ABSTRACTS

आज़ादी का अमृत महोत्सव

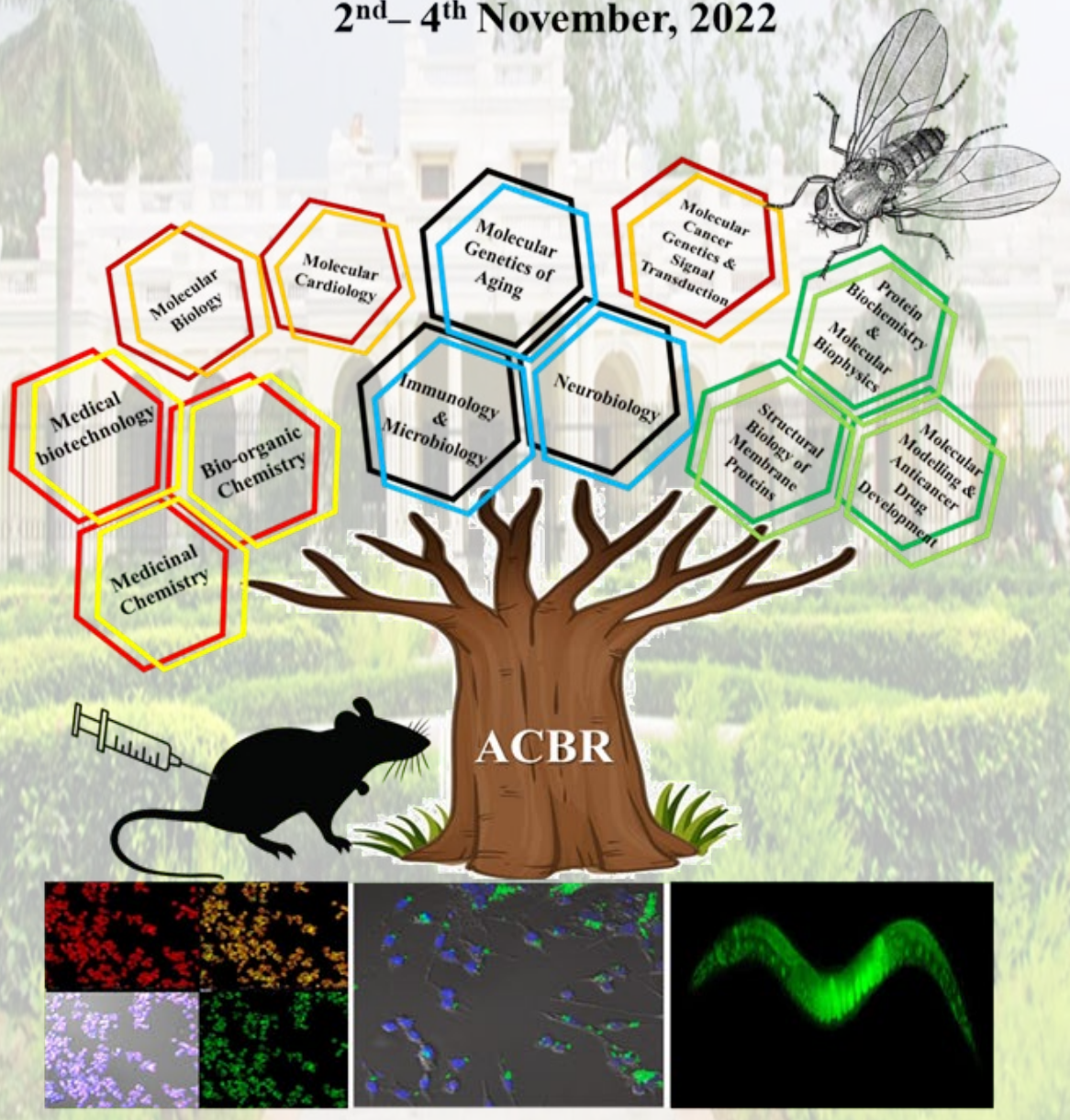
ACBR

YEARS 1922-2022

National Symposium on Frontiers in Biomedical Research 2022 (FBR 2022)

Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

2nd– 4th November, 2022



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

ABSTRACTS

आज़ादी का अमृत महोत्सव

ACBR

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Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

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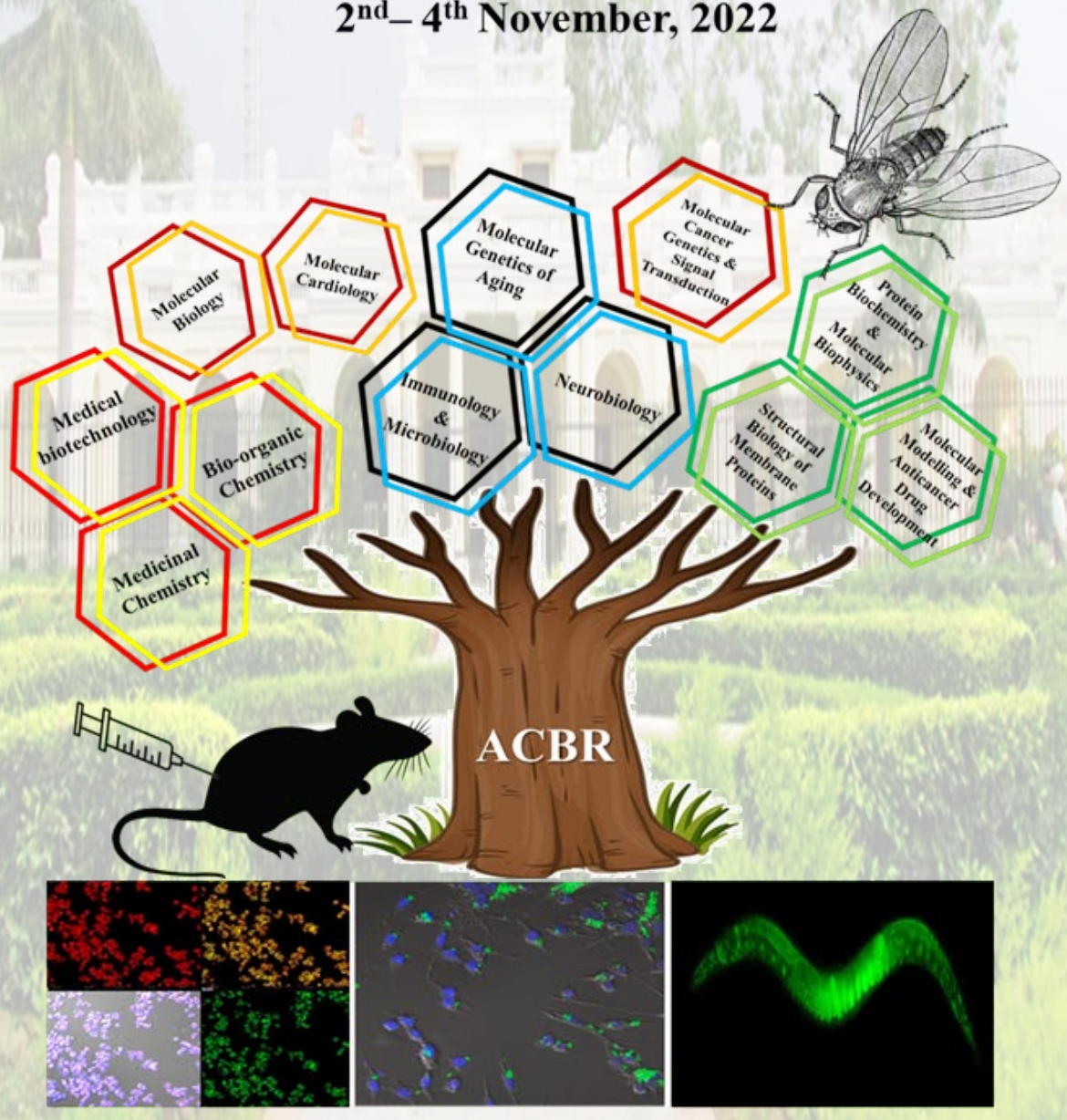

Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi

दिल्ली विश्वविद्यालय
University of Delhi

प्रो॰ योगेश सिंह
कुलपति

Prof. Yogesh Singh
Vice-Chancellor

No. DU/VC/2022/149
17th October 2022

MESSAGE

I am pleased to know that Dr. B. R. Ambedkar Center for Biomedical Research (ACBR), University of Delhi is organizing a symposium on "Frontiers in Biomedical Research" with a themed focus on "Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness" to be held during November 2nd to 4th, 2022 to commemorate the 100th year of University of Delhi. This theme is contemporary and quite relevant in the present context. Health issues need careful consideration in our highly cosmopolitan and populo us country.

For the past several years, University of Delhi has served as a major platform, bringing different parts of the country together by means of National Symposiums like FBR-2022. The theme of the FBR-2022 taken up this year is bound to ignite quest for biomedical sciences in the mind of every scientist. Biomedical research has been unique by its multidisciplinary nature by birth. The scientific utilization of knowledge from such research has helped in targeting chronic and acute human diseases. Such opportunities must be utilized for sharing the rich experience of Researchers, Teachers, Practitioners, so that the entire biomedical fraternity may be enlightened about the clinical- and basic-fundamental developments in the field. At the onset, it's been so appropriate that ACBR is organizing the FBR-2022 with its immense experience and wealth of research with proven track record in biomedical sciences.

I am sure 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 wish FBR-2022 a grand success and look forward to result-oriented deliberations during this national symposium, as evident from the topics being taken up during this program.

Yogesh Singh

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UNIVERSITY OF DELHI
दिल्ली विश्वविद्यालय

प्रोफेसर बलराम पाणी
अधिष्ठाता महाविद्यालय
Professor Balaram Pani
Dean of Colleges

**********MESSAGE**********

I have great pleasure in congratulating the faculty of ***Dr. B. R. Ambedkar Center for Biomedical Research*** *for organizing 13th Symposium on "Frontiers in Biomedical Research", at University of Delhi with a theme "Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness" during November 2nd to 4th, 2022 to commemorate the* ***100th year of University of Delhi.***

At the onset of celebrating the centenary year of University of Delhi, organizing National Symposium has come up as a boost to the University's long tradition to bring scientific minds for stimulating discussions and exchange of ideas. The multidisciplinary nature of biomedical research has made ACBR as the most suitable host for Symposium like FBR-2022. I am sure this will be a wonderful opportunity for the scientists carrying out work in diverse fields of Biomedical Research to discuss their thoughts, approach and findings with students, peers and faculty of ACBR at Delhi University. I am sure that some very important issues of societal relevance will find place in discussion amongst experts.

I wish the FBR-2022 a great success.

Balaram Pani

October 12th, 2022

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कुलसचिव
REGISTRAR

दिल्ली विश्वविद्यालय
University of Delhi

MESSAGE

It gives me an immense pleasure to know that Dr. B. R. Ambedkar Center for Biomedical Research is organizing a National Symposium on "Frontiers in Biomedical Research", during 02nd – 04th November, 2022 at University of Delhi as part of Centenary Celebrations of the University of Delhi. I would like to take this opportunity to congratulate the Director and other Faculty Members of the Dr. B. R. Ambedkar Centre for Biomedical Research for taking such an initiative which will be an amalgamation of scientific thoughts of peers and experts with similar minds in Biomedical Research.

I wish the FBR-2022 a great success.

Vikas Gupta

(DR. VIKAS GUPTA)

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दिल्ली विश्वविद्यालय
University of Delhi

प्रो॰ श्रीप्रकाश सिंह
निदेशक, दक्षिण दिल्ली परिसर

Prof. Shri Prakash Singh
Director, South Delhi Campus

Message

As the Director of University of Delhi South Campus, I am so pleased to know that Dr. B. R. Ambedkar Center for Biomedical Research is organizing a National Symposium on "Frontiers in Biomedical Research", during 2nd-4th November 2022 at University of Delhi to commemorate the 100th year of University of Delhi.

By tradition University of Delhi, has been a scientific hub for the country by inviting researchers from all parts of India for scientific meetings and exchange of ideas. It is needless to say that like several past scientific mind boosting Symposiums, this year too ACBR is organizing the FBR-2022 with a very relevant theme entitled as "Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness". This will surely provide a common interaction mela for young Indian PhD students, MSc students, as well as experienced Teachers, and Scientists in the field of biomedical research. It will boost their minds to pursue further research in the similar field.

I am sure that the symposium will be a grand success to bring together scientists, peers, and students in the field of Biomedical Research for very fruitful discussions and exchange of ideas.

Shri Prakash Singh

वाईस रीगल लॉज, दिल्ली विश्वविद्यालय, दिल्ली-110007
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रसायन शास्त्र विभाग / DEPARTMENT OF CHEMISTRY

दिल्ली विश्वविद्यालय, दिल्ली-110007 / University of Delhi, Delhi-110007

Prof. Ashok K. Prasad
HEAD, DEPARTMENT OF CHEMISTRY

Dean, Faculty of Science

Message

I am so happy to know that Dr. B. R. Ambedkar Center for Biomedical Research is organizing the 13th National Symposium on "Frontiers in Biomedical Research", during 2nd-4th November 2022 at University of Delhi to commemorate the 100th year of University of Delhi. I can assure that the symposium will be a grand success to have brainstorming discussions of the latest developments in the field of Biomedical Research.

On behalf of the Faculty of Science, University of Delhi, I welcome all the delegates. scientists, researchers, and students to this societally relevant National Symposium FBR-2022. The theme of the symposium for this year is so relevant for current need of the country to solve many burning issues to save thousands of lives. ACBR, being a unique center pursuing multidisciplinary research in biomedical sciences, is no doubt the best host for the symposium like FBR-2022. The symposium will surely mingle scientific ideas of experienced teachers, scientists with your researchers and students to motivate them pursue further biomedical research.

I wish the conference a big success.

12/10/22

Ashok Prasad

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E-mail : head@chemistry.du.ac.in | Mob. : +91-8826761666

दिल्ली विश्वविद्यालय
University Of Delhi

Professor K. Ratnabali
Dean Academic Activities & Projects

Message

It gives me immense pleasure to know that the Dr. B. R. Ambedkar Center for Biomedical Research (ACBR) is organizing 13th Symposium on "Frontiers in Biomedical Research" from 2nd – 4th November 2022. ACBR is one of the pioneers in areas of biomedical research in the University of Delhi. It is with pride that I recall that during the challenging time of Covid 19 pandemic, the Centre had been able to develop an assay for the purpose of detecting the presence of the virus within a short span of time. The Centre has been consistently working in several other areas of biomedical research.

The title of the Symposium reflects the readiness of the Centre to discuss those frontiers of biomedical research which will have an important bearing upon the timely detection, prevention and treatment of several communicative and non-communicative diseases as well as evaluate new therapeutics.

I appreciate the efforts made by the Centre to bring in a wide range of experts on one platform to discuss emerging issues in biomedical research. I express a hearty welcome to all the dignitaries and participants on behalf of the University as well as on my own behalf.

My sincere wishes for a successful Symposium.

K. Ratnabali

K. Ratnabali

दिल्ली विश्वविद्यालय, दिल्ली-110007 (भारत)
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Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi

University Road, Delhi-110007, India

Presents

National Symposium on Frontiers in Biomedical Research 2022 (FBR-2022)

Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

Chairperson, Research Council,
Director, ACBR
University of Delhi

Date: 20-10-2022

Message

I on behalf of the University of Delhi, and in my own capacity as the Chairperson of the Research Council and Director, ACBR, welcome all the eminent scientists, academicians, young researchers, and students to the 13th Frontiers in Biomedical Research 2022 symposium. The conference aims to share an insight into the recent research and cutting-edge technologies in the field of Biomedical sciences. This year, ACBR is commemorating the 100th year of the University of Delhi through this symposium as well.

The University doesn't need any introduction which is clear from its quality education and Research portfolio. The University is preparing the next generation of leaders who will carry this path forward in the years ahead. Today, the Dr. B R Ambedkar Center has a distinguished record in both teaching and research. ACBR has already 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 breakthrough ideas related to 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 are looking forward to an excellent meeting with great scientists from different Institutes to share their research and enlighten us through their presentations.

20/10/22

Prof. Daman Saluja

Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi
University Road, Delhi-110007, India

Presents

National Symposium on Frontiers in Biomedical Research 2022 (FBR-2022)

Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

Dr. Sanjay Kumar Dey
Assistant Professor, ACBR

Date: 2nd November 2022

Message from the Organizing Secretary

"विज्ञान का अनुसरण करने के लिए मानव की भागीदारी की आवश्यकता होती है;
और मनुष्य के अस्तित्व के लिए भी विज्ञान की भागीदारी की आवश्यकता होती है"
"Pursuing Science Requires Involvements of Human Being; And
Survival of Human Beings too Requires Involvement of Science"

I am honoured to write this message that FBR-2022, themed "Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness", is being organized by the Dr. B.R. Ambedkar Center for Biomedical Research (ACBR), University of Delhi. On behalf of the Organizing Committee and my own self, we cordially welcome you all to this scientific fest. After a gap of two years, the symposium is going to happen in an off-line mode with only a few talks in online mode thereby marking a resumption of the pre-COVID-19 era. I congratulate one and all for your active participation and overwhelming response in this event as a driving force to make it a grand success. With this symposium, ACBR is also commemorating the 100 years of the University of Delhi and its excellence.

As Biomedical scientists, we are exploiting all resources made by us and from the last several years, we are trying to win over any human diseases to make our life normal. This national symposium will provide the opportunity to researchers and students to experience the effort made by world- and national-leaders to develop various strategies, kits, vaccine, tools etc. to achieve those primary goals. The symposium hosts two keynote/public lectures, 11 plenary lectures, 16 invited lectures, 18 oral presentations, and >101 poster presentations through three poster sessions by budding scientists. Scientific sessions will include research discussions on cancer, leukemia, immunology, neurodegenerative disorders, protein sciences, structural biology, drug discovery, ayurveda, and genetics, among others.

The entire scientific fest could not be possible without a strong financial support from the University of Delhi, DST-SERB, and DBT. Academic, administrative, and infrastructural supports from the University of Delhi and ACBR fraternity are also remarkable to put together this scientific program. I convey my heartiest gratitude to all the faculty members, students, volunteers, and non-teaching staffs from ACBR who have been contributing day and night to make FBR-2022 a scientifically enchanting event. I am thankful to all the invited speakers, and dignitaries for accepting our requests to be part of this event and encouraging their students to join this event.

The students' fraternity of ACBR has also put together a dedicated cultural event which they rightly named as "**परवाज़ (Parvaaz)**" for this 13th FBR.

Finally, credit for anything good in this symposium solely goes to the entire organizing team while anything looks bad in inadvertence goes to me and the later is deeply regretted.

Sanjay Kr. Dey

Sanjay Kumar Dey

PROGRAM COMMITTEES

Chairperson
Prof. Daman Saluja
Director, ACBR

Organizing Secretary
Dr. Sanjay Kumar Dey

Scientific Advisory Committee

Prof. Ashok Prasad, Dean, Faculty of Science, Prof. Swati Saha, Dean, FIAS, Prof. Suman Kundu, Director, BITS-Pilani Goa (Ex-Director, UDSC), Prof. Y. Singh, Honorary Director, DSPH, IoE-DU, Prof. Alok Bharti, Department of Zoology Prof. Daman Saluja, Prof. PM Luthra, Prof. K Natarajan, Prof. Anju Katyal, Prof. Madhu Chopra, Prof. Manisha Tiwari, Prof. Ajay K Yadav, Prof. LR Singh, Dr. Aparna Dixit, Dr. Meenakshi Sharma, Dr. Sanjay Kumar Dey, Dr. Kamna Srivastava, Dr. Praveen Belagal,

Registration Committee

Dr. Meenakshi Sharma
Dr. Aparna Dixit
Ms. Chitra Joshi

Venue Management

Prof. Anju Katyal
Prof. L. R. Singh
Mr. Jegadheesan
Mr. Gajinder Giri

Food Committee

Prof. Manisha Tiwari
Dr. Kamna Srivastava
Mr. Kishan Kumar
Ms. Veenu Bhatia
Mr. Saurabh Dixit
Mr. Jegadeesan

Abstract Committee

Prof. K. Natarajan
Dr. Praveen Belagal
Mr Naterpal Yadav
Ms Kavita Dhar

Transport & Accommodation

Prof. Anju Katyal
Prof. L. R. Singh
Dr Mordhwaj

Treasurer & Finance

Prof. Pratibha Mehta Luthra
Prof. Madhu Chopra
Mr. Ram Narain
Mr. Rajneesh
Mr. Ashraf Ansari
Mr. Praveen Kumar

Memento Committee
Prof. Ajay K. Yadav

We are thankful to

Research Council, University of Delhi
ACBR, DBT, DST-SERB, and CSIR
For their generous support to FBR 2022

STUDENT VOLUNTEERS

Registration

Ms. Sonali Kumar
Mr. Ozasvi R Shanker
Ms. Sandhya
Ms. Kajal
Ms. Diksha Rani

Food Committee

Mr. Chandan
Mr. Bhaskar

Session-I

Ms. Sandhya
Ms. Kajal

Session-II

Mr. Ankush Rana
Ms. Shakuntala
Ms. Aarti Singh
Ms. Akshita Singh

Session-III

Mr. Aman Gangwar
Ms. Divpreet Kaur
Ms. Chanchal Baweja

Session-IV

Ms. Meetali
Ms. Sushmita Pandey

Session-V

Ms. Snigdha

Session-VI

Ms. Sarika Bano
Ms. Diksha Rani

Session-VII

Ms. Sonali Kumar
Mr. Ozasvi R Shanker

Session-VIII

Mr. Shoaib Khan
Ms. Prerna Rajoria

Session-IX

Mr. Sanjay

Session-X

Mr. Siddharth Gosain
Ms. Kajal

Session-XI

Ms. Shelly Aggarwal
Ms. Monika Sharma

STUDENT PARTICIPANTS IN INAUGURATION AND CULTURAL PROGRAM

INAUGURATION

Ms Sakshi Sharma (Compere)
Ms Sarika Bano
Ms Diksha Rani
Mr. Suyash Devgan
Ms Himanshi Sharma
Ms Akanksha Shukla

NATIONAL ANTHEM

Mr. Dheeraj Bansal
Mr. Ashish Yadav
Ms. Shahjahan
Ms. Smaranjot Kaur
Ms. Sumedha Sengupta

SARASWATI VANDANA

Ms. Surbhi Tripathi
Ms. Annu Kumari
Ms. Vidhi
Ms. Mamta Rohilla
Ms. Srishti Srivastava

VANDE MATARAM

Ms. Sumedha Sengupta
Ms. Surbhi Tripathi
Ms. Mamta Rohilla
Ms. Smaranjot Kaur
Ms. Shahjahan

CULTURAL PROGRAMME

Dance Team

Ms. Surbhi Tripathi
Ms. Milky Mittal
Ms. Shreya Bhattacharjee
Ms. Shahjahan
Ms. Smaranjot Kaur
Ms. Neha Dixit
Ms. Diksha Saini
Ms. Bhawna Solanki
Ms. Riya Jain
Ms. Tejaswini
Ms. Shivam Yadav
Ms. Pratima
Mr. Dipesh Talukdar
Mr. Bhashkar Paul
Mr. Wilson Gbedema
Mr. Ashish Yadav
Mr. Altaf Asghar
Mr. Jai Prakash

Anchoring

Ms. Iram Haque
Ms. Neha
Mr. Chandan Kr. Rajak
Ms. Ashmita

Graphics and Sound

Ms. Meghna Birla
Mr. Wilson Gbedema
Mr. Bhashkar Paul

Solo Performances

Mr. Anish Vashisht (Guitar and Poem)
Mr. Srishti Srivastava (Miscellaneous)

Song

Ms. Sumedha Sengupta
Mr. Dipesh Talukdar
Ms. Vidhi

Solo Song

Ms. Sarika Bano

Venue Committee

Compere and Tokens/Memento

Ms. Snigdha
Ms. Sakshi
Ms. Surbhi
Ms. Meetali

Rangoli
Ms. Shushma
Ms. Shweta
Ms. Divya Rajput
Ms. Aradhna
Ms. Ashmita

Audio-Visual team
Mr. Sachin
Mr. Rahul

Floral: Bouquet/Flowers
Mr. Surjalal
Mr. Rahul
Ms. Prerna

Venue Prep./ Banner
Mr. Siddharth
Mr. Zia Khan
Ms. Sushma
Mr Anil Kumar

Helpers for Mic
Mr. Chandan
Mr. Devesh
Mr. Bhaskar

Accommodation
Ms. Snigdha
Ms. Reshmee
Ms. Priya
Mr. Kunwarpal
Ms. Saksham

Miscellaneous Items/ Poster
Ms. Anju
Mr. Kuldeep
Ms. Bhawna
Mr Vijay Sihag

Scientific Program

Day 1: Wednesday, 2nd November 2022

Registration: **8:30 A.M. – 9:00 A.M.**

SESSION I: GENETICS AND EPIGENETICS OF HUMAN DISEASES

Session In-Charge: Dr. Meenakshi Sharma, ACBR

TIME: 9:00 A.M. - 10:30 A.M.

Chair: Prof. Namita Aggarwal, *Dept. of Zoology, DU and* ***Prof. Vani Brahmachari****, ACBR, DU*		
PL-1	**Vani Brahmachari**, *ACBR, DU:* The eloquent language of epigenetics; Our efforts at understanding its alphabets & amp; grammar	9:00 am - 9:30 am
IL-1	**Chandra Shekhar,** *CCMB:* Trophoblast Stem cell derivation and Blastoid generation from pluripotent stem cells follow competing molecular trajectories	9:30 am - 9:55 am
IL-2	**Debabrata Biswas,**, *CSIR-IICB:* Understanding of Eukaryotic Transcriptional Regulatory Mechanisms Involving Super Elongation Complex and Its Implications in MLL Fusion-mediated Leukemogenesis	9:55 am - 10:20 am
OP-1	**Sakshi Sharma** *ACBR, DU:* Elucidating the functional relevance of Sin3B spliced variants in pathogenesis of Oral Squamous Cell Carcinoma	10:20 am - 10:30 am

TEA BREAK 10:30-11:00 A.M.

Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi
University Road, Delhi-110007, India

Presents

National Symposium on Frontiers in Biomedical Research 2022 (FBR-2022)

Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

Programme for Inaugural Function

Venue: Conference Centre, University of Delhi North Campus

Date: November 2nd 2022 **Time: 11:00 AM – 12:15 PM**

Welcoming of Chief Guest and Dignitaries to the Dias	
Lighting of Lamp	
Saraswati Vandana	
Opening Remarks and Welcome	**Prof. Daman Saluja,** Director, ACBR
Felicitation of Dignitaries	
Release of Symposium Abstract Book	
Inaugural Remarks	**Prof. Yogesh Singh** Vice Chancellor, University of Delhi
Introduction to the Inaugural Address Orator	**Prof. RNK Bamezai** Former VC, Shri Mata Vaishno Devi University, Katra
Inaugural Address	**Prof. Randeep Guleria** Former Director, AIIMS-New Delhi
Vote of Thanks	**Dr. Sanjay Kumar Dey** Organising Secretary, FBR-2022

(The function will be followed by Lunch at the venue)

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SESSION II: INFECTION AND IMMUNITY

Session In-Charge: Prof. K. Natarajan, ACBR

TIME: 2:00 P.M. - 3:40 P.M.

Chair: Prof. Suman Dhar, *Special Centre for Molecular medicine, JNU*		
PL-2	**Pawan Malhotra**, *ICGEB, New Delhi*: Unravelling and targeting Plasmodium falciparum merozoite invasion of human RBCs	2:00 pm - 2:30 pm
IL-3	**Udaykumar Ranga,** *JNCASR, Bengaluru:* Sleep like HIV to win the world!	2:30 pm - 2:55 pm
IL-4	**Amit Singh**, *IISc, Bengaluru:* Macrophage heterogeneity promotes drug tolerance in *Mycobacterium tuberculosis*	2:55 pm - 3:20 pm
OP-2	**Shakuntala S. Saraswati**, *ACBR, DU:* Investigations on the Immunological Roles of Host Derived Heat Shock Proteins during Mycobacterial Infection	3:20 pm - 3:30 pm
OP-3	**Dhaneshwar Prusty** *Central University of Rajasthan*: Rational designing of Peptide-Ligand Conjugates for the treatment of complicated malaria	3:30 pm - 3:40 pm

EVENING TEA 3:40 P.M. – 4:00 P.M.

SESSION III: CANCER STEM CELLS & LEUKEMIA

Session In-Charge: Prof. Daman Saluja, ACBR

TIME: 4:00 P.M. - 5:15 P.M.

Chair: Prof. Ramesh K. Bamezai, *Former VC, Shri Mata Vaishno Devi University, Katra*		
PL-3	**Jacqueline Cloos,** *University of Amsterdam Cancer Center, Netherlands:* Relevance of leukemia stem cells for acute myeloid leukemia	4:00 pm - 4:30 pm
IL-5	**Tulika Seth,** *AIIMS, New Delhi:* Leukemias: unanswered questions Leukemia stem cells: holding the answers?	4:30 pm - 4:55 pm
OP-4	**Ankit Mathur,** *ACBR, DU:* Induction of terminal differentiation in leukemic blast cells with esculetin: Role of "axis shifts" of Wnt signaling	4:55 pm - 5:05 pm
OP-5	**Sumeet,** *ACBR, DU:* Ricolinostat suppresses proliferation and promotes apoptosis alone as well as in combination with topotecan/etoposide in cervical cancer cells	5:05 pm - 5:15 pm

Day 2: Thursday, 3rd November 2022

SESSION IV: SYSTEMIC INFLAMMATION VS NEUROINFLAMMATION: THE TWO DRIVERS OF NEURODEGENERATIVE DISORDERS

Session In-Charge: Prof. Anju Katyal, ACBR

TIME: 9:00 A.M. - 10:40 A.M.

Chair: Dr. Shashi Bala Singh, *Director, NIPER, Hyderabad*		
PL-4	**Vaibhav Kumar**, *University of Augusta Georgia:* Immune interaction in brain injury: what we know so far	9:00 am - 9:30 am
IL-6	**Udayabanu Malairaman,** *Jaypee University of Information Technology, Himachal Pradesh:* Quercetin Attenuates Neurological Complications Associated with Chronic Diabetes	9:30 am - 9:55 am
IL-7	**Tauheed Ishrat,** *University of Tennessee Health Science Center (UTHSC):* Role of TXNIP in Brain Aging and Alzheimer's Disease	9:55 am 10:20 am
OP-6	**Meetali,** *ACBR, DU:* PPAR-β/δ agonist GW501516 attenuates neuroinflammation and blood-brain barrier breakdown in Plasmodium berghei ANKA-infected Balb/c mice	10:20 am - 10:30 am

TEA BREAK 10:30 A.M. - 11:00 A.M.

SESSION V: PROTEIN FOLDING DISEASES: MOLECULAR MECHANISMS AND THERAPEUTIC APPROACHES

Session In-Charge: Prof. L. R. Singh, ACBR

TIME: 11:00 A.M. - 12:40 P.M.

Chair: Prof. Rajiv Bhat, *School of Biotechnology, JNU*		
PL-5	**Ipsita Roy,** *NIPER Mohali:* Development of aptamers as therapeutic agents for C9 ALS-FTD	11:00 am - 11:30 am
IL-8	**Krishnananda Chattopadhyay,** *CSIR-IICB, Kolkata:* Metal cofactor Zn and interacting membranes modulate conformation-aggregation landscape in SOD1	11:30 am - 11:55 am
IL-9	**Athi N. Naganathan**, *IIT Madras* ***(Online)****:* Dynamic Homo- versus Hetero-Oligomerization Drives the Thermo-Osmo Responsiveness of Enterobacterial Sensory Proteins	11:55 am - 12:20 pm
OP-7	**Snigdha** *ACBR, DU:* Taurine & derivates as enhancers of thyroxine-binding affinity transthyretin: an insight towards therapeutic intervention of pre-eclampsia	12:20 pm - 12:30 pm
OP-8	**Reshmee Bhattacharya**, *ACBR:* Organosulfurs, S-allyl cysteine and N-acetyl cysteine sequester dicarbonyls and reduces carbonyl stress	12:30 pm – 12:40 pm

LUNCH BREAK AND POSTER SESSIONS **12:40 P.M. – 2:20 P.M.**

SESSION VI: APPLICATIONS OF STRUCTURAL BIOLOGY TO TREAT HUMAN DISEASES

Session In-Charge: Dr. Sanjay K. Dey, ACBR

TIME: 2:20 P.M. – 4:00 P.M.

Chair: Prof. T. P. Singh, *AIIMS, New Delhi*		
PL-6	**Christian Betzel,** *Hamburg University, Germany:* Past and Future in Structure-Based Drug Discovery to identify Lead Compounds	2:20 pm – 2:50 pm
IL-8	**S. Gourinath**, *JNU:* Structural based inhibitor development against cysteine biosynthetic pathway enzymes of E. histolytica	2:50 pm – 3:15 pm
IL-9	**Manidipa Banerjee,** *IIT Delhi:* Molecular pathways for non-enveloped capsid disassembly	3:15 pm – 3:40 pm
OP-9	**Prakash Jha,** *ACBR, DU:* Drug repurposing to treat Tuberculosis and SARS-CoV-2 infections: Insights from computational design into their mechanisms of action	3:40 pm - 3:50 pm

EVENING TEA 4:00 P.M. – 4:30 P.M.

SESSION VII: NEUROBIOLOGY AND EXPERIMENTAL NEUROLOGY

Session In-Charge: Dr. Aparna Dixit, ACBR

TIME: 4:30 P.M. - 6:10 P.M.

Chair: Prof. P. M. Luthra, *ACBR, DU*		
PL-7	**Annamaria Vezzani,** *Department of Neuroscience, Mario Negri Institute for Pharmacological Research in Milano, Italy:* Neuroinflammatory pathways in epilepsy as treatment targets and biomarker candidates in epilepsy	4:30 pm - 5:00 pm
IL-9	**Surajit Sarkar,** *DU:* A multi-target based novel combinatorial approach to dominantly restrict human Tau mediated neurotoxicity in Drosophila disease models	5:00 pm - 5:25 pm
IL-10	**Baby Chakrapani,** *Centre for Neuroscience, Department of Biotechnology, Cochin University of Science and Technology, Kerala:* Differentiation of peripheral blood mononuclear cell (PBMC) into tyrosine hydroxylase expressing Dopaminergic neurons for cell replacement therapy in Parkinson's disease	5:25 pm - 5:50 pm
OP-10	**Nitin Yadav,** *ACBR, DU:* Srk Kinase mediates differential regulation of excitatory synaptic transmission in the hippocampus and ATL in temporal lobe epilepsy	5:50 pm - 6:00 pm
OP-11	**Tuithung Sophronea,** *ACBR, DU:* $A_{2A}R$ antagonists mediate the restoration of mitochondrial calcium dysfunction using the 6-OHDA model of Parkinson's in primary neuronal cells of P_0/P_1 rat pups	6:00 pm - 6:10 pm

You are cordially invited to
join us for

परवाज़

(Parvaaz)

A Cultural Program

On

Thursday, November 3, 2022 at 6:30 PM

at

National Symposium on Frontiers in Biomedical Research 2022 (FBR-2022)
Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness

(Venue: Conference Centre, University of Delhi North Campus)

Featuring

Hindustani Vocal Music

By

Prof. Subhendu Ghosh (Rampur Sahaswan Gharana)

(Former Professor, Department of Biophysics, University of Delhi)

Bharatanatyam

By

Ms. Ishita Bhatia

Solo Performance

by

Ms. Srishti Srivastava and Ms. Sarika Bano

Classical and Semiclassical Group Dance

By

Ms. Surbhi Tripathi, Ms. Milky Mittal, Ms. Shreya Bhattacharjee, Ms. Shahjahan, Ms. Smaranjot Kaur, Ms. Neha Dixit, Ms. Diksha Saini, Ms. Bhawna Solanki, Ms. Riya Jain, Ms. Tejaswini, Ms. Shivam Yadav, Ms. Pratima, Mr. Dipesh Talukdar, Mr. Bhashkar Paul, Mr. Wilson Gbedema, Mr. Ashish Yadav, Mr. Altaf Asghar, and Mr. Jai Prakash

A Short Story with Guitar and Stand-up Poetry

By

Mr. Anish Vashisht

Song

By

Ms. Sumedha Sengupta, Mr. Dipesh Talukdar, and Ms. Vidhi

(The function will be followed by a Banquette Dinner at the venue)

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Day 3, Friday, 4th November 2022

SESSION VIII: NEW PARADIGM IN DRUG DISCOVERY RESEARCH

Session In-Charge: Prof. Madhu Chopra, ACBR

TIME: 9:00 AM - 10:40 A.M.

