

NORTH ZONE IABSCON 2022

North Zone Conference Indian Academy of Biomedical Scientists *"Omics in Biomedical Research –Current and future perspectives"*



Organised by

Department of Biochemistry Postgraduate Institute of Medical Education & Research, Chandigarh

SOUVENIR

November 4, 2022

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स्नातकोत्तर चिकित्सा शिक्षा एवं अनुसंधान संस्थान, चण्डीगढ़ 160 012 (भारत) POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION & RESEARCH CHANDIGARH - 160 012 (INDIA)

Prof. (Dr.) Vivek Lal

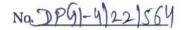
MD (Med), DM (Neuro) Director

Head, Department of Neurology

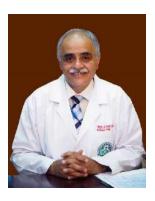
Visiting Guest Faculty, University of Oxford(2016) Former Dean, Baba Farid University of Health Sciences Faridkot, Punjab



प्राध्यापक (डॉ.) विवेक लाल एम.डी. (मैडीसन), डी.एम. (न्यूरो) निदेशक एवं



प्रमुख, तन्त्रिका विज्ञान विभाग



Message

It gives me immense pleasure that the Department of Biochemistry, Postgraduate Institute of Medical Education & Research, Chandigarh is organizing the North Zone Conference of Indian Academy of Biomedical Sciences on November 4, 2022. The IABS society was established to promote translational research in the field of health and medicine. The theme of the conference "Omics in Biomedical Research: Current and Future Perspectives" is very pertinent to all the biomedical scientists actively involved in medical research. With advances in omics technologies like genomics, epigenomics, transcriptomics, proteomics and metabolomics, various therapeutic and diagnostic strategies at the molecular level are becoming feasible for both communicable and non-communicable diseases. Further, integration of different data types using multiomics technologies can provide a better tools for clinical applications.

I welcome all the participants, invited faculty and delegates. I am sure that this one day scientific feast will provide a platform for researchers, scientists, and students to discuss the recent concerns, trends, and innovations in the field of Omics. The scientific program includes lectures from eminent speakers in their respective areas of expertise. The conference will provide an opportunity for oral and poster presentations for young researchers too.

I would like to congratulate the entire team of the Department of Biochemistry for their efforts in organizing NZ-IABSCON 2022. I wish the conference a great success!

Erasmus MC Calmo

Department of Pathology ErasmusMC, University Medical Center 3015 GD Rotterdam *The Netherlands* E-mail: h.sharma@erasmusmc.nl

Hari S. Sharma, PhD, DSc, FIABS Founder President, IABS



MESSAGE

I am pleased to learn that the North Zone Conference of Indian Academy of Biomedical Sciences (IABS) with a special theme on 'Omics in Biomedical Research - Current and Future Perspectives' is being organized by the Department of Biochemistry, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh on November 4, 2022. The global objective of this conference is to translating cellular cues in understanding pathogenesis of disease process and eventually developing novel therapeutics.

In order to promote translational research, **IABS** was established at the renowned Medical Institution, KGMU, Lucknow with keen interest and efforts of various scientists from India and abroad. The main aim of the academy is to disseminate knowledge and academic excellence in the field of biomedical sciences. It is hoped that the achievements and aspirations of **IABS** in promoting collaboration between clinicians and basic scientist will be attained in this auspicious gathering and further set forth guidelines for research and teaching in the area of biomedical sciences.

I extend my heartiest welcome to all clinicians and scientists who are pursuing and those who intend to embark upon translational research to this event of scientific dialogues. Distinguished faculty from India and abroad will speak on various aspects of human diseases and will elaborate on potential therapeutic interventions. I am thankful and congratulate the organizers, Professors Sadhna Sharma and Indu Verma and their team for all the hard work they have put in and extended my best wishes for the success and glory of this **North Zone IABS** conference at Chandigarh.

Prof. Dr. Hari S. Sharma

Dated: 21/10/2022 Rotterdam, The Netherlands



INDIAN ACADEMY OF BIOMEDICAL SCIENCES

(Registration No. 2826-2011-2012, Under the Societies Registration Act-1860)

website: www.iabs.in



MESSAGE

I am happy to know that the Department of Biochemistry, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, is organizing the *North Zone Conference of Indian Academy of Biomedical Sciences* (NZIABSCON) - 2022 on November 04, 2022, under the aegis of the **Indian Academy of Biomedical Sciences** (IABS). The organizers have chosen a catchy theme for this conference "OMICS in Biomedical Research - Current and Future Perspectives".

I am sure that the conference will provide an excellent opportunity to faculties, scientists, residents, Ph.D. scholars and postdoctoral fellows to interact on various emerging trends in OMICS related to Biomedical Research, including recent advances in genomics, epigenomics, proteomics and metabolomics. It is needless to say that the main aim of the Indian Academy of Biomedical Sciences is basically to disseminate knowledge and promote academic excellence in the field of Biomedical Sciences as also to promote translational research.

I am sure that the deliberations of the conference, being organized by a very dedicated, devoted and enthusiastic team of organizers lead by Prof. Sadhna Sharma, will be highly beneficial for the participants in updating their knowledge.

My good wishes for huge success of the conference.

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(Prof. Dr. Abbas Ali Mahdi) Secretary General, IABS Professor & Head Department of Biochemistry, KGMU. Lucknow "संस्थान में हिंदी पत्रों का स्वागत है" जीवरसायन विभाग स्नातकोत्तर चिकित्सा शिक्षा एवं अनुसंधान संस्थान, चण्डीगढ़ -160012 (भारत) DEPARTMENT OF BIOCHEMISTRY POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION & RESEARCH, CHANDIGARH-160012 (INDIA)

डॉ साधना झर्मा Dr. Sadhna Sharma प्राध्यापक एवं विभागाध्यक्ष Professor and Head



HEREN 40.53 BIOCHEM 4053



Message

With immense pleasure, I take the opportunity to announce the North Zone Conference of Indian Academy of Biomedical Sciences, to be hosted by Department of Biochemistry, Postgraduate Institute of Medical Education & Research (PGIMER) Chandigarh, with the theme "Omics in Biomedical Research – Current and Future Perspectives" on November 4, 2022. In recent years, biomedical sciences have made a tremendous progress with rapid developments in latest technologies leading to the concept of 'OMICS' and its uncountable applications. It helps in understanding the cellular alterations at the genomic, transcriptomic, proteomic and metabolomic level. The event is being attended by renowned scientists from prestigious institutes of the country who will be sharing their research work and experience. The conference will provide ample opportunities for interaction amongst faculty, researchers and students. I hope that the proceedings of conference will be a valuable resource addition to all the attendees.

I take this opportunity to acknowledge the passion and unconditional support from the organizing committee. I express my sincere gratitude to all the partners and sponsors for their active participation and support. I extend my best wishes to the organizing committee and all the delegates for excellence in their endeavors and hope that the conference is a great success!

(Prof. Sas na Sharma)

"संस्थान में हिंदी पत्रों का स्वागत है"

जीवरसायन विभाग स्नातकोत्तर चिकित्सा शिक्षा एवं अनुसंधान संस्थान, चण्डीगढ़ -160 012 (भारत) DEPARTMENT OF BIOCHEMISTRY Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012 (INDIA)

डॉ.इन्दु वर्मा Dr. Indu Verma प्राचार्य Professor



संख्या/No**PGIBIOCHEM) 4071** दिनांक/Dated: <u>3 11 22</u>



Message

It is a moment of proud privilege for me to welcome you all; our esteemed speakers, chairs, faculty, residents, researchers and students attending the "North Zone Conference of Indian Academy of Biomedical Sciences (NZIABSCON 2022)". It will be a one-day scientific feast on November 4, 2022 with a theme, "Omics in Biomedical Research - Current and Future Perspectives". The study of larger sets of biological molecules to understand the complex biological processes on levels other than just genome led to the concept of -Omics. With the advent of acquired knowledge and new technologies, the number of types in omics and their applications are constantly increasing; ranging from new biomarker discoveries, studying environmental impacts, understanding pathophysiology down to individual molecular interactions, to its use in pharmacogenomics etc. The organizing committee has put in tremendous effort to gather great minds across the country to share their expertise in this field. I hope that all the attendees will have an enriching experience through the feast of programs including plenary lecture, invited talks, oral and poster presentations. I sincerely thank each and every one of you who are contributing to the success of the conference. Looking forward to having you all with us.

(Prof. Indu Verma)



About Indian Academy of Biomedical Sciences (IABS)

Indian Academy of Biomedical Sciences (Regd.) was established to promote research in the field of translational sciences. The academy has been registered under the Societies Act 1860 of the Government of India, with Registration No. 2826-2011-2012.

The academy's main aim is to disseminate knowledge and promote academic excellence in the field of Biomedical Sciences. The academy was formed with the vision, keen interest and efforts of several scientists from India and abroad.

