Souvenir and Abstracts

44th All India Cell Biology Conference & International Symposium on

Molecular & Cellular Insights of Human Diseases

http://mciohd.uok.edu.in/

September 2-3, 2022

Department of Biochemistry
University of Kashmir (NAAC Accredited A+)
& Indian Society of Cell Biology

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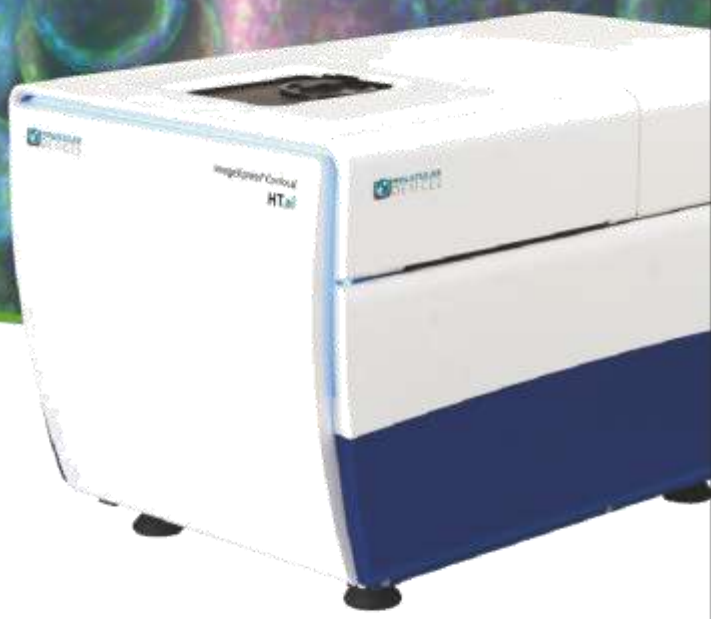

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44th All India Cell Biology Conference and International Symposium

on

Molecular and Cellular Insights of Human Disease

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Supporting staff and volunteers:

- All non-teaching staff, Department of Biochemistry, University of Kashmir
- All research scholars and M.Sc students of the Department of Biochemistry
- All volunteers who helped in the conference arrangements as part of various committees

*We gratefully acknowledge the support of **Mr. Sajad Ahmad Bhat** of **M/S Spectrum Advertising/ Bizwiz Creations**, who helped us on many different fronts to accomplish our designing and printing assignments under very pressing conditions, when things seemed impossible.*

Department of Biochemistry, University of Kashmir

University Of Kashmir
(NAAC Accredited Grade A+)
Hazratbal, Srinagar-190006 Kashmir, J&k

August 12, 2022

Prof. (Mrs.) Nilofar Khan
Vice Chancellor
University of Kashmir
Hazratbal Srinagar - 190006
Jammu & Kashmir (India)

MESSAGE

It is great pleasure that the Department of Biochemistry, University of Kashmir in collaboration with the Indian Society of Cell Biology (ISCB), is organizing the 44th All India Cell Biology Conference on September2-3, 2022. The theme of the conference is "Molecular and Cellular Insights of Human Diseases". It is indeed heartening to know that during this conference; very reputed Cell Biologists of National and International repute will discuss their discoveries, challenges, and experiences.

It is very pleasant to know that more than 500 delegates including scientists, research scholars and students from all over India will attend this conference. I am sure that this event will inspire the young scientists to carry out innovative research, using the latest trends and technologies in the field of biomedical research.

I believe that this conference will certainly provide the participating scientists and scholars a great opportunity to network and collaborate with each other. I am confident that such conference will open new vistas in promoting scientific research and innovation and further inculcating scientific temper among the academicians and researchers.

I extend a hearty welcome to all the participants in this scientific event. I complement and congratulate the Department of Biochemistry University of Kashmir, the Indian Society of Cell Biology (ISCB) for this wonderful initiative. I also wish the organizers of this conference a great success.

Prof. Nilofer Khan

University Of Kashmir
(NAAC Accredited Grade A+)
Hazratbal, Srinagar-190006 Kashmir, J&k

Prof. Farooq A. Masoodi
Dean Academics Affairs,
University of Kashmir

MESSAGE

A better understanding of the principles of science has facilitated a significant advancement in technology, which in turn has resulted in solving many problems of mankind and mitigating its miseries. The cutting edge research in biological sciences, both at the level of basic and translational research has provided new insights into the problems that we face and led to landmark discoveries. Research in cell biology has made an immense contribution in understanding the mechanism of diseases and developing efficient diagnostic, prognostic and treatment strategies at molecular level. Similar progress has also been witnessed in other fields like agriculture, animal science, bio-processing etc.

I am pleased to know that the Department of Biochemistry, University of Kashmir is to organize the 44th All India Cell Biology Conference and International Symposium on "Molecular and Cellular Insights of Human Diseases" on 2nd and 3rd September 2022. This gathering of the intellectuals and scientists from abroad and different parts of the country will provide a great opportunity to deliberate upon some important challenges and come up with recommendations and strategies to combat these issues.

I am sure the conference will provide our students and scholars a platform to share knowledge and ideas, and enhance their understanding about different realms of biological sciences.

On behalf of the organizing committee of this conference, I extend a warm welcome to all the scientists, delegates, and participants and hope they enjoy their stay in the valley. I congratulate the organizing committee for their efforts and wish them all the best for making this conference academically and intellectually productive.