Chair: Prof. Diwan S. Rawat, *Dept. of Chemistry, DU*		
PL-8	**Anil K. Mishra,** *DRDO, INMAS, New Delhi:* Chemical Chaperones in Theragnostic using Nuclear Technology	9:00 am - 9:30 am
IL-11	**Debashisa Mohanty,** *NII, New Delhi:* Designing Allosteric inhibitors for PfCDPK1 by combining atomistic simulations with machine learning	9:30 am - 9:55 am
IL-12	**Tavpritesh Sethi**, *IIIT-Delhi:* Understanding DNA Sequences with Artificial Intelligence	9:55 am - 10:20 am
OP-12	**Priya Poonia**, *ACBR, DU:* Virtual screening combined with molecular modelling and designing approaches to identify HDAC6 selective inhibitors as anticancer agents	10:20 am - 10:30 am
OP-13	**Ayush Thakur,** *Kirori Mal College, DU:* Exploring the Therapeutic Potential of Nanotechnology based Phyto-pharmaceuticals	10:30 am - 10:40 am

TEA BREAK 10:40 A.M. - 11:00 A.M.

SESSION IX: THERAPEUTIC VENTURE TO TARGET CANCER CELL AND ITS REPROGRAMMED BIOLOGY

Session In-Charge: Prof. Ajay K. Yadav, ACBR

TIME: 11:00 A.M. - 12:15 P.M.

Chair: Prof. S. N. Das, *Adjunct Faculty, Jamia Hamdard*		
PL-9	**Durga Prasad Mishra,** *CSIR-CDRI:* Therapeutic Targeting of Metabolic Reprogramming in Glioma	11:00 am - 11:30 am
IL-13	**Ritu Kulshreshtha,** *IIT-Delhi:* miR-210: An attractive target for cancer therapy	11:30 am - 11:55 am
OP-14	**Sachin Bhardwaj**, *ACBR, DU:* SMAC mediating a switching point in TRAIL drive sensitization	11:55 am - 12:05 pm
OP-15	**Akansha Chauhan**, *Amity Univ, Noida UP*: Targeting NF-κB50 DNA binding region through active phytochemicals from Spaheranthus indicus	12:05 pm - 12:15 pm

SESSION X: RECENT ADVANCES IN ALTERNATIVE MEDICINE: WITH EMPHASIS ON AYURVEDA

Session In-Charge: Prof. Pratibha M. Luthra and Prof. Manisha Tiwari, ACBR

TIME: 12:15 P.M. - 1:30 P.M.

Chair: Prof. Veena Aggarwal, *Dept. of Botany, DU*		
PL-10	**VM Bhandari,** *CSIR-NCL:* SWASTIIK Technology- Exploiting knowledge of Ayurveda for water disinfection and for possible health benefits.	12:15 pm - 12:45 pm
IL-14	**Sunita Dhawan,** *CIMAP: Exploration of biosynthetic potential for new therapeutic molecules and nutraceuticals with aim..... in Ocimum basilicum: validations through genomics*	12:45 pm - 1:10 pm
OP-16	**Shruti Shalini**, *ACBR, DU:* Biological evaluation of hydro-alcoholic extract of Bacopa monnieri for the treatment of Alzheimer's disease	1:10 pm - 1:20 pm
OP-17	**Rambir Singh,** *Mizoram University:* Standardization and quality control in medicinal and aromatic plants for phtopharmaceutical drug discovery	1:20 pm - 1:30 pm

LUNCH BREAK AND POSTER SESSION III **1:30 P.M. – 3:00 P.M.**

SESSION XI: ART OF WAR AGAINST CARDIOVASCULAR DISEASE PROGRESSION AND OUTCOMES

Session In-Charge: Dr. Kamna Srivastava, ACBR

TIME: 3:00 P.M. - 4:30 P.M.

Chair: Prof. Jagriti Bhatia, *AIIMS New Delhi*		
PL-11	**Dhavendra Kumar,** *Spire Cardiff Hospital, UK:* Cardiovascular disease in the Genome era	3:00 pm - 3:30 pm
IL-15	**R. Lakshmy**, *AIIMS, New Delhi*: Endothelial progenitor cells in cardiovascular disease	3:30 pm - 3:55 pm
IL-16	**Vivek Chaturvedi,** *Amrita Institute of Medical Sciences, Faridabad:* Art of war against cardiovascular disease	3:55 pm – 4:20 pm
OP-18	**Shelly Aggarwal,** *ACBR, DU:* Elevated expression of SORT1 gene in patients with Coronary Artery Disease	4:20 pm - 4:30 pm

EVENING TEA 4:30 P.M. – 5:00 P.M.

You are cordially invited to

join us for

Valedictory Lecture

By

Prof. Sudhanshu Vrati

(Director, Regional Centre for Biotechnology, Faridabad)

On

"Rotavirus vaccine development: The India story"

On Friday, November 4, 2022 at 5:00 PM

at

National Symposium on Frontiers in Biomedical Research 2022 (FBR-2022)
Communicable and Non-communicable Diseases: Prevention, Cure, and Future Preparedness
(Venue: Conference Centre, University of Delhi North Campus)

Chaired by

Prof. Yogendra Singh

(Former Dean, Life Sciences & Director, DSPH, IoE, University of Delhi)

Poster Awards by Dignitaries

Vote of Thanks

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PLENARY AND INVITED LECTURES

The eloquent language of epigenetics; Our efforts at understanding its alphabets & grammar

Vani Brahmachari

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

Epigenetic regulation occupies the center stage in explaining the lack of correlation between genotype and phenotype. What are the aspects of this regulatory mechanism that makes it so eloquent? Some of the important features of epigenetic modification is that it can be written as well as erased, it acts on several genes, sometimes on a cluster of genes as in the homeotic gene complex. Recent results also indicate that epigenetic marking shows trans-generational inheritance. I was introduced to epigenetics in early 80s, (when it was not the buzzword!), through the amazing system, the mealybugs. It is an excellent model for genomic imprinting and epigenetics, though a difficult system to work with. While our initial effort was to understand the differential regulation of homologous chromosomes using molecular analysis. This work raised the possibility of differential organization of homologous chromosomes being an imprinting mechanism. Later, around 2015, we proceeded to use the genomics tools to understand this system. We completed the sequencing of the genome and the transcriptome of mealybugs at ACBR. Our findings on chromatin organization in mealybugs, led us to raise questions on the effect of sequence dependent chromatin organization in triplet repeat instability, a case of (CGG)n repeats in the Fragile X syndrome. We demonstrated the importance of chromatin organization in dynamic mutations by generating various transgenic mouse lines. The availability of the draft sequence of the human genome and the paucity of well characterized chromatin modifiers in the human genome motivated us to take up a unique in silico approach to identify cellular memory modules. This resulted in the identification of human INO80 and its characterization as a dual function protein. Demonstrating the essential role of INO80 in development in Drosophila, we analyzed the various interactions of INO80, which led us to propose a “LEGO Model” for cellular memory modules; limited number (of proteins), but innumerable unique outcomes by combinatorial interactions! We identified the other partner of this interaction, the DNA binding sites, the PRE/TRE sequences (Polycomb/Trithorax Responsive Elements) in the human genome through in silico approach and characterized their function using human cell lines. hPRE-PIK3C2B and hPRE-HoxA3, are two of the limited number of human PRE/TREs so far characterized. During my talk, some aspects of our work in the area of epigenetics will be described to reflect the journey I undertook with highly committed students, associates, and colleagues.

Trophoblast Stem cell derivation and Blastoid generation from pluripotent stem cells follow competing molecular trajectories

P Chandra Shekar

Centre for Cellular and Molecular Biology, Hyderabad

Unlike Human pluripotent cells which can differentiate to Trophectoderm lineage, mouse embryonic stem cells (mESCs) are pluripotent, they cannot differentiate into extraembryonic layers such as the placenta. By virtue of lacking totipotency they can nether self-organise into blastocyst like structures. Here we show that (trophoblast stem cells) TSCs could be derived from mESC involving a preliminary TE priming stage followed by reprograming to TSC. The TSCs derived from mESCs have a have transcriptome profile similar to embryo derived TSCs and efficiently contribute to placenta of mouse conceptus. We further show that intron-I element of Cdx2 is indispensable for this TSC derivation. The TE potential of mESC prompted a small molecule screen to self to mESC organise into blastocyst-like structures (Blastoid). We have developed an efficient method to generate blastocyst like structures exclusively from ESCs which we refer to as E-blastoids. E-Blastoids expresses all the markers as Blastocyst, undergo implantation and development till 6.5dpc. E-blastoids generation a very high efficiency (>90%) relative the currently known methods. Intriguingly, the molecular pathways that promote torphoectoderm fate of ESC inhibit the self- organisation of ESCs to blastoids.

Understanding of Eukaryotic Transcriptional Regulatory Mechanisms Involving Super Elongation Complex and Its Implications in MLL Fusion-mediated Leukemogenesis

Debabrata Biswas

CSIR-Indian Institute of Chemical Biology, Kolkata

Human MLL protein is a histone H3-Lysine 4 methyl transferase that positively regulates transcription. Balanced chromosomal translocations between N-terminus of MLL and variety of other fusion partner proteins result in misregulation of transcriptional activation during hematopoiesis that ultimately give rise to acute form of leukemia with a survival prognosis of >2 yrs. Majority of MLL fusion partners presumably reside in large megadalton Super Elongation Complex (SEC) containing AFF1/AFF4, AF9/AF9 family-related protein ENL, either ELL or its isoforms ELL2/3, ELL-1 associated factors 1/2 (EAF1/2), and P-TEFb complex. Since these factors have been described recently, mechanistic understanding of their functional regulation in cellular processes is not well known. Since majority of the cases, full-length fusion partner proteins are fused with N-terminus of MLL, it is conceivable that functional mechanistic understanding of these fusion partner proteins would lead to deeper mechanistic understanding of misregulations caused by corresponding MLL fusion proteins that ultimately result in giving rise to leukemia. With these goals in mind, we have set out our initial journey of mechanistic understanding of transcriptional regulation by Super Elongation Complex which contains majority of MLL fusion partner proteins in a large single complex. In this talk, I would discuss our overall research efforts that have led to novel understanding of transcriptional regulation by SEC components/MLL fusion partner proteins. These new mechanistic understandings have further implications in deciphering the novel roles that MLL fusion proteins could play in giving rise to leukemogenesis.

Inaugural Address

Dr. (Prof.) Randeep Guleria

Department of Pulmonary, Critical Care and Sleep Medicine,
Former Director, All India Institute of Medical Sciences
New Delhi

Air Pollution and Health

Air pollution is known to be detrimental to health and environment since ancient times. There has been a surge of pollutants in the atmosphere due to a rapid increase in urbanisation and industrialisation in the last century. Rapid and unplanned industrialization, especially in developing countries has altered our environment in a negative manner. This led to significant increase in premature deaths and air pollution associated disability associated life years lost (DALY), especially in developing countries such as China and India. Air pollution is now also being linked to many non-communicable diseases and infectious diseases. According to the Global burden of disease (GBD) study (2016), air pollution accounted for 6·4 million (5·7-7·3 million) deaths in 2015. Household air pollution (HAP) from solid fuel use was responsible for 2·8 million (95% UI 2·2-3·6 million) deaths and 85·6 million (66·7- 106·1 million) DALYs. In India alone, it was estimated that more than 1.09 million premature deaths, could be attributed to ambient air pollution. While in India, data shows that the numbers have risen by 24% over the past decade, in China deaths have stabilised, with a 3% drop. The annual deaths attributed to air pollution in India in 2015 alone were more than four times as compared to the European Union. It is estimated that global deaths due to ambient air pollution (AAP) could double by 2050. Moreover, the COVID-19 pandemic data has suggested an increase in mortality due to COVID in areas where pollution levels were high. Thus, air pollution mitigation and control is the need of the hour. Efforts are essential from all levels, be it legislative, administrative, community or individuals. Research is needed to further evaluate the burden of air pollution-related diseases, its effect on the vulnerable population, develop simple and effective methods for measuring air pollution exposure and health risks associated with pollutants released from various anthropogenic sources in our country.

Unravelling and targeting *Plasmodium falciparum* merozoite invasion of human RBCs

Pawan Malhotra

International Center for Genetic Engineering and Biotechnology, New Delhi-110067

Invasion of human RBCs by *Plasmodium* merozoites is a multistep process that involves initial attachment of merozoites to RBCs surface, their reorientation and final gliding into RBCs. *Plasmodium falciparum* possesses a unique gliding machinery referred as glideosome that powers its entry into various hosts. The glideosome machinery lies between the plasma membrane and inner membrane complex (IMC) and consists of Myosine A, Mysosine interacting protein and Gliding associated proteins. Here, we define a new set of proteins associated with *P. falciparum* gliding referred as Photosynthesized INA labeled protein ; PhIL1 and its interacting proteins. We initially characterized Pf & Pb PhIL1 proteins and showed that this protein plays an important role in mosquito stages and exists in a complex. Subsequently, we studied the role(s) of three of the PhIL1 interacting proteins; glideosome associated protein-PfGAPM2, an IMC structural protein, PfALV5 and an uncharacterized protein referred here as PfPhIP (PhIL1 interacting protein) by reverse genetic approaches. Microscopic examination of parasites lacking PfPhIP or PfGAPM2 showed that these parasites were unable to glide or invade host RBCs. Although, we could observe attachment of these parasites to RBCs. Downregulation of PfPhIP in transgenic parasites also showed significant defect in merozoite segmentation. Together, the data presented here showed role of PhIL complex in merozoite gliding into RBCs. Presently, we are targeting some of the *P. falciparum* glideosome proteins. One of the proteins; GAP50 has been the target for a Mtb drug, Bedaquiline. Screening of a number of chemical libraries targeting GAP50 have identified about seven potent inhibitors and one of them MMV688271 is working on *P. falciparum* as well as *Mycobacterium tuberculosis* also. We are presently modifying these drugs to achieve better efficacy and are also trying to identify their respective targets.

Sleep like HIV to win the world!

Udaykumar Ranga

Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru

Transcriptional silence (latency) is the fundamental hurdle to HIV cure. By being silent, HIV escapes the immune system, vaccines, drugs, or any other form of disease intervention. The primary factors responsible for the 'ON/OFF decision-making' of HIV are not yet understood. We will provide three lines of experimental evidence to show that Tat, the master transcription regulatory factor of HIV-1, governs the latency decision. Using reporter viruses encoding GFP and Tat tagged to RFP, we show that Tat intracellular concentrations are not limiting at latency decision. Further, by using infectious viruses, several T-cell lines, and primary CD4 cells, we demonstrate that Tat is present in the latently infected T-cell recruited to the silent viral promoter. Lastly, by constructing a novel 'two-viruses-one-cell' model, we offer evidence that the latency decision is hardwired into the master transcriptional regulatory circuit of HIV-1. Our leads have direct implications for HIV cure research.

Macrophage heterogeneity promotes drug tolerance in *Mycobacterium tuberculosis*

Amit Singh

IISc., Bengaluru

Successful treatment of tuberculosis (TB) depends on eradicating its causative agent, *Mycobacterium tuberculosis* (*Mtb*), in the host. However, the emergence of phenotypically drug-resistant *Mtb* in the host environment tempers the ability of antibiotics to cure disease. Host immunity produces diverse microenvironmental niches that *Mtb* exploits to mobilize adaptation programs. Such differential interactions amplify pre-existing heterogeneity in the host-pathogen milieu to influence disease pathology and therapy outcome. Therefore, comprehending the intricacies of phenotypic heterogeneity can be an empirical step forward in potentiating drug action. With this goal, we discovered the interconnectedness between macrophage bioenergetics and bacterial heterogeneity underlying phenotypic drug resistance. We further examined a few clinically-approved host-directed pharmacological agents that manipulate macrophage metabolism to collapse heterogeneity in bacterial physiology, thereby potentiating the lethal activity of anti-TB drugs. Our findings suggest targeting heterogeneity in host-pathogen encounters to shorten TB therapy time.

Relevance of leukemia stem cells for acute myeloid leukemia

Diana Hanekamp, Lok Lam Ngai, Angele Kelder, **Jacqueline Cloos**

University of Amsterdam Cancer Center, Netherlands
(adapted from: Measurable residual disease and leukemic stem cells in acute myeloid leukemia, Thesis Diana Hanekamp 2021)

Acute myeloid leukemia (AML) is a heterogeneous group of clonal and oligoclonal stem cell disorders with variable response to therapy. Despite risk-directed chemotherapy, better supportive care and recent developments of novel therapies targeting specific genetic lesions overall survival (OS) remains low[1]. Current treatment decisions in AML are strongly dependent on a selected number of clinically relevant cytogenetic and molecular genetic markers at diagnosis[2]. Although the majority of patients achieve complete hematological remission (CR) under current intensive induction chemotherapy, relapse rates remain high[3]. Early detecting or prevention of AML relapse, is a high priority clinical need measurable residual disease (MRD) measurements have largely improved relapse risk estimations after intensive chemotherapy treatment[4]. The ultimate MRD assay would allow discrimination between cells without relapse initiating potential and those that can repopulate a new leukemia. At the basis of this conceptual framework of leukemia initiating cells is the notion that leukemia stem cells (LSC) have the same potential for self-renewal, multidirectional differentiation, unlimited proliferation, resistance to cell death and multidrug resistance as normal hematopoietic stem cells. As such, for further refinement in AML relapse prediction, incorporation of LSC frequency at diagnosis and (perhaps more importantly) in MRD is warranted. Our current characterization of LSCs is based on the principle that healthy tissue-derived hematopoietic stem cells (HSCs) do not express lineage-infidelity antigens, nor overexpress myeloid markers. The antigens aberrantly expressed by LSCs are miscellaneous and include, amongst others: CD2, CD7, CD11b, CD22, CD33, CD44, CD45RA, CD56, CD123, CD366 (TIM3) and CD371 (CLEC12A)[5–7]. The leukemic function of immunophenotypically-defined LSCs has been confirmed by studies demonstrating that AML patient-derived LSCs and HSCs generate leukemic- and multilineage engraftment upon xenotransplantation, respectively[8,9]. Recent studies have correlated high immunophenotypically defined CD34+CD38- LSC frequencies at the time of diagnosis with subsequent poor prognosis[10,11]. We found this relevance of LSC frequency for risk of relapse and poor survival for both adult and pediatric patients. As the definition of LSC includes the CD34+CD38- backbone, these LSC cannot be identified yet in AML cells lacking CD34. Patients with CD34- leukemia have a significantly better OS in adults and children with AML.[12]. Based on these observations, immunophenotypic assessment of CD34+CD38- LSCs frequencies at diagnosis would be a good additional marker for risk classification at diagnosis. Furthermore, identification of these LSCs at diagnosis, could pave the path for promising strategies targeting surface markers for eradication of AML LSCs[13].

As is hypothesized based on the stem cell definition, LSCs are more therapy resistant, and thus likely contribute to the total frequency of MRD cells. Interestingly, we found that the number of LSCs after therapy is an independent predictive factor for relapse[11]. Moreover, patients with both MFC-MRD positivity and LSC-MRD positivity have very poor outcome. It can be suggested that in future clinical studies, allogeneic stem cell transplantations should be considered in specific patient groups both positive for MRD and LSC-MRD after induction therapy.

As presence of any CD34+CD38- LSC was associated with worse outcome compared to patients without LSCs, it is critical that sufficient numbers of cells are acquired. However, as the immunophenotype of LSCs are diverse, and many antigens are needed to fully grasp the total LSC

load[8,13], this is a challenge. Using an antibody panel with higher number of fluorochromes reduces the amount of tubes (and thus cells) needed. Advances in the development of new fluorescent dyes, flow cytometers capable of >20-parameter measurements and analysis software push research toward high-content MFC applications. However, for medical and clinical laboratories the number of fluorochromes is limited by the flow cytometers present. The 8-color LSC-tube (containing 13 different immunophenotypic markers) designed by our group[7] is currently best fit for this, which has also recently been validated by others[14]. The development of a dried ready-to-use version of the LSC-tube, and accompanying protocols for use and analysis significantly contributed in dissemination to other laboratories[15,16]. Within the ELN research group, the feasibility of LSC testing, and the prognostic impact of LSCs detection will now be validated both in adult and pediatric AML. Further studies in the prognostic value of LSC frequencies in follow-up time points, and the combination with MFC-MRD are warranted for this patient group and currently ongoing.

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Leukemias: unanswered questions. Leukemia stem cells: holding the answers?

Dr Tulika Seth

Dept. of Hematology, AIIMS, New Delhi

Leukemias are a varied group of cancers which arise from the hematopoietic stem cells. HSC with chromosomal mutations may develop into leukemia by a multi-step process. Most leukemias are treatable however cure is still elusive for many patients, and the possibility of a relapse is a risk which is ever present even years after treatment. As clinicians we take into account the immunophenotype, cytogenetics and molecular mutations in order to group patients for their treatment into risk groups. However we still find patients who despite adequate treatment, continue to have measurable residual disease, or patients who relapse many years later. We often cannot explain these scenarios. Leukemia stem cells (LSCs) also develop as a result of chromosomal abnormalities or mutations, they have been identified in patients even before the development of leukemia and play a role in the etiology of leukemias and have an important role in causing their relapse. This is because the stemness properties of dormancy, replication make these LSCs resistant to most chemotherapy and even many targeted treatments for the leukemias. LSCs reside in a highly specialized micro-environment within the bone marrow. There are complex interactions between the leukemic stem cells and their microenvironment. Expanding knowledge of our understanding of the LSC gene expression profile and phenotype has helped in studying their role in different types of leukemias and different patients groups. By understanding of the nature and role of the microenvironment, LSC and immune signatures, we may have a better understanding of prognosis, deeper knowledge of risk stratification. They may also yield potential therapeutic targets. Yet many questions remain unanswered and research on leukemic stem cells is required to develop more effective targeted treatments and prevent relapse.

Immune interaction in brain injury: what we know so far

Vaibhav Kumar

University of Augusta Georgia, USA

Brain injury such as traumatic brain injury (TBI) and stroke are major causes of neurodegeneration and dementia. Acute inflammation as a result of impact or hemorrhages leads to brain pathology, ventricular changes, edema and BBB damage. It has been seen that patients and animal models display the signs of both local and systemic inflammation post-injury. We have shown that brain injury leads to increased peripheral immune cells migration into injured brain. We further reported that modulating these immune cells in alternatively polarized state helped brain to recover faster from initial injury cascade. One of the important homeostasis system in neuroinflammation is cannabinoids system. Our lab has shown modulating CB receptors help to minimize inflammation. Recently, we observed that brain after injury shows chronic mild inflammation that may drive senescence and inflammaging. In conclusion, brain injury poses a risk of sustained inflammation and expedited senescence. Therefore, timely intervention with adjusted therapeutic measures at various time point in the progression of pathology should be adopted to help individual patient.

Keywords: Brain injury, Inflammation, Senescence, Inflammaging, Cannabinoid, Immune cells

Quercetin Attenuates Neurological Complications Associated with Chronic Diabetes

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Diabetes mellitus (DM) is a complex progressive metabolic disorder arising from variety of pathogenic mechanisms, genetic or environmental, resulting in hyperglycemia. Neurological complications associated with diabetes affects the quality of life of the diabetic patients. We evaluated the effect of Quercetin under stress induced prediabetic and STZ induced chronic diabetic condition and its neurological complications in an experimental animal model. Results showed that Quercetin treatment improved hyperglycemia, glucose intolerance, attenuated Insulin Resistance and behavioral dysfunction. Behavioral deficits in diabetic animals were attributed to hyperglycemia mediated enhanced hippocampal oxidative stress, neurodegeneration and impaired neuronal insulin signaling, which were attenuated by Quercetin treatment. Further, Quercetin upregulated the neuronal insulin signaling pathway and enhanced GLUT4 expression, independent of insulin and InR. In conclusion, Quercetin may find a clinical application in managing neurological complications associated with T2DM and IR by activating neuronal insulin signaling pathway.

Role of TXNIP in Brain Aging and Alzheimer's Disease

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Aging is the greatest risk factor for dementia and Alzheimer's disease (AD). Recent findings indicate that thioredoxin interacting protein (TXNIP), an inducible protein involved in oxidative stress and aging, is essential for NOD-like receptor pyrin domain containing-3 (NLRP3)-inflammasome activation. The NLRP3-inflammasome essentially connects "inflammaging" to senile cognitive decline. According to our preclinical studies cerebral TXNIP was significantly upregulated in aged animals, associated with the NLRP3-inflammasome over-activity in both sexes, and closely linked to klotho depletion in males. TXNIP knock-out reversed age-related NLRP3-hyperactivity and enhanced thioredoxin (TRX) levels in aged brains. Further, pharmacological TXNIP inhibition replicated the TXNIP/NLRP3-inflammasome downregulation in aged animals, with FOXO-1 and mTOR upregulation. These alterations concurred with substantial improvements in both cognitive and sensorimotor abilities. Moreover, our immunostaining shows a significant increase of TXNIP/NLRP3-inflammasome activity in transgenic 5XFAD mice and AD human postmortem hippocampal specimens, supportive of potential mechanistic links between TXNIP and AD. Together, these findings unravel new information about upstream pathways in age-associated neuroinflammation.

Development of aptamers as therapeutic agents for C9 ALS-FTD

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Frontotemporal dementia (FTD) is the second most common origin of pre-senile dementia occurring due to neurodegeneration of frontal and anterior temporal lobes in the brain. It is also referred to as semantic dementia. Amyotrophic lateral sclerosis (ALS) results from degeneration of motor neurons leading to progressive muscle weakening. However, several overlapping characteristics have been identified in the two disorders, which has led to the proposal that these two diseases represent a broad spectrum of the same family of diseases. This hypothesis has gained support from the observations that the two diseases are often reported in the same family and the inheritance pattern of the disease cannot be explained by the unique genetic defects associated with each disease. Expansion of the GGGGCC hexant in the non-coding region of *C9ORF72* gene, either in the promoter or intronic region, has been identified as the most common cause of ALS-FTD. This expansion results in some characteristic pathophysiological symptoms associated with C9 ALS-FTD. Three major disease-relevant consequences, which may not be mutually exclusive, have been proposed: (i) haploinsufficiency (loss-of-function), (ii) sequestration of RNA-binding proteins (gain-of-function), and (iii) toxicity due to dipeptide repeat (DPR) proteins (gain-of-function). Studies have been carried out in the laboratory to inhibit aggregation of DPR proteins using RNA aptamers. Specific and high affinity aptamers were selected against the expanded polynucleotide sequence coding for DPR proteins. These aptamers were able to inhibit aggregation of the target protein *in vitro* as well as in a cell model of C9 ALS-FTD. Inhibition of protein aggregation led to restoration of function of C9ORF72 and improved cell survival. The results obtained show that aptamers can be explored as viable therapeutic agents against this devastating neurological disorder.

Dynamic Homo- versus Hetero-Oligomerization Drives the Thermo-Osmo Responsiveness of Enterobacterial Sensory Proteins

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Environmentally regulated gene expression is critical for bacterial survival under a variety of conditions including extremes in temperature, pH, osmolarity and nutrient availability. Sensing the environment is orchestrated by macromolecules with diverse underlying mechanisms - e.g. changes in protein oligomerization status or DNA superhelicity - that eventually result in the repression or expression of genes in a finely tuned manner. In this talk, I will focus on our attempts to understand the molecular mechanisms of thermo- and osmo-sensing by Cnu and H-NS, two classic sensory proteins ubiquitous in enterobacteria. Employing an array of experimental spectroscopic, calorimetric, hydrodynamic methods and computational modeling we show that H-NS in particular exhibits a large degree of heterogeneity in its helical content and oligomeric nature with osmolarity- and concentration-dependent populations of monomer, dimer, tetramer and octamer. This in turn drives a competition between homo- versus hetero-oligomerization of protein-protein and protein-DNA complexes as a function of osmolarity, temperature and monomer concentration. The dynamic ensemble of these different species effectively drives the stress response behavior and genomic compaction in enterobacteria.

Metal cofactor Zn and interacting membranes modulate conformation-aggregation landscape in SOD1

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Aggregation of SOD1 is the hallmark of motor neuron disease, ALS. About 140 point mutations of SOD1 are associated to fALS. A molecular mechanism linking their stability, aggregation propensity, membrane attachment and disease progression is yet to be established. To investigate this missing link, we used WT, a Zn deficient H72F, a Cu deficient H121F, and Apo protein variants to show that the loss of Zn, and not Cu, influenced membrane association through two loop regions. Conformational change induced by loss of Zn facilitates membrane attachment and triggers aberrant aggregation. These loop regions influenced both Cu intake (the primary function) and aggregation (the gain of function) of SOD1 presumably through a shared landscape. It was also observed that the fibrillar aggregates formed in the presence of membrane inflicted higher toxicity compared to the aggregates formed in absence of membrane. We established here a 'co-factor derived membrane association model' which suggested that mutational stress closer to Zn binding site is responsible for membrane attachment associated toxic gain of function which was confirmed by studying the aggregation kinetics of two disease mutants G37R and I113T in absence and presence of membrane environment. All together our study showed, for the first time, a nice correlation between the membrane binding propensity of the disease mutants based on the variation in their metal contents and mutational stress points with the progression of neurodegenerative disease ALS.

Past and Future in Structure-Based Drug Discovery to identify Lead Compounds

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Within the presentation past and latest methods in Structure based Drug Discovery will be summarized comparative, and procedures to identify effective lead compounds, applying high-throughput X-ray screening. A particular focus will be on new approaches utilizing re-purposing compound data banks [1,2,3]. Structure based Drug Discovery is contributing substantial to the field of drug design for some decades by now, mainly through analyses of the three-dimensional structures of infection-relevant biomolecules and complexes with potential drug lead-molecules, a prerequisite for structure-based development of new anti-infectives. Humanity is facing these days an increasing health threat caused by a variety of multidrug resistant bacteria, parasites [4], and in parallel by already well known and more recent also via emerging viruses, such as SARS-CoV-2. The last, devastating and causing during the last two years extreme high numbers of infections and even death. In this context and considering the growing shortage of new and effective drugs to treat such infectious diseases it is required to identify and optimize new compounds or, or better in parallel to re-investigate the potential of natural compounds in time, which can be applied, or optimized to treat infectious diseases in the near future [5]. In terms of the presentation methods, procedures and results of atomic resolution X-ray structure analysis will be presented and discussed. Highlighting particular the more recent structure based approaches applying drug re-purposing, a method in favor for screening the effectiveness of already approved drugs against a new target molecule, drugs and compounds which have already marketing authorization or are licensed for human use to treat a particular health condition.

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Structural based 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 *L. donavani*, *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, JSB, 2019, IJBM, 2019), as well as the structures of some of their homologues from other organisms for comparative studies (Acta D, 2012; BBA, 2014, Febs J, 2017, Biochem J 2017, Mol Microbiol 2019). We have reported initial inhibitor development (lead like molecules) against the one of the enzyme (OASS) from *E. histolytica* (PLoS One, 2011, Eur J Med Chem, 2020) and been involved in developing high affinity inhibitors and screening for other enzymes. The high affinity inhibitors shown to 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.

Molecular pathways for non-enveloped capsid disassembly

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The capsid shells of non-enveloped viruses are symmetric, stable containers for protecting and transporting viral genome inside host cells. In spite of the symmetry and stability, dynamic behavior of capsid components is expected during cellular entry or disassembly related conformational alterations. We are utilizing a combination of molecular dynamics simulations and cryoelectron microscopy to understand the dynamic behavior of a non-enveloped insect RNA virus – Flock House Virus (FHV) – a model system for non-enveloped viruses. MD simulation of the whole capsid indicates that there are striking differences in the flexibility of sequentially identical capsid proteins occupying different positions in the icosahedral asymmetric units of the capsid, which is consistent with previously described biological behavior. The capsid shell is permeable to the bidirectional movement of water, with the location of water tunnels within the capsid being influenced by the capsid geometry. Certain pathways are more permeable to water than others, indicating the possibility that these may be exploited for genome release. Biochemical and structural studies of two disassembling states of FHV also indicates the involvement of the 2-fold axis in genome release. One of the intermediate structures has been resolved using cryoelectron microscopy to 4.5 Å, and appears to be significantly asymmetric in nature, with icosahedral details preserved in only one half of the capsid. There are significant conformational alterations at the capsid axes of symmetry, however, the release of genome appears to occur from the vicinity of one specific 2-fold axis of symmetry of the capsid. The structures of these intermediates, in conjunction with whole capsid simulation studies, are expected to provide a molecular roadmap for non-enveloped virus structural dynamics.

Neuroinflammatory pathways in epilepsy as treatment targets and biomarker candidates in epilepsy

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Epilepsy is a chronic neurological disease characterized by an enduring propensity for generation of seizures. The pathogenic processes of seizure generation and recurrence are the subject of intensive preclinical and clinical investigations, as their identification would enable development of novel treatments that prevent epileptic seizures and reduce seizure burden. Such treatments are particularly needed for pharmacoresistant epilepsies, which affect ~30% of patients. Neuroinflammation is commonly activated in epileptogenic brain regions in humans and is clearly involved in animal models of epilepsy. An increased understanding of neuroinflammatory mechanism in epilepsy has identified cellular and molecular targets for new mechanistic therapies or existing anti-inflammatory drugs that could overcome the limitations of current medications, which provide only symptomatic control of seizures. Moreover, inflammatory mediators in the blood and molecular imaging of neuroinflammation could provide diagnostic, prognostic and predictive biomarkers for epilepsy, which will be instrumental for patient stratification in future clinical studies. In my talk, I focus on as our understanding of the IL-1 receptor–Toll-like receptor 4 axis, the arachidonic acid-prostaglandin cascade, oxidative stress and TGF-β signalling associated with blood–brain barrier dysfunction, all of which are pathways that are activated in pharmacoresistant epilepsy in humans and that can be modulated in animal models to produce therapeutic effects on seizures, neuronal cell loss and neurological comorbidities.

A multi-target based novel combinatorial approach to dominantly restrict human Tau mediated neurotoxicity in Drosophila disease models

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Human neuronal tauopathies such as Alzheimer's, Parkinson's, Pick's disease(s) etc. are group of neurodegenerative disorders characterised by abnormal tau hyperphosphorylation resulting in formation of toxic paired helical filaments (PHFs) and neurofibrillary tangles (NFTs) in specific areas of brain. Despite several attempt being made; the definite cause of these disorders remains elusive, mainly because of complex disease traits and limitations associated with the human genetics. We have reported earlier that tissue specific downregulation of dmyc (a Drosophila homologue of cmyc proto-oncogene) constrains NFTs mediated tau pathogenesis. Further, in order to unravel the mechanistic insights, our findings suggest a vital role of gsk3β in conferring the dmyc mediated rescue against tauopathies. We noted that adequate expression level of shaggy in essential for the maintenance of the rescue efficacy of dmyc against tauopathy. It was further observed that shaggy works downstream of dmyc to control the phosphorylation status of tau during the disease pathogenesis. We propose that dmyc mediated rescue of human neuronal tauopathies functions via gsk3β (a potent tau phosphorylating kinase). For the first time, our study provides novel molecular insights about the role of gsk3β in tau aetiology which will help in development of combinatorial drug(s) against the devastating human neurodegenerative tauopathies.