Initially, the initiative to form the Academy was taken by Prof. Hari S. Sharma, Department of Pathology, UV University, Amsterdam, Netherlands. Prof. Sharma discussed the idea with Prof. Abbas Ali Mahdi during one of his visits to his laboratory at King George's Medical University, Lucknow, India. After that, Prof. Mahdi got the Academy registered at Lucknow on 7th February 2012.



About PGIMER

Postgraduate Institute of Medical Education and Research, Chandigarh owes its inception to the vision of late Sardar Partap Singh Kairon, the then Chief Minister of Punjab and distinguished educationists of the then combined state of the Punjab and supported by the first Prime Minister of India Pt. Jawaharlal Nehru who considered the institutions of scientific knowledge as temples of learning. The institute was started in 1962 with the mandate to provide high-quality patient care, attain self-sufficiency in Postgraduate Medical Education, provide educational facilities for the training of personnel in all branches of health activity and undertake basic community-based research. It became an Institute of National Importance and an autonomous body by an Act of Parliament (Act 51 of 1966) on April 1, 1967 under the Ministry of Health and Family welfare. The mission of PGI is engraved in its logo which means "Service to the community care of the needy and Research for the Good of all". The founders of the Institute Prof. Santokh Singh Anand and Prof. PN Chuttani, Prof. B. N. Aikat laid the path of excellence for the institute. PGIMER is one of the most prestigious medical institutes of national importance. The infrastructure for patient care includes the Nehru Hospital and Nehru Extension Block, a 2200 bedded hospital and two research blocks for basic sciences. PGIMER is a referral centre for several northern states and provides tertiary care and emergency medical, surgical and intensive care services. The institute has a number of advanced centres with state-of-the-art facilities for the treatment of various diseases and provides excellent patient care services like Advance Pediatric Center, Advanced Cardiac Center, Advanced Eye Center, Advanced Trauma Center, Advance Urology Center, Oral Health Sciences Center, Renal Transplantation and Telemedicine. New OPD Block inaugurated on March 19, 2001 has comprehensive diagnostic and therapeutic services under one roof for a number of special clinics and operation theatres and fully functional Microbiology, Hematology and Biochemistry laboratories. The website of the institute has a link to the patient portal for online registrations. The patients can also login to view the reports of various investigations. Teleconsultation services are also available for the patients.





About the Department

The Department of Biochemistry at the Post Graduate Institute of Medical Education and Research was set up when the institute was established as a centre of national importance for the teaching, research, and patient care. Currently, the department has the strength of ten faculty members, thirty-seven Ph.D./M.D./M.Sc. students, eight Senior Residents/ Demonstrators, and 38 technical personnel. Department conducts various courses like Ph.D., M.D., M.Sc., M.Sc. (MLT), and B.Sc. (MLT) Biochemistry. The faculty of the department have received considerable recognition through the receipt of numerous awards for their outstanding achievements in research, teaching, and patient care. The department is facilitating Prof. R Nath memorial oration by inviting speakers of repute, every alternate year since its institution in the year 2004. The department provides clinical services to more than 2500 patients daily using state of art high throughput machines including photometric and immunochemistry autoanalysers through its clinical laboratories set up at Nehru Hospital and the New OPD Block of the institute. It provides 24 hours emergency services as well. All the laboratories are well equipped with high-end automated equipment and are fully integrated with the hospital administration system (HIS). The department successfully runs EQAS programs namely UKNEQAS, Birmingham, and EQAS for clinical chemistry of Randox. The department has infrastructure facilities for research in the field of Clinical Biochemistry, Molecular Biology, Molecular Genetics, Immunology, and Cell Biology. The department has GCMS, AAS, and Flow Cytometer for patient care as well as clinical research. The faculty members of the department have expertise in a wide array of research fields like Cancer Biology, Human Genetics, Nutrition, Nanomedicine, Infectious Diseases, Molecular Psychiatry, etc. The research is supported by funding agencies that include DST, DBT, ICMR, CSIR, and PGIMER. The department is recommended by the "Fund for Improvement of S&T Infrastructure in Universities and Higher Educational Institutions Advisory Board" (FISTAB) for support in the Level-1 category under DSTFIST2013 to further enhance teaching and research facilities



Organizing Committee

Patron		:	Prof Vivek Lal		
Organizing Secretary		:	Prof Sadhna Sharma		
Co-Organizing Secretary		:	Prof Indu Verma		
Treasurer		:	Dr Sant Ram		
		:	Prof Jyotdeep Kaur Prof Thungapathra M Prof Arnab Pal Dr Deepy Z Dr Prasenjit Mitra		
Poster Management Committee		:	Prof Arnab Pal Dr Deepy Z		
Website/Registration/Souvenir Committ		:	Dr Prasenjit Mitra Dr Shruti Gupta Dr Malavika L Dr Arpana Verma Dr Subhamon Bhattacharya		
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Local Hospitality	Transport	:	Dr Sant Ram Dr Piyush Pathak		
	Food	:	Dr Deepy Z Dr Renuka Sharma Dr Apoorva Ms Anshika Ms Neerja		
	Accommodatio	:	Prof Thungapathra M Dr Saravanan Mr Ravjit		

SCIENTIFIC PROGRAM

8.30-9.30 AM	Registration				
9:30 - 9:50 AM	Inauguration				
9:50 - 10:30 AM	Plenary Lecture Prof J Gowrishankar Director, IISER, Mohali "Omics Research: Separating Signal from Noise" Chairpersons: Dr Venkatesh Thuppil, Dr Abbas Ali Mahdi				
10:30 - 11:00 AM	High Tea				
	Session 01 Chairpersons: Dr Vijay Kumar Kutala, Dr Rajendra Prasad				
11:00 – 12.00 PM	11:00-11:30 AM Dr Arindam Maitra NIBMG, Kalyani "Single Cell Profiling and Identification of Hypoxia Induced Cellular Transitions in Oral Squamous Cell Carcinoma"	11:30–12.00 PM Dr Bushra Ateeq IIT, Kanpur "A Tale of Body Patterning Gene: From Diagnostics to Therapeutic Target"			
	Session 02 Chairpersons: Dr Alpana Sharma, Dr Sunil K Arora				
12.00 – 01.00 PM	12.00-12:30 PM Dr Swasti Tiwari SGPGI, Lucknow "Omics in Kidney Disease"	12:30–1.00 PM Dr Vinod Scaria CSIR-IGIB, New Delhi "Genomes - From Personal to Populations and Back - Learnings from India"			
01.00 - 01:30 PM	Session 03 Chairpersons: Dr Seema Bhargava, Dr Savita Yadav				
	1.00 -1.15PM Dr Prashant Sharma Biorad Laboratories "Accelerate your high quality research with Droplet Digital PCR: Next generation tool in Molecular Biology"	1.15-1.30PM <i>Mr Ravi Sharma</i> Beckman Coulter India Pvt. Ltd. <i>"Future-Proofing Your Lab with Next</i> <i>Generation Automation"</i>			
01:30 - 02:15 PM	Lunch & Poster Viewing Session				

SCIENTIFIC PROGRAM

02:15 – 03.45PM	Session 04 Free Paper Presentations Chairpersons: Dr Ranjana Singh, Dr Savita Attri, Dr Naresh Sachdeva					
03.45 - 4.45 PM	Session 05 Chairpersons: Dr Farzana Mahdi, Dr Rajat Sandhir					
	3.45-4.15 PM Dr Deepak Sharma IMTECH, Chandigarh "Peptide Based Therapeutics Against Parkinson's Disease"		4.15 PM-4.45 PM Dr Moinuddin JNMC, AMU, Aligarh "Glycoxidative Modification of Proteins Results in Generation of Neo-antigenic Epitopes"			
04.45 – 05.00 PM	Теа					
05.00 – 06.00 PM	Session 06 Chairpersons: Dr Khursheed Alam, Dr A S Bhatia					
	5.00–5.20 PM Dr Maryada Sharma PGIMER, Chandigarh "Multi-omics Approaches to Neurosensory and Neuro-immune ENT Diseases: Implications in Liquid Biopsies and Precision Medicine"	05.20–05.40 PM Dr Amit Arora PGIMER, Chandigarh "Molecular Adaptations, Phenotypic Transformations and Resistance Mechanisms of Burkholderia cenocepacia When Exposed to Sub- inhibitory Antibiotic Pressure"		5.40-5.55PM Dr Rana Pratap Singh QIAGEN India Pvt Ltd. "Digital PCR Technology: Insights and Applications"		
06:00 PM	Valedictory					

ABSTRACTS

PLENARY LECTURE

Omics Research: Separating Signal from Noise

J. Gowrishankar

Indian Institute of Science Education and Research, Mohali.