F.A. Masoodi
Dean Academics Affairs

Office of the Dean Research
University Of Kashmir
(NAAC Accredited Grade A+)
Hazratbal, Srinagar-190006 Kashmir, J&k

Prof. Irshad A. Nawchoo
Dean Research,
University of Kashmir

MESSAGE

I am delighted that the Department of Biochemistry, University of Kashmir is organizing 44th All India Cell Biology conference and International Symposium on "Molecular and Cellular Insights of Human Diseases" on 2nd and 3rd September 2022. The world is changing fast, so the challenges mankind faces which warrants dynamic and robust scientific solutions. Improving current understanding for filling information gaps and exploring new domains of research in the essence of science. Identifying difficult questions and deliberations on them among scientific communities are inevitably relevant even in this era of digital world. In this context, the conference being arranged by Department of Biochemistry and Indian Society of Cell Biology makes a gigantic scientific importance and relevance.

Opportunity is created to share research findings, organize deliberations and plan science in these conferences. Given the rudimentary place of cell science in life makes the conference of immense importance. I am optimistic, the conference will serve all delegates a scientific feast and wish organizers a great success

Prof. Irshad Nawchoo
Dean Research

Office of the Dean, School of Biological Sciences
University Of Kashmir
(NAAC Accredited Grade A+)
Hazratbal, Srinagar-190006 Kashmir, J&k

Prof. Zafar A. Reshi
Dean School of Biological Sciences,
University of Kashmir

MESSAGE

I am pleased to know that 500 delegates have registered for presentations during the 44th All India Cell Biology (AICB) conference. We are humbled as well as encouraged by this overwhelming response from the scientific fraternity and thank each participant for his/her valuable contribution. We hope that the deliberations during the conference would be very fruitful and new ideas and approaches would emerge for a better understanding of human diseases at the cellular and molecular level which would pave way for their better and more effective management. We also expect that the conference would provide a platform for transforming the fragmented research landscape into a collaborative and co-operative venture that is urgently needed for realising the ambitious goals of 'one health' approach for better public health outcomes.

We are also grateful to the Indian Society of Cell Biology (ISCB) for entrusting the responsibility of hosting the 44th edition of the All India Cell Biology (AICB) conference to the Department of Biochemistry, University of Kashmir, Srinagar and I am glad that the Organizers of the conference have worked beyond their comfort zone to make this event a success.

I hope that the participants attending the conference physically will have a good time in Kashmir and will visit us again in near future for an even bigger event.

Prof. Zafar A Reshi

DEPARTMENT OF BIOCHEMISTRY
(A DST-FIST Assisted Department)
University Of Kashmir
(NAAC Accredited Grade A+)
Hazratbal, Srinagar-190006 Kashmir, J&k

Dr. Shajrul Amin
Head, Department of Biochemistry,
University of Kashmir

MESSAGE

It is a matter of contentment and pride for us to organize the 44th All India Cell Biology Conference and International Symposium on "Molecular and Cellular Insights of Human Diseases" in collaboration with the Indian Society of Cell Biology from September 2-3, 2022. The conference aims to bring together scientists, academicians, research scholars and students from different domains to share their knowledge and to squeeze out their experiences into valuable suggestions for shaping up the future research strategies. The events of this standard are also indispensable for face-to-face interactions, developing collaborative research and building scientific networks among scientists and students.

The conference has become more exhilarating with the responses that it has received, covering the central/state universities and research institutes, which further adds to the grandeur of the conference.

On behalf of the Department of Biochemistry, I take this opportunity to welcome all the delegates of the conference. I hope all the participants will have a fruitful and memorable time in the paradisiac valley.

I am highly grateful to organizing team for exercising painstaking efforts to materialize the conference. The success of this conference will encourage us to introduce many more initiatives for carrying out innovative research in the coming years.

I wish the conference a great success!

Dr. Shajrul Amin
Head of Department

ACKNOWLEDGMENT

The Department of Biochemistry, University of Kashmir is truly honoured to host the 44th All India Cell Biology Conference and International Symposium on "Molecular and Cellular Insights of Human Diseases" (http://mciohd.uok.edu.in/) to be held at the University of Kashmir on September 2-3, 2022. First and foremost, we are very thankful to the Executive Council (EC) of the Indian Society of Cell Biology (http://www.iscb.org.in) who graciously accepted our request to host the conference at the University of Kashmir. Special thanks go to the president Dr. Jyotsna Dhawan (President), Prof. Pradeep Kumar Burma (Vice-President), Prof. Bhupendra N Singh (Secretary), Prof. Jagat Roy and Prof. Vegesna Radha who offered all the support and guidance needed for organizing this event.

We offer our sincere thanks to the Honourable Vice Chancellor Prof. Nilofar Khan, who provided us all the support for holding this event right from the inception of this idea of holding this event. The support and guidance of the Prof. Farooq A Masoodi, Dean Academic Affairs, Prof. Irshad A Nawchoo, Dean Research, Dr. Nisar A Mir, Registrar, and Prof. Zafar A Reshi, Dean School of Biological Sciences has also been incredible all along. Without their keen interest and involvement, it was not possible to organize this event. We also thank their supporting staffs who helped us in various ways to bring the conference to a reality. The support of all our colleagues in the University and outside is also highly appreciated.