Differentiation of peripheral blood mononuclear cell (PBMC) into tyrosine hydroxylase expressing Dopaminergic neurons for cell replacement therapy in Parkinson's disease

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Parkinson's disease (PD) is a complex neurodegenerative disease where the progressive loss of dopaminergic neurons (DA) in the substantia nigra pars compacta leads to the motor deficit and cognitive decline. There is no definitive cure for PD, and current therapeutic strategies only alleviate the symptoms. However, it may be possible to compensate for the loss of neurons by replacing the lost DA neurons with cell therapy. But the isolation of autologous DA neurons from patients' brains is not feasible, and allogenic transplants are associated with further immune complications. Adult stem cells hold the potential for autologous cell therapy as they can differentiate into multiple cell lineages. As an easy-to-isolate and clinically feasible stem cell source, peripheral blood mononuclear cells (PBMNC) seem ideal for generating autologous DA neurons. The current study used a biomimetic niche to induce rat blood-derived PBMNCs to TH+ve DA neurons and evaluated the potential for cell transplantation. Density gradient centrifugation was used to isolate PBMNCs from adult rat blood, and the isolated cells were then induced to DA neurons on a biomimetic niche containing a fibrin matrix and soluble growth factors. The differentiation was confirmed based on specific DA neuronal markers using immunocytochemistry, western blotting, RNA sequencing and ELISA. The gene expression analysis using qPCR showed significant upregulation of neuronal genes and down-regulation of blood lineage genes. Similarly, immunofluorescence analysis indicated high expression of neuronal markers β-III tubulin, Nurr1, Tuj1, Tyrosine Hydroxylase (TH), Dopamine transporter and Synaptophysin in induced cells. Tyrosine Hydroxylase expression was further confirmed by Western blotting. The dopamine production was confirmed on Day 12 and Day 21 using ELISA, with increased dopamine production on day 21. The gene expression analysis confirmed the upregulation of the DA precursor marker on Nurr1 on day 4, which will be transplanted to rat 6-hydroxy dopamine unilateral lesion models in a fibrin matrix for evaluating the clinical translation potential of these cells.

Ethics Statement: Handling of SD rats was carried out in strict accordance with the guidelines of the Institutional Animal Ethics Committee (IAEC) and Centre for Committee for Control and Supervision of Experiments on Animals (CPCSEA), India

Acknowledgments: This work was supported by Kerala State Council for Science and Technology (KSCSTE) and CUSAT plan fund.

Chemical Chaperones in Theragnostic using Nuclear Technology

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To develop smart and specific tracers to investigate *in vivo* topography, and connections and titration of biochemical's non-invasively using imaging techniques are essence of time in diagnosis and therapy or to use it in the combination as theragnostic. Our ongoing efforts are to innovate and translate multimodal molecular pharmaceuticals of broad interest in health care through state of art construction of chemical chaperons. Imaging probes are a special class of tracers that are used in conjunction with imaging techniques such as MRI, CT, and nuclear imaging (PET and SPECT), allowing healthcare practitioners to see disease and injuries in a non-invasive way. In the post genomics era, there is the opportunity to advance probes to the point where they can target specific biochemical signatures associated with disease. Because changes in biochemistry occur before diseases reach an advanced stage, molecular imaging probes will foster earlier and more personalized diagnosis of disease. Our Lab is focused on bringing the power of modern synthesis to bear on the development of molecular imaging probes and agents. These probes and agents are being developed to visualize specific molecular targets and pathways in live cells, tissues and organism (from plants, mouse to human). The specific aim is to 1) design and synthesize new imaging probes/agents, 2) develop and use novel amplification schemes for the development of 'next generation' imaging probes, 3) optimize pharmacokinetics and 'imagability', 4) efficiently synthesize and produce complex and diverse small molecules, and test their ability as imaging agents. To design and synthesis the next generation of imaging probes/agents for MRI, PET and SPECT, and optical imaging is the core mandate of our research lab.

Designing Allosteric inhibitors for PfCDPK1 by combining atomistic simulations with machine learning

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The talk would give an overview of the studies to investigate the role of the CAD domain in the activation mechanism of calcium dependent protein kinase-1 of *Plasmodium falciparum* (PfCDPK1) and explore the possibility of allosteric inhibition of this kinase (1). PfCDPK1 belongs to CDPK family of apicomplexan kinases which have a C-terminal CAD domain. Microsecond scale MD simulations were performed on modeled structures of complete PfCDPK1 and its kinase domain alone. The simulations revealed that in absence of CAD the salt bridge between Glu116 in αC-helix and Lys85 in β3-sheet of kinase breaks after 200 ns resulting in inactive conformation of the kinase, but the salt bridge stays intact in the complete protein stabilizing it in active conformation. These results highlight the novel CAD mediated allosteric stabilization of the crucial salt bridge which is a hallmark of active conformation of kinase domains. The mechanistic details of the allosteric activation revealed by our study, opens up the possibility for design of allosteric inhibitors of PfCDPK1 kinase by disrupting the kinase:CAD interactions. Using a combination of machine learning and structure-based *in silico* screening, we have identified novel PPI modulators for allosteric inactivation of PfCDPK1 kinase.

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Understanding DNA Sequences with Artificial Intelligence

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Artificial Intelligence has achieved state of the art performance across areas such as text, vision, time series, and multimodal biomedical datasets. In this talk, I will outline how new generation AI architectures such as Transformers can help understand the mutations in DNA sequences, thus helping better drug discovery for infectious diseases. I will use COVID-19 as an example, and our recent work, "Strainflow" and "Strainformer" models for sequence to biological and epidemiological predictions.

Therapeutic Targeting of Metabolic Reprogramming in Glioma

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Aerobic glycolysis or the Warburg effect, is a hallmark of glioma. However the complete understanding of the regulatory mechanisms associated with this metabolic reprogramming is incomplete. Based on this background we analysed clinical glioma samples and cell lines and demonstrated that miR-101 expression was downregulated in both human glioma tissues and cell lines. The overexpression of miR-101 inhibited glioma cell proliferation, induced cell cycle arrest and induced apoptosis. The inhibition of the miR-101 facilitated cell proliferation , cell cycle transition and suppressed apoptosis. Our results revealed miR-101 expression was inversely correlated with CDK8 expression in glioma tissues and cell lines. CDK8 was confirmed to be a direct target of miR-101 by using a luciferase reporter assay. The overexpression of miR-101 decreased CDK8 expression at both the mRNA and protein levels, and the suppression of miR-101 increased CDK8 expression.CDK8 inhibition impaired glucose transporter expression, glucose uptake, glycolytic capacity and reserve, as well as cell proliferation. Furthermore, CDK8 impairment sensitized glioma cells to pharmacological glycolysis inhibition. CDK8 silencing recapitulated the cellular and molecular effects observed upon miR-101 overexpression, and CDK8 overexpression eliminated the effects of miR-101 overexpression on glioma cells. In conclusion our study demonstrates that miR-101 inhibits glioma cell proliferation and induces apoptosis through targeting CDK8 associated glycolysis. These findings suggest that miR-101 plays a significant role in glioma progression and could possibly serve as a potential therapeutic target for glioma

miR-210: An attractive target for cancer therapy

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Hypoxia is a regular feature of the GBM tumor microenvironment and correlated to increased tumor proliferation, migration, invasion and therapy resistance thus, leading to poor prognosis. The molecular mechanisms responsible for the hypoxic survival of neoplastic cells are not well characterized, however it is widely agreed that a better understanding of this process may lead to novel approaches for pharmacological intervention. MicroRNAs (miRNAs) have emerged as critical mediators of hypoxic response and have shown great potential for cancer diagnostics and therapeutics. Using small RNA sequencing approach we identified microRNA signature of hypoxia in glioblastoma (GBM), a highly malignant and hard to treat brain cancer. We studied the roles of hypoxia regulated miRNA- miR-210 in GBM. We found that miR-210 is overexpressed in GBM patients and correlates to negative prognosis. It makes the tumor cells more aggressive by promoting cell proliferation, migration and inhibiting apoptosis. We further unveiled that several tumor suppressive genes are directly regulated by miR-210. We also established that delivery of anti-miR-210 oligos using a cell penetrating peptide not only had a strong anti-cancer effect but also sensitized GBM cells to chemodrug, temozolomide mediated death. Overall, we show miR-210 inhibition may serve as an attractive approach for GBM treatment.

SWASTIIK Technology- Exploiting knowledge of Ayurveda for water disinfection and for possible health benefits

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Ancient Indian literature has vast resources of knowledgebase, and Ayurveda is especially important for health benefits and for naturally protecting ecology and environment. A large number of natural oils, having antimicrobial properties, can be used aptly using modern technologies such as hydrodynamic cavitation for providing safe drinking water that is necessary to prevent occurrence of large number of waterborne diseases; highly important for India. We, at CSIR-NCL have developed a water disinfection technology, SWASTIIK- Safe Water and Sustainable Technology Initiative from Indian Knowledgebase, that can provide safe and possibly healthy drinking water at low cost with substantial ease of operation, scale-up and without harmful disinfection by-products by using a hybrid hydrodynamic cavitation technology. The disadvantages of the commonly used chlorination process, that generates harmful carcinogenic disinfection by-products, can be overcome by the use of SWASTIIK with cost-competitiveness (treated water @ ~0.25 Paisa per liter). Both, harmful gram-negative (*Escherichia coli*) and gram-positive (*Staphylococcus aureus*) bacteria and also antimicrobial resistant (AMR), gram-positive methicillin resistant, *Staphylococcus aureus* and relatively less researched, gram-negative opportunistic pathogen, *Pseudomonas aeruginosa* can be effectively eliminated within minutes. We have researched the effectiveness using some of the most commonly used natural oils such as clove oil, peppermint oil etc. in conjunction with hydrodynamic cavitation. The mechanism involves cell destruction through the rupture of cell wall, oxidative damage and possible DNA denaturation. It is imperative that the extent and the exact nature of the health benefits with different types of natural oils be ascertained and validated by the medical fraternity, since developing sustainable engineering/ technological alternative to the existing technologies is crucial to life -not just for the increased disinfection efficiency but also to possibly alleviate/ eliminate health hazards or provide additional health benefits, crucial in the COVID era.

Exploration of biosynthetic potential for new therapeutic molecules and nutraceuticals with aim to provide new targeted chemotypic variants in Ocimum basilicum: validations through genomics

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Plants produce a vast quantity of diverse chemicals required for their performance. These include primary and secondary metabolites. Primary metabolites are required for the growth and biological processes and are crucial for plant survival, on the other hand, secondary metabolites are very specific and required for their ecological perception. These are the active constituents present in different parts of the plants with immense biological properties and gradually elevated from their traditional claims to modern medicinal necessities. In this relevance, these phytochemicals may be reappraised methodically by scientific validations monitoring their efficacy as well as safety along with biodiversity augmentation, planned growth and processing. India has a unique position worldwide for recognized traditional systems of medicines, the AYUSH have collated around 8,000 herbal remedies from diverse group of natural resources. Ayurveda, an ancient health care system, which was evolved in India about 5,000 years ago have been used successfully for the management of various diseases like bronchial asthma, chronic fever, cold, cough, malaria, dysentery, convulsions, diabetes, diarrhoea, arthritis, skin diseases, insect bite, gastric, hepatic, cardiovascular and immunological disorders. The advantages claimed for therapeutic uses of medicinal plants are their safety besides being cost-effective, availability and effectiveness. The chemotherapeutics from MAPs established herbal therapies, although synthetic drugs enhanced the demand against green remedies because of their rapid-acting implements. Nowadays, research mainly focused on exploring the potential of plant metabolites for curing several diseases by inhibiting the initiation or propagation of oxidative chain reactions by counteracting the reactive oxygen species (ROS) and free radicals during regular metabolism. In Ayurveda, Tulsi (Ocimum spp.) has been well documented for its therapeutic potentials and described as Dashemani Shwasaharni (antiasthmatic) and antikaphic drugs (Kaphaghna). Although this medicinal plant has been used for management of various disease conditions from ancient time but not much is known about the mode of action of Tulsi, and a rational approach is required for establishing this traditional medicine in modern system of therapeutics. Several studies have been carried out to suggest the role of essential oils and their constituents for therapeutic potentials. The essential oils have also been observed to possess membrane stabilizing properties on synaptosomes, erythrocytes and mast cells which account for the therapeutic potentials of Tulsi in management of neurological, inflammatory. allergic disorders. Ocimum basilicum also used in the treatment of gastric ulcer, lowering of uric acid level, as an immune stimulant claiming the therapeutic potential of Ocimum spp. The essential oils extracted from Tulsi leaves possess anti-fungal and anti-viral activity. In contrast to other sources Ocimum basilicum are cheaper sources for commercial extraction of specific metabolites like Linalool, Chavibetol and Eugenol. The estimated global herbal industry is valued at US$ 40 billion mainly in the form of pharmaceuticals growing at 7% per year. Agro-biotechnology aids to increase the biosynthetic ability of nutra-pharmaceutical crops and to produce commercial biopharmaceuticals, functional proteins and edible vaccines in-planta. Research targets are focused on identifying the genes involved in the biosynthesis of secondary metabolites, to be used for treatments of diseases and disorders. Metabolic control through genetic manipulation is the key to regulate biosynthetic pathways. The genetic engineering has led to large-scale biosynthesis of natural products. Harnessing the genetic potential of basil through application of biotechnology is still at infancy. With the availability of genome sequences and understanding of genetic control, basil could be designed to produce diverse metabolites as per the requirement. Basil genotypes with the higher percentage of linalool, chavibetol, eugenol could be utilized in cosmetic perfumery, chewing gum, pan masala, mouth wash, mouth freshener, aromatherapy, antioxidant, antiaging, chest infections also traditional and therapeutic purposes. In view of its importance, there is a need to develop a better adaptable variety at CSIR-CIMAP for diverse metabolites. This will add to the farmers and industries, which are dependent upon the bioactive constituents to formulate value added industrial products. Metabolomics could contribute significantly by identifying targeted by-products of yield metabolism. System biology approach and biotechnology strategies could be used potentially to unravel the potential for exploring novel molecules in Basil. The understanding of the mechanism of action of these bioactive principles has introduced new vistas of scientific methods for the modernization and standardization of several medicines at the genetic level. Newer approaches and insights through scientific validations led to development of abundant traditional remedies and drug discovery systems, which will make an immense impact on the biomedical science.

Cardiovascular disease in the Genome era

Dhavendra Kumar

Consultant in Clinical Genetics and Genomic Medicine, The Genome Clinic, Spire Cardiff Hospital, UK:

Amongst the non-communicable diseases, the enormous burden of cardiovascular disease (CVD) is globally acknowledged. The World Health Organization and many other leading health groups have successively put the CVD as the leading cause of morbidity and mortality. Historically, recurrent advances in bio-medical science have set several benchmarks in the diagnosis, treatment and prevention of CVD. Since the completion of the Human Genome Project (2003) and the beginning of the Genome Era, the practice of modern medicine has revolutionised with the emergence of genomic and precision medicine. Genomics led precision diagnosis and treatment are now available across the broad spectrum of human disease, particularly birth defects, childhood metabolic diseases, CVD, cancer, neuro-psychiatric disorders, immunological diseases, and more importantly the communicable diseases. The modern cardiovascular genomic medicine offers precision diagnosis, treatment and prevention of broad range of common and rare heterogeneous CVD with judicious applications of genomic diagnosis, stratified and precision therapy and targeted prevention. Some of the key genomic advances in CVD include congenital heart defects, coronary artery disease, hypertension, heart failure, cardiac arrest, and the cardiovascular involvement in systemic diseases like obesity, type 2 diabetes mellitus, chronic kidney disease and chronic lung disease.

Endothelial progenitor cells in cardiovascular disease

R. Lakshmy

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Endothelial dysfunction is involved in cardiovascular diseases and is known to be caused by risk factors like diabetes, dyslipidemia, smoking, aging and hypertension. Restoration of damaged entholium has the potential to prevent the progression of atherosclerosis. It was believed that the damaged endothelium is repaired by adjacent endothelial cells until in late 90's it was shown that endothelial progenitor cells (EPC) derived from bone marrow can aid in EC regeneration. The circulating EPC number and function is a surrogate marker for vascular function and cumulative cardiovascular risk and strong predictor of cardiovascular events. EPCs are defined as either early and late EPCs based on their biological properties and their time of appearance during in vitro culture. Recent studies have suggested that early EPCs are not directly involved but only support angiogenesis through paracrine signals whereas that late EPCs also known as endothelial colony forming cells (ECFCs) are the only known endothelial precursor and are directly involved in the process of neovascularization or reendothelization 11 and therefore may be more relevant to study in the context of vascular diseases. Nitric oxide (NO .) is critical for functionality of endothelial colony forming cells (ECFCs). Dimerization of endothelial nitric oxide synthase (eNOS) is must to produce NO and tetrahydrobiopterin (BH4) plays a crucial role in stabilizing this state. We investigated BH4 level in ECFCs and its effect on ECFCs functionality in CAD patients. We observed that ECFC from CAD patients were less proliferative and showed impairment in migration as seen by delayed wound healing capacity in vitro and significant decline in angiogenesis potential as compared to ECFCs from healthy controls. A significant association between ECFC BH4 levels and its wound healing capacity and angiogenesis potential was observed. The talk will focus on role of EPC in cardiovascular diseases and specifically the results of our study on the late EPCs and their functionality in CAD patients.

Art of war against cardiovascular disease

Vivek Chaturvedi

Amrita Institute of Medical Sciences, Faridabad

Cardiovascular diseases are a major cause for death and disability in India. Community based prevention efforts should be the primary and major focus for tackling this enormous burden. However, there is a need to develop effective and resource sensitive management strategies for the large number of people who have pre-existing cardiovascular diseases. In this presentation we discuss the recent advances in management of cardiovascular diseases. Many of them have been made possible with cutting edge technology and scientific discoveries. These include new drugs for heart failure, dyslipidemia, ventricular assist devices, ablation for atrial fibrillation, etc. Equally important, many advances have happened by introspection and repurposing of older tools and drugs, and their active scientific validation. These include use of colchicine, acetazolamide, left bundle branch area pacing, and cervical sympathectomy. Also, many advances have been simply a change in diagnostic strategies, that have translated to real gains in cardiovascular disease management. These include blood pressure measurement, use of natriuretic peptides, ICD use for primary prevention, etc. Finally we outline our philosophy and approach for treatment of heart diseases in the Indian context. We also discuss the urgent unmet need for developing locally context specific technologies.

Valedictory Address: **4:50 – 5:45 PM.**

Prof. Sudhanshu Vrati

Rotavirus vaccine development: The India story

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Rotavirus is the leading cause of diarrhoea-associated hospitalisations and deaths in developing countries, estimated to account for approximately 610,000 deaths annually. It is a particularly important problem in India where nearly one-fourth of these deaths occur and it is estimated that about 1 child in 250 in India will die of this disease. Accordingly, development of vaccines for rotavirus infections has been accorded high priority. As part of the Indo-US Vaccine Action Program, a Department of Biotechnology (DBT), Government of India sponsored activity to promote new vaccine development, two rotavirus strains were identified that demonstrated interesting properties as potential candidate vaccines. These strains were obtained from outbreaks of asymptomatically infected newborns in Delhi (116E) and Bangalore (I321). Having undergone the phase I and II, safety and immunogenicity studies, a randomised double-blind, placebo-controlled, multicentre trial of 116E vaccine was conducted at three sites in Delhi (urban), Pune (rural), and Vellore (urban and rural) that enrolled 6799 infants aged 6-7 weeks. The incidence of severe rotavirus gastroenteritis per 100 person-years was 1·5 in the vaccine group and 3·2 in the placebo group. Prevalence of immediate, solicited, and serious adverse events was similar in both groups. These studies demonstrated that the monovalent human-bovine (116E) rotavirus vaccine was effective and well tolerated in Indian infants. Having established the safety and efficacy, the 116E rotavirus vaccine 'Rotavac' produced by BBIL, Hyderabad was launched for commercial use. The vaccine has since been prequalified by the World Health Organization.

ORAL PRESENTATIONS

SESSION I: GENETICS AND EPIGENETICS OF HUMAN DISEASES

Oral Presentation-1

Elucidating the functional relevance of *Sin3B* spliced variants in pathogenesis of Oral Squamous Cell Carcinoma

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Head and Neck Squamous Cell Carcinoma is the sixth most common cancer worldwide developing from mucosal epithelium in the oral cavity, pharynx, and larynx. By 2030, the incidence rate is anticipated to increase by 30%. With no absolute treatment options, there is a need for new biomarkers and revolutionary treatment strategies to address the urgent clinical need in fighting the disease. Alternative splicing of pre-mRNA is described as an important molecular event allowing protein diversity. Although, it is common in normal cells; evidence suggests that aberrant splicing contributes to a number of diseases including tumoral transformation. Sin3B, also known as a master scaffold is responsible for transcriptional gene repression through chromatin-modifying complexes. Thus, resulting in regulation of important biological processes such as genomic stability, cell cycle progression, homeostasis and embryonic development as a result of its interaction with vast number of repressors and co-repressors leading to modulation of transcription and chromatin structure. Our study suggests the presence of a novel alternatively spliced form of Sin3B in several transformed cell lines and oral cancer tissue samples. We observed the presence of alternatively spliced forms of Sin3B mRNA in some malignant and premalignant cases of oral carcinoma and a few mammalian cell lines connoting the importance of their presence only in the transformed phenotype. This spliced form was found to be strongly expressed in the later stage cancer as compared to early stages suggesting a role in cancer development and progression. The functional relevance of these different spliced forms indicate a possibility for therapeutic implication.

SESSION II: IMMUNITY AND INFECTION

Oral Presentation-2

Investigations on the Immunological Roles of Host Derived Heat Shock Proteins during Mycobacterial Infection

Shakuntala S. Saraswati[1], Ankush Kumar Rana[1], Aayushi Singh[1], Vandana Anang[1], Chaitenya Verma[1], Aarti Singh[1] and Krishnamurthy Natarajan[1]

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Tuberculosis (TB) infection caused by *Mycobacterium tuberculosis (M. tb)* is responsible for around 2 million deaths annually. Drug development and targeted immunotherapy against TB is an urgent need of the hour. Mycobacteria is known to modulate host immune responses for its survival and pathogenesis. Study of host pathogen interactions is important for better understanding of the mode of pathogenesis and controlling the infection. HSPs are stress proteins that help the living system to cope up with various kinds of stresses and also help in the generation of immunological responses. We investigated the role of HSPs in regulating key defence responses to mycobacteria mounted by macrophages. Our study indicate that mycobacteria upregulates the expression of HSP-27 and HSP70. Inhibiting HSPs prior to Mycobacterial infection decreases the bacterial survival in macrophages, increases oxidative burst and induces autophagy and apoptosis. Further, HSPS also associate with critical proteins in the autophagic and apoptotic pathways. These results point towards a unique strategy of mycobacteria to use the host cellular machinery for immune evasion.

Oral Presentation-3

Rational designing of Peptide-Ligand Conjugates for the treatment of complicated malaria

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Complicated malaria is associated with the sequestration of *Plasmodium falciparum*-infected erythrocyte (*Pf*IE) in the capillary microvasculature and is majorly responsible for malaria mortality. In this study, we attempted the *in silico* designing of peptide-ligand conjugates (PLCs) based immunotherapeutic molecules, the first of its kind, for treating complicated malaria. In a nutshell, we target the erythrocyte membrane protein 1 (*Pf*EMP1) that is expressed explicitly on the surface of *Pf*IE and causes the sequestration of *Pf*IE by interacting with vascular endothelial receptors. The Hightrougput Virtual Screening study revealed natural compounds against the receptor binding domain of PfEMP1. Further, these natural compounds are conjugated, by suitable non-cleavable triazole linkers, with highly immunogenic peptides obtained through *in silico* screening from the peptide vaccines of malaria-endemic countries. Upon binding of PLCs to the parasite-infected RBCs, the PLC decorated *Pf*IE may not bind to/detach from the endothelial cells and be eliminated by preexisting vaccine-induced immunity.

SESSION III: CANCER STEM CELLS-& LEUKEMIA

Oral Presentation-4

Induction of terminal differentiation in leukemic blast cells with esculetin: Role of "axis shifts" of *Wnt* signaling

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Background: The "Differentiation therapy" has been emerging as a promising and more effective strategy against acute leukemia relapses. **Objective**: In extension to the revolutionising therapeutic outcomes of All Trans Retinoic Acid (ATRA) to induce terminal differentiation of Acute Promyelocytic Leukemic (APL) blast cells, we decipher the potential effect of a natural compound "Esculetin" to serve as a differentiating agent in Acute Myeloid Leukemia (AML). Underlaying role of Wnt signaling pathways in esculetin mediated blast cell differentiation was also evaluated. **Methods**: Human acute myeloid leukemic cells (Kasumi-1) with t(8;21/AML-ETO) translocation were used a model system. Growth inhibitory and cytotoxic activity of esculetin were analysed using growth kinetics and MTT assay. Morphological alterations, cell scatter characteristics, NBT reduction assay and cell surface marker expression patterns were analysed to detect terminally differentiated phenotypes. We employed RT^2profiler PCR array system for the analysis of transcriptome profile of Wnt signaling components. Calcium inhibitors (TMB8 and Amlodipine) and Transforming growth factor beta (TGF-β) were used to modulate the Wnt signaling axes. **Results**: We illustrate cytotoxic as well as blast cell differentiation potential of esculetin on Kasumi-1 cells. Morphological alterations akin to neutrophilic differentiation as well as the corresponding acquisition of myeloid lineage marker indicate terminal differentiation potential of esculetin in leukemic blast cells. Exposure to esculetin also resulted in downregulation of canonical Wnt axis while upto ~16 fold upregulation of non-canonical axis associated genes. **Conclusions**: Our study highlights the importance of selective use of calcium pools as well as "axis shift" of the canonical to non-canonical Wnt signaling upon esculetin treatment which might abrogate the inherent proliferation to release maturation arrest and induce the differentiation in leukemic blast cells. The current findings provide further therapeutic interventions to consider esculetin as a potent differentiating agent to counteract AML relapses. Key Words: Acute Myeloid Leukemia (AML), Esculetin, Blast cell differentiation, Differentiation therapy, Kasumi-1, Wnt signaling.

Oral Presentation-5

Ricolinostat suppresses proliferation and promotes apoptosis alone as well as in combination with topotecan/etoposide in cervical cancer cells

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Ricolinostat, HDAC6 specific inhibitor exhibits promising anticancer effects alone as well as in combination with various other chemotherapeutic drugs in several cancer types. In this study, we evaluated the effect of ricolinostat in cervical cancer as a single agent as well as in combination with topotecan/etoposide. The effect of ricolinostat alone and ricolinostat/topoisomerase inhibitors combination on cervical cancer cells was assessed using MTT assay, cell-cycle arrest, Annexin V/PI staining assay, ROS measurement, and western blot. Synergism of ricolinostat/topoisomerase inhibitors combination was quantified using the 'CompuSyn' software. Our study showed that ricolinostat, as a single agent suppressed proliferation, and induced G2/M phase cell cycle arrest and apoptosis in cervical cancer cells. Also, ricolinostat treatment resulted in increased ROS production, p21 expression and decreased Bcl-xL expression. We also found that ricolinostat significantly enhanced the antiproliferative activity of both, topotecan and etoposide in cervical cancer cells. Ricolinostat/topoisomerase inhibitor combination induced cell cycle arrest. Ricolinostat potentiated the apoptosis inducing capability of topoisomerase inhibitors in cervical cancer cells. In conclusion, our study showed that ricolinostat as a single agent suppresses proliferation by inducing G2/M phase arrest and promotes apoptosis, indicating that ricolinostat, as a single agent may be a promising antitumor agent in cervical cancer. Also, ricolinostat synergistically potentiates the antiproliferative activity and apoptosis inducing capability of topotecan/etoposide in cervical cancer cells. Hence, these findings provide cellular evidence that ricolinostat may be a promising anti-cancer drug alone and its combination therapy with topotecan/etoposide might turn out to be effective for cervical cancer treatment.

SESSION IV: SYSTEMIC INFLAMMATION VS NEUROINFLAMMATION: THE TWO DRIVERS OF NEURODEGENERATIVE DISORDERS

Oral Presentation-6

PPAR-β/δ agonist GW501516 attenuates neuroinflammation and blood-brain barrier breakdown in Plasmodium berghei ANKA-infected Balb/c mice

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Cerebral malaria (CM) is a neurological complication of *Plasmodium falciparum* making it the fourth major cause of morbidity in children <5 years of age. The currently available anti-malarial drugs fail to combat the CM related complications and mortality. Thus, there is an urgent need to establish novel therapeutic targets to alleviate CM. In this context, PPAR β/δ receptors can prove to be potential therapeutic targets. PPAR-β/δ are highly expressed nuclear receptors in the central nervous system, which have recently emerged as important mediators in regulation of blood-brain barrier integrity and inflammatory responses. Thus, we investigated the involvement of PPAR-β/δ in CM and utilized a selective PPAR-β/δ agonist GW501516 as a potential therapeutic agent. In the present study, Balb/c mice infected with *Plasmodium berghei* ANKA (PbA) were treated with GW501516 and the modulations in salient features of CM were analysed. In PbA-infected mice a decrease in cortical PPAR-β/δ expression negatively correlated with progressing parasitaemia, cerebral symptoms, and brain pathology. GW501516 administration in the infected mice significantly alleviated parasite infiltration, blood-brain barrier damage as indicated by FITC-dextran assay, restoration of tight junction proteins (ZO-1, Claudin-3), and VEGF-A. Furthermore, decreased cytokine and chemokine expression following GW501516 administration, emphasizes the pivotal importance of PPAR-β/δ in anti-inflammatory response's regulation, substantiated by a decrease in CD8+ T-cell infiltration in the brain. Thus, our results provide novel insights into the involvement of PPAR-β/δ in CM, establishing it as a potential therapeutic target. However, further work is required to validate the exact molecular mechanism involved in this pathway.

SESSION V: PROTEIN FOLDING DISEASES: MOLECUALAR MECHANISMS AND THERAPEUTIC APPROACHES

Oral Presentation-7

Taurine & derivates as enhancers of thyroxine-binding affinity of transthyretin: an insight towards therapeutic intervention of Pre-eclampsia

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Transthyretin (TTR) is an evolutionary conserved 55kDa serum and CSF protein, synthesized mainly in the liver, retinal epithelium, choroid plexus, placenta and uterus. The main function of the protein is transport of thyroid hormones T_4 & T_3, and retinol-binding protein (RBP). In fact, it's the only known thyroxine transporter in brain and across placenta which makes it crucial in different pathologies. Thus, functional regulation of TTR has colossal utility in various physiological complications involving hypothyroidism, especially in neuronal and gestational impairments. During pregnancy, TTR is 77ynthesized from the placental syncytiotrophoblast cells at the placental-maternal interface and the native TTR tetramers aids in the transport of maternal thyroxine to developing foetus which is crucial for proper placenta formation and maturational processes of foetal nervous system. Additionally, TTR initiates the process of uterine spiral artery remodelling. Dysregulation in TTR levels or functions leads to major pregnancy complications including but not limited to preclampsia.Preclampsia is characterized by sudden onset hypertension and proteinuria after 20 weeks of gestation. It is associated with reduced placental and serum TTR levels and dissociation of the TTR tetramers into partially unfolded monomers which oligomerize into amyloid fibrils. The deposition of these fibrils in the placental tissue as well as maternal vasculature facilitates the establishment of the disease. In the present article, we attempted drug-repurposing of FDA-approved small molecule taurine & its derivatives i.e. NAC-taurine and γ-glutaurine as enhancers of thyroxine-binding affinity of TTR. They also proved to be effective against the aggregation propensity of TTR. This highlights the importance of taurine administration in pregnancy, mainly preeclamptic patients.

Oral Presentation-8

Organosulfurs, S-allyl cysteine and N-acetyl cysteine sequester di-carbonyls and reduces carbonyl stress

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Diabetes, characterized by high blood glucose level, is a progressive metabolic disease that leads to serious health complications. One of the major pathological consequences associated with diabetes is the accumulation of highly reactive carbonyl compounds called advanced glycation end products (AGEs). Most of the AGEs are dicarbonyls and have the potential to covalently modify proteins especially at the lysine residues in a non-enzymatic fashion (a process termed as glycation) resulting in the functional impairment and/or toxic gain in function. Therefore, non-toxic small molecules that can inhibit glycation are of interest for the therapeutic intervention of diabetes. In the present study, we have investigated the effect of organosulfurs (S-allyl cysteine, SAC and N-acetyl cysteine, NAC) that are major principal components of *Allium sativa* against the glycation of different proteins. We discovered that both SAC and NAC are potent anti-glycating agents. We also found that both SAC and NAC reduce ROS level and inhibit apoptosis caused by protein glycation.

SESSION VI: APPLICATIONS OF STRUCTURAL BIOLOGY TO TREAT HUMAN DISEASES

Oral Presentation-9

Drug repurposing to treat Tuberculosis and SARS-CoV-2 infections: Insights from computational design into their mechanisms of action

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Tuberculosis (TB) continues to pose a serious threat to the world's population, with over 10 million new cases each year. Nevertheless, during the past ten years, mortality has reduced by almost a third and tuberculosis incidence has steadily decreased. But the COVID-19 pandemic abruptly reversed this upward trend, causing a significant drop in tuberculosis testing and case reporting in many regions of the world, as well as an increase in death. This set back efforts to control the disease by nearly ten years. As a result, it is critical to identify potential therapeutic agents and strategies for both infectious diseases i.e. Tuberculosis and COVID-19 Drug repurposing can speed up the discovery of new medications by discovering existing medications that are useful in treating infectious disorders. Therefore, in 1st part, we are targeting RNA-dependent RNA Polymerase (RdRp) of SARS-Cov-2 because of its significant role in viral transcription and replication. Herein, we generated the structure-based pharmacophore model by using the RdRp complexed with Remdesivir (PDB Id: 7BV2). The selected pharmacophore model consisted of five features (3 hydrogen bond acceptors and 2 donor features, AAADD). Next, we screened the DrugBank database (9506 compounds) and filtered out 271 compounds based on fit value criteria. Out of 198 successfully docked compounds, nine compounds were further selected based on high cDocker energy and interactions. Finally, MD simulation studies identified three potent drugs which may be repurposed as potent inhibitors for RdRP of SARS-CoV-2. Our in-silico predictions were experimentally validated using vero E6 cells infected with SARS-CoV2 virus in vitro testing at Regional Center for Biotechnology (RCB). Interestingly, two out of five tested molecules showed good inhibition against SARS-CoV2. C2_MC and C3_MC have shown good inhibition at highest non-cytotoxic concentration (100µM) tested. Further, the IC50 will be determined by studying virus inhibition at different conc. to generate a 7-point inhibition curve. The 2nd study aimed to describe the development of a pharmacophore model from a structurally diverse series of Pantothenate kinase (Pank) inhibitors. Pank would be an essential target for the development of antimicrobials because of its crucial role in the metabolism pathway. A total of 25 well-defined training set molecules were selected for hypothesis generation using Discovery Studio 2020. The best pharmacophore model (Hypothesis 1) consists of 4 features, namely, two hydrogen bond acceptor (HBA) and two hydrophobic (HY) features, correlated (r) of 0.976, an 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 the DrugBank database. The top 20 compounds were filtered based on their cDOCKER energy score as well as fit value and consensus scoring parameter. Next, the five compounds were identified based on their MM-PBSA score as well as 100 ns MD trajectory analysis. The present pharmacophore models can thus be helpful for the identification, development, and design of potent inhibitors which can be used as potential lead compounds for the development of anti-infectious agents.