As with any new toy introduced to children, the excitement of generating and interpreting the reams of data from high-throughput Omics experiments has tantalised the biomedical research community. Notable successes have included identification of genetic loci conferring disease susceptibility, elucidation of evolutionary relationships between species and of human ancestry, and delineation of pathways for tissue differentiation or cancer development. At the same time, big data also imply an abundance of noise, and researchers must especially beware pitfalls of statistics, effects of small magnitude, and dangers of over-interpretation from such data. The Omics technologies also underscore the value of collaborative interdisciplinary approaches in biomedical research.

INVITED SPEAKERS

1. Single Cell Profiling and Identification of Hypoxia Induced Cellular Transitions in Oral Squamous Cell Carcinoma

<u>Arindam Maitra</u>¹, Sillarine Kurkalang¹, Sumitava Roy¹, Arunima Acharya¹, Paramita Mazumder², Somnath Mazumder¹, Subrata Patra¹, Sumanta Sarkar¹, Shekhar Ghosh¹, Sandip Ghose², Partha Pratim Majumder¹

¹ National Institute of Biomedical Genomics, Kalyani, West Bengal. ² Dr R. Ahmed Dental College and Hospital, Kolkata, West Bengal

Tumors are complex ecosystems composed of diverse cell types, including malignant, immune and stromal subsets. Interplay between these diverse cell types are the major driver for initiation, progress and response of tumor. Our recent bulk tumor sequencing studies have led to identification of some of the genomic, epigenomic and transcriptomic alterations which drive tumorigenesis in gingivobuccal oral cancer (OSCC-GB), the most predominant cancer of men in India, but information on heterogeneity of cell types and cell states within the tumors is yet to be explored.

To address this question, we undertook single cell transcriptome profiling of tumor biopsies of treatment naïve OSCC-GB patients. We identified cell types present in the tumor ecosystem and have inferred the dominant gene expression programs of the malignant and non-malignant cells, classified by a novel method developed in house. We identified unique malignant and non-malignant cell types and states which might have important impact on tumor initiation and progress. Our results provide novel information on heterogeneity of gene expression in OSCC-GB which might lead to improved understanding of cell type diversity and cellular transitions in oral cancer.

2. A tale of body patterning gene: from diagnostics to therapeutic target

Dr. Bushra Ateeq

Joy Gill Chair Professor, Department of Biological Sciences & Bioengineering, Indian Institute of Technology Kanpur

Deregulation of homeobox genes has been associated with several human malignancies. For instance, Distalless homeobox-1 (DLX1), which is involved in the development of craniofacial features and GABAergic interneuron, is also highly upregulated in prostate cancer. We showed that ~60% of advanced-stage prostate cancer patients display higher DLX1 levels, and are associated with metastatic disease and poor survival. We established the oncogenic role of DLX1 in prostate cancer, and deciphered its transcriptional regulation involving ERG, AR/AR-V7 and FOXA1. Moreover, we showed that BET inhibitor and/or anti-androgen drugs disrupt ERG/AR-mediated *DLX1* transcription leading to its reduced expression and downstream oncogenic effects. Taken together, we offered a strategy to include BET inhibitors and anti-androgens for treatment of DLX1-positive prostate cancer patients.

3. Omics in kidney disease

<u>Swasti Tiwari</u>

Department of Molecular Medicine & Biotechnology, Sanjay Gandhi Postgraduate Institute of Medical Sciences

Chronic Kidney Disease (CKD) accounts for 1.2 million deaths globally. The diagnosis of CKD depends primarily on the albuminuria and estimated glomerular filtration rate (eGFR), as per the kidney disease improving global outcomes (KDIGO) guidelines. CKD is known to progress to end-stage kidney disease, where only 10% of the kidney remains functional, eventually leading to premature mortality. Regular screening and timely identification of kidney disease can lessen the Global Disease Burden. However, the

existing screening methods are limited in their ability to predict the onset of the disease and lack specificity. Thus, there is undoubtedly a need for more specific and less invasive biomarkers for kidney disease diagnosis. In recent years, Omics has emerged as an effective tool for unbiased gene profiling in various disease conditions. In my lab at SGPGI, we are using the approach to explore urinary exosomes for potential molecular predictors of CKD in humans. We are the first Indian laboratory to establish the isolation and characterization of exosomes from human urine and demonstrate its usefulness for the early diagnosis of CKD. In addition, we tapped kidney-specific databases to get insight into the pathophysiological mechanisms and molecular targets for kidney disease. I will present some of these interesting data obtained using omics approaches.

4. Genomes - from Personal to Populations and Back - learnings from India

Vinod Scaria

Principal scientist, CSIR-IGIB, New Delhi

The last decade has seen tremendous developments in the capability to sequence genomes. This has seen the unprecedented growth of personal genomics spilling over to population-scale genome initiatives across the world which now has provided insights which can significantly add value to interpreting personal genomes. One of the areas in modern medicine that has immensely been impacted by these developments have been clinical genetics - today impacting the diagnosis and potential precise treatment of thousands of patents and families suffering from rare genetic diseases. We have over the last decade from the initial personal genomes, build GUaRDIAN, a clinical network for undiagnosed and rare diseases in India - today impacting thousands of families through genomic diagnosis. The follow-up initiatives as part of the IndiGen initiative for population genomics have provided insights and the much-needed basal data to start implementing genomic medicine in India. This would only be possible with close collaboration and partnership towards enabling Predictive, Preventive, Precise, Personalised and Participatory Medicine.

5. Peptide based therapeutics against Parkinson's disease

Dr Deepak Sharma

Principal Scientist, CSIR- IMTECH, Mohali

Parkinson's disease (PD) is the second most common neurodegenerative disease. Once thought to be uncommon, the prevalence of PD is on rise worldwide, including in India. Though multifactorial, the presence of α -synuclein amyloid aggregates in dopaminergic neurons in substantia nigra region of brain is a common feature seen in PD patients. Thus, numerous studies have focused on identification of inhibitors of α -synuclein aggregation but little therapeutic progress have been made and the disease remains incurable. In the present study we screened and identified a potent peptide that inhibit α -synuclein aggregation in vitro. We further characterized the peptide and its derivatives for binding to α -synuclein. Further study showed the therapeutic effect of the peptide in *C. elegans* and mice model of PD.

6. Glycoxidative modification of proteins results in generation of neo-antigenic epitopes

Moinuddin¹, Minhal Abidi¹

¹Department of Biochemistry, J.N. Medical College, Faculty of Medicine, Aligarh Muslim University, Aligarh

Structural rearrangements and condensation of proteins under glycoxidative stress have been implicated in various pathological disorders. Novel immunological epitopes on glycoxidatively modified proteins have been discovered and multi-specific natural antibodies against them have been identified.

NORTH ZONE IABSCON 2022

Here we present some of the studies on the glycoxidative modification of low-density lipoprotein (LDL). Methylglyoxal (MGO), a reactive dicarbonyl compound, has been reported to alter the protein structure with physiological implications for various diseases. The study has probed MGO mediated structural alterations in the protein and its immunological implications in diabetes type 2 (T2DM). Glycoxidation perturbed the structural integrity of LDL and affected their aromatic micro-environment leading to the generation of advanced glycation end products (AGEs) and aggregate adducts. Generation of N-epsilon-(carboxymethyl) lysine (CML) was observed under HPLC and LCMS studies.

The modified protein showed altered secondary and tertiary structure that would also affect its functions. Glycoxidation caused disordered or amorphous type aggregation in the modified protein, as confirmed by electron microscopy. It enhanced carbonyl content and reduced the free lysine and arginine content. Modified LDL presented novel antigenic determinants that lead to an aggressive immune response in the immunized rabbits. The antibodies had high affinity towards the immunogen. Auto-antibodies derived from T2DM patients exhibited strong affinity towards the modified LDL in comparison to the unmodified protein. Specificity of serum antibodies from T2DM patients was further confirmed by competitive-inhibition ELISA and gel retardation assays.

We report that neo-antigenic determinants on glycoxidatively modified proteins generate specific immune response in T2DM; the results exhibit potential for biomarker development for the disease.

7. Multi-omics approaches to neurosensory and neuro-immune ENT diseases: implications in precision medicine and liquid biopsies

Maryada Sharma

Associate Professor, Department of Otolaryngology & Head and Neck Surgery, PGIMER

Neural crest (NC) stem cells that delaminate from the neural tube during the developmental neurulation process are unique cells of neuroectodermal descent; however, their developmental progenitor potential is panoptic owing to their ability to differentiate into multiple cell types of ecto-mesodermal lineages. Further, the NC cells have remarkable migratory potential whereby they migrate (and differentiate) to distant location outside the head region giving rise to cardiac/vagal (aorticopulmonary septum, enteric ganglia, cardiomyocytes), and trunk (adrenal chromaffin cells, dorsal root ganglia, sympathetic ganglia, Schwann cells) neural crest cells. The NC cells confined to the head region give rise to the cranial sensory ganglia (in collaboration with the cranial placodes), and participate in glialgenesis and skeletogenesis in the facial region. As NC cells make appreciable neurogenic, glia, mesenchymal, and skeletal system contributions to the head and neck (HAN) region, we were encouraged to establish a NC stem cells model with the potential of differentiating into diverse tissues of HAN to understand the mechanistic developmental pathways and pathogenesis of the HAN.

