers and was first identified in yeast. Apart from the chromatin remodeling function, INO80 is also shown to function as a transcription factor, regulating the expression of many types of target genes. The *Drosophila*Ino80 (dINO80) protein is recruited by Pho but it was hypothesized that dINO80 can regulate the expression of its target genes independently too. The rescue of Pho null mutants by over-expression of dIno80 suggests that Ino80 can function independent of Pho (Jain Ph.D. thesis). A 7mer consensus DNA sequence for dIno80 binding has also been identified (Jain S, Ph.D. thesis).

The current project aims to identify the regulatory effect of dINO80 on protein coding genes in *Drosophila melanogaster*. To identify the genes in the *Drosophila* genome, that have a high probability of being regulated by dINO80, we adopted an in-silico strategy. The regulatory regions, i.e regions 2kb upstream of TSS and 2kb downstream of the polyA site, of all the protein coding genes in the *Drosophila* genome were screened for the presence of dINO80 binding sites (consensus sequence and 4 variant of it) and also Pho binding sites. The list of genes which had dINO80 binding sites exclusively in their upstream region was compared with the ChIP seq data available in the public domain. The genes common in both were suggested as plausible target candidates of dINO80. Some of these candidate genes were further selected for validation on the basis of 3 criteria: the number and type of dINO80 binding sites present, their distance from the TSS, and the biological functions that the genes were involved in.

To determine the effect of tissue specific knock down of dINO80 on phenotype and expression of target gene, we are using the Gal4/UAS system. After determining the phenotypic effect, the expression levels of few of the above selected genes will be checked by quantitative RT-PCR, to determine the precise genes and the way in which they are affected by the knockdown of dINO80.

P58: Silver Nanoparticle Synthesis via Green Chemistry: Characterization and Biological Evaluation

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Development of nanomedicine/ nanoparticle using green synthesis approaches considered to be a bench mark in current scenario as chemical approaches have higher adverse effects in comparison to therapeutic effects. Green synthesis has several advantages such as cost effective, easy availability, less side effects, profound therapeutic efficacy, and human-friendly. From decades, silver have been known to possess unique physical, chemical and biological properties. We selected Aeglemarmelos(Indian Bael) as first approach as a reducing agent in Ag-NPs synthesis as it has been reported with antioxidant, anti-inflammatory, antiasthmatic, antibacterial properties along with peptic ulcer and diarrheoa relieving remedy. Further, we selected gymnemasylvestre(Gurmar) as second medicinal plant due to its antidiabetic, antiasthmatic, anti-inflammatory, antimicrobial activities. It used as natural remedy for symptomatic relief in arthritis, constipation, cardiopathy. Herein we demonstrate the design and synthesis ofsilver nanoparticles using herbal extract of above two fruitsviz. dried rind of Aeglemarmelosanddried powder of gymnemasylvestre. Silver nanoparticles were subjected to physicochemical characterization as well as biological evaluationalong with antimicrobial evaluation on disparate bacterial strains i.e. gram-positive bacteria and gram-negative bacteria. In present study, we evaluated the syngeristic effect of silver nanoparticles synthesized using herbal extract of Aeglemarmelosand Gymnemasylvestre along with their therapeutic index on different pathophysiologic conditions like cancer and microbial infection respectively.

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