SESSION VII: NEUROBIOLOGY AND EXPERIMENTAL NEUROLOGY

Oral Presentation-10

Src kinase mediates differential regulation of excitatory synaptic transmission in the hippocampus and ATL in Temporal Lobe Epilepsy

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INTRODUCTION: Src family kinases are crucial points of convergence for various signaling pathways. NMDARs, which are regulated by Src kinase, are important in the process of epileptogenesis and play a crucial role in excitatory synaptic transmission in the brain. Therefore, this study is designed to test the hypothesis that altered Src kinase functions may contribute to hyperexcitability in MTLE

MATERIALS AND METHODS: Hippocampal and ATL tissue samples from MTLE patients who had undergone surgical resection were acquired for this investigation. Real-time PCR & Western blotting was used to examine the mRNA and protein expression in the hippocampal and ATL areas of both acute and chronic TLE rats and humans. Kinase assay was used to determine functional Src activity. On paraffin-embedded tissue sections, immunohistochemistry and histopathological examinations were carried out. Functional validation using EPSCs was done using Patch-clamp.

RESULTS: Src was found to be upregulated in the histopathological, immunohistochemical and protein level findings of hippocampus. Kinase activity was higher in TLE model as compared to control. Significant increase in Src was observed in chronic model of TLE as compared to respective control with no significant changes in acute TLE model. PP2 blocker resulted in alterations in EPSC from MTS patients.

CONCLUSION: Our results are indicative of the role of Src in hyperexcitability via modulating the regulation of NMDA receptors in MTLE. These findings will greatly improve our understanding of the molecular mechanisms and synaptic plasticity involved in the pathogenesis of MTLE, and Src may represent new potential therapeutic drug targets.

Oral Presentation-11

$A_{2A}R$ antagonists mediate the restoration of mitochondrial calcium dysfunction using the 6-OHDA model of Parkinson's in primary neuronal cells of P_0/P_1 rat pups

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Deterioration in neuronal intracellular calcium ($[Ca^{2+}]_i$) and mitochondrial calcium ($[Ca^{2+}]_m$) has been reported to induce Parkinson's disease (PD). Recently, we have demonstrated that A_{2A} R modulates the $[Ca^{2+}]_i$ through PKA to induce IP_3 levels. An increase in $[Ca^{2+}]_i$ coupled with alterations in mitochondria tethering, is reported to cause $[Ca^{2+}]_m$ overload, which is linked to excessive reactive oxygen species (ROS) generation, mitochondrial dysfunction, protein aggregation and progressive neuronal, all prominent features of PD pathogenesis. Although 6-OHDA-induced toxicity led to increased cytosolic and mitochondrial calcium leading to cell death, however, the role of NCLX, MCU and VDAC in deteriorating the calcium homeostasis by 6-OHDA has not been explored. In the present work, we investigated the role of A_{2A} R antagonists in restoring $[Ca^{2+}]_m$ overload induced by 6-OHDA via NCLX, MCU and VDAC. The measurement of protein levels of NCLX, MCU B, VDAC, alpha-synuclein, caspase-3, alpha-synuclein and β-actin was assessed by western blot in 6-OHDA-induced primary neuronal cells with or without A_{2A} R antagonists treatment. Moreover, mitochondrial SOD, mitochondrial membrane potential and mitochondrial calcium were also measured by MitoSOX, rhodamine 123, and Rhoda-2 AM respectively. The result showed that 6-OHDA-induced primary neuronal cells decreased the protein expression of NCLX while increasing MCU protein expression, however, there was no significant difference in the protein expression of VDAC. As anticipated, A_{2A} R antagonist treatment increased NCLX expression and decreased MCU expression as compared to untreated 6-OHDA-induced primary neuronal cells resulting in the restoration of $[Ca^{2+}]_m$ overload, mitochondrial SOD and mitochondrial membrane potential. Therefore, these results provide a link between mitochondrial calcium channels and mitochondrial dysfunction suggesting $[Ca^{2+}]_m$ channels like NCLX and MCU as potential therapeutic targets in PD and $A_{2A}R$ antagonists as a good candidate for the therapy of PD.

SESSION VIII: NEW PARADIGM IN DRUG DISCOVERY RESEARCH

Oral Presentation-12

Virtual screening combined with molecular modeling and designing approaches to identify HDAC6 selective inhibitors as anticancer agents

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To date, many HDAC6 inhibitors have been identified and developed but none is clinically approved as of now. Through this study, we aim to obtain novel HDAC6 selective inhibitors that are druggable and possess anticancer activity. To achieve this goal, we targeted two databases together; ZINC and Drugbank to attain maximum output by using molecular modeling and drug repurposing approach in a single study. HDAC6 pharmacophore-based virtual screening of the databases was performed followed by molecular docking. ZINC database hits obtained were subjected to modification via molecular modeling to obtain novel HDAC6 inhibitors. ADMET and TOPKAT analysis of modified ZINC hits provided 9 novel potential HDAC6 inhibitors with better docking scores and 2D interactions as compared to the control molecules. The process of designing these novel inhibitors provides new information towards the "structural requirement" of the HDAC6 selective inhibitors. The drugbank hits obtained after *in silico* screening provided 8 potential HDAC6 inhibitors. Further, the *in vitro* enzyme inhibition results of Drugbank hits indicate that these molecules possess HDAC6 selective activity, and cytotoxicity assays performed in cervical cancer cell lines (SiHa and HeLa) showed their anticancer potential. Western blot analysis showed that 'Compound A' is capable of increasing the acetylation levels of alpha-tubulin while at the same time levels of acetylated Histone H3 remain unaltered thus indicating that 'Compound A' is HDAC6 selective inhibitor. Moreover, we found that 'Compound A' inhibited proliferation, and induced G0/G1 phase arrest and apoptosis in cervical cancer cells. The results indicate that this compound has a high potential to be repurposed as an HDAC6 selective anticancer agent.

Oral Presentation-13

Exploring the Therapeutic Potential of Nanotechnology based Phyto-pharmaceuticals

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The biologically active constituents in herbal plants have low bioavailability and efficacy due to their high solubility in water, low absorption because of inability to cross the cell lipid membranes and large molecular size. Nanomaterials have the potential to significantly improve the pharmacokinetics and therapeutic index of plant-derived drugs by the development of nano-based drug delivery systems (NDDSs) for herbal constituents which not only reduce the need for repeated administration, but also contribute to increased therapeutic values by lowering toxicity and increasing the bioavailability. Recent advancements in camptothecin (an anticancer agent) drug delivery systems have increased the efficacy of drug by the development of nano-sized dosage forms of camptothecin-derived drugs. The plant virus based nanoparticles (VNPs) have been explored as nanocarriers for cancer therapy. Using nanobiotechnological techniques the higher demands for artemisinin for malaria treatment and cancer chemotherapy has been successfully achieved. The new research progress in NDDSs and future prospective for nano-carriers in drug delivery and their safety will be reviewed.
Keywords: *Nanomaterials, Nano-based drug delivery systems (NDDSs), chemotherapeutic effects, Nanocarriers, virus based nanoparticles (VNPs)*

SESSION IX: THERAPEUTIC VENTURE TO TARGET CANCER CELL AND ITS REPROGRAMMED BIOLOGY

Oral Presentation-14

SMAC mediating a switching point in TRAIL drive sensitization

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Drug resistance in gliomas is a major concern in developing therapeutic approach. Tumor necrosis factor related apoptosis inducing ligand (TRAIL) shows a promising therapeutic potential as it kills cancerous cells without affecting normal cells. Various glioma cells like T98G and U87 MG reported to shows moderate to high resistance against TRAIL, but the relevant cell resistance is yet to understand. TRAIL was known to mediate apoptosis through crosstalk in between extrinsic and intrinsic pathway of apoptosis. SMAC, a known apoptotic protein participates in apoptosis along with release of cytochrome C from mitochondria, after inhibiting IAP family proteins. Whereas in our study, expression of SMAC (apoptotic protein) is suppressed in TRAIL sensitive T98G glioma cells, however SMAC upregulation induces TRAIL resistance in U87MG glioma cells. Additionally, *Withania somnifera's* (WS) fruit methanolic extract downregulates SMAC in both TRAIL co-treated glioma cell lines. SMAC degradation pathway was also observed using inhibitor against proteosomal degradation pathway and lysosomal pathway. TRAIL dependent USP5 cleavage was showed to be effective in inducing more apoptosis, revealed also by knocking down USP5, which leads to ~90% apoptosis in TRAIL treated and WS cotreated cells. Another, TRAIL resistant U87 MG glioma cells where USP5 knockdown showed apoptosis, and necrosis or autophagy in *Withania somnifera* (WS) extract treated. This concludes that in TRAIL treated SMAC plays a key role in between apoptosis or autophagy, where presence of USP5 or its cleavage supports the subsequent cell death pathway.

Oral Presentation-15

Targeting NFκB p50 DNA binding region through active phytochemicals from Spaheranthus Indicus

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Transcription factor of Nuclear Factor kappa B (NF-κB) signaling pathway govern important physiological processes to maintain homeostasis, which includes inflammation, cell proliferation and apoptosis. Inhibition of NF-κB signaling pathway act as important therapeutic target, mainly in situation where the pathway is often constitutively active and plays a central role in chronic inflammation driven disease pathogenesis like cancer. Different components of NF-κB pathway can act as modulator at several levels. In this study phytochemicals from Sphaeranthus Indicus were investigated for their NFκB p50 inhibiting properties through in silico methodologies. Docking with 19 phytochemicals at DNA binding region of p50 was performed. Gallic acid, a known p50 inhibitor was used as positive control. Drug likeness and physiochemical properties of the phytochemicals were also investigated. our data revealed 15 of the studied phytochemicals exhibited good drug like properties. Outcomes of the study also suggest that these 15 phytochemicals can also act as p50 inhibitors. Moreover, four phytochemicals, 2-Hydroxycostic acid(1), Ilicic acid(2), β-Sitosterol(3) and 7 Hydroxyfrullanolide(4) exhibited better inhibiting properties then the known p50 inhibitor Gallic Acid.

Keywords: *Sphaeranthus Indicus, Phytochemicals, Cancer, NFκB, p50, p50 inhibitor*

SESSION X: RECENT ADVANCES IN ALTERNATIVE MEDICINE: WITH EMPHASIS ON AYURVEDA

Oral Presentation-16

Biological evaluation of hydro-alcoholic extract of Bacopa monnieri for the treatment of Alzheimer's disease

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Alzheimer's disease is a multifaceted neurodegenerative disorder manifested by various cellular and molecular changes. The discovery of drug molecules targeting the multifaceted nature of AD from natural products would reduce the side effects, costs and time required in the drug development stages and would significantly assist in the disease therapy. Plant derived drugs like physostigmine, rivastigmine, galantamine, and huperzine are known AChE inhibitors, implicating the possibility of discovering more potent anti-AD agents from plant sources. The aim of this study is to explore the effects of *bacopa monnieri* on the major AD targets, viz. acetylcholinesterase (AChE), amyloid beta aggregation, antioxidant, metal ions and neurodegeneration. Extensive biophysical studies that included kinetic studies, fluorescence quenching experiments, UV-spectroscopy and confocal microscopy established the multipotent nature of extract of *Bacopa monnieri*. Whole extract showed non-cytotoxic activity in the tested range and protected cells from H_2O_2 induced neurotoxicity in the brain cell line. Bacopa extract showed significant memory retrieval of mice during elevated plus maze, passive avoidance and social recognition tasks in scopolamine induced mice model of AD. Histopathology data revealed the potential of *Bacopa monnieri* in retrieving the structural damages caused in the cortex and hippocampus by scopolamine in mice.

Oral Presentation-17

Standardization and Quality Control in Medicinal and Aromatic Plants for Phytopharmaceutical Drug Discovery

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Globally, herbal medicine has been considered an important alternative to modern allopathic medicine. Although the allopathic medications offer fast relief, however, due to many adverse effects associated with them, herbal medicine have good community acceptance. This field is bringing forward new drug leads as well as safe and efficacious plant-based medicines. In spite of the fact that the herbal medicines are very popular in the society, only few medicinal herbs have been scientifically evaluated for their potential. In most countries, the herbal drugs are poorly regulated and are often neither registered nor controlled by the health authorities. The Indian System of Medicine largely encompasses AYUSH (Ayurveda, Unani, Siddha, and Homeopathy) systems. Although Ayurveda is being practised in the Indian subcontinent since millennia, its usage is largely limited. The consistency in Ayurvedic formulations among manufacturers and batch to batch variations are the major cause of concern. 'Phytopharmaceutical drug' class has been introduced in India in 2015. This drug class is under regulatory control of Central Drugs Standards Control Organization (CDSCO), Ministry of Health and Family Welfare, Govt. of India. Phytopharmaceutical drug is defined as purified/ standardized fraction with defined minimum four bioactive or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation, or prevention of any disease or disorder but does not include administration by parenteral route. Standardization and quality control is an essential regulatory requirement of phytopharmaceutical drugs. We have performed marker compound-based standardization of selected medicinal (*Withania somnifera, Curcuma longa, Zingiber officinale*) and aromatic (*Cymbopogon flexuosus, Cynbopogon nardus, Cynbopogon khasianus*) plants and their formulations using HPLC/LCMS/GCMS. The microbial quality control in *Chlorophytum borivilianum and Withania somnifera* roots have been carried as per pharmacopeial regulatory requirements. Total microbial load and presence of *Escherichia coli* and *Salmonella sp.* contamination were assessed in the fresh and processed roots of these medicinal plants.

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SESSION XI: ART OF WAR AGAINST CARDIOVASCULAR DISEASE PROGRESSION AND OUTCOMES

Oral Presentation-18

Elevated expression of SORT1 gene in patients with coronary artery disease

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Background: Background: Genome-wide association studies demonstrate that SORT1 gene expression affects lipid metabolism, identifying it as a risk gene for coronary artery disease (CAD). Sortilin protein enhances low density lipoprotein (LDL) absorption, form cell development, and atherosclerosis in macrophages. Thus, inhibiting this protein in immune cells can provided cardiovascular risk protection, and hence, we explored SORT1 expression in CAD patients and its gene expression's predictive usefulness for the severity of CAD. **Objectives**: To analyse the expression of SORT1 gene at mRNA and protein level in patients with CAD. **Method**: Quantitative real-time polymerase chain reaction (qPCR) and western blotting were used to determine the expression of SORT1 gene at the mRNA and protein levels in 200 healthy controls and 200 patients with various CAD syndromes (chronic stable angina (CSA), myocardial infarction (MI), acute coronary syndrome (ACS). The Sandwich ELISA also measures Sortilin protein concentration in plasma. **Results**: CAD patients exhibit a significant difference in average delta-Cycle Threshold (delta-CT) value (approximately a 6.9-fold change, $p<0.0001$) as compared to the healthy individuals. In addition, Circulating levels of Sortilin proteins were higher as compared to healthy controls (5.049±0.56 v/s 9.196±1.25 ng/ml, $p<0.0001$). The expression of the SORT1 gene differs between patients with CSA, MI, ACS, diabetes, and CAD according to the increasing percentage of stenosis. The highest expression is found in ST-Elevation myocardial infarction (STEMI) patients and expression of SORT1 gene was positively correlated with the severity of the disease (number of coronary arteries affected). **Conclusion**: Differential SORT1 gene expression in various CAD syndromes may be a potential biomarker for the disease.

Keywords: *Coronary artery disease, SORT1 gene, Biomarker.*

POSTER PRESENTATIONS

Day-1

SESSION I: GENETICS AND EPIGENETICS OF HUMAN DISEASES

P-01

Expression and Functional characterization of all SR family of proteins in cancer

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Alternative splicing is a post-transcriptional modification which yields generation of many proteins and RNA from one pre–mRNA, contributing to the heterogeneity of mammalian cells. It is a tightly regulated by splicing machinery components and yet one of known established reason behind many oncogene activation leading to cancer progression.

Dysregulation of splicing machinery component and its associated proteins accelerate cancer progression. Serine/arginine-rich Splicing Factors (SRSF or SR family of proteins) are well-studied RNA splicing families regulating gene expression. Having the intrinsic capacity to activate splicing, they are found to be responsible for the regulation of alternative splicing events leading to enhanced production of pro-oncogenic isoforms and reduced tumor suppressive isoforms. SRSFs have been reported to be upregulated in various cancers (Breast, lung, kidney, skin) strengthening their association with altered gene expression during cancer progression, making them a potential therapeutic target for certain cancers.

We studied the mRNA level expression of all SR family of proteins- SRSF1-SRSF12, on 22 transformed cell lines of different origins and in normal healthy adult tissues. Mainly three splicing factors namely SRSF1, SRSF3, and SPF45 showed a higher expression in almost all the tissues and cell lines. Among transformed cell lines SiHa, HCT116 and H1299 had the highest expression of, SRSF1, SRSF3 and SPF45. Among adult tissues, the testis, placenta, and pancreas, had higher expression of these three splicing factors. Functional characterization of these splicing factors might establish its clinical and pathogenic significance in cancer.

P-02

Coordination between PHA-4 and SIN-3 for transcription regulation responses in *Caenorhabditis elegans*

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The central dogma determines gene expression in eukaryotes with the help of several core machinery enzymes, transcription factors and regulatory proteins. In the context of global transcriptional regulation, SIN-3 is an essential regulatory protein that acts as a scaffold for Histone Deacetylase (HDAC) enzymes in the Sin3/HDAC complex. This protein is known to regulate various processes like cell fate specification, and nematode male tail mating organ morphogenesis. Previously, our lab has demonstrated that deletion of *sin-3* in *C. elegans* reduces the lifespan of the mutant worms even with increasing ROS production and cell death, yet the mechanism followed by the SIN-3 protein in regulating these biological processes is still not clear. Recently, we found several protein-protein interactors of the *C. elegans* SIN-3 protein which are known to be implicated in apoptosis, autophagy and longevity. Among these interactors, the PHA-4 protein was observed to have a significant transcriptional up regulation in case of sin-3 deletion. PHA-4 functions as a transcription factor in cell differentiation, macroautophagy, and pharynx development. Pha-4 mutants also phenocopy sin-3 mutants. In addition, there is evident co-occupancy of SIN-3 with PHA-4 proteins at several promoters in the epigenome. Therefore, we anticipate PHA-4 to be an enabler for SIN-3 in transcription regulation of various processes like autophagy and thereby affecting aging in *C. elegans*.

Keywords : *Lifespan , Transcription Regulation, Autophagy, Aging.*

P-03

Identifying key genes involved in EMT metastasis pathway along with associated mi-RNA's in gastric cancer through juxtaposition of gastric cell-line versus tumor data, proclaiming cell line an ideal tumorigenic model

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Cell line development has been largely accepted in medicine and has been employed for understanding the genetic expression and therapeutic viability of substances against immunological disturbances. Cancer cell lines have been adopted as tumorigenic models, juxtaposing tumor development and pathophysiology into an artificial environment. In the present study, the same superimposition was taken into a comparative account - between gastric cancer cell line and gastric tumor, with the genomic data sourced through literature surveys and bioinformatic databases.

The research aims at proclaiming gastric cancer cell line as a suitable model for gastric tumor research and helps identify differential genes participating in metastatic proliferation through EMT along with respective suppressor miRNAs. The data procured was run through analytical tools helping identify 380 common differentially expressed genes (DEG's) between gastric tumor and gastric cell line, followed by pathway enrichment and miRNA identification of the key genes. Four of these common DEG's were expressed as differential EMT markers, of which two were identified in an over-expressive state namely, ITGB1 and TGFB1. Kaplan-Meier survival plots for both the EMT genes exhibited a regressing survival curve, confirming the lethal potency of these up-regulated tumorigenic genes. Further, ITGB1 and TGFB1 were found associated with 9 tumor-suppressing mi-RNA's.

Thus, despite the nominal deviation in genetic composition of the cell line, it provides a functional environment for pathophysiological analysis and can also be employed as drug-models, owing to its induced versatility.

P-04

Deciphering complexity of Venous thromboembolism by studying epigenetic regulation mediated by methylation

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Background: Epigenetic play an important role in pathogenesis of many diseases. Recently, several complex multigenic diseases have been associated with alterations in DNA methylation patterns. Present study aims to understand Pathophysiological mechanism of multi-factorial disease venous thromboembolism (VTE). Etiology of VTE is influenced by genetic, acquired and environmental factors, such as exposure to high altitude (HA). Role of methylation in pathophysiology of VTE is yet to be completely elucidated.

Methodology: Study was conducted on a total of 18 Indian Army volunteers, in accordance with the ethical guidelines laid by ICMR. Study volunteers were divided into four groups; VTE patients from HA (HA-VTE), VTE patients from sea level (SL-VTE), healthy controls from HA (HA-Con) and healthy controls from SL (SL-con). DNA was isolated from blood followed by qualitative and quantitative check. Global methylation pattern were studied by genome bisulfite sequencing. Differentially methylated pathways and genes in the study groups were identified after bioinformatic analysis of the sequenced data.

Major Findings: Distinct methylation patterns were observed in HA and SL patients in comparison to respective healthy controls. HA-VTE patients had 296 differentially methylated genes (DM), in which component of hypo-methylation was predominant, whereas SL-VTE patients had a total of 1162 DM genes, wherein hypermethylation was predominant. DM pathways included cell adhesion, platelet activity, trans membrane receptor and immune response.

Conclusion: Present study demonstrates that global DNA methylation is associated with primary VTE. Differential methylation pattern in VTE patients (both HA and SL) could be further investigated to establish potential role of methyaltion as diagnostic or preventive biomarker.

P-05

Effect of Naringenin on GPCR signaling with emphasis on behavioral response in *Caenorhabditis elegans*

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G-Protein Coupled Receptor (GPCR) signaling is one of the most important signaling systems with well-known clinical applications. GPCR genes account about 4% of the human genome. The aim of this study was to investigate the impact of natural compounds on genes related to GPCR signaling in *Caenorhabditis elegans*. First, ten natural compounds were selected through a literature search, of which five were chosen for further research based on pharmacokinetic features. Naringenin, a naturally occurring flavanone, was studied. The effect of Naringenin was assessed in behavioral responses and further on the gene expression of selected GPCR pathway genes. The pharyngeal pumping was assessed in the Naringenin treated worms. The effect of Naringenin was studied for reverse mutation and gene conversion in *Saccharomyces cerevisiae* D7 strain. Mitotic gene conversion is monitored by appearance of tryptophan non requiring colonies on selective media. Mutation induction can be followed by appearance of isoleucine non requiring colonies on selective media. In results, Naringenin treated worms showed decreased muscle activity as observed by pharyngeal pumping as compared to untreated worms. We found that naringenin was moderately toxic in ADMET toxicity analyses. Gene expression analysis for selected genes involved in GPCR signaling was analyzed by semi quantitative rtPCR technique. The gene expression data showed downregulation of *unc-68* and upregulation of *egl-19* gene level in naringenin treated worms. The reverse mutation and gene conversion analysis in *S. cerevisiae* suggest that naringenin act as mutagen specifically causing reverse mutation and is independent of mitotic gene conversion.

***Keywords**:* GPCR, Naringenin, *C. elegans*, *S. cerevisiae*, *unc-68*, *egl-19*, Behavioral responses, rtPCR, Reverse mutation, Mitotic gene conversion

P-06

Autism Spectrum Disorder: Genetic Factors and their Modifiers

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The poster aims at elaborating upon the causes of Autism or Autism Spectrum Disorder (ASD) as a neurodevelopmental condition that affects how a person communicates with others, interacts, learns and behaves. There is no one single cause of this complex neurological condition. Autism can occur as a result of both genetic and environmental factors. Inheritable mutations as well as de novo mutations in various genes contribute to the etiology of this disorder. Proteins encoded by these susceptibility genes or risk genes have broadly 2 functions- (I) synapse regulation and (II) transcriptional regulation and chromatin remodelling pathways. Mutation in genes such as NRXN1, NLGN3, MeCP2, CHD8 lead to synapse pathology and alteration in cellular processes like DNA methylation, transcriptional regulation, regulation of RNA synthesis, etc. Another key aspect of ASD is that it is a highly heterogenous disorder i.e., individuals with similar pathological variants exhibit varied phenotypes. This can be attributed to the role of modifiers- factors that regulate the expression of other genes, thereby modifying the phenotypic outcome of the condition. Genetic modifiers include CNVs (copy number variations), epigenetic genes and double-hit mutations. Non genetic modulators such as environmental exposure (increased parental age, maternal complications or infections during pregnancy, or prenatal exposure to anticonvulsants) and sex-linked modifiers also affect the penetrance of risk genes. In 15% cases of autism, the cause is known and this is referred to as Secondary ASD, caused by genetic abnormalities like Fragile X syndrome, tuberoses sclerosis.

P-07

Molecular mechanisms of Vascular Smooth Muscle Cell dysfunction in accelerated Diabetes Cardiovascular Disease

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Diabetes, one of the most prevalent chronic diseases worldwide, is associated with accelerated cardiovascular disease (DCVD). Diabetic patients continue to develop CVD even after implementing glycemic control through therapeutic interventions due to metabolic memory of prior glycemic status. Current therapies targeting Angiotensin II (AngII), such as Angiotensin converting enzyme (ACE) inhibitors and AngII receptor blockers, are not fully efficacious. Thus, it is imperative to identify novel mediators of AngII action in accelerated DCVD that could be therapeutically targeted.

Vascular smooth muscle cells (VSMCs) that line the blood vessel walls play pivotal roles in CVD. Under diabetic conditions and in the presence of CVD promoting hormone AngII, mature VSMCs can de-differentiate through a phenotypic switching process that leads to a decrease in contractile gene expression. Decreased contractile function of the endothelium results in increased stiffness of arteries. Phenotypic switching also increases VSMC proliferation, migration, inflammation, and extracellular matrix production, contributing to vascular dysfunction and CVD. In this project, I propose to understand the molecular mechanisms of diabetes and AngII- mediated VSMC dysfunction in accelerated DCVD. It is possible that diabetes conditions and AngII coordinately re-program the VSMC transcriptome and epigenome, which lead to persistent dysregulation of genes promoting phenotypic switching to unique cell states underlying VSMC dysfunction and accelerated DCVD. An in-depth understanding of the genetic and epigenetic mechanisms underlying AngII- and diabetes-induced DCVD will allow us to discover novel therapeutic targets for patients with DCVD.

P-08

Mapping of hervs gene expression in human diseases

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Human endogenous retroviruses (HERVs) are relics of ancient retroviruses that infected humans and became integrated into our genome millions of years ago. Presently HERVs account for about 8% of human genome but most of them are inactive and silent due to mutations and other epigenetic reasons. However, HERVs have been shown to play potential pathological role in several diseases including autoimmune diseases like multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis and several neurodegenerative diseases. The abnormal expression of HERVs has been noted in various disease conditions however, the data for tissue specific expression of HERVs is missing from literature. This important information can help the scientific community to peep into the mechanisms utilized by HERVs and henceforth devising the applications of these mechanisms for various applications. The data was collected from available databases for in-silico analysis of HERVs related genomic and epigenomic features and marks that can point out specific details. A total of 9 tissues were selected based on data availability and interesting observations have been chalked out after comparison with diseased and normal states. These revating observations emphasize the need for further analysis of HERVs their expression and regulation in human genome

P-09

Association of rs9890617(C/T) polymorphism of *BECN1* with the risk of CHB in the North Indian population

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Beclin 1, a key autophagy protein encoded by *BECN1* gene plays a central role in the autophagy process and protein sorting. Autophagy is a cellular pro-survival mechanism that maintains homeostasis by recycling cytoplasm, eliminating excess or aberrant organelles and clearing the pathogens. Autophagy is subverted by hepatitis B virus (HBV) for its own replication and survival. Despite the availability of vaccines, HBV continues to be a serious health concern. Recently, WHO estimated 296 million people infected with chronic hepatitis B (CHB) which is associated with an enhanced risk of developing HCC which is one of the leading causes of liver related deaths globally. 'Autophagopathies' is a term recently proposed for human diseases including HBV infection resulting from genetic defects in autophagy machinery. Intronic variants have been linked to genetic predisposition to various diseases including tumorigenesis. In this study, we predicted potential alteration of splicing signals due to *BECN1* variant rs9890617 using Human Splicing Finder v.3.1. Further, we genotyped 231 CHB patient samples and 218 age and gender matched healthy controls using PCR-RFLP to determine if the *BECN1* intronic variant rs9890617(C/T) was associated with the risk of CHB infection in the North Indian population. The statistical analysis revealed a significant association between the mutant T allele and disease risk in the allelic (OR=1.62; 95%CI=1.11-2.39, p=0.01), dominant (OR=1.64; 95%CI=1.07-2.52, p=0.02) and co-dominant model (OR=1.55; 95%CI=1.00-2.40, p=0.04). The results conclude that 'T' is a risk allele in genetic predisposition to chronic HBV infection.

†Sargeet Kaur

P-10

A Pan-cancer Biomarker Study for better diagnosis of Digestive System cancers

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The three digestive system cancers viz, gastric, pancreatic and colon cancer are a leading cause of death worldwide. Approximately, 10M deaths were reported in 2020 due to digestive cancers in the world. The global digestive cancer burden is higher in young males and apart from the genetic factors, socioeconomic status also plays an important role. Also, it is difficult to differentiate between the individual types of digestive cancers due to common symptoms. The diseases are diagnosed at a later stage after the onset of metastasis and surgical removal of the organs is also not successful. Therefore, we have performed a pan-cancer approach to study multiple datasets of the three digestive cancers and identify the biomarker genes responsible uniquely for the three cancers. RNA-seq datasets from various studies are taken from NCBI SRA and investigated through the NGS pipeline using RNAseq analysis. The highly overexpressed and under expressed genes in each of the digestive cancers are selected to study the pathways involved using DAVID GO Ontology Tool.

So far, we have identified 10 genes overexpressed and low expressed in each of the three cancers and we are studying the structural features of these genes and the pathways they are involved in. Further, we will use this biomarker study to identify and analyze the symptoms encountered by patients in their early stages of cancer and use this approach as a good therapeutic target so as to minimise the dependency of treatment on the crucial stage.

P-11

Regulation of immune responses to mycobacteria by Toll Like Receptors on epithelial cells

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In addition to providing a physical barrier against the invasion of pathogen, a major function of the epithelial layer in the mucosal immune system is to serve as the inductive sites to initiate immune responses and thus provide the first line of defence for the host against pathogens. The epithelial cells express a range of innate receptors that provide initial signals to the adaptive immune system to mount responses to invading pathogens. The role of epithelial cells and Toll Lile Receptors (TLRs) on these cells during mycobacterial infection is not understood in detail. In this report we show a dynamic and differential regulation of TLRs by mycobacteria. Specific roles for calcium homeostasis have been identified. TLR7 appeared to be most dynamically regulated both by different TLRs as well as calcium homeostasis on epithelial cells. Further, TLRs also cross-regulate the expression of each other. The data also indicate that TLRs regulated by calcium homeostasis have functional significance in regulating defense responses and intracellular bacterial survival.

P-12

Elucidating the immunological role of C-Type lectin Receptors (CLRs) during *Mycobacterial* infection

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C-type lectin receptors (CLRs) are pattern recognition receptors (PRRs) which are expressed by various innate immune cells say monocytes, macrophages, DCs, and Langerhans cells (LCs). They are crucial for recognition and induction of adaptive immune responses. Successful pathogens, like *Mycobacterium tuberculosis,* have evolved to subvert defense functions to establish pathogenicity. In this report we explore the roles of various CLRS during *Mycobacterial* infection in macrophages. The CLRs under study were CLEC-7A (Dectin-1) and CLEC-4E (Mincle). Their expression level was monitored in macrophages after 24 hours of BCG infection, along with other associated responses like ROS and bacterial load. The results suggested that the expression of these CLRS is upregulated by BCG. Furthermore, their modulation with respect to calcium homeostasis was also studied. Inhibiting the release of intracellular calcium from ER (using TMB8) leads to reduction in these CLRs expression levels. The functional role of this homeostasis was also investigated by intracellular bacterial persistence and oxidative burst. Results point towards a differential role of Dectin-1 and Mincle and also indicates a role for that homeostasis in regulating their expression

P-13

Comparative analysis of alternate methods of genomic DNA isolation from Sputum samples of MTB patients

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Tuberculosis is one of the most contagious airborne diseases caused by *Mycobacterium tuberculosis,* transmitted through droplets of infected individual. Rapid detection can help cure and prevent the transmission of disease but conventional diagnostic methods are less specific and very time consuming. Recently developed NAAT based diagnostic assays are comparatively rapid, specific and sensitive but the major challenge for these NAAT based assay is the successful extraction of Genomic DNA from the sputum specimen. The quality and quantity of isolated DNA influences the amplification efficiency, causing interference on the sensitivity and respective inhibitors for detection.

Sputum being highly viscous and gluey especially in patients with heavy bacterial load is difficult to homogenise and liquify. Various chemical and physical methods are used for liquification but those are expensive and require installation of large equipment therefore, cannot be used resource limited settings for use as a point-of-care device.
In this study different method of genomic DNA extraction are compared with the Standard USP method. Quantitative and qualitative assessment was done by comparing amount of DNA extracted and by comparing the amplification profile of each method by in-house sdaA PCR and sdaA LAMP

In conclusion, out of all the methods compared NP-40 & Triton X-100 method is further standardised to achieve maximum yield and can be used as a potential extraction method for extraction of genomic DNA owing to its speed and simplicity in resource limited settings.
Keywords: MTB (Mycobacterium tuberculosis), sdaA LAMP, genomic DNA extraction, Tuberculosis, Diagnosis

P-14

A study of the ecology, evolution and resistance mechanism of *C.auris* in a tertiary care center in North India

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AIM – To study the ecology, evolution and resistance mechanism of *C.auris*, using samples from patients, healthcare workers, hospital and environmental niches, using amplified fragment length polymorphism (AFLP) and antifungal susceptibility testing (AFST). **METHODS-**The screening for *C. auris* involved 854 samples in total, including surface swabs from hospital locations, clinical samples(tissue, body fluids) from crtically ill patients(ICUs/Wards) with prolonged history of hospital stay, antibiotic therapy, catheterization and co-morbidities; surveillance samples from patients with *C.auris* reported in urine and blood (axillar/groin swabs) ; swabs and water samples from environmental locations and objects, and screening samples from medical staff for hand carriage of C. auris. Samples were cultured on CHROMagar and Sabouraud Dextrose agar (SDA). By using Matrix Assisted Laser Desorption - Time of Flight (MALDI - TOF) to identify colonies that had C. auris-like morphology, isolates were then tested for antifungal susceptibility using the broth micro-dilution method. Amplification-Fragment-Length Polymorphism (AFLP) and cluster analysis were used to analyse the DNA. For the creation of the heat map and dendrogram, the amplicons were subjected to capillary electrophoresis and fluorescence amplified length polymorphism (FALP)**. RESULTS-** C. auris was isolated and identified by MALDI-TOF from 50 of the 854 samples, including 37 from routine patient samples, 12 from the 674 axillar/groin surveillance swabs, and 1 from the 66 samples taken from the hands of healthcare professionals. No environmental samples or hospital surfaces harbored C. auris. According to AFST, a substantial percentage of isolates were resistant to fluconazole, voriconazole, and amphotericin B, respectively, 93.22%, 38.98%, and 52.54% of isolates. Fewer isolates (1.81%) were resistant to echinocandins - caspofungin and micafungin. Additionally, only intermediate sensitivity to both voriconazole and caspofungin was exhibited by 18 isolates. Amphotericin B and azole resistance rates were highest in blood isolates (62.5% of isolates) and axillar/groin swabs (44.5% of isolates), respectively.14.28% of the isolates from both groups exhibited caspofungin resistance. The isolated DNA underwent AFLP and capillary electrophoresis, which revealed 188 polymorphisms between 300 and 662 nucleotides. Ten samples were designated as "constant" since the nucleotides were constant. Two distinct clusters, cluster I and cluster II, were generated by the dendrograms obtained by the bioinformatic analysis of the FALP findings. Sub-clusters Ia and Ib of Cluster I could be differentiated further, indicating further polymorphisms**. CONCLUSIONS-***Candida auris* is a pathogen of emerging importance in our centre, with significant levels of resistance to several important antifungal drugs. Incidence of both the pathogen and antifungal drug resistance were observed in samples collected from crtically ill patients admitted to various ICUs and wards with an overwhelming preponderance of prolonged hospital stays, antibiotic therapies and co-morbidities, which predisposed the patients to *C.auris* infection and colonization. AFLP findings indicate 188 polymorphisms (SNPs and SNVs) between 300-662 nucleotides catering to increased resistance to routinely administered antifungals, which hinders patient treatment. Due to increasing resistance to major class of antifungals, our findings suggest that combination therapy has an increased improvement rate as compared to monotherapy. Our findings suggests that the source of most *C. auris* infection is colonizers from the patient rather than environmental sources or healthcare workers, and infection control measures should be tailored accordingly.