We discuss the multi-omics driven characterization of a novel NC model generated by reprograming of blood cells by plasma-based complement-coagulation serine proteases. The RNA transcriptomics of these cells facilitated our understanding of the NC lineage intermediates induced under proteolytic cellular stress (heightened complement coagulation activity). Importantly, the multiomics of the NC cells guided us to establish a novel basis of neuro (ecto)-immune (mesodermal) cross talk in the above model. The model was further used to decipher potential neurosensory pathways of cochlear development and morphogenesis. The whole exome sequencing of sensorineural hearing loss (SNHL) patients is regularly carried out in our lab to identify the genetic variants of pathogenicity underlying SNHL. Based on our NC stem cell model, we were able to establish a neurosensory model of cochlear development and regeneration for disease modeling of SNHL. We employed this model for predicting the pathogenicity of a novel variant of MYO7a identified in a 4-year-old child who presented with non-syndromic hearing loss. In silico analysis of RNA transcriptomic data of the neurosensory model predicted this variant to be associated with Usher Syndrome Type 1B (deaf-

blindness). The ophthalmology follow-up of the patient indicated early signs of retinal changes suggestive of retinitis pigmentosa? Importantly, early diagnosis and hence management of Ushers 1B is challenging due to the late onset (progressive) vision loss in second decade by when the retinal degenerative changes are appreciable. We leveraged the multiomics tool toward strengthening of an early and faithful diagnosis of Usher1B. We are currently trying to establish gene editing tools in the patient-derived NC stem cell model for neurosensory disorders like SNHL to develop precision medicine approaches for SNHL patients and predicting the communication outcomes in the cochlear implantees. The NC model also has implications in precision medicine for the craniofacial anomaly patients and patients with Ushers Syndrome of Type 2.

To validate the strength of the NC model, the identified and proposed potential neuro-immune biomarkers and therapeutic nodes for COVID-19 and CAM were investigated in the pathological COVID-19 and CAM plasma samples using metabolomics and proteomics approaches; and for Laryngotracheal Stenosis (LTS), the tracheal aspirates of LTS patients were subjected to proteomic profiling using LC-MS approach. Interestingly, we observed an appreciable correspondence in the in vitro NC multi-omic data and the neuroimmune disease samples derived from COVID-19, CAM, and LTS patients thereby suggesting the potential of developing liquid biopsies for neuro-immune ENT diseases in near-future.

8. Molecular adaptations, phenotypic transformations and resistance mechanisms of *Burkholderia cenocepacia* when exposed to sub-inhibitory antibiotic pressure

Dr Amit Arora

Associate Professor (Bioinformatics), Department of Medical Microbiology, PGIMER

Recent studies have shown that sub-clinical levels of antibiotics (AB) have significant impact on microbes. Most prominent of these being the acquisition of resistance by means of mutations, recombination's or by lateral gene transfer events. These sub-inhibitory concentrations (SIC), by exerting selective pressure over the microorganisms, have major biological consequences as they perturb microbial molecular mechanisms. This results in the generation of diverse phenotypes adapted towards survival. These SIC levels of ABs are particularly worrisome in the case of nosocomial pathogens as by undergoing adaptive changes, they could further evade AB treatment strategies. *Burkholderia cenocepacia*, a gram-negative bacterium, is such an organism that is exposed to SIC levels of ABs. It possesses intrinsic resistance to major classes of antibiotic treatment. It is an important opportunistic pathogen in immune compromised, cystic fibrosis, granulomatous disease patients and has emerged as a major pathogen, causing life threatening bacteremia and respiratory tract infections. Thus, considering the role of SIC in development of resistant bacterial phenotype and ability of *Burkholderia* to adapt to antibiotic pressure it becomes utmost important to understand how SIC levels of an antibiotic influences the survival strategies of its resistant and sensitive strains.

We employed a novel integrated NGS based whole genome sequencing approach along with transcriptomic profiling of resistant and sensitive *Burkholderia cenocepacia* isolates. SIC of antibiotic ceftazidime under *invitro* and *invivo* conditions in Balb/c mice were analysed. Network models of host-pathogen interactions during antibiotic treatment were also analysed.

ORAL PRESENTATIONS

O01

A FACS-based strategy identified phenotypic and transcriptomic heterogeneity in Circulating tumor cells, associated with poor prognosis in Oral Squamous Cell Carcinoma

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Background: Detection of Circulating tumor cells (CTCs) in cancer patients is an essential component of "Liquid Biopsy", a tool for non-invasive diagnosis and monitoring in cancer patients. Detection of CTCs is very challenging because of their extremely low abundance, while their presence in circulation of solid cancer patients, predicts early metastasis.

Objective: To study the presence of CTCs and its association with Oral Squamous Cell Carcinoma (OSCC) prognosis

Materials and methods: We developed a novel in-house FACS-based strategy for isolating CTCs from OSCC patients. After isolation, CTCs were characterized using Giemsa staining (morphological characterization), Immunostaining (phenotypical characterization), and qRTPCR (molecular-level characterization). Ultra-low cell RNA sequencing was also performed to analyze whole transcriptome of CTCs and paired primary tumors (n=24).

Results: Seventy-one percent (45/63) of patients were positive for CTCs, expressing CTC specific markers (EpCAM, EGFR, CK and Vim) in various combinations, suggesting extensive phenotypic heterogeneity in the CTCs. There was no difference in CTC-positivity proportion between patients with early (23/33;69%) and late (22/30;73%) TNM staging, which suggest that CTC positivity is independent of staging. Overall survival (OS) and Disease-free survival (DFS) was less in CTC-positive patients as compared to CTC-negative patients. EpCAM-positive CTCs were detected only in 46% (n=29/63) patients, indicating importance of multi-marker approach for CTC isolation. Moreover, we found that patients having EpCAM-negative CTCs had worse OS (p=0.044*) as compared those with EpCAM-positive CTCs. We also found extensive transcriptomic heterogeneity in CTCs by RNA sequencing (n=24) while primary tumors were less heterogeneous. Unsupervised hierarchical clustering of the CTC transcriptome data stratified the patients in two different cohorts having highly significant decrease in OS (p=0.0004***) and DFS (p=0.0097***).

Conclusion: We suggest importance of molecular profiling of CTCs as a tool for individualizing cancer therapy as identified by a sensitive, specific, in-house developed FACS based tool.

002

Role of Cornulin in pathophysiology of Head and Neck Squamous Cell Carcinoma (HNSCC)

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Background: Cornulin (CRNN), a relatively unexplored protein, localized in the epidermal differentiation complex region of chromosome 1. Low tissue Cornulin level is associated with oesophageal and oral squamous cell carcinomas.

Objective: Our objective was to analyse the salivary and tissue levels of CRNN in HNSCC patients and healthy controls to identify the role of CRNN in pathophysiology of HNSCC.

Materials and methods: The salivary CRNN levels were measured by sandwich ELISA while tissue levels were estimated with Immunohistochemistry. Whole transcriptome by RNAseq of CRNN upregulated and downregulated cell line was done to explore the molecular pathway.

Results: The salivary levels of Cornulin were significantly downregulated (p<0.0001) in HNSCC patients ($n=128,146.4\pm5.589$ pg/mL) in comparison to the healthy controls ($n=84,185.2\pm7.170$ pg/mL) while and the tumour tissue expression of Cornulin (n=113, H-score=12.70±2.396) were also significantly downregulated (p<0.0001) with respect to the tumour free margin tissue (n=72, H-score=139.6±10.34). The patients showing complete clinical response to therapy have a regain in the levels of Cornulin to the normal level after six to eight months of completion of treatment (p<0.0001). During the follow up, decreased salivary Cornulin levels were associated with poor overall survival (p=0.0282). RoC analysis for the potential diagnostic biomarker resulted an area under the curve of 66% significant score (p<0.0001), with 189.6pg/mL as a cut-off. Analysing the RNAseq data, CRNN was found to be involved in PI3K/Akt/mTOR signalling pathway.

O03

Serum and urine metabolomics after traumatic brain injury indicates altered systemic metabolism

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Background: Traumatic brain injury (TBI) is a not a single insult to the brain but can lead to a sequalae of secondary response to the physiological system. To understand the neurotrauma induced alterations and identify mechanism underlying non-neuronal issues like, bladder and bowel incontinence, and systemic metabolic dysregulation in patients, metabolomics serves as an important tool.

Objective: Identification of systemic metabolic fingerprint to identify systemic metabolic alterations and help in prevention of chronic abnormalities and long-term impairment after TBI.

Methods: The present study involved induction of weight-drop injury to rats using modified Marmarou's weight drop injury model. The serum and urine samples were collected, and data was acquired using NMR spectroscopy for metabolite quantification. The metabolites identified were subjected to multivariate analysis and biomarker identification.