The success of the programme was of couse heavily dependent upon the speakers. We requested them to come to this event and share their knowledge, research findings and experience with us. They are very well known in their fields and come from very reputed institutes in India and abroad. They are: Prof. V. Radha, Prof. Khurshid Andrabi, Prof. L.S. Shashidhara, Prof. Sanjeev Galande, Dr. M. Ayub Qadri, Dr. Sagar Sengupta, Dr. Rashna Bhandari, Dr. Pritha Ray, Dr. Nazir A Dar and Dr. Aamir Nazir. Despite their very busy schedule, they kindly accepted our invitation and agreed to grace us on this occasion. We are also honoured to have Prof. Arshad Desai from UCSD, USA and Prof. Jonathan Higgins from the Newcastle University who kindly agreed to give talks in the online mode, despite their very busy schedule. We are also honoured to have the distinguished scientists who will receive the Memorial Awards from the Indian Society of Cell Biology: Prof. Chandrima Shaha (President INSA), Prof. Umesh Varshney (IISC, Bangalore) and Dr. Md. Imtaiyaz Hassan (Jamia Millia Islamia, New Delhi). We also thank them for agreeing to come to this event and share their research findings with us.

The work of the conference started immediately with the designing of the website, which was the most effective way to reach out to the participants. We thank Dr. Maroof N Qadri who provided us support right from the beginning on this front. We want to specially mention the immense contribution of Mr. M. Aasim Banday who put tireless efforts in initially designing a good website and improving as well as updating the contents very regularly. We admire his ability as well as sincerity to help us on this front. The support of EMMRC & ITSS is also highly appreciated in anticipation who will cover this event on September 2-3 during the conference. We also thank the support of Ms Lubna Bhat who graciously agreed to provide all the support and the facility to hold this event in the beautiful Convocation Complex of the University. Only because of the support of the Registrar, University of Kashmir and Ms Lubna Bhat, we could convene the programme at this venue and accommodate the large size of the participants during this event.

Organizing conferences is never easy, and the magnitude of the conference also kept on increasing as we moved closer to the date of the event. Our organizing committee including the teachers, non-teaching staff, research scholars, non-teaching, M.Sc students and many other volunteers were the backbone of this conference. Without the support of all of them, it was impossible to organize this event. The support of all of them is deeply appreciated.

ACKNOWLEDGMENT

We also thank our Advisory Committee members who provided valuable suggestions during this time. The names of Prof. Akbar Masood, our colleague and now the Vice Chancellor of Baba Ghulam Shah Badshah University, Prof. Khurshid Andrabi, our colleague and former Vice Chancellor, University of Kashmir, Prof. M.A. Zargar, our colleague and Registrar, the Central University of Kashmir, Prof. Qayyum Hussain, Vice Chancellor of the Cluster University of Kashmir, who also supported us in so many ways. We could not have organized the programme so efficiently had it not been their support and guidance.

We are so thankful to all other people who have contributed in so many ways to organize this event. The support of the University Guest House to host our esteemed guests needs a very special mention. We also thank all the vendors who provided us all the things that are needed to conduct this event successfully. We thank Mr. Feroz Ahmad of M/S Mehak Printing Press who took all the pains to print all the material that is for this event. We also thank Javed Ahmad who helped us in so many ways: arranging the registration material, hotels, transportation, catering as well as providing help and guidance on many different fronts.

We also thank our sponsors who supported us financially for this event. It would have been very difficult to organize the event of this size without their generous support. They are: University of Kashmir (Honourable Vice Chancellor, Registrar and Dean Research), Indian Society of Cell Biology, BD Biosciences, Molecular devices, Leica Microsystems, Carl Zeiss, ThermoScientific and Biomed Systems. We also thank in anticipation the support of the Department of Biotechnology, Ministry of Science and Technology, New Delhi and the J&K Science Technology and Innovation Council (JKSTIC) who have shown their keen interest to

The time for holding this event was very limited (about 2 months) and the task was huge. At times, it seemed impossible to be able to get the printing material ready for the event. We therefore gratefully acknowledge the support of Mr. Sajad Ahmad Bhat of M/S Spectrum Advertising/Bizwiz Creations, who helped us on many different fronts up to the last minute, particularly with regards to the designing/printing of various materials like certificates, momentos, Abstract book etc. He made our task much easier under very pressing conditions, putting aside many of his own projects and deadlines.

We also want to thank all the participants who showed keen interest to attend this event and convert this originally conceived mini-conference to a full conference. The response was so good, but the time was so limited that we had to finally stop accepting any further registrations, just within 3 weeks of time of our announcement. Your presence will make this event memorable, successful and worthy. We are very hopeful that all of you would like this conference and enjoy your stay in Kashmir. We hope to hold many such events in the future. We are sorry for those who wanted to come but we had to deny them for logistic reasons.

Finally, we want to thank all those who are not mentioned here, though unintentionally. You all have contributed to the success of this event in many ways. We apologize to those who deserved mention in case we have missed you. We are also sorry for any inconveniences, delays or shortcomings that may have occurred during this event. We all wish our participants a great time and stay during the conference.

Thank you all.

Organizing Committee:

- **Dr. Sharul Amin** (Convenor)
- **Dr. Shaida Andrabi** (Organizng Secretary)
- **Dr. Nazir A. Dar** (Co-organzing Secretary)
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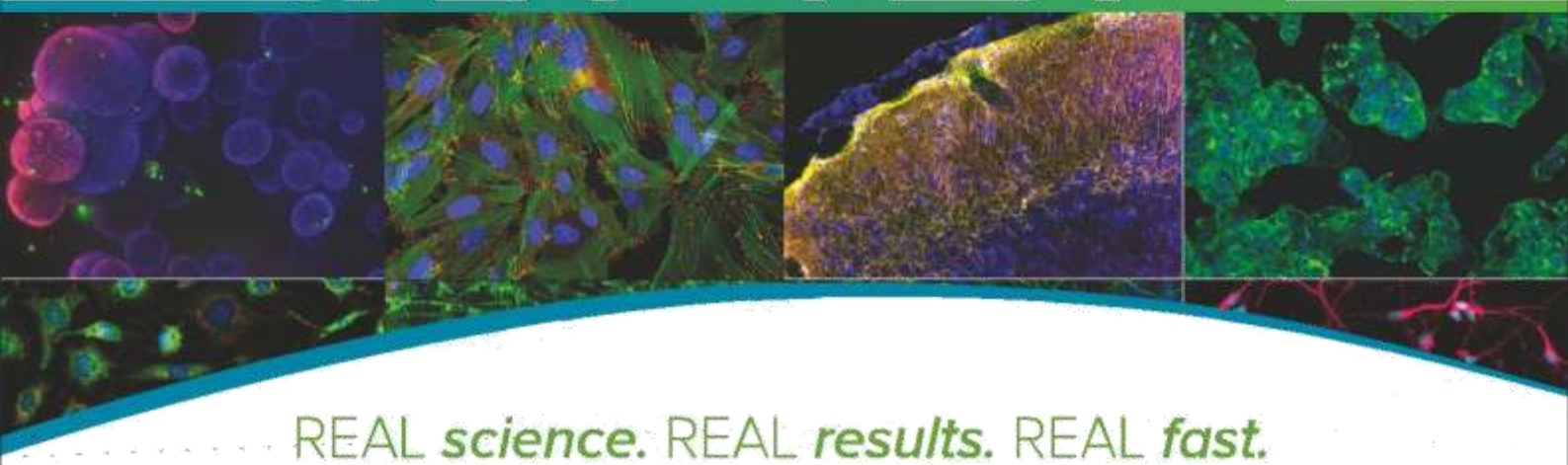

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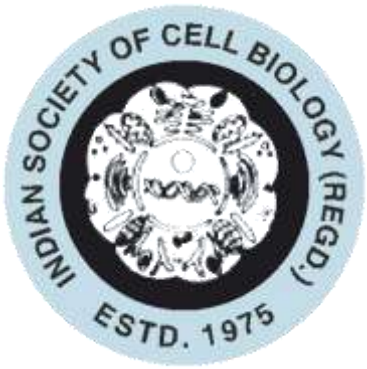

Distinguished Memorial Awards

by Indian Society of Cell Biology

for 2020 and 2021

The XVIII Prof. S P Ray- Chaudhuri 75TH Birthday Endowment Lecture Award

Prof. Chandrima Shaha
Indian Institute of Chemical Biology, Kolkata 700032

'Intracellular parasitism: succeed to survive'

In the context of infectious diseases, the processes that drive cell death in both the host and the pathogen are important as co-evolution of the two has shaped both the assault and the defense systems. A surprising number of intracellular pathogens of public health importance, survive within macrophages countering the host cell's potent microbicidal activities and antigen presentation capabilities. These pathogens, including the trypanosomatid parasites, have evolved mechanisms to thrive despite the strong assault from the host. Some parasite proteins function as dynamic players with multiple functions helping infections to succeed. The hosts have evolved mechanisms to interfere with such molecules to prevent pathogen survival. Cellular processes like autophagy and apoptosis are important participants in the success or failure of infections. Apoptosis being the preferred form of death when host assault with reactive molecules becomes overwhelming, cellular autophagy is used as a possible survival strategy. Enormous progress has been made in understanding intracellular pathogen survival, with novel findings adding to recognize cellular processes amenable to targeting for reducing or preventing infections.

The Eleventh Prof. J Das Memorial Lecture Award

Prof. Umesh Varshney
Department of Microbiology and Cell Biology,
Indian Institute of Science, Bangalore

'Initiator tRNA centric view of translation initiation and ribosome maturation in *Escherichia coli*'

Translation initiation in bacteria involves assembly of initiator tRNA (tRNAfMet), mRNA, initiation factors (IFs) on 30S ribosome to form 30S pre-initiation complex (30S pre-IC), which rearranges and joins 50S ribosome to form 70S IC. Upon releasing IFs, 70S IC becomes elongation-competent 70S (70S EC). The recruitment of tRNAfMetto the ribosomal P-site, crucial for accurate initiation, is attributed to formylation of the amino acid attached to it and, the presence of three consecutive GC base pairs (GC/GC/GC or 3GC pairs) in its anticodon stem. We showed that formylation of tRNAfMet is crucial for its initial targeting to the 30S ribosome whereas the 3GC pairs are critical in the later stages in initiation.

The 3GC pairs in the initiator tRNAs are conserved in all domains of life, and are vital fortranslationinitiation. However, using a reporter system, we isolated Escherichia coli suppressors that allow initiation with tRNAfMet wherein the 3GC pairs (GC/GC/GC) were changed to UA/CG/AU pairs (tRNAfMetua/cg/au). Our studies with these strains have revealed that, (i) one-carbon metabolism (producing methionine, S-adenosylmethionine and N10-formyl-THF) contributes to the fidelity of translation initiation; (ii) deficiency of the chromosomally encoded tRNAfMet allows initiation with tRNAfMetua/cg/au and elongator tRNAs, suggesting a novel mechanism to generate proteome diversity. Further, E. coli with the canonical number of four tRNAfMet genes are favored in nutrient-rich environments, and those with three are favored in nutrient-poor environments; (iii) RluD, a pseudouridine synthase that isomerises uridines to pseudouridines in H69 of 23S ribosomal RNA in 50S ribosomal subunit is involved in ribosome maturation by a novel mechanism of the removal of ribosome biogenesis factor A (RbfA) from 30S ribosomal subunit; (iv) extended interactions between Shine-Dalgarno sequence (SD) in mRNA and the anti-SD in 16S rRNA compromise fidelity of initiation; (v) the 3GC pairs play a critical role in transitions of tRNAfMet from 30S pre-IC to forming the 70S EC, and in release of IF3 during this process, and in the final stages of rRNA maturation.IF3 interaction with tRNAfMet elbow modulates translation initiation and growth fitness in E. coli. Further, we show that a mutation (V93A) in IF3 leads to a relaxed fidelity of initiation and allows poor growth of E. coli sustained solely on tRNAfMetcg/GC/cg mutant. Interestingly, a subsequent mutation of either V32L or H76L in uS12 (known for its role in fidelity of tRNA binding in the A-site) salvages the retarded growth by enhancing the fidelity of translation. Thus, our studies using a simple system of E. coli are allowing us to understand the intricate mechanistic details of translation initiation in bacteria.