P-15

Deciphering the role of Sodium Butyrate in macrophages upon mycobacterial infection

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Adaptations and alterations into the metabolic pathways of host are the key targets by pathogen for its persistence and disease progression. *Mycobacterium tuberculosis* is one of the known pathogen which does these adaptations and alterations to cause tuberculosis. SCFAs (small chain fatty acids) have strong influence on host immunity against infection. Sodium Butyrate is one of SCFA which have potent anti-microbial activity in gut and believed to modulate host immune system. SCFAs are produced in gut by microbial dietary fermentations and enter in circulation through portal vein. In this study, we deciphered the role of Sodium Butyrate in macrophages upon *M. bovis* BCG infection. We found that sodium butyrate mount protective responses in host immunity upon mycobacterial infection. These include significant increase in reactive oxygen species which subsequently leads to apoptosis, up-regulation of co-stimulatory molecule expression such as CD40, CD-54 & CD86 and down-regulation of cytokine IL-10 receptor expression. Importantly, there was a significant reduction in bacterial survival inside macrophages upon butyrate treatment. Further, supplementation of mycobacterial growth medium with Butyrate attenuated mycobacterial growth. These results suggest that Butyrate mounts pro-inflammatory and protective responses against mycobacterial infection.

P-16

Investigating the Prevalence and Associated Risk Factors of Irregular Menstrual Cycle Among Undergraduate College Girls During COVID-19 Second Wave in India

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Background: Several studies demonstrated various symptoms and disease severity post COVID-19 outbreak which had enduring effects on people's health. Globally a lot of women are reporting reproductive health issues post-COVID-19. Therefore, the objective of the present study was to investigate the prevalence of and associated factors of irregular menstrual cycle among undergraduate college girls (aged 16-24 years).

Methods: A cross-sectional survey study was conducted using a self-designed reproductive health questionnaire pertaining details of the menstrual pattern, features of hyperandrogenism, lifestyle, and comorbidities among college girls. The responses from 530 girls collected between April to May 2021 and responses (N=508) fulfilling the inclusion criteria were analyzed using GraphPad Prism 5 software.

Results: The prevalence of irregular menstrual cycles was found to be 29.1%. The risk factors associated with irregular menstrual cycle were found to be depression, and stress. Further analysis of data revealed that out of 508 responses, 58 girls were diagnosed with PCOS. Moreover, the girls having PCOS also found to have various comorbidities. The most prevalent comorbidity among girls having PCOS was found to be obesity (60%) followed by an eating disorder.

Conclusions: A significant increase in irregular menstrual cycles in college girls were found during the second wave of COVID-19. The risk factors for causing the irregular menstrual cycle were found to be insomnia, stress, and depression.

Keywords: *Menstrual cycle; COVID-19; Reproductive health; Young girls; Polycystic ovarian syndrome (PCOS)*

P-17

Advancement of Hepatitis B Virus Therapeutics

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Despite being curable by vaccination, hepatitis B virus (HBV) infection is nevertheless a major contributor to chronic liver disease. HB Virus, a small encapsulated virus with a reverse transcribed DNA genome, can infect the liver either acutely or persistently. Hepatitis B virus (HBV) affects 250 million people globally, causing cirrhosis and hepatocellular cancer. Established HBV infections are difficult to treat, but new infections can be vaccinated. Antiviral medications halt viral reproduction, not healing. WHO wants viral hepatitis eliminated by 2030. This requires reducing vertical viral transmission. Since hepatitis B and C cause 96% of all hepatitis-related deaths in India, they are increasingly recognised as a public health concern. It is generally known that hepatitis B vaccination has greatly reduced the incidence of acute and chronic hepatitis B infections and carriage. In order to effectively treat this ailment, the scientific community has focused on developing cutting-edge treatment plans. New treatment strategies that address all HBV genotypes as well as recently emerging viral variants will soon be required. The creation of novel direct-acting anti-viruses that function via a number of mechanisms, including as the degradation of hepatitis B antigen, transcriptional silencing, viral entry, and capsid assembly, will be made possible by a full understanding of the HPV life cycle. Combination therapy that targets several stages of the HBV life cycle and immunomodulators may be the best approach for establishing a long-lasting functional or complete cure. The vaccine should be improved to address issues including low or non-existent response in some risk groups and declining anti-HBs titters that result in occult infections. Biosensors incorporate biological and physiochemical aspects to detect HBV in screen samples, enabling quick viral control. This paper reviews the rationale for progressive treatment strategies and the newest HBV therapeutics findings.

Keywords:- *Antiviral medications, Biosensors, HB infection, HB Therapeutics, HB Vaccination, Transcriptional silencing*

P-18

Identification of Novel Inhibitors against NDM-1 in urinary tract infections

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Uropathogenic *Escherichia coli* (UPEC) is a major cause of urinary tract infection (UTI) and treatment of UTI has been challenging due to increased antimicrobial resistance (AMR). One of the most important types of AMR is carbapenem resistance (CR). CR bacteria are known as an important threat to global public health today among which Class B metallo-beta-lactamases (MBLs) are one of the major factors for resistance against carbapenems**.** Metallo-β-lactamases (MBLs) are an emerging class of antimicrobial resistance enzymes that degrade β-lactam antibiotics, including last-resort carbapenems. Infections caused by carbapenemase-producing Enterobacteriaceae (CPE) are increasingly prevalent, but treatment options are limited.

The enzyme New Delhi metallo-ß-lactamase-1 (NDM-1) provides bacterial resistance by its hydrolytic activity against the β-lactam ring of antibiotics. Inhibition of NDM-1 may prevent the hydrolysis of β-lactam ring of the antibiotics, and therefore, plays an important role against antibacterial resistance. This review summaries β lactam/lactamase Inhibitor combinations that could be potentially used to treat infections caused by NDM producers pathogens. Here, the crystal structure, outer membrane vesicles, Zn(II) as cofactors, surrounding important amino acid residues, newly discovered inhibitors and their mechanism of action are classified which can be used as a reference for the characterization of Novel Inhibitors against NDM-1 in UTIs.

P-19

Prediction of novel and potent inhibitors of Lanosterol-14 alpha demethylase: Structure-Based Drug Designing Approach

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Candida glabrata is the second most common cause of invasive fungal infection. In the limited antifungal drugs, azole antifungals are commonly used to treat candidiasis. Lanosterol 14-alpha demethylase (LDM) is the main target of the azole antifungals. High-level resistance against the azoles indicates the need for novel inhibitors of LDM. In this study, we have screened a large number of small molecules from different chemical databases (ZINC, Drugbank, ChEMBL, and ChemDiv) to find out novel and potential inhibitors of LDM. As a result, from more than a hundred thousand molecules, the two best candidates (ZINC000299817826 and ZINC000095786149) were selected from the top-scoring compounds and further validated in molecular dynamic simulation. Glide score of selected compounds ZINC000299817826 and ZINC000095786149 were -19.33 kcal/mol and -19.13 kcal/mol, suggesting that these compounds bind with LDM with higher binding affinity than the benchmark compound (Itraconazole), which has a Glide score of -6.85 kcal/mol. During molecular dynamics simulations and binding free energy calculations, the protein-ligand complexes of selected compounds also show stable binding.

Keywords**:** *Lanosterol 14-alpha demethylase, molecular docking, molecular dynamic simulation, virtual screening, free energy calculation, phytochemicals*.

P-20

Multiple interactions of CagV and its role in Cag-Type IV secretion system of *Helicobacter pylori*

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Antibiotic resistance in *Helicobacter pylori* urges us to decrypt its pathogenesis machinery bit by bit till we can have a suitable vaccine or a fool proof treatment of *H. pylori* infection. *H. pylori* infected individuals may show severe gastrointestinal maladies ranging from chronic gastritis to peptic ulcer, gastric adenocarcinoma, and mucosa associated lymphoid tissue (MALT). It is also to be noted that *H. pylori* infections are no longer limited to GI tract. Including idiopathic thrombocytopenic purpura, various skin, liver, cardiovascular, neurodegenerative diseases are being reported as clinical outcomes of *H. pylori* infection. The virulent Type I strains of *H. pylori* have been declared as the first bacterial class 1 carcinogen by IARC, a unit of World Health Organization.

One of the primary virulence factors, Cytotoxin associated gene A (CagA) is encoded by 40kb genomic region named as Cag Pathogenicity Island (cag-PAI) along with other Cag proteins which assemble together to form a functional Cag-Type IV secretion system (T4SS). Among these 27 Cag-T4SS components, CagV, a VirB8 homolog, is reported as an inner membrane protein, essential for CagA translocation to host cells and also influence the formation of pilli. Despite of being an inner membrane protein, CagV also interacts with outer membrane subcomplex via CagX. Thus it may considered to be a bridging component between inner membrane and outer membrane complex. The detailed investigations of multiple interactions of CagV with other Cag proteins will help us to have a better understanding of molecular architecture of Cag T4SS and thereby attain an advanced therapeutic control over *H. pylori* infections.

In this present study we performed protein-protein docking between CagF, CagZ and CagV to identify the interacting residues and domains. Our lab has some preliminary data of physical interaction of CagV with CagF and CagZ, essential protein for CagA translocation into host cells.

P-21

In-silico analysis of the unique Cagδ protein of *Helicobacter pylori* type IV secretion system

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Helicobacter pylori is a Gram-negative bacterium which is found in the gastrointestinal tracts of more than half of the world's population. *cag*-PAI genomic region comprises about 27 Cag proteins including an 'Oncoprotein' CagA, a cargo protein. These Cag proteins, altogether, constitute a type 4 secretion system (T4SS) that is known as Cag-Type 4 Secretion System (Cag-T4SS). Cagδ is one of the key components of Cag-T4SS that is essential for both, translocation of CagA and IL8 induction in the host cell. This is the foremost study involving secondary structure, 3D structure prediction as well as interaction analysis of unique protein, namely Cagδ (HP0522). 3D structure prediction was performed utilising the I-TASSER workspace and model was evaluated through generation of Ramachandran plot by PROCHECK. Further protein-protein interactions are studied using STRING tool indicating the interaction of Cagδ with other associated proteins helping in translocation of CagA oncoprotein to the host cell. As a result, we are providing better understanding of structural characteristics and interaction analysis of Cagδ protein. This interaction predicted with other proteins can be further verified through wet-lab experiments. This research may further lead to analysis of structural organization of *H. pylori* T4SS involving Cagδ.

P-22

Identification of natural compound inhibitors of *E. coli O157:H7 MurI* using molecular docking and molecular dynamic simulation-based approach

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The chances of disease outbreak through contaminated fresh produce are high since it is consumed raw. Thus, food borne pathogens are becoming a burden on socioeconomic development and are emerging as a serious global concern. Even though most of the Escherichia coli (*E.coli*) strains are harmless but pathogenic strains like Shiga Toxin-Producing *E.coli* (STEC), can cause significant food-borne illness. *E. coli O157:H7* which is one of the most researched serotypes, has often been linked to significant disease outbreaks. Due to the advent of several resistant *E. coli* strains and the rise in side effects from currently available treatments, there is an urgent requirement to get improved antibacterial agents to fight the emerging problem of antibacterial resistance. Natural compounds are emerging as a cutting-edge therapy that can stop bacterial development. Moreover, glutamate racemase of *E.coli* (EC-MurI) has become a desirable target as it is an important enzyme involved in peptidoglycan (PG) biosynthesis. Thus, in this study insilico screening of different natural compounds was done to identify potential inhibitors of enzyme EC-MurI. Initially, computational methods were adopted to identify the target sites on EC-MurI and subsequently molecular docking studies resulted in a few potential hits which were further assessed for their structural activity and binding. Finally molecular dynamic simulation studies revealed that amongst the screened 1200 compounds, one of the compound proved to be the most stable that can be taken forward for further studies as a potent EC-MurI inhibitor and a potential lead molecule for treating *E. coli* associated food borne illnesses.

P-23

Effect of Boldine and Morin on the Intracellular Growth of Mycobacteria in Human Macrophages

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Even after the worldwide efforts to combat the global threatening diseases tuberculosis (TB), it is still remaining a major cause of mortality in many developing countries including India. TB globally cost millions of people's life till now and its main causative agent is *Mycobacterium tuberculosis*. The main reason for this globally tremendous diseases, TB is the uniqueness of its causative pathogen *Mycobacterium tuberculosis*, because it has ability to preserve in the host and can strongly affects the several host defence mechanisms like autophagy, apoptosis, phagosome-lysosome fusion etc. In the past year research experiment, scientists have found that host directed therapy can be an efficient strategy to combat the *Mycobacterium tuberculosis* infection because that potentiates host's anti–TB effector mechanism. Hence, induction of house hold mechanism by the drugs can be proved beneficial in the context of TB treatment. Our current study was attempted to understand the anti-mycobacterial effect especially hosts immune mechanism by inducing the effect of drugs on the different strains of Mycobacterium. For this study, we have used Boldine and Morin (plant product) which may help in shorting the treatment period by enhancing the host immune response against tuberculosis.

P-24

Non-tuberculosis mycobacterial pulmonary infection: a neglected disease of today but a concern for tomorrow

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Non-tuberculosis mycobacterial pulmonary infection (NTM-PI) has increased tremendously in the last decade. It is closely related to *Mycobacterium tuberculosis* and have over 170 identified species but most of them are non-pathogenic. *M. abscessus* is one of the distant relatives of *M. tuberculosis* known to be present in environment (soil, wastewater etc.). It causes disease in cystic fibrosis (CF) patients or individuals with defective lung structure or immunocompromised people. Several cases have also been reported in immunocompetent individuals having vitamin-D deficiency and elderly white post-menopause women with low body mass index (Lady Windermere syndrome). However, the exact reason why only a certain portion of population is infected with NTM-PI is still unknown. Based on phylogenetic characteristics *M. abscessus* group (MABS) is recently considered as a separate clade named *Mycobacteriodes abscessus*. The MABS group is generally antibiotic and disinfectant resistant, and generally do not get affected by pH change. The NTM-PI is difficult to manage as it require prolonged antibiotic regimens with a complexity in the microbiology, radiology, medical treatments, and drug–drug interactions. The major difference between NTM-PI and tuberculosis is that the former is non-communicable except in CF patients infected with MABS. Further studies should focus on deciphering the factors such as Vitamin-D deficiency causing NTM-PI, and why only a certain portion of population is susceptible to it. The diagnosis for NTM-PI take months or often misdiagnosed as they have very similar symptoms as tuberculosis. The diagnosis is, therefore, one of the major challenges for NTM-PI patients.

Keywords: *Mycobacterium abscessus*, MABS, NTM, pulmonary infection

P-25

On Water Pictet-Spengler Reaction of Tryptophan for the Synthesis of Natural Products Stellarines A, B and *β*-Carboline Derivatives: Their Molecular Docking against SARS Covid Protease

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An Environment friendly synthesis of 1-benzoyl-9H-pyrido[3,4-b] indole-3-carboxamide β-carboline derivatives has been reported via Pictet-Spengler Reaction of tryptophan methyester with 2-oxoaldehydes in water. Two natural products Stellarines A and Stellarines B having anti-inflammatory activity against *i*NOS inhibition (IC50 value of 19.3 and 18.6 µM) isolated from the root of Stellaria dichotoma L. var. lanceolata Bunge were also synthesized from □-carboline derivatives by amidation followed by Buchwald coupling. The synthetic strategy has advantage of using nontoxic and inexpensive condition for producing excellent yields. These functionalized *β*-carboline carboxamide derivatives have been evaluated against SARS Covid Protease using molecular docking studies.

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P-26

An Efficient Synthetic Approach towards the Natural Product Herdmanine D: Their Docking Studies against HSA Protein

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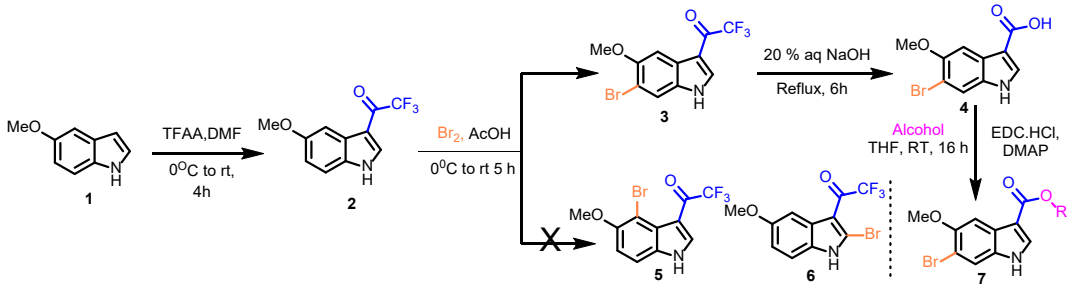
The synthetic approach was developed for the preparation of the regioselective 6-bromo-5-methoxy-1-H-indole-3-carboxylic acid by doing hydrolysis of trifluoroacetylated indole. The formation of mono-bromine substituted product is the most advantageous step of this approach which was confirmed by ^{1}H-NMR data. The brominated 5-methoxy-3-trifluoroacetylated indole is the key intermediate for the synthesis of the natural product, Herdmanine D. These developed bromo-indoles having carboxylic acid functional group were further treated with a variety of aliphatic / aromatic alcohols to form ester derivatives, which were evaluated against HSA Protein by docking studies.



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P-27

Identifying Non-Invasive Diagnostic Protein Markers in Urine Samples Of Malaria Patients

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Malaria is a life-threatening disease caused by the protozoan parasite, *Plasmodium.* According to WHO, in 2020, around 241 million cases of malaria were reported across the world. When the parasite infects the host, there is a continuous reciprocation of metabolites between the two which may disturb the biochemical profiles of both. Hence, detection of the metabolites whose levels are altered in infected patients in comparison to healthy individuals may be a sign of parasite activity or the host's response to the infection. Microscopy of Giemsa-stained blood smears is the gold standard method for malaria detection. Other methods used for malaria diagnosis include PCR based tests, rapid diagnostic tests (RDTs), automated blood cell analysers. So, several diagnostic methods are available for malaria but most of them are based on invasive methods and have certain limitations. Therefore, there is a need for an effective non-invasive method for malaria diagnosis. The methodology includes sample collection, proteomics analysis by LC-MS/MS, cloning of selected proteins by PCR, purification and characterization of proteins, ELISA based quantitative detection of proteins. In the mass spectrometry analysis, *Plasmodium* proteins such as rifin, PfEMP1, merozoite surface protein, GAPDH, a 31 kDa antigen, plasmodial isoform of actin have been found. The cloning of selected proteins is being done. The outcome of this project will be the identification of diagnostic biomarker proteins in the urine of patients infected with *P. falciparum* and/or *P. vivax.* The outcome will help in developing better diagnostic techniques for malaria using non-invasive procedures.

P-28

Human immune-deficiency virus co-infection with *Mycobacterium tuberculosis*

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Co-infection may significantly inhibit the host's immune system, increase antibacterial therapy intolerance and be determined the prognosis of the disease. On the other hand, the Co-infections of *Mycobacterium tuberculosis* and Human immune-deficiency disease/AIDS constitute the main burden of health care systems and pose particular diagnostic and therapeutic challenges. Tuberculosis (TB) is a devasting disease that accounts for high proportion of infectious disease morbidity and mortality worldwide. HIV Co-infection exacerbates tuberculosis. Infection with HIV is most powerful known risk factor for *Mycobacterium tuberculosis* infection and to active disease which increases the primary infection or reinfection and also the risk of TB reactivation for patients with latent TB. In the individual, the host, the two-pathogens relationship in TB and HIV is required. In addition, the Bacillus Calmette-Gurein vaccine is primarily used against *M. tuberculosis*. TB is the most common cause of AIDS-related death. Thus, the *M. tuberculosis* infection also has a negative impact on the immune response to HIV, accelerating the progression from HIV infection to AIDS. The clinical management of HIV associated with TB includes the integration of anti-TB treatment, use of antiretroviral therapy (ART) prevention of HIV- related comorbidities, and management of drug cytotoxicity and prevention/treatment of immune reconstitution inflammatory syndrome (IRIS). Enhanced Understanding the nature of the interactions between *M. tuberculosis* and Human immune-deficiency disease will be crucial for the development of therapeutic strategies against co-infection. In this review, we provide an overview of clinical and immunological features of HIV and TB co-infection followed by an introduction to systems approaches and concrete examples of how such approaches are useful.

Keywords: ART, HIV, Immunological, Mycobacterium Tuberculosis.

P-29

Identification of novel compound inhibiting Uropathogenic *E. coli* biofilm formation

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Background: Biofilms are multicellular communities held together by a self-produced extracellular matrix which are resistant to antimicrobials. Antimicrobial resistance in Uropathogenic *E. coli* (UPEC) is a crucial problem in patients with Urinary Tract Infections (UTI) as UPEC accounts for approximately 80% of UTI. Therefore, there is a demand for the discovery and development of novel antibiofilm compounds for preventing and treating biofilm-related infections successfully and safely. In this lieu, we have identified a novel compound STL 522171 targeting Uropathogenic *E. coli* biofilm formation.

Material/methods: In the present study we have reported the effect of STL 522171 against UPEC strain CFT073 biofilms. (ATCC # 700928; United States). In order to evaluate the cytotoxicity of STL 522171 on T-24 cells, MTT proliferation assay was conducted. Biofilm formation was quantified by crystal violet staining and further confirmed fluorescence microscopy.

Results: The viability of T-24 cells remained above 60% at STL 522171 concentrations, ranging from 0 to 300 µM post 48 hours of treatment. The significant (36%) reduction in UPEC biofilm (p-value <0.0001) was observed at 300 µM STL 522171 as determined by crystal violet assay. The same results were qualitatively observed in fluorescence microscopy and SEM analysis.

Conclusion: Our study revealed that STL 522171 effectively reduced UPEC biofilm formation and thus provide a theoretical foundation for the prevention of biofilm-associated uropathogenic *E. coli* infections.

P-30

Uropathogenic *E. coli* and Commensal *E. coli* CRISPR-Cas system Spacers Show Differential Targeting to Viral Genes

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In many Bacteria and most Archaea, clustered regularly interspaced palindromic repeats (CRISPR) act in a sequence-specific manner by providing acquired immunity against viruses and plasmids. The CRISPR region consists of several direct repeats separated by spacer sequences which are unique sequences against bacteriophages or plasmids. Here, we amplified the CRISPR-loci by PCR of both Uropathogenic *E.coli* (n=70) and commensal *E. coli* (n=70) strains isolated from urine of suspected UTI patients and faecal matter of healthy individuals respectively. After purification of PCR products, all sequences retrieved were analysed by CRISPR Finder webtool and later, CRISPR spacers were predicted for their most likely targets by CRISPR Target. We have annotated these CRISPR spacers sequences to their viral and phage genomes to know their biological relevance. The comparative analysis of CRISPR content of UPEC and commensal *E. coli* isolates unfolds some interesting theory of CRISPR-Cas system. UPEC has more CRISPR array content than commensal *E. coli* and a total of 751 unique spacers were extracted from both groups. In addition, the CRISPR spacers matched against 110 viral and 109 phage genomes. After Manual curation of all hits to genes, UPEC spacers showed preferential matching to structural genes while commensal showed to host-pathogen interaction and DNA Repair/ recombination genes. Interestingly, some important host- pathogen interaction proteins were identified ranging from Host cell lysis, Immune evasion and DNA translocation. These findings might aid in the development of new antiviral and antiphage therapies by elucidating the innovative methods utilised by bacteria to combat phages and viruses.

P-31

"B-10" regulatory B cells (Bregs) suppress osteoclastogenesis and ameliorates inflammatory bone loss under post-menopausal osteoporotic conditions

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Background: In 2002, a subset of B-cells has been identified named as regulatory-B-cells "Bregs". Several evidence suggest that B-10-Bregs plays a vital role in inflammatory-disease-conditions. Nevertheless, no study till date has revealed the significance of Bregs in modulating-osteoclastogenesis and its probable-contribution in inflammatory-bone-loss associated with post-menopausal-osteoporotic-(PMO)-conditions. To-our-knowledge, this study for the first-time investigated the anti-osteoclastogenic-potential of Bregs and their subsequent-role in PMO. **Aim & Objectives:** To determine the Immunoporotic-potential of Bregs in PMO-conditions. **Material and Methods:** Firstly, to investigate the bone-heath-modulating-potential of Bregs, co-culture between bone-marrow-cells-(BMCs) and differentiated-Bregs were carried out. TRAP-staining was performed for evaluating presence of multinucleated-TRAP-positive-osteoclasts. Trans-well and IL-10-neutralization-assay was performed. Lastly, for *in-vivo* experiments C57BL/6-mice were divided to two-groups: Sham and ovariectomy (Ovx-ovaries-removed-bilaterally). After 45 days, various lymphoid-organs mainly bone-marrow (BM) and spleen, bones, blood were harvested for assessing several osteo-immune-parameters. ELISA was done for serum-cytokine-analysis. For-human-studies, PBMCs were isolated and cultured in the presence of Bregs-stimulating-conditions (CpG and CD40L) for 48 h and flow-cytometry was done to evaluate the percentage of Bregs. **Results:** Our *in vitro* BMCs and Bregs-co-culture assays suggested that Bregs suppressed RANKL-induced-differentiation of osteoclasts in a density-dependent-manner. Furthermore, our trans-well and neutralizing-antibody-experiments revealed that Bregs inhibited-osteoclastogenesis in an IL-10-cytokine-dependent-manner. Our F-actin-ring-polymerization assay clearly indicated that along with suppressing-osteoclastogenesis, Bregs also inhibited the functional-activity of mature-osteoclasts. Moving-ahead-in-our-study, we further-explored whether these "B-10" Bregs plays any role in mediating-inflammatory-bone-loss in ovariectomy-induced-postmenopausal-osteoporotic-mice-model (Ovx). Interestingly, our *in-vivo* data suggest that frequencies of both total B cells-($CD19^{+}IL\text{-}10^{+}$) and B10-Bregs-($CD19^{+}CD1d^{hi}CD5^{+}IL\text{-}10^{+}$) were significantly-reduced in BM (major-site-of-osteoclastogenesis) and in spleen (prime-site-for-Bregs-differentiation) of Ovx-mice in comparison to sham-group. In addition, our serum-cytokine-analysis data indicated towards significant-reduction of IL-10 cytokine-levels in serum of Ovx-mice, thereby further supporting our observations. Of note, suppression-assay clearly indicated that Bregs-harvested and generated from Ovx-mice showed-reduced-tendency to suppress the proliferation of CFSE-labelled-effector-T-cells in comparison to sham group thus suggesting towards reduced immunomodulatory-potential of Bregs under estrogen-deficient-conditions. In consistent to this, our *in-vitro* data further demonstrated that exogenous addition of 17β-estradiol significantly-enhanced the percentage of IL-10 producing Bregs and its efficacy to modulate the immune-cells. Importantly, in our clinical-studies we observed that the percentage of peripheral-Bregs ($CD19^{+}CD38^{hi}D27^{hi}IL\text{-}10^{+}$) was significantly-reduced in post-menopausal osteoporotic-patients in comparison to the healthy-control. **Conclusion:** Altogether, our-research clearly establishes that Bregs inhibit-osteoclastogenesis in an IL-10-dependent-manner. Additionally, both our pre-clinical and clinical-results showed that numerical-defects in the percentage of Bregs as well as their diminished capacity to produce IL-10 along with their compromised-immunosuppressive-efficacy collectively are responsible for exacerbated inflammatory-bone-loss-under-estrogen-deficient-conditions. In summary, our study for the first-time explores the "Immunoporotic" role of Bregs in bone health.

P-32

Li-Koff: Genetically Engineered *E. coli* to Detect and Degrade Nitrosamines

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Nitrogen pollution is currently very concerning owing to the dearth of awareness and research on it. Nitrogen that is biologically, photochemically, or radiatively active is known as reactive nitrogen. Reactive nitrogen can cascade through the ecosystem, creating smog, acid rain, biodiversity loss, and other problems. Its levels in drinking water, packaged foods, etc have grown substantially, and it is not even looked for at a scale that it demands. N-nitrosamines are by-products of reactive nitrogen and water reaction and are recognized as mutagenic and potential carcinogens to humans and as contaminants of the environment including water resources. There is still limited scientific data about N-nitrosamines, stressing the need to understand their long-term impact on human health better and determine their concentration in various sources.

It was this realization that led to the inception of our project and motivated us to develop Li-Koff which is a genetically engineered E. coli to detect and degrade N-nitrosamines. It is a whole cell-based bio-sensing solution in which we have exploited nitosamine's alkylating property.

E. coli has a natural adaptive DNA damage repair mechanism known as ADA response. The DNA gets damaged upon methylation by alkylating agents like nitrosamines and the damaged DNA is repaired using four Ada response proteins, encoded by three different operons of the "Ada Regulon". We have manipulated this regulon to make *E. coli* generate fluorescence which will confirm the presence of nitrosamines.

The DNA damage repair mechanism of *E. coli* gets induced by an O6-methylguanine (O6-MeG) lesion formed due to methylation of DNA in the presence of nitrosamines. The methyltransferase activity of the ADA response protein aids in a methyl shift reaction from the O6-MeG lesion to the Ada protein which repairs the DNA. For the purpose of our project, we have selected the ADA-AlkB operon which gets induced by methylated Ada, which acts as a transcriptional activator, in the presence of an O6-methylguanine lesion. We have placed a fluorescence reporter gene downstream of the ADA-induced promoter in the operon so that when the methylated ADA protein binds to the promoter, it transcribes the gene placed downstream and generates fluorescence.

These genetically engineered *E. coli* will later be immobilized on papers and transformed into easy-to-handle dip-sticks and paper-based kits ultimately providing a substitute for the expensive detection of nitrosamines.

P-33

Comparative Analysis of Symptoms, Severity and Breakthrough Infections During Three Waves of COVID-19 in India

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India has experienced three COVID-19 epidemic waves characterized by clinical spectrum of symptoms and severity of infections varying from mild to severe. However, the variation in symptoms and severity is hinge on coronavirus strain and vaccination status of infected individual. Therefore, the aim of the present study was to investigate and compare the clinical characteristics such as symptoms, severity and breakthrough infections of COVID-19 patients among three waves of epidemic in India. This cross-sectional survey study included data from 3404 Indian participants. Data were analysed based on SARS-CoV-2 infection, associated symptoms, severity, vaccination status, comorbidities and re-infection during epidemic three waves. Out of 3404, 37.19% (n=1266) individuals (364 during the first wave, 663 during the second wave and 239 during third wave) had experienced COVID-19 with 14.37% breakthrough infection. The percentage of asymptomatic infection, SARS-CoV-2 infections and re-infection post vaccination found to be increased and symptomatic infection decreased from first wave to third wave. Intriguingly, the vaccination was found to reduce rate of symptomatic infection. Symptoms such as fever, persistent cough were found most prevalent during first wave while cold/running nose and shivering were found most prevalent during third wave predisposing the mild illness. The high prevalence of asymptomatic infection during third wave could be the major reason in rapid dissemination of infections resulting in high breakthrough infections and higher asymptomatic infection post vaccination confirms the importance of vaccination in ameliorating the severity and symptoms of COVID-19 infection during third wave.

P-34

Cross-talk between canonical/non-canonical wnt components upon esculetin mediated leukemic blast cell differentiation

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Background: *Wnt* signaling is an evolutionarily conserved pathway, and the role of canonical and non-canonical Wnt axes in various cellular processes is well established. However, the interplay between canonical Wnt/β-catenin and non-canonical Wnt/PCP, /Wnt/Ca^{+2} axes during cellular differentiation remain poorly understood. **Objective:** To delineate the interplay of both the major Wnt axes upon esculetin-mediated leukemic blast cell differentiation. **Methodology:** Human acute myeloid leukemic cells (Kasumi-1) were used as a model system. Effect of esculetin on the expression profile of 84 canonical/non-canonical Wnt associated genes was analysed using RT^2 PCR profiler array. Manual analysis of differentially expressed genes was carried out to determine esculetin-mediated cross-talk between different Wnt axes and associated phenotypic alterations. **Results:** Analysis of the **Wnt-associated gene expression profile revealed that esculetin exposure resulted in the downregulation of canonical Wnt-associated genes (**β-catenin and LEF) and their downstream targets (**c-Myc, Cyclin D1). On the other hand, non-canonical Wnt/PCP-related genes *viz.* VANGL, PRICKLE, DAAM1, and NKD1 were markedly upregulated upto threefold. These alterations were coupled with upto ~16 fold upregulation of** Wnt/Ca^{+2} associated genes **such as Wnt5a, FZD5, KREMEN1, NFAT. Increased levels of intracellular calcium upon esculetin treatment further confirmed the activation of non-canonical Wnt/Ca^{+2} axis. Additionally, negative regulators of canonical axis (WIF, DKK, IDAX),** together with specific canonical Wnt targets associated with cellular **differentiation were found to be upregulated upto ~6 fold. The differentially regulated wnt genes upon esculetin treatment were accompanied by growth inhibition and induction of terminal differentiation in Kasumi-1 cells as indicated by upregulation of maturity CD38/CD11b while downregulation of immaturity marker (CD34) expressions.** Conclusion: The present study demonstrates the importance of selective activation of non-canonical while suppression of canonical Wnt axes during induction of differentiation upon esculetin treatment in leukemic blast cells.

P-35

Pre-clinical standardization and development of oral squamous cell carcinoma (OSCC) model in rats

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Preclinical model of oral squamous cell carcinoma (OSCC) is very crucial for identifying therapeutic targets and strategies. The validity of a model is very essential for looking into the intricacies of the disease. Recent advancements in the field of OSCC have been achieved, but still identification of Lymph node metastasis is a challenge. Therefore, the present study identifies the challenges faced during the standardization and development of the chemical carcinogen-induced OSCC rat model.

Sprague Dawley Rats (n=40, ♂) were divided into 4 groups: control (C); 4-NQO-50 µg/ml (N50); 4-NQO-100 µg/ml (N100); Arecholine + 4-NQO-100 µg/ml each (NA). Food and water were provided ad libitum (Drug added to drinking water except for Control group). Behavioral studies were carried out post 1month. Daily monitoring of health and behavioral aspects was carried out in the first week, followed by biweekly monitoring. Hyperplasia and dysplasia in tongue were monitored as the endpoints.