Results: Both serum and urine samples showed distinct metabolites in injured rats as compared to the control rats. The metabolites identified as the classifiers after injury showed impaired systemic metabolism after injury.

Conclusion: The study highlights that TBI can lead to alteration in the physiological system and the classifying metabolites can further strengthen the knowledge of the diagnostic markers and mechanistic changes after injury.

O04

MicroRNA expression profiling to study the impact of aberrant miRNAs on the association of diabetes with tuberculosis.

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Background: Type 2 Diabetes (DM) is a significant risk factor of development of tuberculosis (TB). Diabetes causes immune dysfunction and leads to alterations in immune responses thereby increases susceptibility to TB. Thus, comprehending the impact of DM on TB and the biomarkers of comorbidity is crucial for the diagnosis of TB and to plan improved treatment strategies. *M. tuberculosis* infection causes dysregulation of microRNAs expression involved in inflammation, autophagy and apoptosis etc. hence serves as marker for the diagnosis of TB.

Objective: The objective of this study was to examine the genome wide microRNA expression profile of peripheral blood mononuclear cells (PBMCs) of DM and TB+DM patients to identify differentially expressed microRNAs that can be used to diagnose TB among diabetics.

Methods: MicroRNA expression profiling in the PBMCs of DM and TB+DM patients was done using microRNA microarrays. Differentially expressed microRNAs in TB+DM compared DM group were identified using GeneSpring software. Functional relevance of microRNAs and their role in the pathogenesis of TB+DM was depicted by gene ontology and KEGG pathways.

Results: Microarray data showed that 45 miRNAs were differentially expressed in TBDM compared with DM group (17 upregulated & 28 downregulated). Following qRT-PCR, hsa-miR-31-5p, -532-3p, -199b-5p, -148a-3p and -582-5p were significantly altered in TBDM compared to DM and these results were in line with microarray data. *In silico* analysis revealed that these miRNAs are involved in apoptosis, macrophage polarization, MAPK signaling, chemokine signaling and insulin signaling pathways etc.

Conclusion: Differentially expressed microRNAs may deserve further evaluation as candidate biomarkers for the screening of *M. tuberculosis* infection among diabetic patients and better targets to plan therapeutic interventions in the near future.

O05

Synovial fluid Cathepsin G and SERPINA3 disequilibrium shows potential for characterization of Early and Late Osteoarthritis

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Background: Despite rising prevalence of Knee Osteoarthritis (OA), pathophysiology is yet partly understood, and no early-stage markers are available for differential diagnosis of OA.

Material and Methods: Synovial fluid (SF) and blood were collected from Grade 2 (Early) and Grade 4 (Late) OA patients categorized as per Kellgren Lawrence system after Institute ethics committee approval. For discovery phase, 7 SF samples of each OA grade were run on Triple TOF 6600, followed by SWATH-MS for protein quantification. After data normalization, relative peak area ratio of \pm 2-fold and p-value <0.05 was used as differential protein expression criteria.

Results: Early and Late OA comparison revealed 26 significantly modulated protein signatures. Shortlisted proteins were validated by ELISA in SF and serum (n=25 and n=15 for each grade, respectively). Among shortlisted proteins, Cathepsin G (neutrophil derived serine proteinase) showed significant upregulation (p = $<0.0001^{****}$) while SERPINA3 (inhibitor of Cathepsin G) showed significant downregulation (p = $<0.0002^{***}$) in SF with OA progression, while serum levels remained non-significant. Noteworthy, validated proteins showed great potential to distinguish early and late OA in SF with ROC curve (p= $<0.0001^{****}$) having AUC, sensitivity and specificity of 94%, 100% and 88% for Cathepsin G while 80% (p = 0.0003^{***}), 72% and 80% for SERPINA3, respectively.

Conclusion: This study demonstrates Cathepsin G and SERPINA3 potential in characterizing early and late OA. Moreover, it highlights that an imbalance between serine proteinases and their inhibitors might augment OA progression.

O06

Identification of PPAR modulators as therapeutic targets in Alzheimer's Disease

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Background: Neurodegenerative diseases (NDDs) affect millions of people worldwide. Alzheimer's Disease (AD) is the most common form of dementia. Presently, scarce treatment options are available for AD. Peroxisome Proliferator Activated Receptors (PPARs) are ligand activated transcription factors which bind to enhancers of their target genes to regulate their expression. Fatty acids and eicosanoids can activate PPARs, which further, triggers the lipid and fat metabolism in the liver. Imbalance in PPAR activation disrupts numerous pathways and consequently leads to disorders like AD and Metabolic Syndrome. The beneficial effects PPAR activation are via multiple pathways and it was hypothesized that selective PPAR modulators may help in alleviating neurodegenerative symptoms.

Objective: The present study was initially aimed to investigate the role of PPARs in AD by screening differentially expressed genes (DEGs) in microarray datasets.

Method: After gene enrichment and selection based on expression, the study was designed for virtually screening the binding affinities of 5,000 synthetic ligands of PPARs and manually curated library of 300 natural compounds against PPARs using molecular docking and ADMET analysis. Top 10 natural and synthetic compounds with most stable binding affinities were selected for ADMET analysis and their interactions with protein structure were investigated. High throughput data meta-analysis showed the critical role of PPARs in AD progression.

Result: The docking results showed that all selected compounds bind PPARs in the cavity of the binding pocket with strong hydrogen and hydrophobic bonds. The ADMET results indicate good drug-like properties in selected lead compounds.

O07

Novel target exploration in highly virulent uropathogenic Escherichia coli strain CFT073 using protein-protein interaction network analysis

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Background: Urinary tract infections (UTIs) are one of the commonest bacterial infections worldwide. The most common etiological agent is uropathogenic Escherichia coli. The occurrence of high rates of antimicrobial resistance among UPEC has complicated therapeutic management and emphasized the need for new drug targets or newer approaches to tackle the increasing trend of antimicrobial resistance. The use of OMICS technologies provides an attractive alternative to experimental methods to provide momentum in the discovery of drugs and decrease the chances of drug failure in later stages of drug development.

Aim: The present study was performed to identify and characterize promising drug targets against a highly virulent UPEC strain CFT073 by utilizing a novel hierarchical in silico approach.

Objective: We conducted the study in four phases. In phase 1, three sets of proteins were mined through a chokepoint, virulence, and resistance genes analysis. The proteins selected from phase 1 were further subjected to the nonhomology analysis in phase 2. In phase 3, co-evolution analysis was done to find nonhomologous proteins which interact with virulence and resistance genes at high correlation values (≥ 0.9).

Results: We found eight putative drug targets (MurB, MurC, HisC, HyaB, HybO, FliN, FliH, and MotB) that interacted with five virulence (chuU, chuW, iucA, fepA, and hylD) and two resistance genes (arnA and acrB). Most of the identified drug targets are part of distinct metabolic pathways (viz., peptidoglycan biosynthesis, histidine biosynthesis etc.). In phase 4, qualitative characterization of the above drug targets including protein location in the bacterial cell, broad-spectrum analysis, interactome analysis, evaluation of druggability by similarity search against drug-target database, and essentiality analysis was performed. PCR-based confirmation of identified drug targets in clinical isolates of UPEC was also carried out.

Conclusion: The findings of this study may aid in the discovery of new antibacterial agents for better treatment of E. coli UTIs.

O08

Identification of common biological pathways between Alzheimer's Disease and Metabolic Disorders through transcriptomic analysis

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Alzheimer's Disease (AD) is a prominent age-related neurodegenerative disorder, which leads to deterioration in cognitive ability, progressive loss of memory and major behavioral changes. It is the most common form of dementia and approximately accounts for 60-70% of total dementia cases reported all over the world. Recent evidence has revealed that people afflicted with metabolic disorders like Diabetes and Obesity have a higher chance of developing AD than the normal population. As number of individuals affected by metabolic disorders reaches epidemic proportions in developed and developing nations, the

patients impacted by AD will also exponentially grow. However, the exact mechanism responsible for this association is not fully understood. Therefore, it is essential to discover the underlying pathways and molecular targets which might aid in unravelling this mystery. The current study aimed to discover novel associations between AD, Diabetes and Obesity through in-silico means. Briefly, gene expression datasets from NCBI Gene Expression Omnibus (GEO) were downloaded and subjected to transcriptomic analysis to discover Differentially Expressed Genes (DEGs) in all three diseases through GEO2R (a R package to determine significant DEGs in datasets). Additionally, pathway enrichment analysis was carried out by MolSig database to discover common pathways and categorize the DEGs into significant pathways. From MolSig, a hub of pathways, mainly linked through MAPK signalling, was shortlisted for further studies. The pathways identified included Neurotrophin signalling pathway, Chemokine signalling, Insulin signalling pathway, Calcium signalling, Endocytosis, Focal Adhesion and Lysosome. Further, these pathways were categorized into wider sub-headings to get a clearer idea about the overall related functioning of the systems involved. Moreover, we also discovered common genes between the datasets to delineate the reason behind AD progression and understand it's pathophysiology better. The results obtained from this study have identified novel cellular and molecular mechanisms that might link AD progression with metabolic disorders and will further aid in formulating new treatment regimens.