The Third Prof. Rita Mulherkar Lecture Award

Md. Imtaiyaz Hassan
Centre for Interdisciplinary Research in Basic Sciences,
Jamia Millia Islamia, New Delhi

'Design and development of potential Map/Microtubule-affinity regulating kinase 4 inhibitors: Targeting microtubule dynamics to control cancer'

MAP/Microtubule-affinity regulating kinase 4 (MARK-4) is a Ser/Thr protein kinase that relates structurally to the AMPK/Snf1 subfamily of the CaMK kinases. The protein kinase modulates several major signalling pathways such as NF-κB, mTOR and the Hippo-signalling pathway. MARK4 is associated with various cancer types due to disrupted microtubule dynamics and subsequent cell division. Aberrant expression of MARK4 is linked with several pathologies such as cancer, Alzheimer's disease, obesity, etc. We have designed a series of MARK4 inhibitors bearing excellent binding affinity and consequential inhibition. These compounds inhibit cell proliferation and migration in MCF-7, MDA-MB-435s and HepG2 cells (very high IC50 values). In addition, we exploited a series of natural compounds known to possess anticancer properties and dissected their mechanism of action using cutting-edge computational, molecular and cellular biology-based methods. We showed that rutin, quercetin, ferulic acid, hesperidin, citral, gallic acid, cholic acid, rosmarinic acidand vanillin potentially inhibit MARK4 and thus employed for cancer therapeutics. Cell proliferation, ROS quantification and Annexin-V staining studies. These compounds cause oxidative stress resulting in apoptosis and showing a remarkable MARK4-specific selectivity profile. In addition, these compounds inhibit cell viability, induce apoptosis and lower the tau-phosphorylation in cancer cells. In addition, we have developed isatin-triazolehydrazones, aryl-substituted heteroarylchromones and acridone-derivatives, showing binding affinity to the MARK4 in the nM range and possessing admirable anticancer properties. Our findings provide evidence for these herbal products' apoptotic potential and their further implications against MARK4-associated diseases.The design, synthesis and biological evaluation of potential inhibitors of MARK4 will help conceive new therapeutic strategies for discovering a first-in-class small molecule for the cancer, metabolic and neurodegenerative diseases.

Keywords: Microtubule-affinity regulating kinase 4; Drug discovery; Kinase Inhibitors; Anticancer Therapy; Microtubule Dynamics; Natural Products

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Abstracts
of Invited Speakers

Professor Arshad Desai
Professor of Cellular and Molecular Medicine,
Member Ludwig Institute for Cancer Research,
University of California, San Diego

Time is (not) on your side: mitotic control of G1 progression

Professor Vegesna Radha

CCMB, Hyderabad

RAPGEF1 orchestrates embryonic cell division and differentiation

During embryonic development, altering cell fate from proliferation and committing to lineage specific differentiation is under the control of signaling molecules that specify gene expression and cytoskeletal dynamics. Identifying molecules that control cell fate allows us to understand development and the underlying cause of developmental defects. Using mESCs, and zebra fish, we identified RAPGEF1, a multifunctional signal transducer, as an essential regulator of cell division and differentiation for normal embryonic development. We show that RAPGEF1 is required for maintaining the activity of signaling and cell adhesion molecules. RAPGEF1 is ubiquitously expressed, but human brain organoids, mouse and zebra fish tissues show developmental regulation, and tissue specific expression of distinct RAPGEF1 isoforms. We also identify functional defects caused by missense mutations in RAPGEF1 associated with developmental disorders.

Professor Khurshid Andrabi
University of Kashmir

mTOR signalling as an integrated circuit to regulate cellular fate for survival and growth

Cellular growth and proliferation is regulated by a series of signal networks predominated by mTOC1 pathway. Ribosomal S6 kinase 1, the terminal effector of this pathway assumes significance in modulating the prospect of growth and survival. The classical view of signal propagation through mTORC1 relies on its ability to interact with and phosphorylate S6K1 at its hydrophobic motif for its activation. The dogma however, fails to synchronize metabolic and autophagy dynamics with its nutrient and growth factor dependence. In deviance with common understanding, we present evidence that role of mTOC1 is restricted to priming S6K1 for phosphorylation for its subsequent activation by mTORC2 to realign the bonafide of S6K1 as an AGC kinase in the process. We also present data to identify a novel signalling circuit induced by energy crisis through which AMPK brings about growth factor and nutrient independent activation of mTORC1 to integrate autophagy with cell survival. Our data identifies AMPK as a novel backup for cell to sustain mTORC1 activity under extreme nutrient deprivation for survival and switch to aggressive growth during normal nutritional state.