N50 rats were stable throughout the study. However, the N100 group rats showed severe reduction in body weight, which were supplemented with black gram. NA group rats presented a 50% death rate and severe loss in body weight. Anxiety and aggressive behavior, head tilt, vision loss, circling behavior, mobility issues, poor grooming behavior, hair loss, swollen gonads and nasal burns in 70% of rats in N100 and NA groups observed. In conclusion, Arecoline treatment along with 4-NQO, and high concentration 4-NQO treatment (100 µg/ml) resulted in drastic death loss as well as neurological deficits, making them unsuitable for further studies and thus had to be discontinued. 4-NQO at 50 µg/ml dose was suitable to initiate hyperplasia and dysplasia over a period of 7 weeks in rats.

Keywords: *OSCC, rat models, chemical carcinogen-induced, behavioral studies*

P-103

Identification of biomarker genes and significant pathways of pancreatic cancer

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Pancreatic Cancer is the leading cause of cancer death, more than 5 lakhs new cases were reported in 2020. The global digestive cancer burden is higher in the young generation and apart from socioeconomic status, the genetic factor plays an important role. Due to the common symptoms of digestive cancers, it is difficult to identify pancreatic cancer. Therefore, it is of paramount importance to identify the potential biomarkers, correlate and interpret the early prediction possibilities to avoid metastasis, undergo timely treatment and plan prevention strategies. In the present study, we have conducted comprehensive bioinformatics analysis and identified crucial genes uniquely responsible for pancreatic cancer. RNA-seq datasets from various studies are taken from NCBI SRA and investigated through the NGS pipeline using RNA seq analysis. The highly overexpressed and under expressed genes in cancer are selected to study the pathways involved using DAVID GO Ontology Tool. Until now, we have identified 10 genes overexpressed and under expressed in pancreatic cancer and we are studying the structural features of these genes and the pathways they are involved in. Further, we will use this biomarker study to identify and analyze the symptoms encountered by patients in their early stages of pancreatic cancer and use this approach as a good therapeutic target to minimize treatment dependency at the crucial stage.

Day-2

SESSION IV: SYSTEMIC INFLAMMATION VS NEUROINFLAMMATION: THE TWO DRIVERS OF NEURODEGENERATIVE DISORDERS

P-36
Neuroprotective effect of Novel adenosine $A_{2A}R$ antagonist of (4E)-4-(4-bromobenzylideneamino)-3-phenyl-2,3-dihydro-2-thi-oxo-thiazole-5-carbonitrile (BBPT) in 6-OHDA induced Parkinson diseases

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Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by dopaminergic neuron damage in substantia nigra pars compacta which involved in neuro-inflammation, dysregulation in calcium signalling, autophagy and apoptosis. A_{2A} R antagonist has been suggested to have a neuroprotective effect in PD models. Earlier we had reported the therapeutic potential of (4E)-4-(4-bromobenzylideneamino)-3-phenyl-2,3-dihydro-2-thioxothiazole-5-carbonitrile (BBPT) as A_{2A} receptor antagonist. Novel adenosine A_{2A} receptor antagonist with high binding affinity, selectivity towards A_{2A} receptor and good water solubility. The present study was aimed to investigating the efficacy of BBPT in counteraction of free radical-scavenging and superoxide scavenging activities by 6-OHDA induced oxidative stress in primary dopaminergic neuronal cell lines from Po and P1 SD rats. Herein, we have investigated the effect of BBPT as antioxidant and biochemical study with standard like DPPH, H2O2, ABTS, SOD, Iron chelating, nitric oxide associated biomarkers such as MDA, catalase, superoxide dismutase, nitric oxide and reduced glutathione level. The findings suggested that the BBPT may act as a powerful antioxidant by reducing oxidative damage caused by 6-OHDA. Thus, the research amply supported BBPT' as a potent anti-parkinsonian drug with a significant capacity to prevent neurodegeneration.

Future research will focus on the A_{2A} R antagonist in 6-OHDA-induced Parkinson's disease (PD) in primary dopaminergic cells and in-vivo SD rat models, which primarily cause cell death by reducing intracellular Ca^{2+} excess and oxidative stress by ROS, SOD, and neuro-inflammation. This might have an impact on the pathophysiology of PD and potential treatment targets in the future.

P-37

The Role of BDNF gene in Diabetes

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Brain-derived neurotrophic factor (BDNF) is a Neuro-trophin, which plays an important role in the central nervous system, and systemic or peripheral inflammatory conditions, such as acute coronary syndrome and type 2 diabetes mellitus (T2DM), expressed in several non-neuronal tissues, and platelets are the major source of peripheral BDNF. Here, the reviewed potential role of BDNF in platelet reactivity in T2DM and its association with selected inflammatory and platelet activation mediators. Besides that, we focused on adipocytokines such as leptin, resistin, and adiponectin which are considered to take part in inflammation both lipid and glucose metabolism in diabetic patients as previous studies showed the relation between adopocytokines and BDNF. The evidences of the anti-diabetic effect of BDNF and the association with circulating inflammatory cytokines in T2DM.Diabetes, one of the most prominent Non-communicable diseases, is affecting Indian population, much faster rate compared to other nations. Our study has revealed significant structural details which can be useful in understanding the signaling pathways and downstream targets that can get affected in the diseased state.

P-38

The inhibitory effect of methyl ammonium compounds on acetylcholinesterase activity

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The human brain consists of around 86 billion cells, which are classified into neuronal, glial, endothelial, epithelial, and immune cells. Neuronal cells secrete neurotransmitters, the chemical messengers that carry nerve impulses to another cell across a synapse. Increasing evidence suggests that a class of compounds, methylamines which are alkyl-derivatives of ammonia may modulate neuron firing. Methylamines (e.g., sarcosine, betaine, DMG) arise during amine catabolism endogenously and target voltage-operated potassium channels in neurons, inducing the release of neurotransmitters. Few methylamines like sarcosine effectively regulate surface trafficking of glutamate receptors, N-methyl-D-aspartate receptor (NMDAR), and also regulate brain glycine levels. Several clinical reports also suggest that betaine has been associated with improved cognition and neuroprotection. Sarcosine and dimethyl glycine (DMG) have also been reported to affect glycine binding site of NMDARs where sarcosine and DMG act as full and partial agonists respectively. These brain methylamines come under the class of quaternary ammonium compounds which are, indeed, inhibitors of acetylcholinesterase (AChE). AChE is an enzyme present in the synapse and is responsible for the degradation of the neurotransmitter, acetylcholine (ACh). To date, no studies have been conducted about the effect(s) of these molecules on human AChE and, therefore, their role in the human brain is not clearly understood. In the present study, we have systematically investigated the effects of 4 different methylamines (betaine, DMG, gamma butyrobetaine, and sarcosine) on the functional activity of AChE. We discovered that all methylamines inhibit AChE and extent of inhibition depends on the number of methyl groups present in the molecules.

P-39

Effect of Homocysteine-thiolactone on the reservoir protein, Hemoglobin

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In an error-editing reaction, homocysteine-thiolactone (HTL), a hazardous reactive thioester, is created from homocysteine (Hcy) by methionyl-tRNA synthetase. It is thought that the development of an adduct with the protein's lysine residues—a process known as "N-homocysteinylation"—is the primary source of HTL's toxicity. Different serum proteins that have been altered by HTL have been discovered thus far, and their reactivities have been clarified. Another class of proteins, however, is impervious to changes brought about by N-homocysteinylation. Here, we have looked at the structural and functional effects of N-homocysteinylation by HTL utilizing Hemoglobin (Hb) as a model protein. Intriguingly, we discovered that the protein's structural conformation did not change significantly at first when it was incubated with HTL; however, as the concentration of HTL is increased, the protein tends to form a partially unfolded intermediate structure with a subtly distorted secondary structure. The research could shed light on the latest pathogenic effects of hyperhomocysteinemia.

P-40

Effect of Quinoline based Ionic Liquids on the aggregation and amyloid fibril formation of Bovine Serum Albumin

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Proteins are momentous biomacromolecules with marked biological essence. The unfolding of proteins under stressful conditions is one of the prevailing challenges in maintaining their stability. In this regard, we present the molecular chaperon activity of quinoline-based biocompatible ionic liquids (ILs) against the thermally induced amyloid fibril formation in Bovine Serum Albumin (BSA). Herein, a series of Quinoline-based ionic liquids (1-Dodecylquinolin-1-ium bromide {[C_{12}quin]Br}, 1-Hexadecylquinolin-1-ium bromide {[C_{16}quin]Br}, 1-Eicosylquinolin-1-ium bromide {[C_{21}quin]Br}) is synthesis and validated using Nuclear Magnetic Resonance (NMR) spectroscopy and Infrared Spectroscopy. The structural changes induced in BSA before and after encountering the synthesized IL is further corroborated with several spectroscopic analysis such as UV-Visible, Steady-State Fluorescence, Circular Dichroism (CD) spectroscopy and Dynamic light scattering (DLS) measurements. The morphology of the BSA amyloid fibrils was characterized using Scanning Electron Microscopy (SEM) and Transmission Electron microscopy (TEM). Quinoline and its derivatives are recognized to manifest bioactive and medicinal properties and hence are utilized in the formulation of a wide range of antimicrobial compounds. The antimicrobial activity of the synthesized ILs is substantiated using disc diffusion assay against various pathogenic microbes. Overall, this study not only highlights the mechanism of BSA fibril formation but also demonstrated the antimicrobial and chaperon activity of the synthesized Quinoline based ILs.

Keywords: Serum Albumin, Quinoline-based IL, molecular chaperon, amyloid fibrils, antimicrobial activity.

P-41

Plumbagin induced conversion of protofibril into fibril of human serum albumin is an accelerated process

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Plumbagin (PL) is a naphthoquinone generally isolated from the roots of the medicinal plant *Plumbago zeylanica* L (Chitrak). The roots of *Plumbago zeylanica* have been used in Indian medicine for more than 2,500 years for treatments of various ailments. In this work, we study the effect of Plumbagin binding on the biophysical properties and aggregation process of human serum albumin (HSA) using multi-spectroscopic methods. The PL–HSA binding studies were performed using UV/Vis difference spectroscopy and fluorescence quenching method. Plumbagin was found to strongly bind HSA with association constant (K_{bind}) ~ 10^5 M^{-1} and binding capacity of ~1. The PL binding significantly expose the lone Try-214 to the solvent indicating disruption of tertiary structure of the protein. However, small increase in α-helical content was noted. Thermal and chemical unfolding of the proteins indicated only a marginal stabilisation of the protein. Interestingly, PL was found to modulate temperature-induced aggregation pathway of the protein. It converted biexponential kinetics of HSA aggregation into a rapid single exponential kinetics curve. The PL binding changes the morphology of HSA aggregate from small protofibril like structure to long fibrillar structure. Far-UV circular dichroism study of aggregates indicated that fibrils in the presence of PL contained more extended beta sheet structures as compared to in its absence. This study offers opportunities to explore the fine differences existing in the mechanism of formation of ligand-induced different aggregate species in their precise molecular structure.

P-42

Chrysin binding modulates conformational dynamics of human serum albumin

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Human Serum Albumin is the most abundant plasma carrier protein. Protein-ligand interaction studies are important to understand the biological mechanisms. Structural changes in proteins caused by the binding of ligands are an essential part of the mechanism of action and regulation of biological activity. These binding studies form the basis of the drug discovery process. In this work, we investigated the potential of chrysin to interact with Human Serum Albumin using spectroscopic techniques. Chrysin (CHR), a dihydroxyflavone, shows a variety of pharmacological properties comprising antioxidant, dietary supplement, antiapoptotic, anticancer, and neuroprotective effects. We showed that chrysin binding to HSA induces local conformational alterations in it. Further, we also found that binding of chrysin to HSA decreases the conformation dynamic of the protein. Binding and conformational studies as followed by various secondary and tertiary structure studies revealed effects of chrysin binding to HSA.

Keywords: *Human Serum Albumin, Chrysin, Protein-ligand interaction, fluorescence spectroscopy.*

P-43

TMAO influences Acute phase protein

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Atherosclerosis is a chronic multifactorial disease characterized by mainly aberrant lipid metabolism and inflammation in vessel wall. The cardiovascular diseases based on atherosclerosis is currently the major cause of mortality. TMAO is a gut metabolite well known to cause atherosclerosis. Concentration of TMAO is very well known to increase in blood in atherosclerotic condition. Based on several findings TMAO can upregulate pro-inflammatory cytokine release (for instance IL-6, IL1B) and can also disrupt lipid homeostasis by upregulating CD36 cholesterol efflux receptor and downregulate ABCA1 receptor in macrophage and also upregulate adhesion molecule expression like SELE, ICAM1, MCP1 and proinflammatory cytokine release in endothelial cells but the exact mechanism of how TMAO increase the expression of adhesion molecule and proinflammatory cytokine is unknown. Here, we will try to find out that TMAO may bind to protein upregulate in atherosclerosis like Acute phase proteins (Antitrypsin, Thrombin, fibrinogen) and modulate them in such a way which can increase plaque vulnerability. Acute phase proteins are well known to increase in inflammatory condition and also increases several fold in chronic inflammatory condition like in atherosclerosis and these Acute phase protein are also well known to bind with metabolite like TMAO and drugs. Several phytochemicals such as resveratrol is well known to decrease plaque vulnerability in vitro and in vivo model and also the phytochemicals like curcumin have shown a very well effect on plaque size with no adverse effect. Therefore, we will screen the thousands of phytochemicals from HERB database and find out 2-3 phytochemicals which can inhibit atherosclerosis induce by TMAO modulated proteins.

P-44

Trans-acting regulatory molecules of Human Prdx6

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The moonlighting protein, Prdx6 exhibits peroxidase activity, phospholipase activity and lysophosphatidylcholine acyl transferase (LPCAT) activity. Enzymatic activities of Prdx6 can be regulated by multiple factors. However, till now any domain responsible for the functional regulation has not been known. Prdx6 consists of thioredoxin fold and C-terminal domain. Thioredoxin fold is responsible for all activities that Prdx6 exhibits. Role of C-terminal domain is not properly unveiled. Any sequence change in C-terminal region might be responsible for structural differences in the thioredoxin fold. On this aspect, there is existence of some work in which they made systematic mutations in a segment of C-terminal region which exhibited increase in activity. That means there is a crosstalk between thioredoxin fold and C terminal domain. C-terminal domain might be acting as cis-acting regulatory site and there must be some trans acting elements that can regulate the structure and function of enzyme. One important possibility of such trans acting regulatory molecule is small molecule metabolites that specifically accumulated by organisms along with antioxidant enzymes such as Prdx6 in order to protect themselves from stressful conditions. In our study on such small molecule metabolites , Myo-Inositol and Beta-Alanine specifically indicated that they could be a trans acting regulatory molecule for Human PRDX6 that binds to cis acting regulatory site of prdx6 and regulates its function.

P-45

ROLE OF EXTREMOLYTES IN PREVENTING TOXIC PROTEIN INCLUSIONS

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Extremolytes are organic osmolytes obtained from extremophiles. Extremophiles are able to survive in extreme conditions because these compounds protect the biological macromolecules and cells from damage by various stresses. These extremolytes are low molecular weight, polar compounds and can be zwitterionic, non-charged or anionic. They can be accumulated by cells to exceedingly high levels without disturbing vital cellular functions. Extremolytes can be of various types belonging to polyols (glycerol, mannitols, sorbitols), amino acid and its derivatives (proline, ectoine, hydroxyectoine), sugars (trehalose, sucrose), phosphorylated compounds (di-myoinositol phosphate, di-glycerol phosphate, cyclic diphosphoglycerate), heterosides (α-D-mannosylglycerate, α-D-mannosylceramide etc.). Studies done on extremolytes have shown that they are one of the excellent protein stabilizers and influence enzyme activities. But no systematic studies have been done to date regarding the identification of the most potent anti-aggregating molecules. As such, we investigated the effects of 10 extremolytes on two model proteins – Carbonic anhydrase and Catalase. Our results indicate that ectoine and glycerol, so far, shown to have a good anti-aggregating properties. Such promising effects to suppress protein aggregation indicates that these class of molecules have the potentials to be use for therapeutic intervention of diseases cause by protein aggregation. Further research to be conducted on these molecules to be use as an anti-aggregating drug.

P-46

Pharmacoperons: An emerging therapeutic approach for protein misfolding disease

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A protein must undergo a folding mechanism to achieve a distinct 3D shape in order to be functionally active. When this cannot happen, it leads to protein misfolding and aggregation which may cause numerous degenerative and neurodegenerative illnesses, including Alzheimer's, Parkinson's, Huntington's disease. Misfolded forms of protein, such as Prions are known to cause CJD: Creutzfeldt-Jakob Disease in humans. It has been found that cellular molecular chaperones, as well as newly discovered chemical and pharmacological chaperones, are helpful in preventing the misfolding of several disease-causing proteins, effectively reducing the severity of a number of neurodegenerative diseases. Pharmacological chaperones (Pharmacoperones) have a promising future as therapeutics to improve the underlying mechanism of protein misfolding diseases. They work by binding to misfolded proteins with high specificity, either as enzyme substrates or receptor ligands. This results in reduced folding energy barriers and promotes misfolding correction. In this poster, we aim to provide a comprehensive overview of this exciting area of research, surveying the literature from in vitro studies and clinical trials in a variety of protein misfolding diseases. We look into the possible molecular mechanisms of protein misfolding diseases in humans, as well as potential therapeutic options with specific approaches towards pharmacoperones in preventing the negative effects of protein misfolding in humans.

P-47

Molecular Mechanisms and Therapeutic Strategies of Protein Misfolding Disorder

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The abnormal accumulation of unfolded or misfolded proteins is emerging as a potential cause of human diseases. Mutations or collisions between neighboring proteins can occasionally cause protein misfolding. Some misfolded proteins continue to exist despite using numerous strategies to address the misfolding issues. Then, several mechanisms like ubiquitin-proteasome system, autophagy, and ER-associated degradation are activated to degrade the incorrectly folded proteins. Any one of these dysfunctional mechanisms can result in protein misfolding diseases. Dominant-negative mutations, inappropriate degradation, mislocalization, and amyloid build-up, are some examples of protein misfolding events that lead to illnesses. One well-known example is sickle cell anemia, in which the globin chain has a missense mutation that replaces glutamic acid with valine, which alters protein conformation. This improper protein conformation in the deoxygenated environment reveals its hydrophobic patch, which causes polymerization in those who are homozygous for the mutation, leading to decreased elasticity of RBCs, which results in severe discomfort and anemia. There are numerous different therapeutic strategies, such as blocking the chaperones and co-chaperones system in cystic fibrosis to stop the maturation of CFTR or using enzyme replacement therapy in Gaucher's disease to prevent chaperons from binding to the enzyme and preventing the build-up of -glucosidase, or using protein-specific drugs like Nutlins in cancer to stop the degradation of p53. In addition, misfolded proteins can be rescued via the use of proteostasis regulators and pharmacological chaperones, suggesting that treatments with small molecules might be developed for a range of genetic diseases.

Keywords – Protein misfolding; Mechanisms**;** Degradation; Dysfunction**;** Therapeutics

Note – All the authors have equal contributions.

P-48

Development of small molecules inhibitors of SOD1 aggregation as therapeutics agents for Amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease which is characterized by the loss of upper and lower motor neurons. Death occurs within 3–5 years from disease onset. The worldwide annual incidence of ALS is 2.1 per 100,000 people, with an estimated prevalence of 5.4 cases per a population of 100,000. Cu/Zn superoxide dismutase (SOD1) is one of the genes associated with the familial form of the disease (fALS). The mechanism of neuron degeneration by SOD1 is not clear, it is hypothesized that there is a toxic gain of function in the protein which leads to the downstream effects. Currently, there are only two FDA approved drugs; Riluzole and Edaravone, which are non-curative and marginally slows disease progression by a few months. In the present study, we aim to stabilize the mutant SOD1 dimer by synthesizing novel carbazole derivates, thereby preventing its aggregation. *In- silico* studies have shown that our compounds bind to both the chains of the SOD1 mutant proteins with significant C.Docker energies. Using ThT binding assays, TEM imaging, DLS and other techniques, we demonstrate that our compounds inhibit the aggregation of three mutant forms of purified SOD1 protein.

P-49

Molecular Dynamics-Based elucidation of BIBR1532 Binding Site in hTERT and identification of lead compounds targeting telomerase using structure guided drug repurposing approach

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Replicative immortality caused by increased telomerase activity is a hallmark in about 85% of cancer malignancies, making it an attractive target to develop anti-cancer therapeutics. However there has not been much success in part due to unavailability of a crystal structure of human telomerase enzyme. In 2015, Skordalakes and co-workers reported the structure of a highly specific telomerase inhibitor BIBR1532 bound to TcTERT catalytic subunit with cues of its potential binding in a highly conserved and clinically relevant hydrophobic FVYL pocket in human telomerase. Due to unavailability of a co-crystalised structure of BIBR1532 with hTERT thumb domain, we devised a unique Molecular dynamics-based method to first identify the exact binding site of the inhibitor in the hTERT thumb domain followed by a two-way pharmacophore generation approach to identify lead compounds. The two pharmacophore models so generated were virtually screened through Drug Bank database. The models were validated on the basis of fit value of the BIBR1532 and selectivity value indicating the favourable feature set required. The top hits obtained were filtered using Lipinski, ADMET and TOPKAT filters followed by redocking into their binding site. Structural investigation, molecular docking studies and confirmatory molecular dynamics indicated that the exact binding site of BIBR1532 is away from the reported FVYL pocket strikingly with some of the characteristic interactions conserved. Finally, lead drugs that were able to dock in the new pocket were validated using MD simulation studies and MM-PBSA score calculation as potential telomerase inhibitors.

P-50

Structure based studies of a novel potassium channel to exploit it as a drug target to combat various non-communicable human diseases

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The alarming continuous increase in morbidity and mortality due to various non-communicable human diseases like cardiovascular, neuronal, and cancers, has made it imperative to identify new drug targets and drug candidates for these diseases. In the current work, we attempted to investigate ion channels as a potential new therapeutic target since ion channels are evolutionarily conserved. After an extensive literature search, we found that Slo (slowpoke) is a family of potassium channels that are activated by elevations in intracellular sodium and chlorine concentration and is inhibited by intracellular ATP (1). The SLICK/KCNT2 is a member of this Slo family and it is a sodium-activated potassium (K_{Na}) channel. Inner mitochondrial membrane of cells as well as cell membranes of heart and brain are where it is currently known to be expressed (2). While KCNT2 has a clear role in case of neural dysfunctions, its involvement in cardiovascular diseases, and cancers are less explored. Hence, to further understand KCNT2, we used structure-based *in-silico* methods, such as conserved domain, sequence alignment, molecular modelling, and molecular interaction analyses.

According to conserved domain and sequence similarity analyses KCNT2 exhibit Ca^{2+} sensitivity and it is evolutionarily conserved. Further, molecular modelling has helped in molecular interaction studies of existing small molecular activators of different potassium channels with KCNT2. Couple of such small molecules showed significant binding affinity/energy towards KCNT2 which will be further investigated via wet lab experiments. Currently, we are recombinantly expressing human KCNT2 channel in specific cell lines and baculovirus mediated methods to investigate its role in various non-communicable human diseases.

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P-51

Structure-based identification of small molecule antivirals to combat Monkey pox infection by targeting its DNA polymerase

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DNA polymerases (DNAP) are a diverse group of small, hydrophilic, cytosolic proteins present in Monkey pox (MP) virus with functional resembles to DNA directed RNA polymerase. Since these enzymes are essential for MP viral DNA replication, their inhibition could help the treatment of MP virus. Till date no experimental structure is solved neither a good inhibitor is available for MP DNAP.

Thus, in the current study, we have solved these issues by building an in-silico molecular model of DNAP to investigate its three-dimensional structure. Upon physiochemical (bioinformatic) validations, the model was used for structure based virtual screening against >100 FDA-approved small molecule antivirals from various databases, revealing three drugs as prospective inhibitors of MP DNAP, with better efficacies than the known inhibitors (i.e., cidofovir and acyclic nucleoside analogues) providing confidence in the outcome. Pharmacokinetic (in-silico ADMET) study shown these DNAP inhibitors having very high cell permeability, inability to cross the BBB, and thus promising for further experimental studies. Molecular dynamics simulations of the DNAP model have also been initiated to understand the effect of PTM and metal ions (at the active site) on the modelled structure and dynamics of the enzyme. Furthermore, proteomics, metabolomics, and enzymatic assays related to DNAP upon exposure to inhibitors should be performed as confirmatory tests. Combination of all of these efforts may ultimately save thousands of human lives by curbing MP viral infection as well as future viral epidemics, if any.

P-52

Characterisation of wild type Envelope and ORF8 viroporins of SARS-CoV-2

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Viroporins of SARS-CoV-2, such as Envelope (E), and ORF8 have no sequence homology with ion-channels of human hosts, therefore investigating such viroporin will open up opportunities for basic and translational research to cope up with the current and future pandemics (Rizwan et al., 2021). Many electrophysiological and biochemical studies of E and ORF8 proteins are yet to be done to fully understand their effects on COVID-19 infected patients. Extensive mutational studies of these two proteins from SARS-CoV-2 variant strain are also required to compare that with the wild type to determine the roles of specific amino acids in each of these viroporins for their functional implications. Thus, in the present work, we have cloned, expressed, and purified the E and ORF8 proteins using chromatographic methods. We have further characterized the ORF8 biophysically by using CD, fluorescence, and UV-Visible spectroscopies. *In silico* screening of FDA approved drugs was also done against these two viroporins to design prospective antivirals. Current work to provide a platform for further research in understanding the molecular mechanism of these two viroporins with special emphasis on COVID-19 infection.

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P-53

Medicinal plants as a potential antiviral

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Viral infections (both communicable and non-communicable) and their outbreaks are a major concern since they are the source of various newly emerging infectious diseases (human immunodeficiency virus; HIV, Influenza, Monkeypox, coronavirus, lumpy virus, etc) and challenged mankind survival. Although there are several antivirals available in the market like remdesivir, flavipiravir, zanamivir, acyclovir, etc. but due to high cost, their side effects and viral resistance researchers are back to traditional formulations to extract therapeutic phytochemicals from medicinal plants that can treat a mild to fatal viral infections. Phytochemical extracts as primary and secondary metabolites and many medicinal herbs produces essential oils with great therapeutic window. *Pyrrosia lingua* (tongue fern), *Artemisia annua* (sweet wormwood), *Lycoris radiata* (red spider lily) and *Lindera aggregate* (spice bush) are few plants whose phytochemical extracts were used against coronavirus recently during the COVID outbreak. Phytochemicals like quercetin (flavonoid in onion, apple, berries etc.) accounts for inhibition of viral transcription, protein synthesis and endocytosis in influenza and rhinoviruses. Many flavonoids like quercetin, baicalein (flavonoid in root of *Scutellaria baicalensis*) and myricetin (flavonoid in fruits and vegetables) inhibits DNA polymerase and reverse transcriptase in HIV and Rauscher murine leukemia virus (RMLV). *Syzygium aromaticum* (clove) has high antiviral activity against coxsackievirus, polioviruses and adenoviruses. Studies reported that the phytochemicals have similar mechanism of action against viruses as conventional antiviral drugs. The list of traditional medicinal plants is huge; however, further advanced investigations are required with the objectives of development of effective and affordable antiviral drugs from plants.

***Keywords*:** *Antivirals, Phytochemicals, Flavonoid, Traditional medicine*

P-54

Actionable miRNA in embryonal Rhabdomyosarcoma

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Orbital Rhabdomyosarcoma is a highly malignant neoplasm of embryonal origin, prone to metastasis into the lungs and bone marrow if left untreated. Recent evidence has suggested that muscle-specific miRNAs are downregulated in RMS tumours. In this study, Embryonal and Alveolar rhabdomyosarcoma samples were analysed using GEO2r platform to identify target genes that are common in both, in addition, miRNET platform provided a visual representation of the miRNA-target gene networks. We identified 9 significant differentially regulated key miRNAs in ERMS against ARMS samples through GSE135518 dataset. On KEGG analysis of miRNA-target genes:- RTK, Ras, apoptotic and several cell cycle regulatory pathways were found to be involved in RMS. Analysing these interactions, we found BCL2, PTEN, CDK2 and YMHAQ to be key miRNA targets in RMS. We also identified hsa-miR-214-3p & hsa-miR-660-5p as top differentially regulated miRNAs in ERMS samples, which induce apoptosis, myogenic differentiation and inhibition of tumorigenesis.

P-55

Investigating the role of *Mycobacterium tuberculosis* transcriptional regulator VirS in acidic responses and identification of inhibitors against it

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The ability of *M. tuberculosis* to respond to intramacrophage stresses such as oxygen/nitrogen radicals and low pH is important for its persistence. It has been reported earlier that an AraC/XylS type transcriptional regulator, VirS, is induced under low pH and regulates cell envelope architecture. However, a comprehensive understanding of how VirS mediates its influence on gene expression to coordinate pH response remains uncharacterized. Here, by using multiple approaches, we investigated the contribution of VirS in maintaining intramycobacterial pH homeostasis. Using a genetic biosensor of cytoplasmic pH, we demonstrated that VirS is required to maintain intramycobacterial pH in response to acid stress. Furthermore, loss of VirS reduced *M. tuberculosis's* ability to block phagosomal-lysosomal fusion, indicating that VirS regulates phagosomal maturation. Transcriptomics data indicate that VirS affects the expression of genes involved in cell wall synthesis, efflux pumps, ion transporters, metabolic enzymes, transcription regulation and growth under acid stress. Furthermore, we performed EMSA, DNA footprinting and 3-D structure generation. Structure guided mutational studies revealed key residues required for its interaction with DNA. Importantly, we performed structure based virtual screening to identify inhibitors against VirS. We identified a few hit compounds that inhibited VirS DNA binding activity as well as the growth of *M. tuberculosis in vitro* broth culture. Taken together, our findings establish an empirical role of VirS in mediating *M. tuberculosis's* response to acidic stress and suggest that targeting of VirS can be effective anti-mycobacterial strategy. These studies also pave way to design novel *M. tb* inhibitors targeting VirS.

P-56

Elucidating the Binding site of VX-222 on hTERT, Pharmacophore generation, and virtual screening

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Telomeres are DNA-protein structures that are localized at the ends of eukaryotic chromosomes to prevent degradation, and fusion and maintain genome stability. Telomere decides and limits the number of replications a cell can undergo, and are maintained by telomerase – conferring cell immortality & obstruction of cell senescence. Therefore, telomere conservation via telomerase reactivation is considered a hallmark of cancer cells. Telomerase represents an attractive target for highly selective cancer therapeutics. Telomerase activity in various cancer cells can be inhibited by natural products (curcumin, quercetin) from plants, microbial products (daunomycin, trichostatin A, telomastatin) marine products (meridine), and synthetics inhibitors (Imetelstat (GRN163L), BIBR1532). There are many available targets like HDAC, CDK, and tyrosine kinases for the treatment of cancer but with the emergence of various drug-resistant forms of cancer, there is an urgent need for discovering novel anti-cancer drugs for its effective therapy. The structure of hTERT and hepatitis C virus (HCV) RdRP is quite similar. A rigorous literature study was done and we found VX-222 which is a non-competitive selective inhibitor of HCV NS5B genotype 1a and 1b. It binds to the allosteric pocket of HCV RdRP on the thumb domain and shows an inhibitory effect. This HCV RdRP inhibitor VX-222 showed a remarkable inhibitory effect on RdRP activity in human hTERT as well. In this study, we used the available crystal structure of the thumb domain of hTERT (PDB: 5ugw) and VX-222, showing an inhibitory activity on RdRP of hTERT, to generate a structure-based pharmacophore. This pharmacophore was later used to screen the DrugBank database and the hits obtained through virtual screening were further filtered using Lipinski's rule of five, Veber's rule, ADMET, and TOPKAT studies. The screened hits were further studied using molecular docking by CDOCKER docking protocol and various energy scores were calculated. Through this study, we obtained four approved, twenty experimental, and three investigational drugs from the DrugBank database. We have obtained potential drugs which can be repurposed as potential drug candidates for the treatment of cancer.

P-57

Lipidomics using mass spectrometry reveals altered lipid patterns in brain tissues resected from individuals with focal cortical dysplasia (FCD): a precursor to rapid evaporative ionization mass spectrometry (REIMS) based iKnife surgery

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Introduction: FCD, being one of the most common pathologies of drug-resistant epilepsy (DRE), accounts for one-third of the cases referred to surgery. Failure to precisely localize the epileptogenic zone (EZs) is a major reason for poor surgical outcomes in FCD. Currently, no molecular or cellular biomarkers are available to aid in defining EZs. In this study, we used liquid chromatography coupled high-resolution tandem mass spectrometry to identify altered lipid profiles in the resected tissues from FCD patients obtained during electrocorticographically (ECoG)-guided surgery compared to autopsy.
Method: Lipids were extracted from frozen brain tissues using a modified Bligh & Dyer method and separated on an ExionLC™ system with a Waters AQUITY UPLC BEH HILIC column. A SCIEX QTRAP® 6500+ LC-MS/MS system with polarity switching, Turbo V™ source, and electrospray ionization probe was used. For identification and relative quantification of all the lipid species, theoretical multiple reaction monitoring (MRM) library was generated using LIPIDMAPS. Lipids were quantified by MultiQuant™ 3.0.2 quantitation software. The intensity values (mz/rt) were normalized with spiked internal standards. MetaboAnalyst software (v5) was used for missing values imputation.
Results: Mass spectral profiles of a total of 1224 lipids with 607 in positive mode and 617 in negative mode were detected. A total of 13 lipids (8 upregulated and 5 downregulated) were altered in FCD compared to autopsy ($p<0.05$ and fold-change ≥ 2). The upregulated lipids in FCD comprised neutral triacylglycerols (TAGs) and downregulated lipids included phosphatidylcholine (PC) and phosphatidylethanolamine (PE).
Conclusion: Distinct lipid mass spectra of TAGs, DAGs, PC, and PE were observed in FCD tissue in comparison to autopsy. As a proof-of-concept, lipid signatures could be used for developing REIMS-based techniques for defining epileptogenic zone in FCD.

P-58

Differential Regulation of Casein Kinase 2 (CK2) in Mesial Temporal Lobe Epilepsy

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Introduction: In the brain, NMDA receptors (NMDARs) are important mediators of excitatory synaptic transmission. Studies have demonstrated that phosphorylation of GluN2B Ser1480 by CK2 affects the NMDAR activity, resulting in phosphorylation dependent endocytosis of NR2B and an increase in synaptic NR2A expression Therefore, this study is designed to test the hypothesis that altered CK2 functions may contribute to hyperexcitability in MTLE.

Methods: For this study, surgically resected hippocampal tissue specimens of 23 patients and 17 controls were obtained. mRNA levels of CK2α, CK2β, NR2A and NR2B were evaluated by quantitative real-time PCR. Expression of proteins were studied by western blotting. CK2 activity was measured by kinase assay. Expression of mRNA and protein were also evaluated in acute and chronic pilocarpine model of TLE. **Results**: A significant increase in CK2α1, CK2β1 and NR2A expression was observed in MTLE patients. Kinase activity was significantly higher in MTLE patients. Significant increase in CK2α2 was observed in chronic model of TLE as compared to respective control with no significant changes in acute TLE model. **Conclusion:** Our findings show that casein kinase 2 may contribute to hyperexcitability by altering NMDA receptor regulation in MTLE. This new insight contributes significantly to our understanding of the molecular processes and synaptic plasticity involved in the pathogenesis of MTLE, and CK2 may offer new potential therapeutic targets.