O09

Protein biomarker identification in gastric lavage samples of pulmonary tuberculosis children for disease diagnosis.

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Background: Pediatric TB diagnosis is still a major challenge as the currently used diagnostic methods miss out many positive cases. So, identification of better biomarkers in the commonly available samples, which can increase the sensitivity is required. Though sputum is considered as a potential sample for pulmonary TB diagnosis, but as the infants and young children tend to swallow sputum, so gastric lavage is a useful sample type for biomarker discovery.

Objective: Identification of host specific protein biomarkers from gastric lavage of pulmonary tuberculosis pediatric patients which may aid in the development of better diagnostic tests.

Material and methods: Gastric lavage samples from culture positive pediatric TB (n=8) patients and lisease controls were processed for mass spectrometry via Shotgun proteomics and data was analyzed. Thereafter, ELISA was carried for the validation of LC-MS/MS results.

Results: 256 human proteins were identified in gastric lavage samples by shotgun proteomics among which 80 were specifically identified in TB samples. One of the host protein, α -1-acidglycoprotein showed exclusive or predominant detection in TB samples, so its expression was further validated by ELISA. The expression of α -1-acid glycoprotein proteins was significantly high in gastric lavage samples of pediatric TB patients than disease controls as indicated by mean OD values and the protein was able to diagnose pediatric PTB patients with sensitivity of 74%. And specificity of 85.19 %

Conclusion: In gastric lavage samples, α -1-acid glycoprotein showed encouraging results as a biomarker for diagnosing pediatric tuberculosis.

010

Metabolite profiling in the evaluation of SSADH deficiency

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Background: Succinic semialdehyde dehydrogenase (SSADH) deficiency, also known as 4- hydroxybutyric aciduria, is a rare, autosomal recessive, neurometabolic disorder of the γ -amino butyric acid (GABA) metabolic pathway. The clinical and neuroimaging presentation may mimic dyskinetic cerebral palsy, Leigh or Leigh-like disease. In this study, clinical profile of patient with SSADH deficiency was evaluated at our center.

Methods: The study was conducted in the Pediatric Neurology unit of a tertiary care hospital. Ethical clearance was obtained from institutional ethical committee. The clinical, laboratory, genetic and neuroimaging findings were recorded in a predesigned proforma.

Results: We report a case of SSADH deficiency presented with global developmental delay, epilepsy, choreoathetosis and language delay. He had microcephaly and dystonia. TMS profile showed slightly elevated hexa-enoyl carnitine C6. GC/MS analysis showed elevated 4- hydroxybutyric acid and 4,5-dihydroxyhexanoic acid. MRI showed involvement of bilateral globus pallidi, bilateral crus cerebri and substantia nigra. Based on metabolite screening preliminary diagnosis was SSADH deficiency and treatment was started. Further, genetic analysis based on targeted next generation sequencing revealed homozygous, missense mutation, c.608C>T; pPro203Leu in exon 3 of ALDH5A1 gene. The variant was likely pathogenic as per ACMG classification and was predicted as deleterious by multiple computational software.

Conclusion: SSADH is a neurometabolic disorder with diverse phenotype. A simple urinary test to detect 4 hydroxybutyric aciduria can help in clinching the diagnosis.

P01

Codon usage behavior distinguishes pathogenic *Clostridium* species from the nonpathogenic species

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Genus *Clostridium* is comprised of anaerobic, spore-forming, gram-positive bacteria. Members of this genus have been implicated as causal organisms of different human diseases like food poisoning, tetanus and botulism. This includes C. perfringens, C. tetani and C. botulinum. On the other hand, various clostridial species have been used for industrial production of different enzymes, acetone and biohydrogen etc. Clostridial species can be grouped into pathogenic, opportunistic and non-pathogenic. Because of the diversity this genus presents promising opportunities in medical and environmental sustainability fields. We performed genomic analysis of 76 clostridial species belonging to the three different groups. A significant difference in genomic G+C% content of the three representative groups was observed. The lower GC content of the pathogenic clostridia bodes well for the microbial energy economics. Our study also demonstrated the pathogenic group to use lowest number of codons implying a strict bias in usage of synonymous codons suggesting shedding of extra synonymous codons to shrink genomic size and number of encoding genes. Preferred and optimal codons were also observed to be AT rich. We found preference for purines over pyrimidines in all the genomes. Dinucleotide analysis suggested lowest CpG level in pathogenic group as compared to other two suggesting higher immune evasion property. A significant role of gene expression in shaping the amino acid and codon usage pattern was observed. Our data showed definitive differences in codon usage patterns of the three representative groups, shaped significantly by compositional constraints and translational selection pressure.

P02

Comprehensive Genome Analysis of the Pathogenic and Non-Pathogenic *Escherichia* Species

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Genus *Escherichia* is comprised of rod-shaped, gram-negative, facultatively anaerobic bacterial species. While a majority of strains are known commensals in the human intestine, pathogenic strains of *Escherichia* have also been found to cause a number of infections. We performed genomic analysis focusing on codon, dinucleotide, and amino acid usage patterns of 56 *Escherichia* strains.

We found a strong influence of natural selection on the codon usage pattern employed by the genomes under study. Moreover, the P2 values ~0.49 also highlighted a major role of translational selection in shaping codon usage. The average GC-content of *Escherichia* genomes was found to be ~50%, and average eNc values as ~47 indicating minimal codon usage bias. Amongst the analyzed genomes, CUG was the most preferred codon and AGG was found to be the least preferred codon. In the case of preferred and optimal codons, the GC-rich codons were highly preferred as compared to AT-rich codons. Upon assessing the dinucleotide

frequencies, GpC and ApA were found as overrepresented dinucleotides. On the other hand, ApG and TpA were under-represented dinucleotides in all the genomes.

P03

Cystatin A in pathophysiology of Head and Neck Squamous Cell Carcinoma

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Background: Cystatin A (CSTA) is dysregulated in different cancers and documented to have both tumor progressive and tumor suppressive roles. In our previous study, a number of dysregulated proteins in the saliva of HNSCC patients were identified using shotgun proteomics approach, Liquid Chromatography-Mass Spectrometry (LC-MS) analysis. Among those proteins, CSTA protein expression was found to be 5-30-fold upregulated depending upon the tobacco habits.

Objectives: In this study, we wanted to explore the role of CSTA in pathophysiology of HNSCC. Methodology: CSTA expression was checked in HNSCC cell lines (CAL 27 and FaDu). CSTA was knockdown in both the cell lines using the lentiviral shRNA pLKO vector. The same plasmid expressing a non-targeting shRNA sequence was used as scrambled control. The effect of CSTA downregulation on various cancer hallmarks such as cell proliferation (MTT staining), migration (wound healing assay), invasion (trans-well assay), colony formation and cisplatin-induced apoptosis (Annexin V-PI staining) was elucidated.

Conclusion: Our data is suggestive of tumor progressive role of Cystatin A in HNSCC, indicated the possibility of therapeutic targeting

P04

Proteomic analysis of Cartilage unravelled dysregulation of Coagulation Cascade in Osteoarthritis

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Background: Cartilage degradation is a frontline player in Osteoarthritis (OA). Proteomic analysis of cartilage has been performed to understand OA pathogenesis. However, no study is cited till date where proteomic analysis of healthy, early and late grade OA cartilage has been performed.

Objective: Study aimed to analyze and validate differentially expressed proteins (DEP) in cartilage tissues to better understand OA pathogenesis.

Material and methods: Normal cartilage from healthy individuals (n=5) and early and late grade cartilage from OA patients (n=5) was microscopically evaluated and processed for protein quantitation by LC- MS/MS analysis. Shortlisted proteins were validated in cartilage tissues (n=8), synovial fluid (n=25) and serum (n=15) by ELISA.

Results: 1185 proteins were found in comparative cartilage proteomic analysis of which 945 proteins were found to be consistent in all three respective cartilage tissues groups. Total 97, 135 and 120 proteins were found to be significantly dysregulated in late grade vs normal, late vs early grade and normal vs early grade comparisons, respectively. Pathway analysis of DEP by Reactome showed coagulation cascade as the top pathway constituting Serpin F2, Fibrinogen alpha, beta and gamma chain proteins. Fibrinogen gamma chain, being ultimate protein in coagulation cascade was validated in cartilage, synovial fluid and serum samples. Significant upregulation ($p < 0.0001^{****}$) in cartilage samples with disease progression was observed, however, protein levels showed significant down regulation in synovial fluid and serum with disease progression.

Conclusion: Coagulation cascade showed significantly dysregulation with OA progression. Moreover, fibrinogen showed great potential to act as diagnostic marker in distinguishing early and late OA.