Professor Jonathan Higgins
Newcastle University, UK

Chromosomes, Kinases, and Cancer

Jonathan Higgins received his DPhil at the University of Oxford, and then carried out postdoctoral work at the Brigham & Women's Hospital, Harvard Medical School, working on lymphocyte-epithelial cell adhesion. While there, he serendipitously discovered the mitotic kinase Haspin, leading to a significant change in research direction and the establishment of his lab working on protein kinases and histone modifications in mitosis. He returned to the UK in 2014, becoming Professor of Eukaryotic Molecular Cell Biology at Newcastle University, where he is Theme Lead for Chromosome Biology and Cell Cycle. He will discuss recent work on the functions of histone phosphorylation during cell division and describe a new method to identify protein kinases responsible for specific phosphorylation events in cells.

Professor Sanjeev Galande

Center of Excellent in Epigenetics,
Department of Life Sciences, Shiv Nadar University
Department of Biology, Indian Institute of
Science Education and Research, Pune

Repurposing statins for colorectal cancer therapy

Statin family of drugs has been extensively used as the most potent therapy for hypercholesterolemia. Vast body of research has presented strong evidences wherein statins have been used effectively for treating and/or controlling coronary heart disease, atherosclerosis, diabetes mellitus. In the past few years, reports have suggested it's anti-tumor effects as well, where it was shown that statin treatment prevented the tumor growth. A few indirect mechanisms were also suggested via which statins could prevent tumorigenesis specifically in solid tumors. However, report suggesting any direct mechanism is lacking. We have been interested in the mechanisms and pathways responsible for colorectal cancer and also look for potential therapeutic targets. Here, using a multi-pronged approach we studied the effects of statins both in-cellulo and in-vivo. Through the integrative analysis of our transcriptomics, proteomics and lipidomics data, we have observed that statins downregulate tumor promoting pathways including Wnt/β-catenin signaling. I will discuss the effect of statins on this pathway and it's major molecular players including β-catenin and chromatin organizer proteins. Collectively, we propose a molecular mechanism for how statins affect tumor progression.

Professor L. Shashidhara
Ashoka University, Sonepat

Cell biology of organ development: a case study - specification of wing and halter development in Drosophila

Dilsha, C1, Inamdar, M.M2 and Shashidhara, L.S1, 3
1IISER Pune, 2IIT Bombay and 3Ashoka University

Studying structure-function relationship is key to understand biological systems across all scales of size and complexity. We would present experimental data coupled with mathematical modelling on the differential development of wing and halters in Drosophila. These two organs develop as functionally two distinct organs, although their development begins from near identical progenitor cells and thus they provide a good model system to understand specification of organ size and shape. We first trace how bio-mechanical properties of cellular components such as membrane, actin-myosin and microtubular complexes determine cell size and shape. We then present how forces exerted by the extracellular matrix and how behaviour of individual cells when they are part of larger community of cells determine size and shape of these two organs during development.

Dr. Ayub Qadri

School of Health Sciences,
Islamic University of Science and Technology,
Awantipora, J&K

Tête-à-Tête between Salmonella and the host

Pathogenic Salmonella continues to be a major health problem in the developing world. The clinical manifestations produced by this pathogen vary from self - limiting localized gastroenteritis to more serious systemic infection, typhoid, or invasive non-typhoidal Salmonella disease, depending on Salmonella serovar and the type of host. During systemic dissemination, this pathogen, after breaching the gut, colonizes peripheral organs including spleen, liver, gall bladder and bone marrow. It employs several intricate and highly regulated strategies to invade the gut epithelium, and modulates host defense mechanisms in order to establish a niche in otherwise highly combative immune cells. In this presentation, I will discuss our work on some of the conversations that Salmonella engages in with host cells during its establishment of infection.

Dr. Sagar Sengupta

National Institute of Immunology,
Aruna Asaf Ali Marg, New Delhi 110067, India

MITOL-dependent ubiquitylation negatively regulates the entry of PolγA into mitochondria

Mutations in mitochondrial replicative polymerase PolγA, lead to progressive external ophthalmoplegia (PEO). While PolγA is the known central player in mitochondrial DNA (mtDNA) replication, it is unknown whether a regulatory process exists on the mitochondrial outer membrane which controlled its entry into the mitochondria. We now demonstrate that PolγA is ubiquitylated by mitochondrial E3 ligase, MITOL (or MARCH5, RNF153). Ubiquitylation in wildtype PolγA occur at Lysine 1060 residue via K6-linkage. Ubiquitylation of PolγA negatively regulates it binding to Tom20 and thereby its mitochondrial entry. While screening different PEO patients for mitochondrial entry, we found that a subset of the PolγA mutants are hyper-ubiquitylated by MITOL and interact less with Tom20. These PolγA variants cannot enter into mitochondria, instead becomes enriched in the insoluble fraction and undergo enhanced degradation. Hence mtDNA replication, as observed via BrdU incorporation into the mtDNA, was compromised in these PEO mutants. However, by manipulating their ubiquitylation status by two independent techniques, these PEO mutants were reactivated which allowed the incorporation of BrdU into mtDNA. Thus, regulated entry of non-ubiquitylated PolγA may have beneficial consequences for certain PEO patients.