P-59

DECIPHERING THE ROLE OF PROTEIN TYROSINE KINASE 2 BETA (PYK2) IN MEDIATING EPILEPTOGENESIS IN TEMPORAL LOBE EPILEPSY

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Introduction:

It is estimated that more than 65 million people worldwide suffer from epilepsy. Mesial temporal lobe epilepsy (MTLE) is the most common form of intractable epilepsy. However, as of today it is not possible to cure or prevent epilepsy with a specific drug. Pyk2 is a non-receptor tyrosine kinase that is highly enriched in forebrain neurons. Previous studies have demonstrated the activation of Pyk2 in response to seizures. Thus, this study aimed to assess the levels of phosphorylated and un-phosphorylated forms of PYK2 in surgically resected tissue specimens from patients with MTLE and animal model of MTLE.

Methods:

For this study, western blotting was used to analyse the protein level of Pyk2 and phospho-Pyk2 in the hippocampus, ATL and neocortex tissue resected from animal model of TLE as compared to control. The cell specific expression of Phospho-Pyk2 was determined by immunofluorescence assay and qRT-PCR was employed to analyse the mRNA levels of Pyk2 in a region specific manner. The results were clinically correlated in patient samples.

Results:A significant increase in the activated form of PYK2 was observed in the animal model of TLE as compared to control in a region specific manner and similar results were obtained in surgically resected tissue specimens of MTLE patients.

Conclusion: This was the first study to assess the activation of Pyk2 in a region specific manner in an animal model of TLE and validate it in patient samples suggesting the possible contribution of Pyk2 in the pathogenesis of epilepsy.

P-60

POTENTIAL ROLE OF DEREGULATED HISTONE DEACETYLASE 2 (HDAC2) IN THE PATHOGENESIS OF TEMPORAL LOBE EPILEPSY

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Introduction: Temporal lobe epilepsy (TLE) is a neurological disorder, characterized by recurrent seizures and debilitating cognitive deficits. Nearly a third of TLE patients do not respond to conventional pharmacological treatments. As a result, it is imperative to identify novel therapeutic targets with limited side effects. Previous studies have demonstrated the effectiveness of HDAC inhibitors as effective anti-epileptic drugs and an alteration in the level of HDAC2 has been reported in TLE patients. Thus, this study was designed to investigate the region specific expression of HDAC2 in temporal lobe structures of pilocarpine model of epilepsy and validate it in surgically resected specimens of MTLE patients. **Methods:** Western blotting and qRT-PCR was performed to analyse the protein and mRNA levels of HDAC2 respectively. Immunofluorescence assay was conducted to determine the subcellular distribution and expression of HDAC2 in brain tissue resected from pilocarpine model of TLE and surgically resected specimens.

Results: HDAC2 levels were found to be significantly upregulated in a region specific manner at the mRNA and protein level in pilocarpine model of epilepsy as compared to control. Upregulation in the expression was confirmed at the cellular level as well. Similar results were obtained in patient samples.

Conclusion: This was the first study to demonstrate an alteration in the levels of HDAC2 in a region-specific manner in the pilocarpine model of TLE and tissues resected from MTLE patients which will further aid in identifying potential mechanisms contributing to the emergence of independent epileptogenic networks in the temporal lobe structures.

P-61

IDPU prevents apoptosis, reduces autophagy, and stimulates the survival of 6-OHDA-induced primary neuronal cells isolated from rat pups

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IDPU (1-(7-imino-3-propyl-2,3-dihydrothiazolo[4,5-d]pyrimidin-6 (7H)-yl)urea) has been established as an A_{2A} antagonist and has demonstrated to deplete the oxidative stress in 6-OHDA induced SH-SY5Y cell line and in, in– vivo model of Parkinson's disease(PD). In the present work, we have investigated the role of IDPU in the neuronal survival and apoptotic pathways using primary neuronal cells isolated from the rat pups (P0-P1). 6 -OHDA induced primary neuronal cells isolated from rat pups were treated with IDPU following which cellular proteins were isolated. The apoptotic proteins (Caspase-3, Bcl2) and autophagic proteins (Beclin) were then identified using specific antibodies. Western analysis of the isolated cellular proteins on SDS gel indicated that the presence of Caspase 3 (17, 35 kDa), Bcl2 (26 kDa), and Beclin (51kDa) protein reduced, thus indicating that IDPU prevents apoptosis and reduces autophagy as well, in 6 -OHDA induced primary neurons, thus promoting survival.

Future research will focus on the mechanism of action of A2A antagonists in neuroprotection in PD, pathways promoting neuronal survival, Ca^2 homeostasis, neuroinflammation, etc thus improving the pathophysiology of PD.

P-62

Effect of AW00032 as potential Adenosine $A_{2A}R$ antagonist in 6-OHDA induced SH-SY5Y cell line

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Parkinson's Disease (PD), a neurodegenerative movement disorder, is pathologically characterized by a progressive loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc), and accumulation of misfolded α-synuclein (α-SYN) inclusions called Lewy bodies and Lewy neurites. The current dopamine-centered treatments aim to restore motor functions of patients without slowing the disease progression. Long-term usage of these drugs is associated with diminished efficacy, motor fluctuation, and dyskinesia. Adenosine A_{2A} Receptor antagonists have emerged as potential treatment for PD in the past decade.

In this regard, pharmacophore modelling with the tricyclic, bicyclic and monocyclic compounds synthesized in our lab using Maybridge, ZINC15 databases gave 20 novel hit compounds as potential Adenosine A_{2A} Receptor antagonists. Among those 20 hits, AW00032, a potent and selective monocyclic compound, exhibited drug-like property for A_{2A} Receptor. This compound was further used to investigate its role in neuroprotection using 6-OHDA induced cell death in dopaminergic SH-SY5Y cells.

In the present study, the 6-OHDA induced SH-SY5Y cells were treated with standard positive control (ZM241385 and L-DOPA) and the combination of AW00032 with ZM241385 and L-DOPA. AW00032 concentration-dependently increased the cell viability as measured in MTT compared with 6-OHDA-injured cells (IC50= 60 uM). ZM241385 and L-DOPA, used as positive control, had similar effect to AW00032.

Future research will focus on the further validation of neuroprotective role of AW00032 on autophagy, genetic mutations, pathways promoting neuronal survival, Ca^{2+} homeostasis etc. thus improving the pathophysiology of PD.

P-63

Potential of Hypoxia in Glucose Metabolic Reprogramming - a cure for Neurodegenerative Diseases

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The adult brain's primary circulating energy substrate is glucose. Because brain cells require a lot of energy, glucose is aggressively oxidised through glycolysis to create ATP and works in coordination with mitochondria in metabolic pathways. ATP serves as the electrochemical foundation for the upkeep of both neurons and non-neuronal cells. As a result, sustaining proper neuronal function depends on mitochondrial and glucose metabolism.

The development of neurodegenerative diseases has been linked to abnormal glucose metabolism, including mitochondrial dysfunction, therefore, it is promising to find a cure for these changes, which could enhance the quality of life and prolong the survival of patients with neurodegenerative diseases.

Hypoxia is a lack of oxygen from the circulatory system that may play a part in metabolic reprogramming. Hypoxia-inducible factor (HIF) is a crucial transcription factor that controls oxygen consumption and morphological changes in response to hypoxic stress. HIF triggers the transcription of numerous genes involved in oxygen delivery, angiogenesis, cell proliferation, cell differentiation and metabolism. In living organisms, cells have evolved strategies to adapt to oxygen deprivation including oxygen-independent ATP synthesis which results in increased glycolysis and the other is mitochondrial metabolic suppression.

Here we present the metabolic reprogramming caused by energy metabolism in neurodegenerative disorders like Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and Huntington's disease (HD) and provide a summary on hypoxia as a viable therapeutic option.

P-64

Motor learning, memory deficits, and cerebellar histopathology as a consequence of Low-dose irradiation during the early organogenesis period

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The cerebellum has recently been implicated in cognitive processing in addition to motor functions. Furthermore, the developmental period is more susceptible to low-dose radiation. Studies are unavailable on the later life effects on the cerebellum of low-dose irradiation (LDIR) at the early gestational stage (early organogenesis stage i.e., E5.5). Therefore, this study for the first time investigated the delayed effects of exposure to LDIR on E5.5 in terms of histopathological analysis of the cerebellum and behavioral consequences.

Pregnant mice (C57BL/6) were irradiated with 0.2Gy ϒ radiation (IR) on gestational day E5.5 and the control (C) mice progeny were subjected to motor learning and memory tests at 3, 6, and 12-month age. Motor strength, motor learning, and memory were assessed through grip strength and rotarod, carried out over 5 trials, 3 sub-trials. Correlative histopathological analysis (Calbindin positive; quantitative and qualitative) was conducted.

Male progeny (3 months IR) showed derangement of the Purkinje cell layer in addition to reduced dendritic arborization. Though reduced dendritic arborization was observed in 3-month-old females as well, however, the derangement was not observed. Motor learning was significantly affected in both 3-month-old (IR) males and females. Recovery at 6-month time point was observed in the learning graph in both males and females. However, recuperative ability in learning performance and histopathology was observed only in 12-month irradiated females. 12-month-old males (IR) showed significant learning deficits compared to controls.

In conclusion, a low dose of 20 cGy is adequate to elicit motor learning and memory deficits and histological alterations in both the male and female cerebellum. Male mice were more prone to motor learning and memory deficits as a consequence of prenatal (E5.5) low-dose irradiation.

Keywords: *Cerebellum, low-dose radiation, Motor deficts*

P-65

Calmodulin Modulates the Gating Properties of Voltage-Dependent Anion Channel on Bilayer Lipid Membrane

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Calmodulin (CaM) is a primary signaling protein that plays an important role in mitochondrial Ca^{2+} maintenance and signaling and modulates mitochondrial membrane properties in the mammalian brain. It is proposed that the Voltage-Dependent Anion Channel (VDAC), one of the most abundant outer mitochondrial membrane (OMM) proteins in neurons, could be one of the sites of action for mitochondrial regulation. VDAC is known to play a crucial role in the mitochondrial Ca^{2+} signaling mechanism. Our bilayer electrophysiology results suggest that CaM significantly reduces VDAC's conductivity and modulates its gating as well as permeability properties. Also, spectrofluorimetric analysis indicates the possibility of binding CaM with VDAC. Theoretical analysis of fluorescence data shows that the above-mentioned protein-protein interaction is not linear, but rather a complex nonlinear process. In VDAC, CaM binding site has been predicted using various bioinformatics tools. It is proposed that CaM could interact with VDAC's outer loop region and regulate its gating properties. Our findings suggest that VDAC-CaM interaction could play a crucial role in the transport of ions and metabolites through OMM and regulate the mitochondrial Ca^{2+} signaling mechanism through the alteration of VDAC's gating and conductive properties.

P-66

Extracellular Signal-Regulated Kinase1 (ERK1)-Mediated Phosphorylation of Voltage-Dependent Anion Channel (VDAC) Suppresses its Conductance

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ERK1 is one of the members of the mitogen-activated protein kinases that regulate important cellular functions. VDAC is located at the outer membrane of mitochondria. Here, an interaction between VDAC and ERK1 has been studied on an artificial planar lipid bilayer using in vitro electrophysiology experiments. We report that VDAC is phosphorylated by ERK1 in the presence of Mg2+- ATP and its single-channel currents are inhibited on the artificial bilayer membrane. Treatment of Alkaline phosphatase on ERK1 phosphorylated VDAC leads to partial recovery of the single-channel VDAC currents. Later, phosphorylation of VDAC was demonstrated by Pro-Q diamond dye. Mass Spectrometric studies indicate phosphorylation of VDAC at Threonine 33, Threonine 55, and Serine 35. In a nutshell, phosphorylation of VDAC leads to the closure of the

P-67

Protective effects of herbal drugs in the treatment of Alcoholic Neuropathy

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Background: Among the various medical complications of neuropathy, the one with the most dreadful and griming outcome is alcoholic neuropathy, which grounds serious and severe damage to the nerves; caused by the long term consumption of alcohol which is a potent cytotoxic agent. It provides an impact on the social, psychological, medical, economic and religious spheres of life. In the pathogenesis of alcoholic neuropathy, there is axonal damage and demyleination of sensory and motor fibres resulting in the damage to the nervous system. The progression of alcoholic neuropathy is increasing at an alarming rate and research needs to be done effectively in order to have a check on the progression of the disease.

Result: Looking at the severity of this disorder, various researches have been conducted to find as many ways to treat it as possible. This review is aimed at giving an account of the various herbal plants – such as Allium Sativum, *Pinus Pinaster, Azadirachta Indica, Ginkgo Biloba* and *Gymnema Sylvestre* – which have till now shown successful results in their employment as a possible treatment of alcoholic neuropathy.

Conclusion: Some more studies need to be done for their validation so that they can not only actively substitute or be used in conjunction with the present options of treatment in order to summon the best results which can prevent or cure this disorder effectively but also restore the damage done to the neuropathic patient.

Category: Biological Sciences

Day-3

SESSION VIII: NEW PARADIGM IN DRUG DISCOVERY RESEARCH

P-68

Structure-guided pharmacophore and docking-based virtual screening of databases, and molecular dynamics to obtain novel inhibitors against SARS-CoV-2 Mpro

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The outbreak of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) has received significant attention on the global risks and urges to identify potential therapeutic agents. In this regard, *in silico* approaches are productive to discover potential inhibitors of various targets of SARS-CoV-2. The main protease enzyme, Mpro is an important target for discovering SARS-CoV-2 inhibitors as it plays a pivotal role in viral replication and transcription. Here, we have used two approaches. In 1st approach, plant-based natural compounds database (TIPDb, Taiwan Indigenous Plant database) was virtually screened via molecular docking-based approaches to identify potential inhibitors of Mpro. Molecular docking of TIPdb using Libdock followed by Cdocker-docking protocol was performed with PDB code:7BQY followed by ADME analysis. Best hits were selected based on high –CDOCKER interaction energy and high –binding energies. The top scored ligands having important Protein-Ligand 2D interactions were selected as the best 10 hits. One derivative of each top hit was designed using the proposed best inhibitors in the literature as template. The designed novel derivatives were also docked using CDOCKER and similar scoring functions were performed. The best hits were chosen for the MD simulation studies.

In 2nd approach, we aim to identify potential inhibitors of SARS-CoV-2 Mpro via structure-guided pharmacophore-based virtual screening. The multicomplex-based pharmacophore (MCBP)-guided method was used to generate a comprehensive pharmacophore based on ten crystal structures of Mpro-inhibitor complexes. Further database screening, ADME analysis are to be performed. The top 10 hits will be subjected to MD simulations and in-vitro testing in future.

P-69

The curious case of Glutamate racemase (MurI): the key player to tackle the antimicrobial resistance. A computational drug discovery aspect

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Background *Neisseria gonorrhoeae*, has developed resistance to most of the drugs and hence declared as 'Superbug'. Glutamate racemase (MurI) considered as an important drug target for its role in bacterial cell wall synthesis. Therefore, identification of novel drugs for the treatment of gonorrhea is urgently required.

Methods The amino acid sequence of MurI from *Neisseria gonorrhoeae* (YP_208550) was retrieved from NCBI. Homology model was generated by Modeller programme of Discovery Studio. Best model was selected based on DOPE score and PDF energy score and further verified. Receptor binding site was identified after superimposition of template structure and modelled structure. Best pose was selected and receptor-ligand pharmacophore model was generated. Virtual screening was performed, best hits were selected based on ADMET profile and further refined.

Results The best homology model generated was selected based on the verify score of 107.93. Validation of the selected model by Ramachandran plot showed 214 residues (91.8%) fall in most favored region. Root-mean-squared deviation (RMSD) of 0.2475 A^0 was generated by superimposition of query and template structures. Six pharmacophores were generated using best docking pose between D-glutamate and MurI. Virtual screening with ZINC library was done. 586 hits so obtained were filtered by fit value of 3.51which resulted in 268 hits. These were subjected to energy minimization and docking to obtain the best hits.

Conclusions The study identifies potential compounds that interact with active site of MurI protein, opening new avenues for the treatment option against multidrug resistant strains.

Keywords: *Antimicrobial resistance, drug targets, homology modelling*

P-70

Metformin as an anti-cancer molecule: Curious case of repurposing

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Drug repurposing is considered as an efficient approach to propagate already approved drug molecule for a condition for which it is currently unapproved, with new pharmacological activities or therapeutic properties. In the last couple of decades, drug repurposing has been shown to be a highly cost effective and efficient way to tackle diseases. Metformin, which currently is the first line oral anti-diabetic drug for type 2 diabetes, has been shown in various studies to be an efficient anti-cancer molecule as well. Many *in vitro* and *in vivo* evidence have established the direct inhibitory effects of metformin on cancer cells along with regulation of several cell signalling pathways like AMP kinase and the induction of autophagy, apoptosis, and cell cycle arrest of tumor cells. Substantial preclinical and clinical studies along with various meta-analyses have illustrated the relationship between metformin and its cancerous properties. Treatment with metformin has demonstrated improved responses of radiotherapy and chemotherapy on various types of tumors. As the safety profile of metformin has very well been established and documented, it will be exciting and equally beneficial to carve out various molecular mechanisms of metformin on cancer growth inhibition.

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P-71

A machine learning based approach to predict therapeutic candidates as potential Inhibitors of the BCR-ABL Tyrosine Kinase for Chronic Myeloid Leukemia (CML)

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Introduction- Chronic myeloid leukemia (CML) is usually caused by a reciprocal translocation between chromosomes 9 and 22. This produces the carcinogenic gene bcr-abl, which, when translated, forms the protein p210 BCR-ABL in more than 90% of individuals with CML. The protein's constitutive tyrosine kinase activity triggers downstream pathways, allowing myeloid growth to go uncontrolled. Drug resistance and side effects limit the use of BCR-ABL tyrosine kinase inhibitors (TKIs) such imatinib (Gleevec), nilotinib, dasatinib, bosutinib, and ponatinib. To overcome the difficulties with existing medications, new chemicals must be produced. "Omics", “Artificial Intelligence (AI)” and “Machine Learning (ML)” techniques make it easier to find pharmacological targets and pathways.

Materials & Methods- To address this challenge, we created a machine-learning model for predicting anti-bcr-abl molecules. This work employed feature selection and machine learning methods to develop optimal classifiers based on hyperparameters using the grid-search technique. Using this data, predictive models for bcr-abl inhibitors and non-inhibitors were constructed. We employed 10 fingerprint descriptors to describe bcr-abl inhibitors and created prediction models. Before model building, we tried to achieve high classification accuracy by describing inhibitors/non-inhibitors as a large number of molecular descriptors. Tenfold cross-validation was used in conjunction with the robust machine learning approaches of Support Vector Machine, Random Forest, Logistic Regression and K-Neural Network.

Result-The best performance was obtained on CDK fingerprints using Random Forest (RF) having an accuracy of 81% on independent dataset in discriminating bcr-abl inhibitors from non-inhibitors.

Conclusion- The knowledge offered here can be used to design and prioritize more effective BCR-ABL drugs for CML treatment.

P-72

Design and Development of CDK1 Subtype-Selective Inhibitors

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Cell cycle CDKs are frequently deregulated in all major types of cancers and are considered important anti-cancer therapeutic targets. As pan inhibitors pose a risk of major side effects and toxicity issues, the development of subtype-selective CDK inhibitors has been the aim of researchers in this area. However, designing a subtype-selective inhibitor has been a challenge due to the homologous structure of the ATP binding pocket of the CDKs. Three generations of CDK inhibitors have been developed, approved, or investigated over the years for different cancer types (Flavopiridol, Purvalanol B, Olomoucine etc. with high toxicity issues, Dinaciclib with better pharmacologic profile but toxic at high doses). There has been measurable success in the case of third-generation CDK4/6 inhibitors like Palbociclib, Ribociclib and Abemaciclib which got FDA-approved in recent years, however, there has not been much success for CDK1 except for drugs like ro3306 which is not suitable for clinical use due to rapid clearance from the bloodstream. In our study, we are working to develop subtype-selective CDK1 inhibitors. We performed ligand-based 3D QSAR pharmacophore modelling to generate a query model used to screen the Drugbank database of ~11,500 compounds, the Selleckchem Kinase Inhibitor library containing ~1814 compounds and the Selleckchem Natural Products Library containing ~2661 compounds. The screened hits were then subjected to secondary screening using filters like Lipinski, ADMET and TOPKAT. The final screening hits were then docked into the binding site of CDK1 and 18 approved or investigational hits were selected based on C-Docker scores. These hits were further analyzed by examining the 2D interactions of each compound with binding pocket residues. Finally, 5 hits were taken for MD simulations. These hits will be validated by in-vitro testing in near future.

P-73

Identification of novel PARP1 inhibitors using Ligand-based Pharmacophore Modeling and predictive Machine Learning Models

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Poly (ADP-ribose) polymerase-1 (PARP-1) is a crucial component of many biological processes and is considered a potential target for various diseases, including cancer. Even though several PARP-1 inhibitors have been reported for cancer therapy, their clinical application is limited due to drawbacks such as weak affinity, low selectivity and adverse side effects. Therefore, in this study, we have utilized two approaches - Pharmacophore modeling and AI/ML based model development to identify novel PARP-1 inhibitors.

A three-dimensional chemical-feature-based (3D-QSAR) pharmacophore model was developed to identify the essential chemical features for PARP1 inhibition. The best model (Hypo1) with the highest correlation coefficient (0.963) and the lowest RMS (0.791) consists of four features, namely, hydrogen bond acceptor, hydrogen bond donor, hydrophobic group and aromatic ring. The model was further validated using external test set, cost analysis, Fischer's randomization method and decoy data set, thereby proving the reliability of the predictive pharmacophore model. An integrated protocol of pharmacophore mapping, virtual screening using the pharmacophore as a query and molecular docking can be employed to retrieve novel molecules as potent leads.

To build predictive ML-based models, PARP1 inhibitors were described by different sets of descriptors (1D, 2D and molecular fingerprints) using various algorithms. The performance of these models was evaluated and the best model was determined based on parameters like accuracy (87%) and correlation coefficient (0.85) for classification and regression models, respectively. This model can be utilized for predicting the biological activities of potential PARP1 inhibitors prior to the costly and time-consuming in-vitro studies.

P-74

Reconnoitering moonlight enzyme, glutamate racemase, of *Neisseria gonorrhoeae* as a target for anti-gonococcal drug discovery

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Neisseria gonorrhoeae causes a highly infectious sexually transmitted disease, Gonorrhea, and has progressively developed resistance against antibiotics prescribed for its treatment. Upon fluoroquinolone resistance in *N. gonorrhoeae*, cephalosporin antibiotics were recommended for treating gonorrhoea. However, the emergence of cephalosporin-resistant strains has posed a big challenge to treat gonorrhoea. It is becoming imperative to continuously monitor resistance patterns in *N. gonorrhoeae* and encourage the development of new treatment regimens. Novel drug targets, their cellular pathways, and inhibitors targeting them are under investigation. In this study, we are focusing on a protein, glutamate racemase (MurI) encoded by *mur*I gene. This enzyme has an interesting property of sequestering DNA gyrase enzyme and thereby exhibits its moonlight function. Owing to its multifunctionality, we propose a two-pronged strategy of targeting this enzyme. First, a 3D-model of *N. gonorrhoeae* MurI (NG-MurI) was prepared through homology modeling as there is no structural information of *N. gonorrhoea* is available. AutoDock Vina tool was utilized to identify potential inhibitors, screened based on the modelled active site architecture. Three compounds namely, agrocybyne C, ficifuranone A, and nitrofurazone with high binding affinity to NG-MurI from natural and FDA approved compound databases were selected. To determine the stability of enzyme-inhibitor complexes, molecular dynamics simulations were carried out and it was found that NG-MurI has strong affinity for nitrofurazone. Secondly, we propose to use combinatorial drugs to target *N. gonorrhoeae*. For this, nitrofurazone and ciprofloxacin are being studied for its ability to target *N. gonorrhoeae.*

Keywords: *Moonlight proteins; Glutamate racemase; Homology modeling; Neisseria gonorrhoeae; Multidrug resistance*

P-75

Characterization of SARS-CoV-2 Proteins and Their Potential Drug Targets

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The COVID-19 pandemic was fuelled by the unprecedented global spread of the SARS-CoV-2 virus. The SARS-CoV-2 genome, its role in immune modulation, and vaccine development have been extensively studied. However, the viral proteome, its composition and function across hosts are poorly understood and it is obscure how the host and SARS-CoV-2 interacts to determine the severity of COVID-19 at the molecular level. Our study provides insight into the molecular details of the disease as well as potential new therapeutic candidate drugs by using drug–target–pathways–disease networks. The proteome of SARS-CoV-2 was characterized using bioinformatics and structural analysis based on physiochemical parameters such as isoelectric point, molecular weight, the primary sequence of amino acids, and globularity. Our results reveal that majority of SARS-CoV-2 proteins are acidic, low molecular weight (> 50kDa); highly globular, and contain few intrinsically disordered protein regions (IDPRs). We have identified 2812 protein-protein interactions between SARS-CoV-2 and human proteins. Pathway enrichment analysis (KEGG and Reactome) on the virus-interacting proteins provides insight into 14 potentially impacted pathways. Results show overlap of 90 potential virus-targeted host proteins. Within these, we observed 25 druggable human proteins that may be targeted by 370 approved drugs using DGIdb. We validated our findings against the STITCH database and recognized SUNITINIB, SORAFENIB, IMATINIB, PAZOPANIB, DASATINIB, and LAPATINIB as potential treatment options that may further lead to a therapeutic treatment of COVID-19.

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P-76

Gut Microbiome: A New Therapeutic Opportunity

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In recent years, scientific evidence has shown putative correlation between intestinal dysbiosis due to intestinal microbiota alteration by a pathogen or risk factors such as obesity and the progression of chronic Non Communicable Diseases (NCDs). Given this association, there may be significant therapeutic utility in altering microbial composition through diet by finding which group of bacteria is more associated to cause the prevailing disease in the patient and so its treatment by limiting that bacteria as a treatment. Biomarkers could contribute to more accurate risk prediction models and by applying trajectory analyses of related biomarkers in managing risk factors such as obesity via nutritional modulation can be applied for the prevention of metabolic diseases. Evidence shows that the use of Genetically modified probiotic strains which is Next Generation Probiotics (NGP), synbiotics and parabiotics have been investigated as a promising and alternative future therapy, particularly by reversing gut dysbiosis associated with various disorders such as Non Alcoholic Fatty Liver Disease (NAFLD),Inflammatory Bowel disease (IBD)and Irritable bowel syndrome (IBS), thus improving the symptoms, enhancing biomarkers of the disease. Faecal microbiota transplantation (FMT) has gained increasing attention for the use of healthy human donor flora, and appears to be the most complete probiotic treatment available today. Owing to the great advances in tools for microbial analysis, therapeutic strategies such as prebiotic, probiotic and parabiotic treatment and fecal microbiota transplantation are seen as a potential approach to treat several chronic diseases.

P-77

Functional characterization of endolysins derived from mycobacteriophage *RitSun* as effective antimycobacterial agents

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BACKGROUND Tuberculosis is one of the leading causes of death and calls for an urgent need for exploring bacteriophages and encoded lysins as non-antibiotic strategies to treat drug-resistant TB, which could potentially shorten the treatment regimen of tuberculosis when given in combination with TB drugs. Mycobacteriophages encode LysinA and LysinB, which target the peptidoglycan and ester bonds (link arabinogalactan with the myco-membrane) in the mycobacterial cell wall, respectively.

METHODS We isolate mycobacteriophages using *Mycobacterium smegmatis* mc^2155 as the bacterial host and derive endolysin gene sequences from the novel mycobacteriophages followed by their purification as recombinant proteins. In this study, functional characterization of Lysin and LysinB as lytic proteins are presented. The mycobacterial growth inhibition studies with the recombinant endolysins were done using spot assay, turbidity reduction method and colony count. The biochemical activity was estimated using *in vitro* assays: lysozyme assay for LysinA and esterase assay for LysinB. **RESULTS** The analysis of domain organization of *RitSun* endolysins shows multiple modules in lysinA: chitinase domain embedded in a lysozyme-like domain and the amidase domain embedded in peptidoglycan recognising protein (PGRP); LysinB: a C-terminal linker domain besides the characteristic alpha/beta hydrolase fold. Both the lysin enzymes showed anti-mycobacterial activity when tested against *M.smegmatis*. LysinA showed lysozyme-like activity comparable to chicken lysozyme and the esterase activity of LysinB was found comparable to LysinB activity of MS6 and D29, which are the reported mycobacteriophages against *M.tuberculosis*.

CONCLUSIONS The LysinA data in this study is a significant addition to the existing knowledge as only limited reports are available on LysinA derived from mycobacteriophages. Lysozyme activity and the 'lysis from without' effect of Lysin A on *M.smegmatis*, without the aid of an outer membrane permeabilizing agent, are indeed encouraging. Further investigation of the effectiveness of *RitSun* lysins on the pathogenic mycobacterial spp. can expand their scope as therapeutically relevant protein biopharmaceuticals, alone or in combination with antibiotics.

P-78

In-silico screening of coumarin derivatives as xanthine oxidase inhibitors

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Recent years have seen a remarkable resurgence in the methods used by academic and industry scientists to find novel medications, with several innovative and interesting procedures being created in the last decades. In this overview, we'll try to summarise the recent technique i.e., In-silico screening, being used by chemists and biomedical researchers to develop novel medications rapidly for the inhibition of xanthine oxidase. This enzyme is needed to break down purine nucleotides into uric acid [1,2]. The organism may suffer negative consequences from both the uric acid itself and the reactive oxygen species that are generated during the enzymatic activity. This pathway leads to increased uric acid production, which is a common cause of gout [3,4]. Hence, there is an urge for finding novel targets that can inhibit this enzymatic activity. The present study aims to screen a library of coumarin derivatives using various in-silico tools, like the Lipinski rule, and ADME studies to filter active leads having the ability to inhibit Xanthine oxidase. Further Molecular docking studies with simulations of these derivatives have been performed using AutoDock 4.2 tools on the crystallized structure of bovine milk. The results will be discussed at the conference.

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P-79

Subtyping of advanced lung cancer based on PD-L1 expression, tumor histopathology and mutation burden (EGFR and KRAS): a study from North India

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Objectives: Immune checkpoint inhibitor (PD-L1) therapy of advanced NSCLC has variable outcomes. Tumor Subtypes based on PD-L1 expression, histopathology, mutation burden is required for patient stratification and formulation of treatment guidelines.

Methods: Lung cancers (n=57) diagnosed at Pathology department, VPCI (2018-2021) were retrospectively analyzed. PD-L1(SP263) expressed by tumor cells (low (<1%), medium (1–49%), high (≥50%) was correlated with histopathology, microenvironment, EGFR, KRAS,expression.

Results: Patients were categorized into high and low risk based on their: (i) Gender-males (n=47, 30-89 years), females-(n=10, 45-80 years), (ii)smoking history-males-26/47 (45.61%), females-1/10 (10%). (iii) tumor subtyping: squamous cell carcinoma-15/57 (26.32%), adenocarcinoma-6/57 (17.54%), NSCLC-undifferentiated-24/57 (42.10%), adenosquamous carcinoma-5/57 (8.77 %), carcinosarcoma-4/57 (7.02%), small cell carcinoma-1/57 (1.75%). (iv)Inflammatory tumor microenvironment/TILs-44/57 (77.1%).(iv) PD-L1 positivity-31/57 (54.3%)(v) concomitant EGFR/KRAS positivity. PD-L1positive cases showed squamous/undifferentiated histopathology, concomitant EGFR+(9/20, 45%)and KRAS+ (8/15, 53.3%), smoking+ (21/31,67.74%).PD-L1 negative cases (26/57, 45.6%), were EGFR+(2/14, 14.28%) and KRAS+(6/19, 31.5%). Conclusion: The high risk lung cancer subtypes show squamous/undifferentiated histopathology, inflammatory microenvironment, male preponderance, smoking history, higher concomitant PD-L1, KRAS and EGFR positivity. Lung cancer subtyping can predict clinical response/resistance of patients prior to initiation of PD-L1 inhibitor therapies and can be used to guide therapy.

Keywords: *Subtyping-lung cancer, PD-L1, coexisting EGFR/KRAS mutations, tumor histopathology, North India*

P-80

SINE the new revolution for multiple myeloma

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Multiple myeloma (MM) is a plasma cell disorder set apart by clonal proliferation of malignant plasma cells in the bone marrow or sometimes in extramedullary tissues. MM in most cases is incurable. Recent therapeutic advancement has made the treatment of multiple myeloma both more complex and expensive. But, the median survival of patients with multiple myeloma has been markedly prolonged through the use of targeted drugs which include combination and sequential treatments with corticosteroids, alkylating agents, proteasomal inhibitors, immunomodulators, and monoclonal antibodies while effective their efficacy decreases and ultimately becomes ineffective. When the nucleo-cytoplasmic transport of proteins is dysregulated they become a potential cause of carcinogenesis. Exportins are proteins responsible for transport and the activity of these depends on the nuclear export of proteins. The transport of about 220 proteins is mediated by Exportin 1(XPO1). Hence, the only exporter of growth regulatory and tumor suppressor proteins is XPO1. So under physiological conditions, these proteins on export prevent the cells from overreacting on detection of oncogenic situations or absence of DNA injury. However, in case of cancerous cells, the tumor suppressor activity is inhibited by the protein export and tumorigenesis is promoted. Elevated levels of XPO1 have been reported in several solid tumor and hematologic malignancies. Hence, XPO1 inhibition floats up to the surface as a budding option of treating the fatality caused by Multiple Myeloma. The collective term for future anti-tumor drugs SINE has the capability of blocking the export of TSPs and GRPs thereby maintaining intranuclear concentration and bringing to action anti-cancer activity, becoming a major topic of discussion further in this review.

Keywords: *Multiple myeloma, SINE, cancer, Nuclear export*

P-81

Emerging Role of Nitric Oxide (NO) as a therapeutic and diagnostic tool in health and diseases

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Nitric oxide is an endogenous gasotransmitter molecule that plays a regulatory role in various pathophysiological processes and disease states. NO is produced in the body via L-Arginine dependent and L-Arginine independent pathways. Modulation of various signaling pathways are the cornerstones for the development of NO based therapeutics. NO donors/mimetics such as L-Arginine, Citrulline and organic nitrates, cGMP potentiators like Sildenafil and NOS inhibitors such as L-NAME and L-NMMA has established its place in clinical and experimental pharmacology and physiology. Further research has shown that in addition to be a therapeutic strategy in a variety of disease states, NO may also act as a diagnostic tool. The role FENO has been proposed as an important diagnostic tool for airway diseases. Further the competitive inhibitor of NOS, (ADMA) is now being increasingly recognized as a predictor of endothelial dysfunction and associated CVS mortality and morbidity. In view of the unstable nature of the NO (half-life=5-10 sec) stable NO metabolites (Nitrates & nitrites) are considered as effective biomarkers of NO activity in various tissues. Inhaled NO gas is now considered as a crucial therapeutic modality in HAPE (High altitude pulmonary edema), Pulmonary HTN and ARDS. Salivary NO measurement can also be an important biomarker/diagnostic tool for infectious diseases. Dietary Arginine and citrulline supplementation results in increased NO production and can have therapeutic effects on NO deficiency-related diseases. Hence, even after three decades of the discovery of NO and award of the Nobel Prize, NO continues to be a rapidly expanding field of research with newer emerging roles in health and diseases.

P-82

Inhibitory and Disruptive effect of novel Mycobacteriophages on Mycobacterium biofilm

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Background-Bacteriophages(phages) are natural viruses infecting bacteria, and are promising alternative to antibiotics to treat multidrug resistant infections. The biofilm forming bacteria add up to the antibiotic resistance crisis as they contribute in bacterial resistance and drug tolerance. In this study, we have isolated novel mycobacteriophages and examined their inhibitory and disruptive effect on *M.smegmatis* biofilm.