P05

In silico identification of novel LXR modulators as a key regulator of cholesterol and lipid homeostasis against Alzheimer's diseases

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Liver X Receptors (LXRs) are members of the nuclear receptor superfamily that regulate cholesterol metabolism. LXRs have been suggested as promising targets against Alzheimer's disease (AD). The present study was aimed to identify novel non-steroidal molecules that may potentially modulate LXR activity. The structure-based virtual screening (SBVS) was used to search for suitable compounds from the Asinex library. The top hits were selected and filtered based on their binding affinity for LXR α and β isoforms. Based on molecular docking and scoring results, 24 compounds were selected that had binding energy in the range of -13.9 to -12 for LXR α and -12.5 to -11 for LXR β , which were higher than the reference ligands (GW3965 and TO901317). Further, the five hits referred to as model 29, 64, 202, 250, 313 were selected by virtue of their binding interactions with amino acid residues at the active site of LXRs. The selected hits were then subjected to absorption, distribution, metabolism, excretion, and toxicity (ADMET) analysis and blood-brain permeability prediction. It was observed that the selected hits had better pharmacokinetic properties with no toxicity and could cross blood-brain barrier. Further, the selected hits were analyzed for dynamic evolution of the system with LXRs by molecular dynamics (MD) simulation at 100 ns using GROMACS. The MD simulation results validated that selected hit possess a remarkable amount of flexibility, stability, compactness, binding energy and exhibited limited conformational modification. The root mean square deviation (RMSD) values of the top-scoring hits complexed with LXRa and LXRB were 0.05–0.6 nm and 0.05–0.45 nm respectively, which is greater than the protein itself. Altogether the study identified potential non-steroidal LXR modulators that appear to be effective against AD involving perturbed cholesterol and lipid homeostasis.

P06

Interplay between Interleukin-22 and its receptor in peripheral blood of Tuberculosis patients

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Background: Disease progression of Tuberculosis (TB) is determined mainly by the balance between the microorganism and the host defense systems. T cell-mediated immune response begins after dissemination of *Mycobacterium tuberculosis* in the body. Interleukin-22 (IL-22) helps in cell proliferation, regeneration, and provides protection against microbial diseases. It acts via receptor IL-22R1 that signals various downstream signaling cascades. IL-22 plays an important role in mycobacterial infection but its role is not fully understood.

Objective: To estimate circulating IL-22 levels and correlate it with IL-22R1 relative gene expression levels in the peripheral blood of TB patients and healthy controls.

Methodology: 80 sputum positive TB patients and 80 asymptomatic healthy subjects were enrolled in the study. After obtaining due informed consent, 5mL venous blood was withdrawn in plain and EDTA vacutainers from all participants. Serum IL-22 levels were estimated using ELISA and relative gene expression of IL-22R1 using real time PCR technology. Statistical analysis was performed using SPSS.

Results: The median (IQR) of serum IL-22 was significantly lower in TB patients compared to controls (18.55(5.08) vs 49.38(162.88) pg/mL); p<0.0001). IL-22R1 expression was significantly upregulated with a fold change value of 2.04 in TB patients. Significant positive correlation was observed between the protein levels and the expression of its receptor. On ROC analysis, IL-22 discriminated TB patients from healthy controls at 21.67pg/mL with an AUC of 0.904.

Conclusion: IL-22 levels were found to be significantly decreased in patients, with a plausible compensatory increase in its receptor expression. IL-22 appears to have a good diagnostic efficiency in discriminating TB patients from healthy controls.

P07

Relationship between Malondialdehyde as an Oxidative Stress Marker and Total Antioxidant status in Pre and Postmenopausal Women to assess their predisposition to oxidative stress induced disorders

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Background: Menopause is the natural step in the process of aging. Women face various physiological, psychological and sociological changes which impair the quality of life. In the menopausal women, the oxidative stress is due to decrease in the estrogen level in the body, which in turn decrease the antioxidant status of the body, leading to various complications i.e., osteoporosis, cardiovascular disease etc. Due to osteoporosis, there is maximum chance of bone fractures.

Aim & Objectives: To find out the association between Malondialdehyde (MDA) and Antioxidant status in Pre-and Post-Menopausal women.

Methods & Materials: This is a cross sectional type of study, which was conducted in the department of Biochemistry in collaboration with Department of Obstetrics & Gynecology at LN Medical college, Bhopal, Madhya Pradesh, India during the period of July 2019 to August 2022. For the analysis total 310 subjects had been enrolled with the age between 30 to 60 years.

Results: It has been observed that there are significant changes in the level of MDA & antioxidant status of Menopausal women. The Oxidative stress marker (MDA) level was significantly lower (1.5 ± 0.69), (p-value-0.0005) in Premenopausal women than that of Postmenopausal women (2.84 ± 0.69). But Antioxidant status level was found to be significantly higher (15.1 ± 2.4) in Premenopausal women than that of Postmenopausal women.

Conclusion: Menopause is associated with oxidative stress which predisposes to the development of various diseases like osteoporosis, depression, diabetes, and hypertension. Dietary management, antioxidant supplementation, and moderate physical activity would help to prevent diseases related to menopause.

P08

Effect of paternal folate deficiency on imprinting of various genes in the placenta

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Background: As both paternal and maternal alleles provide their DNA sequences equally to a fertilized egg, the paternal allele may influence the epigenetic reprogramming of fetuses. Therefore, we hypothesize that paternal folate deficiency might affect placental folate status via folate transporters, disrupting the expression of the imprinted genes by altering DNA methylation patterns.

Objective: To study the effect of paternal folate deficiency on the expression of folate transporters and imprinted genes in the placenta.

Materials and methods: Four-week-old C57BL/6 male and female mice were fed experimental diets with folate modulations (PNMN: paternal normal maternal normal, PDMN: paternal deficient maternal normal, POMN: paternal over supplementation maternal normal, PDMD: paternal deficient maternal deficient). Mating was carried out after four weeks and the study was extended to the next generation to see the effects of paternal folate deficiency. Pregnant mice of the F1 generation were sacrificed on the 21st day of gestation, and placentae were isolated. mRNA levels of folate transporters and imprinted genes were studied in the placenta by qPCR.

Results: There was an overall reduction in total body weight of the paternal folate deficiency group in the F1 generation. $FR\alpha$ and RFC (folate transporters) expression was decreased in the case of the PDMN group. Among imprinted genes, expression of *IGF2R*, *CDKN1C*, and *PEG3* was decreased, while *H19* expression was increased in the placenta of the PDMN group.

Conclusion: Paternal folate deficiency affects the expression of folate transporter genes and imprinted genes in the placenta.

P09

Genomic analysis of clinically suspected cases of maturity onset diabetes of the young (MODY)

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Background- Maturity Onset Diabetes of the Young is an early onset, non-insulin dependent, monogenic heterozygous form of diabetes with autosomal dominant mode of inheritance affecting mostly the young non-obese individuals. Till date, 14 genes have been identified in the human genome, a mutation in which leads to pathophysiology of this disease. MODY has been minimally explored and knowledge about its genetic predisposition is obscure especially in Indian populations. The disorder can be treated with diet and lifestyle changes but unfortunately it is mostly misdiagnosed due to its overlapping presentation with the more prominent, Type1 and Type 2 forms of diabetes mellitus.

Objective- The main objective of this study was to elucidate the prevalent variants of the known MODY associated genes in North Indian population and assess the efficacy of biochemical parameters to diagnose patients with MODY.

Materials and Methods- Patients with age of onset of diabetes between 15 to 40 years with family history of diabetes for at least three generations were recruited for the study. No AMP Targeted Gene Sequencing was performed by Illumina Nova Seq 6000. NGS results were then compared and correlated with biochemical parameters (FPG, HbA1c, lipid profile, Insulin, C-peptide, hs-CRP, GADA).

Results- Mutations were found in 18.18% of the study population in *NEUROD1*, *BLK*, *GCK* and *MT-TL1* genes. This is the first study where *NEUROD1* mutation has been identified in Indian population. hs-CRP levels were found to be significantly lower in MODY patients. The blood glucose, HbA1c and lipid profile levels were also lower in MODY patients.

Conclusion_– Based on the small pilot study, it is evident that a significant proportion of young diabetics could be MODY patients. Screening of patients through various biochemical markers combined with molecular diagnosis technology may lead to efficiency in detection of undiagnosed MODY cases in our population. As utilization of research outcome, the team also plans to establish a complementary tool of transcriptomics to identify novel transcripts /signatures to enhance the definitive diagnosis of MODY phenotype.

P10

Validation of Dunkin-Hartley Guinea pig as spontaneous model of osteoarthritis

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Background: Osteoarthritis (OA) is a condition of synovial joints characterized by progressive deterioration of articular cartilage and spontaneous animal models simulate natural human primary osteoarthritis. Numerous studies have focused on expression profiling of miRNAs in various animal models of knee OA but their knee joint pathology doesn't mimic idiopathic OA as in humans.

Objective: We aimed to identify deregulated miRNAs in Dunkin Hartley guinea pig, a well-characterized model of idiopathic OA.