Dr. Rashna Bhandari

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Fingerprinting and Diagnostics,
Hyderabad 500039, India

Protein pyrophosphorylation – an enzyme independent posttranslational modification

Proteins undergo an array of posttranslational modifications that influence their abundance, activity, and interaction with other proteins. Phosphorylation on Ser/Thr residues catalyzed by protein kinases is one the most frequently occurring and best-studied posttranslational modifications. We have shown that a subset of phosphorylated Ser residues can undergo pyrophosphorylation by accepting an additional phosphate moiety. The phosphate donor in this case are inositol pyrophosphates – a class of energy-rich metabolites present in all eukaryotic cells that consist of an inositol ring substituted with mono- and di-phosphate groups. Serine (and in rare cases threonine) pyrophosphorylation is achieved by Mg2+-dependent, but enzyme independent transfer of a β-phosphate moiety from an inositol pyrophosphate to a prephosphorylated serine residue located in an intrinsically disordered region of the protein, amidst acidic amino acid residues. We have demonstrated that serine pyrophosphorylation regulates diverse cellular processes, including rRNA synthesis, dynein-driven vesicle transport, protein stability, and DNA repair. Our understanding of the molecular details of this phosphotransfer process from pyrophospho-inositol to generate pyrophospho-serine, is still nascent. Our current knowledge of the importance of protein pyrophosphorylation, and recent advances in understanding the mechanism of this important yet under-appreciated posttranslational modification will be discussed.

Dr. Nazir A Dar
University of Kashmir

For fueling cancer, NFKB attenuates the control of p53 on G6PD for promotion of pentose phosphate pathway

Bashir Ahmad Malla, Mohammad Amin Hajam, Adil Manzoor Baba and Nazir Ahmad Dar*
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One of the antitumor activity of p53 is executed by inactivation of Glucose 6 phosphate dehydrogenase (G6PD) that catalyze the rate limiting step of pentose phosphate pathway (PPP). But in tumors with functional p53, how cancer cells get energy and building material, remains to be known. Here we show, the antitumor activity of p53 is attenuated by NFkappaB (p50/p65) by enhancing its degradation. Decreased p53 level releases the inhibitory effect on G6PD. With increase in NFkappaB expression, PPP is upregulated as demonstrated by increased level of NADPH- the biomarker specific to PPP. On using the p53 stabilizer - the MG132, the G6PD activity decreases. In esophageal tissue, high level of NFkappaB and G6PD and almost absence of P53 as compare to adjacent normal tissue demonstrates the biological importance of our finding. We unveil another layer of regulation of biosynthetic pathway. The carcinogenesis in presence of normal p53 is possible as high energy and metabolite demands by use of glycolysis (by phenomenon called Warburg effect) and PPP is feasible.

Dr. Pritha Ray
ACTREC, Mumbai

Implication of active autophagic flux in chemoresistance and cancer stem cell differentiation

Pratham Phadte[1,3] , Aniketh Bishnu[4] , Pranay Dey[2,3], Abhijit De[2,3] and Pritha Ray [1,3]

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Autophagy, a catabolic cellular pathway regulates the balance between survival or death of a cell in response to external and internal cues. Cancer cells often exploit autophagy to avoid drug induced lethality and thereby promote resistance. It is however, not clear whether active autophagy is required incessantly from initiation/early stage to completion/highly stabilized stage during the dynamic evolution of chemoresistance. Using several cellular models of acquired chemoresistance of Epithelial Ovarian Cancer, we demonstrated that completion of autophagic flux is an indispensable feature of early resistant (ER) cells when treated with drugs, but not for late resistant (LR) cells. Differential levels of hyperactivated ERK (in ER cells) and hyperactivated AKT (in LR cells) was found to be the key modulators of such stage specific autophagy induction. Utilizing a novel autophagy reporter and molecular imaging techniques, the kinetics of drug induced autophagy modulation was monitored in live mice. Next to inspect whether autophagy is truly a dispensable pathway for maintenance of resistance in LR cells, basal autophagic flux was examined in Cancer stem cell (CSC) and non-CSC population. Intriguingly, the CSC population was characterized with an active autophagy flux and further promotion of autophagy led to enhanced differentiation of these CSC into non-CSC population while blockade of autophagy had no effect. Through a detailed literature search, we identified Inhibitor of Differentiation (ID) proteins as probable molecular player/s in connecting autophagy and CSC differentiation. Indeed, pharmacological inhibition of these ID proteins (AGX51 treatment) enhanced CSC differentiation into their less resistant, non-CSC compartment. A bioinformatic analysis identified three E box transcription factors (TCF 3, 4 and 12) as probable interacting partners of ID proteins in autophagy modulation and stem cell differentiation. Detailed molecular characterization of this TCF12-ID axis in cancer stem cell differentiation, chemoresistance and autophagy are under progress. Simultaneously, we investigated the autophagy flux in cancer associated spheroids (putative CSC population) isolated from malignant ascites of relapsed EOC patients. An intriguing association of active autophagy flux with a platinum influx transporter was observed in the relapsed patient's group who exhibit better response when re-challenged with platinum agents. Altogether our data divulge an intricate association between autophagy, cancer stem cell differentiation and chemoresistance from established cell lines to patient derived spheroid population.