Methods-Mycobacteriophages were isolated using the Double Agar overlay method and used for determining their inhibitory and disruptive effect on *M.smegmatis* Mc^2155 biofilm formation in 24-well plates. To each well, *M. smegmatis*(0.8 OD_{600}) were mixed with phages at a titre of 10^8PFUs/ml for inhibition and phages were added to the preformed biofilm(2 days) for disruption. The plates were incubated at 37°C for 96hours and the quantitative estimation was carried out by Crystal Violet staining method.

Results-In this study, a total of 23 mycobacteriophages were isolated from soil samples and their inhibitory effect on biofilm was investigated. The effect ranged from the absence of measurable inhibition to more than 50% inhibition. While 3phages showed no effect at all, 2phages showed mild inhibition(10%), 8phages within 11-40%, and 10phages exhibited inhibition in the range of 41-60%. Disruptive effect of 6phages was investigated where 4showed mild disruption(10-20%), 2phages exhibited nearly 40% disruption.

Conclusion-Few reports are available on the effect of bacteriophages on mycobacterial biofilms as yet. We find the preliminary results observed here as promising. The ongoing work on their disruptive effect and synergistic effect with the antibiotics can further help us understand their potential as antibiofilm agents.

P-83

Elucidation of mechanism of action of isoflavones in amelioration of Prostate Cancer.

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Prostate cancer is the second most frequent cancer after lung cancer in males. It is known that as the prostate cancer progresses several tumor suppression genes are downregulated including Estrogen Receptor beta (ER-B). ER-Beta Promoter is hypermethylated during prostate cancer advancement. This epigenetic modulation can be reversed by the downregulation of DNA Methyltransferases that is mediated by an isoflavone, Genistein. However, the ability of genistein to evade prostate cancer is limited thereby it will be crucial to further investigate other novel isoflavone compounds that show more pronounced effect against prostate cancer. In the present study, Bioinformatics tool have been deployed for identification of key isoflavones that target the ER-Beta promoter. A library of around 200 isoflavones were screened with the help of Molecular docking. DNA Methyl Transferases were selected as the receptor as they are the suggested key targets during Genistein mediated amelioration of Prostate cancer. Molecular Docking against three DNMTs: DNMT1, DNMT3a and DNMT3b was scrutinized. Top Hits obtained post docking were analysed and compared through software and compounds showing optimum activity against all three DNMTs were selected. The activity of isoflavones identified by preliminary bioinformatic study was further inspected by studying their effect on two prostate cancer cell lines. These studies involve the utilization of Cell Cytotoxicity assay predominantly the MTT assay in order to elucidate their ability to evade prostate cancer. Initial studies have established the higher potency of one of the two isoflavone compounds in cytotoxicity assays in comparison with Genistein. Taken together these results, Isoflavones can be deemed to have potential to ameliorate prostate cancer.

P-84

Synthesis and Characterization of biocompatible Zinc Oxide based nanostructure for biomedical application

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Cancer is a deadly disease responsible for huge fatality rates around the globe. According to WHO reports, around 19.3 million new cancer cases have been diagnosed and about 10.0 million cancer deaths have been reported in 2020. Amongst all cancers, lung cancer is responsible for the highest mortality around the globe. Although, lung cancer treatment has advanced greatly in recent years, is still highly prevalent and continues to be the leading cause of malignancy-related deaths. To address the existing challenges, metal oxide nanoparticle has gained interest of the scientific community over the past two decades in the fields of biomedical sciences, materials science and nanotechnology. Zinc oxide nanoparticles (ZnO NPs) are one of the most utilized nanomaterials. In biological fluids, ZnO NPs are easily soluble and have a propensity to assemble under various physiological conditions which is must for drug delivery. With their specific targeting abilities and advantages as carrier agents, ZnO NPs are proved to be a successful alternative to currently used cancer treatments. In this work, we have created a ZnO-PDA-Ag nanocomposite that shows a promising potential for its application in biomedicine, particularly in anticancer and antibacterial agents due to its powerful ability to liberate zinc ions, increasing the generation of reactive oxygen species (ROS), and causing cancer cell death. The prepared nanocomposite is characterized by different characterization techniques like Fourier-transform infrared spectroscopy **(FTIR**), X-Ray Diffraction (XRD), Scanning electron microscopic (SEM) and energy dispersive X-ray (EDX) techniques.

Keywords: *Lung Cancer, Zinc-Oxide nanoparticles, Nanomedicine*

P-85

Synergetic Effect of *Bacopa monnieri* and Molybdenum Disulfide Nanoparticles in Cancer Cells

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Cancer remains a leading cause of death worldwide, in spite of extraordinary progress in cancer treatment. Therefore, new cancer treatment modalities are required and there are reports suggesting nanomedicine as the promising therapy option. The development in nanostructures including metallic nanostructures, quantum dots (QDs), lipid nanoparticles (NPs), silica nano-vehicles and polymeric NPs with high specificity and significant properties have made NPs as a feasible option to permeate the blood–brain barrier (BBB). Especially, Molybdenum disulphide (MoS_2) NPs have got attention in cancer diagnosis and treatment because of their specific physical and chemical properties such as absorbance of biomolecules and drug molecules via covalent or non-covalent interactions, promising tumor targeting and colloidal stability, accuracy and good sensitivity for detecting specific biomarkers, response to tumor microenvironment, exhibit high specific surface area, enhanced drug accumulation in the tumor site and less side effects on non-cancerous tissues and improved therapeutic effect. Therefore, we checked the cyto-toxicity of synthesized MoS_2 NPs via green chemistry on glioblastoma and breast cancer. Moreover, Bacopa also have been identified for treatment of brain illness and our focus is to use bacopa-MoS_2nanoparticles (B-MS-NP) as a carrier for targeting chemo-resistant population of glioma. Here, the B-MS-NP have been synthesized using nano-precipitation technique and modulated in a way so as to sensitize them toward brain tumor microenvironment. The characterization techniques Fourier-transform infrared spectroscopy (FTIR), *X-ray diffraction* (XRD) and Nuclear Magnetic Resonance (NMR) have been carried out to investigate the structural and chemical properties of B-MS-NPs. In this study we discuss the synergetic effect of B-MS-NPs for their synthesis, characteristic, properties, surface modifications, health risk and biomedical applications and comparative analysis of B-MS-NPs against Breast cancer and Glioblastoma cell line. The challenges that limit their use for various purpose like control over size distribution, shape, composition and surface modifications of nanoparticles have also been investigated in this study. The risk assessment of these nanoparticles via different exposure routes is important for further investigation in clinical use.

Keywords: *NPs, Bacopa and MoS_2, nano-precipitation, cancer treatment, cell line*

P-86

Study the Pro-oxidant effect of Hydrogen Peroxide (H_2O_2) on U87 cell lines

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ROS homeostatis is important for survival and proliferation of cells in normal conditions. In cancers such as Glioblastoma, ROS help cancer cells to proliferate, migrate and make them invasive by upregulating pathways such as PI3K/AKT/mTOR and MAPK/ERK. ROS levels are modulated in cancer by upregulation of antioxidant pathways like Nrf2/ARE. It is found that, if ROS concentrations are increased, it causes cell cycle arrest and cell death by downregulating Cyclins, CDKs and CDC25 and upregulating Bcl2 and Caspase 9 proteins. H_2O_2 has been reported to generate ROS, leading to apoptosis, necrosis and cell cycle arrest in breast cancer cell line, whereas, increased p53 activity and decreased cancer cell migration in lung cancer cell line.

In order to attenuate cell proliferation, higher levels of ROS generation is desired, therefore, we used H_2O_2 to increase ROS concentrations and reduce proliferation of U87 glioma cells. Herein, we have investigated the toxicity of H_2O_2 in U87 cell lines using MTT assay and compared with ascorbic acid. The results showed that H_2O_2 was able to kill U87 cells at a concentration of 100uM while ascorbic acid killed the cells at concentrations of 200uM.
In future, the effect of H_2O_2 and Ascorbic acid alone and in combination with DMC, a curcuminoid already reported in killing glial cells via production of ROS, will be measured, on U87 cell line. Then, the effect of the drug combination will also be determined for cell cycle arrest and apoptosis.

P-87

In situ Fabrication of Noscapine Loaded Collagen Coated Silver Nanoparticles

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Collagen scaffold, a naturally occurring polymer, has been extensively used in biological investigations involving nanotechnology for the delivery of medicinal compounds. Particularly those made of noble metals, metal nanoparticles exhibit excellent qualities for biotechnology applications. Majority of biomedical investigations have demonstrated a wide variety of applications for AgNPs in particular. In this study, a single-step in situ approach to encapsulate the anticancer drug Noscapine in collagen-based silver nanoparticles (Ag@Col@Nos) was developed. Despite the fact that noscapine is insoluble in water, the current nanostructured formulation with collagen enhances the transport and solubility of the anticancer drug and seeks to give enhanced targeted efficacy. The produced NPs will be termed to as Ag@Col@Nos throughout the paper because the structure of the suggested NPs had a Collagen-stabilized Ag0 centre where Nos molecules were bound. FTIR, EDX, UV-Vis, DLS, and other spectroscopic techniques were used to characterise Ag@Col@Nos nanoparticles. The synthesized Ag@Col@Nos were also examined for cellular toxicity and drug release over time in an in vitro model of non-small cell lung cancer.

Keywords*: Silver Nanoparticles, Collagen, Noscapine, Anti-cancer activity, Collagen Coated Silver Nanoparticles*

P-88

Demethoxycurcumin modulates the expression of Bcl-2, LC3/ Beclin proteins and cytochrome c release concurrently in U87 cell lines

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Background: GBM (Glioblastoma), a grade four astrocytoma, is the most aggressive and frequent of all primary brain tumors. Demethoxycurcumin (DMC), a derivative of curcumin has been shown anti-glioma effects. The previous work from laboratory demonstrated that the G2/M cell cycle arrest induced by DMC is associated with Reactive oxygen species mediated reduced protein expression of CDC25C , Cyclin B1 and p-CDK1 in U87 MG glioma cells. The prior study demonstrated that DMC induced apoptosis via ROS dependent pathway. DMC may be a potential anti-cancer drug targeting glioblastoma. In this work effect of DMC was measured simultaneous on expression of autophagy and apoptotic proteins.

Methods: SRB assay used to access the effect of DMC on cytotoxicity. Cellular ROS level was determined by flow cytometry. Flow cytometry were used to evaluate apoptosis by Annexin V-APC apoptosis detection kit. Western blot analysis of Bcl-2, cytochrome c (cyt c) release from mitochondria, LC3 II, Beclin 1 were carried out to study the effect of DMC on autophagy and apoptosis.

Results: DMC inhibited cell viability in concentration and time dependent manner in U87 cell lines. DMC decreased the expression of Bcl-2 and increase cytochrome c (cyt c) release in concentration dependent manner. DMC also modulates the expression of autophagy proteins LC3 II/Beclin 1. However more work will be required to confirm observation.

Conclusion: The results showed that there might be interaction between apoptotic and autophagy proteins, however further work will be required to confirm the hypothesis.

Keywords: *Demethoxycurcumin (DMC), Apoptosis, Autophagy, Glioblastoma, Reactive oxygen species (ROS)*

P-89

Bisdemethoxycurcumin mediated targeting of MnSOD associated mechanism of apoptosis in U87 MG Cell Lines.

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Glioblastoma, a grade four astrocytoma, is the most aggressive, diffuse and frequent of all primary brain tumors. Current treatments involving Temozolomide, however develops resistance. In continuation of our previous work in the laboratory on the isolation and purification of Demethoxycurcumin to study their anticancer effect on U87 malignant glioma (MG) cell lines. We propose to carry anticancer effect of Bisdemethoxycurcumin (BDMC).

BDMC, a curcuminoid isolated from Curcuma longa, was reported to have biological activities such as anti-inflammatory, anti-oxidative and anti-carcinogenic properties. In lung cancer, BDMC was found to induce autophagy, apoptosis, DNA Damage and decrease cell migration and invasion via ROS production. BDMC has been found to induce apoptosis and supress migration and invasion of glioma cells via NF-kB, MMP2 and MMP9 signalling pathways. MnSOD is an antioxidant, overexpressed in various types of human malignancies which helps in tumor proliferations by regulating the ROS levels. In the current study, the drug likeness, ADME and toxicity properties of bisdemethoxycurcumin were assessed. The compound showed significantly drug like properties, no toxic effect in ADME profile. Therefore, the binding interaction of BDMC with MnSOD were carried using molecular docking analysis.

The results showed that BDMC showed stable binding with MnSOD. We have investigated the effect of BDMC on U87 MG cells using MTT assay. Future study will used to determine role of BDMC-induced ROS generation on cell viability in U87 MG and BDMC-mediated inhibition of MnSOD leading to accumulation of superoxide anions to trigger the inhibition of survival pathways and induction of apoptosis.

P-90

DECIPHERING THE ROLE OF p53 AND ITS MUTANTS IN CANCER CELL METABOLISM (PART-I)

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TP53 is a critical regulator of major metabolic pathways. Metabolic reprogramming one of the "hallmarks of cancer" and drives tumorigenesis. Frequent p53mutations not only eradicate tumor suppressor capacities but also confer various GOF activities that impact in alteration of metabolic pathways now regarded as central for tumor development and progression. We selected three hotspot mutants (R175H, R273H and R249S) and wtp53 to evaluate the effects in human non-small cell lung carcinoma cell line (NSCLC-H1299). Our study highlights the effect of different mutp53 and glucose/glutamine deprivation in terms of their effect on metabolism and tumor aggressiveness, RT-PCR (Real Time-PCR) and western blotting were used to check the expression of p53 and its mutants at mRNA and protein level. The seahorse is used to measure the Oxygen Consumption Rate and Extra Cellular Acidification Rate. The cell cycle analyzed by Flow cytometry. Cell proliferation and migration were studied by SRB (Sulforhodamine B) and wound healing assays. Differential expression of p53 mutants observed in normal and stressful circumstances. However, WTp53 wasn't affected. Both glucose and glutamine starvation inhibited the development and migration of mutant cells. In glutamine-starved conditions, growth inhibitory and migratory activities were more prominent than in glucose-starved. Non-mitochondrial oxygen consumption, maximal respiration, and proton leakage decreased in glucose-stressed mutants and p53-/-cells, whereas basal respiration and ATP generation increased. Our research show that mutp53 influence several metabolic processes and decreases aggression in starvation of main carbon source. Increased mitochondrial activity and use alternative pathways for mutp53 survival are observed after glucose starvation in NSCL cells. This might provide a foundation for the development of more effective targeted therapeutics/pharmacological approaches toward variants of mutant p53.

Keywords: *TP53, mutant p53, cancer metabolism, NSCLC.*

P-91

Deciphering the role of p53 and its mutants in cancer cell metabolism (Part II)

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Background: Fundamental metabolic pathways have been shown to alter during carcinogenesis. Role of dysregulated p53 in cancers has been well established. However, the association between p53 and its mutants with altered cancer metabolic pathways have not been well established. **Objective:** To decipher the role of p53 and its mutants in reprogramming the metabolism which ultimately drive the aggressive phenotypes in cancer cells. **Methodology:** We used non-small-cell lung cancer line (NSCLC) (H1299) as a model system. Key metabolic pathways of H1299 with p53 wild-type gene were compared with cells harboring p53 hotspot mutation (R273H). Glucose/glutamine starvation was provided to cells to modulate the metabolic pathways. p53 expressions at transcriptome as well as protein level was analysed using real-time PCR and western blotting respectively. Constitutive levels of metabolites in cells with different p53 mutational status were examined using liquid chromatography-mass spectrometry (LC-MS). Differentially regulated metabolic pathways were delineated by manual analysis. **Result:** In the cells with R273H p53 mutation, the relative abundance of metabolites of urea cycle were found to be increased by four fold while Tricarboxylic Acid Cycle (TCA) precursors/metabolite levels were significantly reduced. Upon glutamine starvation, p53 protein expression was increased in R273H mutant but not in the cells with wild type p53. Cell cycle analysis revealed inherent shortened G2/M phase when compared to cells with wild type p53. We found no significant change in cell proliferative and migratory potential upon p53 mutation. Glutamine starvation to p53 mutated cells resulted in shutting down the TCA cycle as indicated by reduced levels of urea cycle metabolites. However, glutamine starvation could not alter the metabolic pathways in cells with wild type p53.
Conclusion: Metabolic reprogramming of cancer cells and tumorigenesis is associated with the mutational status of p53. We report that urea cycle might be associated with cell cycle alteration in R273H mutant of p53.

P-92
Indian Perspective of Cervical Cancer

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Cervical cancer is the fourth most common cancer among women and is one of the leading causes of cancer-associated death in females. In India, it is the second most common cancer with 123907 diagnoses and 77348 deaths annually. Nation-wide low screening and minimal Human Papilloma Virus (HPV) vaccination rates contribute to the progression of the disease to advanced stages. The high-risk HPV is the causal factor behind the development of cervical cancer. HPV-16/18 is responsible for nearly 83.5% of invasive cervical cancers. Infection by HPV and the integration of the HPV genome into the host chromosome of cervical epithelial cells are the early key events in the neoplastic progression of cervical lesions. Cervical cancer poses a significant global burden and remains a serious therapeutic challenge. Chemoradiation and Brachytherapy (BT) are recommended as the standard care for locally advanced cervical cancer (LACC) by the National Cancer Grid of India and the Indian Council of Medical Research. Current therapies to treat cervical cancer are often associated with debilitating side effects and tumour drug resistance. As a result, alternative therapies are being developed which include immunotherapy, targeted therapy, and genetic approaches such as CRISPR/Cas9 [Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein 9] and RNAi [RNA Interference]. This poster explains that despite being easily preventable, cervical cancer continues to threaten a large segment of the female population. It further elucidates the evidence-based recommendations for the application of the most suited screening tests for use in resource-poor field settings. Tests, like VIA/VILI [Visual Inspection with Acetic acid or with Lugol's iodine] are not only affordable but, can also be easily taught to grass root health workers, who can help in conducting the screening program in remote areas. The elimination of cervical cancer calls for society-based preventive and control measures, educating women, screening activities and HPV vaccination.

P-93

PHYTOCHEMICALS TARGETING METABOLIC REPROGRAMMING TO INHIBIT PYRUVATE DEHYDROGENASE KINASE FOR CANCER THERAPY

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Tumor microenvironment has dearth of nutrients and oxygen which leads to hypoxic conditions. Tumor initiation and progression demands high energy, therefore metabolic reprogramming occurs in hypoxic cancer cells. Hypoxic conditions cause induction of Hypoxia- inducible factor 1(HIF-1α), a crucial modulator of metabolic reprogramming. The common metabolic phenotypic changes are increased glucose uptake for glycolysis and lactate production, known as Warburg Effect. HIF-1α activates Pyruvate Dehydrogenase Kinase (PDK 1,3), which inhibits Pyruvate Dehydrogenase Complex (PDH), consequently impairing pyruvate conversion to acetyl-CoA causing a shift from OXPHOS (krebs cycle) to anaerobic glycolysis. Induction of glycolysis together with inhibition of PDH favours lactate production, which in turn stabilizes HIF-1α further.

Besides metabolic switch to glycolysis, neovascularisation or angiogenesis is required to improve delivery of oxygen and nutrients into hypoxic regions. HIF-1 induces vascular endothelial growth factor (VEGF) which promotes neovascularization, a key mechanism for promotion of angiogenesis during tumor development.

PDK regulates various metabolic processes including aerobic glycolysis, mitochondrial OXPHOS and TCA cycle in cancer cells therefore PDK inhibition can prove a potent therapeutic target. Few PDK inhibitors are known but failed due to toxicity issues when tested on laboratory models of multiple cancers. Therefore, an ideal plant based PDK inhibitor needs to be explored from existing databases, having more specificity and less toxicity.

P-94

Non-viral gene delivery using PEI-HA conjugated Nanoparticles for curing retinoblastoma caused due to deletion of RB1 gene.

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Retinoblastoma (RB) is the main pediatric intraocular tumor in children. It is caused by the mutation of tumor suppressor gene RB transcriptional corepressor 1 (RB1). Herein, we have proposed that hyaluronic acid (HA) grafted linear polyethyleneimine (hyperbranched-star PEI-HA) can be used as the polycationic gene carrier for preparing the nonviral vectors with efficient uptake and hypotoxicity for potential retinoblastoma gene therapy application. HA is less cytotoxic according to previous studies and also receptors of HA are majorly expressed in the tumor cells, hence HA adds to the specificity to NPs to target the tumor cells. The pDNA (cargo) with functional RB1 gene transfection should indicate that different functional proteins can be expressed in the retinoblastoma cells. The functional genes is encapsulated in the PEI-HA based nonviral gene vectors. The hyperbranched-star PEG-HA is a promising nonviral carrier for ocular gene delivery, hence can be used effectively for retinoblastoma.

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P-95

Understanding the role of the Sf-URI1 ortholog in the intrinsic radioresistance of Sf9 insect cells

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Acute exposure to high doses of ionizing radiation (IR) is known to cause cell and tissue damage, followed by organ failure and death of an organism. The responses of an organism to the lethal effects of IR vary considerably among different species. Among all known radioresistant organisms, insects are considered evolutionarily closest to mammals, where many biomolecular signaling components are highly conserved. Among insects, lepidopteran insects or insect cells display extreme radioresistance. The lepidopteran Sf9 cells, (derived from *Spodoptera frugiperda*, Fall Army Worm) are approximately 300 times more radioresistant than mammalian cells and serve as an excellent model to study stress responses. A recent study has indicated the role of unconventional prefoldin RPB5 Interactor 1 (URI1 or RMP1) protein in radioresistance of mammalian gastrointestinal cells (*Chaves-Pérez et al., Science, 2019*). However, its role in Sf9 radiation response is not yet understood.

As the URI1 protein in *S. frugiperda* remains uncharacterized, in-silico analysis comprising of a series of BLAST searches using lepidopteran URI1-like protein sequences from *Trichoplusia ni* against NCBI and Spodobase datasets was performed to identify an ortholog of this protein in *S. frugiperda*. One ORF from this sequence codes for a 266-residue long protein highly similar to the N-terminus and central region of human and drosophila URI1 proteins. The protein coded from the open reading frame (ORF) is predicted to contain two major conserved functional domains of human URI1 protein, i.e., the alpha-Prefoldin domain and the RPB5 mediating domain. Moreover, the structure of the prefoldin domain of the *S. frugiperda* URI 1 (SfURI1) like sequence was identical to that of the human URI1 (hURI1) prefoldin domain. The western blotting analysis using anti-hURI1 pAb (binding to central conserved region in hURI1) of Sf9 whole cell lysates showed the presence of a specific protein band at 31KDa, which is the predicted molecular weight of the SfURI1-like protein. Furthermore, immunocytochemistry (ICC) analysis of Sf9 cells γ-irradiated with 500, 1000, 1500, and 2000 Gy (using Co-60 source) at 24 h post exposure showed cytosolic localization of Sf-URI1 protein, while the URI1 protein translocated to the nucleus with increasing IR dose in mammalian cells. These findings are in concurrence with the *in-silico* analysis as the nuclear localization signal (NLS) of URI1 protein resides in the 339-343 region towards the C-terminus of the protein, which was not present in the SfURI1-like sequence.

Studies are underway to further characterize SfURI1 and its functional crosstalk with already known factors contributing to the intrinsic radioresistance of Sf9 cells. Understanding the mechanistic insights into URI1 cooperation with accessory radioprotective mechanisms has implications for radiation protection as well as the treatment of radioresistant tumors.

P-96

Deciphering the differential regulation of novel long non coding RNAs and their mechanismof action in p73 dependent manner

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The p53 tumor suppressor family is classically activated after DNA damage andplays a central role in cell fate decisions. Although, the p53 family activates many of the same genes in response to DNA damage, p73 plays distinct biological functions in development and metastasis. It is likely that p73 activates a unique transcriptional network which is critical for its anti-metastatic and anti-invasive action. Long non-coding RNAs (lncRNAs) are a class of mRNA- like transcripts longer than 200 nucleotides. They lack protein-coding ability and are believed to be involved in various kinds of biological processes. Increasing evidence suggests that lncRNA are frequently aberrantly expressed in cancers. Therefore, the roles of dysregulated functional lncRNA in human malignant tumors have attracted considerable scientific interest. The objective of our study is to find out novel long non-coding RNAs that can act as transcriptional targets of p73 and to delineate their role in p73-mediated anti-metastatic response. For this purpose, we performed transcriptome sequencing in HCT116p73wt and HCT116p73KD cells and screened the data for modulation of expression of lncRNAs in differential manner. Quantitative Real Time PCR was further carried out to validate the data obtained after screening RNA seq Data. Promoter analysis was carried out for the identification of p73 binding sites in the selected upregulated or downregulated lncRNAs which was further confirmed by Luciferase reporter, ChIP and site directed mutagenesis assays. About six lncRNAs were observed to be significantly upregulated while four were down-regulated upon knockdown of p73. The promoters of selected lncRNAs were analysed *insilico* using TF Bind and JASPAR software for p73 binding sites and luciferase reporter assays suggested regulation of lncRNAs by p73. Chromatin immunoprecipitation showed promoter enrichment of the selected lncRNAs. Together, our study provides insights into the differential regulation of long non-coding RNAs in p73 dependent manner which further will provide the mechanism of their action at the genome level.

P-97

Potential role of melatonin in sensitizing cancer stem cells towards therapy

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The most important loophole of present-day cancer treatment is resistance to therapy as the widely used treatment regimens often make the cancer cells aggressive due to increase in their stemness properties, alters cellular metabolic pathways and thus unresponsive towards therapy. The most important factor that offers resistance to cancer therapy is the presence of cells having stem cell like properties, generally termed as cancer stem cells (CSCs). Cancer stem cells subpopulation of the tumor has been held responsible for therapy resistance (both chemo- and hormone resistance), aggressiveness and instances of tumor recurrences. CSCs, which have received a great deal of research interest recently, pose considerable challenges for cancer treatment. Thus, modulation of CSCs might aid to overcome endocrine resistance and thus alternative therapeutic options are the need of the hour. Melatonin, a physiological hormone released by the pineal gland, possesses excellent anticancer properties and research has shown that melatonin can cause cancer cells to undergo apoptosis and can prevent tumor metastasis and angiogenesis in various malignancies. Moreover, several studies have confirmed melatonin's potential therapeutic use in the treatment of cancer stem cells. This review focuses on the role of melatonin in treating cancer stem cells thereby sensitizing cancer cells towards therapy.

P-98

Potential role of melatonin in targeting anti-cancer pathways in cancer

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Melatonin (N-acetyl-5-methoxy-tryptamine) is the main pineal gland hormone synthesized from tryptophan in response to darkness. Studies have indicated an inverse correlation between progression of various cancer and melatonin concentrations. Several epidemiological studies have shown that women who had experienced over 20 years of night shift work had a statistically significantly increased risk of breast cancer. Researchers have shown that melatonin is an excellent free radical scavenger and antioxidant properties. It possesses anti-apoptotic, cyto-protective, immune-enhancing, and anti-tumor properties. The oncostatic and tumor-inhibiting properties of melatonin has been documented in various experimental models of different types of cancer. Moreover, Melatonin, being an excellent antioxidant agent can also be potentially used as an adjuvant in cancer treatments: increasing the therapeutic effects of various conventional anticancer drugs and minimising the adverse effects of the therapeutic regimes, thereby improving the overall well-being of the cancer patient. It has been reported that the anticancer effects of melatonin are mediated through the modulation of the hallmarks of cancer. Through its interaction with the melatonin receptor MT1 and MT2, melatonin promotes apoptosis, blocks pro-survival signalling, disrupts tumor metabolism and energetics, suppresses angiogenesis and metastasis, induces epigenetic change, and reverses immune evasion. This review summarises the preventive and therapeutic aspects of melatonin as far as cancer treatment are concerned and focuses on the molecular and biological mechanisms by which melatonin inhibits different types of cancer by the modulation of the various cancer cells hallmarks.

SESSION X: RECENT ADVANCES IN ALTERNATIVE MEDICINE: WITH EMPHASIS ON AYURVEDA

P-99

Moringa oleifera: an Ayurvedic cure for community-acquired infections of MRSA

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A formidable medical challenge has presented itself to health systems and clinicians because of the emergence of SARS-CoV-2. Among those diagnosed with COVID-19, *Streptococcus pneumonia* and *Staphylococcus aureus* caused a majority of community-acquired co-infections. *Staphylococcus aureus* is a major human pathogen that causes a wide range of clinical infections. Two distinct shifts have occurred in the epidemiology of *S. aureus* infections over the last two decades: healthcare-associated infections and community-associated infections. It wasn't long after methicillin was introduced in 1961 that Methicillin-resistant *Staphylococcus aureus* (MRSA) was discovered and soon it became resistant to most oral antibiotics, hence a safe and efficient alternative was needed.

Natural products are becoming more popular because of their potent antibacterial, anti-inflammatory, immunomodulatory, and antioxidant properties. Since ancient times the use of these natural plant metabolites to treat a variety of ailments is in Hindu medicinal manuscripts. To discover the potent cure for *S. aureus*, the antibacterial activity of various plants was tested. Among them, *Moringa oleifera* showed a positive result. The antibacterial activity of different extracts (ethanolic and methanolic extracts) of *M. oleifera* leaves and bark was investigated against *S. aureus.* Ethanolic leaf extract showed maximum antibacterial activity (with an inhibition zone size of 17 mm diameter for 0.16 gm ethanolic leaf extract). With various nutritional and medicinal properties, *Moringa* can be seen as a potent neutraceutical.

Keywords: *SARS-CoV-2, Staphylococcus aureus, MRSA, Moringa oleifera, Secondary Metabolites*

P-100

Multi-model Ayurveda Management of Gestational Diabetes Mellitus - A report from the single-arm pilot study

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Background: Gestational diabetes mellitus (GDM) is increasing in prevalence and corresponds to the drastic increase in the prevalence of overweight and obesity in women of childbearing age. Worldwide, there are guidelines with recommendations for appropriate management strategies for GDM. This study deals with Ayurveda management of Gestational Diabetes Mellitus based on heterogenicity model. The diagnosed cases were stratified based on phenotype (*Prakriti*) and intervention was administered. This study reports cases of GDM managed with interventions of Ayurveda – Oral medication, diet and yoga.

Objective: To determine the effectiveness of Ayurveda interventions in management of GDM Cases. The secondary objective was to investigate the therapeutic utility of the therapy, taking onto consideration maternal as well as foetal outcomes.

Study Intervention and Data Collection:

The intervention included Nishamalaki Tablets (NA) and Sarvamehahara Kashaya Ghana Vati (SKG) , dietary modifications and Yoga interventions in the diagnosed cases of GDM. The outcomes were measured were 1) Glucose Monitoring – Objective & Subjective 2) Maternal Outcomes 3) Foetal Outcomes.

Results: 11 pregnant women with a mean age of 25.44 years (range), SD ± (±5.175) and mean period of gestation 29.78 (± 3.416) years were enrolled in the study. One dropped out of the study, but all remaining ten participants were followed up, for glycaemic control maternal and foetal outcomes were assessed at the end of treatment. No adverse were reported during the study.

Conclusion: Ayurveda management of Gestational diabetes mellitus was found effective in the cases. The heterogenicity in pathophysiology of GDM, can be translated to treatment guidelines. This study is an attempt to validate the approach with management of Ayurveda. It is important to investigate the mechanism of action of the treatment with a larger sample and suitable research methodology.

SESSION XI: ART OF WAR AGAINST CARDIOVASCULAR DISEASE PROGRESSION AND OUTCOMES

P-101

Correlation between GDF15 -3148C/G polymorphism and coronary artery disease in population of Northern India

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Background: GDF -15 associates with increased risk of coronary artery disease. Two studies have investigated the association of GDF-15 3148 C>G with CAD in Chinese population but with contradictory results. The present study investigates correlation between GDF15 -3148C/G polymorphism and CAD in population of Northern India.

Methods: GDF-15 3148 C>G polymorphism was analyzed by PCR-RFLP technique. The GDF-15 expression at protein level was investigated in 200 CAD patient samples and 200 control samples by western blot analysis.

Results: - The present study observed the distribution of genotypes in patients as well as in the controls in the order of CC>GC>GG. The allele frequency was found to be 0.93 and 0.07 for C and G allele respectively in patients while it is 0.87 and 0.13 for C and G allele respectively in controls. A significant association was observed in the GDF-15 genotypes (CC vs CG) with CAD with odds ratio 2.25[1.31 to 3.85] at 95% confidence interval [p =0.0030]. A significant association was also observed in CC vs GG+CG genotypes with odd ratio 2.21[1.30 to 3.75], at 95% confidence interval [p= 0.0032]. A significant difference (p = 0.003) in the protein expression of GDF-15 level was observed in the plasma of patient samples (1.73) as compared to control samples (1.02).

Conclusion: The findings suggested a correlation between GDF-15 -3148C/G polymorphism CG + GG genotype with CAD. It is also observed that protein expression of GDF-15 gene in CAD patients is higher when compared to control group for the studied population.

P-102

Prediction of cardiovascular diseases using risk factor-based diagnostic for precision medicine

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According to several studies, cardiovascular disease (CVD) has surpassed cancer as the world's leading cause of death. Healthcare expenditures have predominantly been aimed toward health promotion in the battle against cardiovascular disease, with a focus on causes, prevention, and alternative treatment findings. We can further predict distinctive CVD events with the help of risk factor evaluation; foundations have been driven by population-based scoring algorithms based on existing risk factors. Incorporating conventional risk factors as well as using noninvasive measures purposefully may help identify people at higher risk in addition to people at seriously low risk, allowing for more precise treatment intensity targeting. Numerous new diagnostic techniques, aside from blood tests, ECG, and Echo, have emerged in this field, including an exercise stress test, HRV (Heart Rate Variability), Nuclear Cardiac Stress Test, Coronary Angiogram, MRI (Magnetic Resonance Imaging), and Coronary Computed Tomography Angiogram (CCTA). We can implement an effective evidence-based strategic plan to analyze and minimize CVD risk utilizing scientific evidence, professional judgment, and discussion among both physician and patient.

Keywords: *Cardiovascular diseases, Diagnostic, Risk factor*

P-104

Multifactorial effects of Vitamin C against latent Infection of Mycobacterium tuberculosis

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Tubercle bacilli persists in dormant state during latent tuberculosis infection (LTBI). In Latent TB individuals Mycobacterium tuberculosis (Mtb) localizes in the granuloma, an immune microenvironment, acts as a barrier to dissemination but also it acts as a favorable zone for long term survival of the bacterium. As a fact, within granuloma, Mtb encounters multiple stresses like hypoxia, acidic pH, oxidative stress and nutrient limitation etc. However, very little is known about host cell responses against dormant Mtb so far. Macrophages maneuver as major defense cells against microbial pathogens. Our lab observed that Vitamin C treated Mtb infected THP-1 cells (macrophage cell line) mimics multiple intracellular stresses of granuloma which leads to growth arrest and dormant population of Mtb. Therefore, our main objective of the study is to investigate the immunomodulatory effects and host cell defence responses of Vitamin C on Mtb infected THP-1 model in-vitro. Our findings suggests that Vitamin C induces a hypoxic environment to host cell thereby intracellular Mtb attain dormant state to survive. Simultaneously, it seems that presence of Vitamin C in macrophage induces cellular oxidative stress that switches narcotic state of the infected cell towards the apoptotic state. Altogether, Vitamin C increases the viability of infected macrophages via inducing the hypoxic environment within infected macrophage that reduces the detrimental effects of replicative or active Mtb.

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Abstract book cover page designed by: Kajal Sharma