Materials and methods: Histological analysis of guinea pig cartilage tissue from control (3months), Early OA (7months) and Late OA (12months) groups was performed to analyze the severity of OA development as described by OARSI (Osteoarthritis Cartilage Histopathology Assessment System). RNA from cartilage tissue was extracted for miRNA profiling. Mapping of the human and guinea pig miRNome fetched from miRBase was done to find out the common miRNAs (n=503) which were further screened for potential miRNAs to be involved in OA. We profiled the expression of selected miRNAs (n=100) in cartilage tissue using miRNA RT-qPCR arrays.

Results: Histological observations showed significant osteoarthritic changes as the age progressed. miRNA profiling results revealed 4 miRNAs with a significant trend of downregulated expression as the age of animals increased. In Late OA group, 39 miRNAs were significantly downregulated in comparison to the control.

Conclusion: The development of spontaneous OA in Dunkin-Hartley guinea pig makes it a suitable animal model for exploring OA pathogenesis and our study opens up prospects for a new therapeutic approach by targeting deregulated miRNAs to delay or reverse disease progression.

P11

Serum Cystatin C – An Emerging & Reliable Marker for Diabetic Nephrology

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Clinically, there is lack of predictors for diabetic nephropathy (DN) in diabetes mellitus (DM) without microalbuminuria, macroalbuminuria or retinopathy.

PubMed, Chinese Biomedical Database, Cochrane Library, EMBASE and Elsevier Database are searched. Studies involving patients with DM and containing data on cystatin C measurements and the measured glomerular filtration rate (mGFR) were included. Pooled sensitivity, specificity, positive predictive value, negative predictive value and other diagnostic indices were evaluated using a random effect model.

In conclusion, our presentation shows that serum cystatin C is a significant predictor of Diabetic Nephropathy among patients with Diabetes Mellitus and that the cystatin C test is more accurate and predictable than the standard creatinine method for GFR. With the development of medical treatment level, Diabetic Nephropathy remains a therapeutic challenge with major diabetic complications. The early detection of Diabetic Nephropathy is very important and can improve patient outcomes. Serum cystatin C is an early predictor of Diabetic nephropathy among patients with DM.

P12

Proteomic insight into the venomous protein mixtures from selected Hymenopteran insects and their antibacterial activity

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Hymenopteran stinging insects' secretions contain peptides that are significant parts of their immune systems and play a crucial role in their defence against predators.

For the study, the proteome of three different hymenopteran insect species-ants, bees, and wasps-was examined using LC-MS/MS analysis to identify the potential for hymenopteran toxins and validate their identification as well as their antimicrobial effectiveness against bacteria. Insects (Camponotus compressus (CC), Apis mellifera (AM), Polistes wattii (PW)) were collected manually and the extracts were prepared by homogenization. Subsequently, protein quantification (bicinchoninic acid assay) was done and samples were subjected to LC-MS/MS analysis. We detected 1731 proteins in total, 339 of which were shared by all the groups. From the overall comparison of differentially expressed proteins (DEPs) between two groups that is AM vs. CC, there were 646 proteins found to be upregulated and 11 were downregulated. Similarly, a comparison between AM vs. PW, 762 proteins were upregulated and 32 proteins were downregulated. However, when a comparative analysis between and CC vs. PW was performed, we identified 28 proteins were upregulated and 516 proteins were downregulated. For determining antibacterial activity (MIC) of AM extract against Escherichia coli (MTCC739) (0.62 mg/ml) and Pseudomonas aeruginosa (MTCC1688) (5 mg/ml), CLSI guidelines were followed using broth microdilution method. In conclusion, AM, shown potent antibacterial activity against Gram-negative bacteria in vitro, which presumes the encouragement of other stinging hymenopterans to be considered under potential class for development of new molecules as clinical candidate for combating antimicrobial resistance.

P13

Comparison of 16S metagenomics to conventional microbiological cultures in soft tissue Infections (STIs).

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Background: Soft-tissue infections (STIs) encompass all infections of the dermis to the muscles. The severe cases of these STIs have shown very high mortality rates despite low incidence mainly due to diagnostics challenges. The microbiological culture has been used to understand the milieu of organisms causing this infection; however, in most of the polymicrobial STIs, the microbial diversity is usually underreported as the fastidious organisms are missed. The prokaryotic 16S ribosomal genes along with the intergenic regions have been used to determine the taxonomy since they are conserved as well as variable at difference sequence stretches. We investigated the direct microbial diversity of STIs from patient tissues targeting V3-V4 region of 16S rRNA next-generation sequencing (NGS).

Objective: Comparison of microbial diversity using the conventional and omics technique

Methods: Thirty-nine tissue biopsies of the patient were collected with STIs. Illumina MiSeq Sequencing was employed for pathogen-identification in tissue biopsies using 16S rRNA NGS.

Results: The conventional culture techniques revealed *Enterococcus faecium* as the prominent Gram-positive agent. *Acinetobacter baumannii* as commonly found Gram-negative infectious agent in STIs. Using Illumina MiSeq 16S rRNA gene amplicon sequencing identified *Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterococcus faecalis* as most prominent causative pathogens.

Conclusions: We employed the method to compare the conventional microbiological processing with the latest metagenomics approach for the diagnosis of soft tissue infection from the tissue biopsies by partial-length 16S rRNA gene amplicon analysis using Illumina MiSeq. This strategy will be suitable for quicker routine diagnostics and surgical assessment in developing countries

P14

Imbalance of high folic acid and low vitamin B12 impacts placental development and foetal growth

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Background: The common practice of supplementing folic acid during pregnancy and the absence of such guidelines for vitamin B12 lead to an imbalance in the levels of these vitamins, especially in developing countries like India, where many women are vitamin B12 deficient.

Objective: To explore the effect of low vitamin B12 in combination with different levels of folic acid in the parental diet on fetal growth parameters and maternal reproductive performance in a transgenerational manner.

Materials and Methods: C57BL/6 mice were fed with different dietary groups and mating was carried out within each group in the F0 generation. After weaning for 3 weeks in the F1 generation one group of mice was continued on the same diet (sustained group) while the other was shifted to a normal diet (transient group) for 6-8 weeks (F1). Mating was carried out again within each group, and on day 20 of gestation, the maternal placenta (F1) and fetal tissues (F2) were isolated.

Results: Vitamin B12 deficiency and different levels of folic acid resulted in the decreased placental and fetal weight of the F1 generation. Surprisingly, a decreased placental weight, low fetal weight, and reduced crown-rump length and head circumference were observed in F2 fetuses of vitamin B12 deficient with folate over-supplemented (BDFO) transient group, i.e., when F1 mice were shifted to normal diet conditions. Reduced follicles in ovaries and alteration in placental pathology in all the F0 groups and BDFO of the F1 transient group were also seen.

Conclusion: Overall, the study revealed that dietary imbalance of vitamin B12 and folic acid, particularly B12 deficiency with over-supplemented folic acid, negatively affects placental and fetal development and maternal reproductive performance. Such effects are passed on to the next generation too.

P15

Association of TNF- α (-509 A/G) and TGF- β (-308 C/T) gene polymorphisms with Progression of Chronic Cervical Spondylitis

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Background: Chronic cervical spondylosis (CCS) is a common chronic and progressive degenerative disorder of cervical spine that affects majority of older people. However, people of younger age are also being affected with CCS. Previous studies have shown role of Genetic variations and their associations with disc degenerations, while it lacks evidence in North-Indian population with CCS.

Objectives: We aimed to study the association of IL-1 β (-511 C/T), TNF- α (-509 A/G) and TGF- β (-308 C/T) gene polymorphisms with Progression of Chronic Cervical Spondylitis.

Materials and Methods: 252 subjects including 126 CCS cases and 126 healthy controls were enrolled from Department of Neurosurgery, AIIMS Rishikseh. Whole blood was collected and were processed for ESR estimation by standard Westergren method and DNA isolation. PCR-RFLP technique followed by non-denaturing Agarose gel electrophoresis was employed for genotyping.

Results: ESR was significantly different in CCS and Controls. We found significant associations of C-allele and C/C genotypes of IL-1 β , G-allele of TNF- α and genotypes T/T, C/T, C/C of TGF- β on comparison among CCS and controls. While frequencies of T-allele of IL-1 β , heterozygous A/G genotype and A-allele of TNF- α ; and C/C genotype of TGF- β were simultaneously higher in CCS as compared to controls. Alleles and genotypes of TNF- α were significantly associated among smokers of CCS and controls.

Conclusions: IL-1 β (-511 C/T), TNF- α (-509 A/G) and TGF- β (-308 C/T) gene polymorphism may influence the susceptibility to CCS, but do not reflect the disease active state. C-alleles and G-alleles of IL-1 β (-511), TNF- α (-509) and TGF- β (-308) were protective in CCS progression while T-alleles and A-alleles were common risk alleles associated with severity of CCS.