Dr. Aamir Nazir

Division of Toxicology and Experimental Medicine
CSIR-Central Drug Research Institute
Lucknow

Functional Genomics and Epigenetic Modifications in Neuronal Development, Degeneration and Repair: Studies Employing Transgenic *C. elegans* Model

The advancement in research on disease physiology and pathophysiology has generated significant interest in the aspects of functional genomics and epigenetics pertaining to specific disease conditions. Studying neurodegenerative diseases, the importance of protein quality control and role of non-neuronal cells like glial cells, have provided intriguing insights. In C. elegans model, the glial cells are enriched with specific genes like patch related family gene ptr-10. We endeavored to study the role of this specific "enrichment" in neuronal function, especially in development of neurons or in healing of damaged neurons. We assayed the expression pattern of PTR-10 across various developmental stages, employed RNAi induced silencing and knock-out based studies towards carrying out functional, behavioural and transcript profiling studies in C. elegans model. We also established a model for studying neuronal damage and repair towards exploring the role of ptr-10. We extended the studied towards identifying functional genomics and epigenetic modulators associated with ageing and related processes. Our studies revealed that PTR-10 has an increased expression during the stages of neurogenesis and eventually the expression declines as the worm's age. Loss of ptr-10 led to partial loss of anterior dopaminergic neuron ADE and associated neuronal processes. Neuronal damage as a result of catecholaminergic-toxicant assault was not effectively repaired by neuroprotectant when ptr-10 was absent. The transcriptomic analysis of ptr-10 knockout revealed changes in the expression a subset of 5 genes having role in axonal regeneration. We also identified a novel chromatin modulator and studied functional genomics associated with protein quality control. The studies provide interesting insights on why PTR-10 is enriched in glial cells and that the understanding can be employed towards exploring possible ways of exploiting its protective or repair functions during the conditions of neuronal demise associated with ailments like Parkinson's disease.

Dr. Romsha Kumar

Application Scientist for
Single Cell Multi-omics in
BD BioSciences India.

BD RhapsodyTM Single-Cell Analysis System: A robust microwell-based single-cell partitioning system for high-dimensional biology research

Dr. Romsha Kumar is working as an Application Scientist for Single Cell Multi-omics in BD BioSciences India. Before joining BD, she worked as a Scientist in the Department of Biochemistry, AIIMS, New Delhi. She has more than 13 year of research experience in the field of Immunology with expertise in HIV pathogenesis and Chemokine Receptor signaling. She has published multiple papers in international journals and participated in various national & international conferences. She has an excellent experience in Single cell Multi-omics, Cell sorting and Multi-color Flow cytometry. Dr. Romsha received her PhD from AIIMS, New Delhi.

Dr. Madhujit Damle

General Manager, India and South Asia
Molecular Devices

Molecular Devices ImageXpress platform

Cell Biology has been an important tool to study biological processes over the years. Several experimental tools reveal the changes which are measured by analytical instruments to interpret the biological processes. Microscopy unravels these biological changes in visual form. Taking a step further, this talk will focus on Molecular Devices ImageXpress platform of instruments that help open a new dimension of Quantitative Imaging in 2D and 3D to put a number to the beautiful images and help biological interpretation.

MOLECULAR DEVICES

From Eye to Insight

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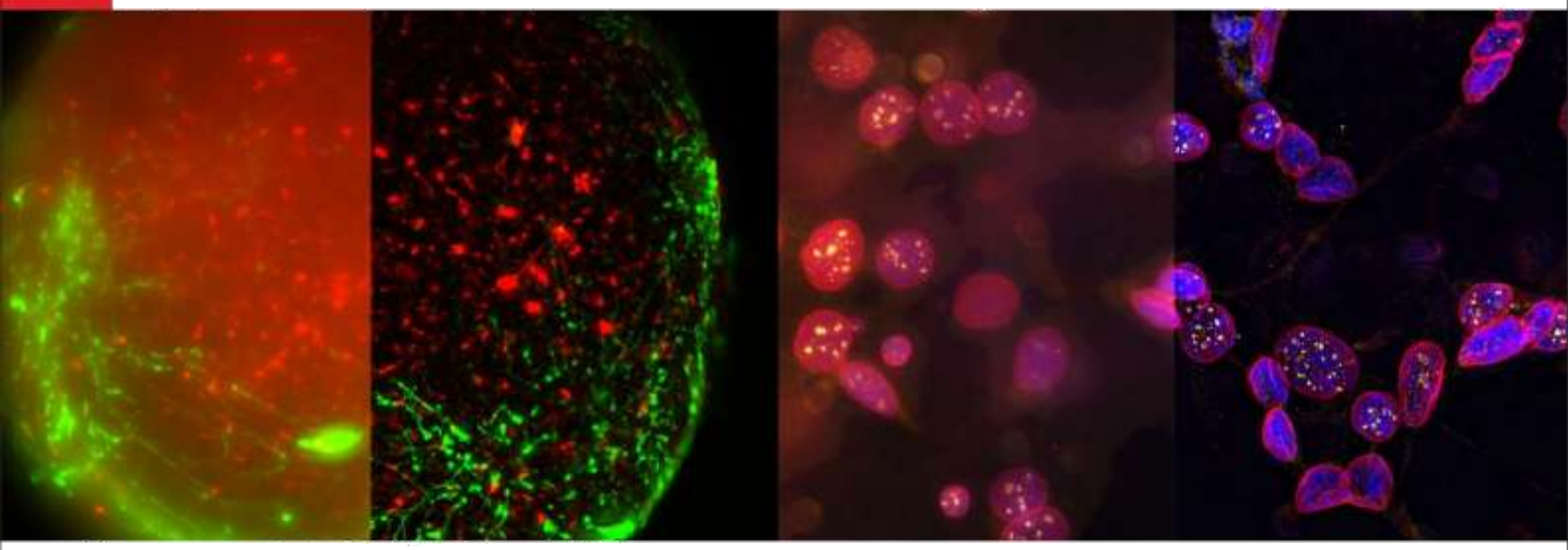

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Abstracts Selected For Oral Presentation

BCH-5 ORAL

EYA-SCAMP3 Facilitate Wntless Trafficking

Hilal Reshi and Dr Maddika Subba Reddy
Centre for DNA Fingerprinting and Diagnostics, CDFD, Hyderabad

Eyes Absent proteins (EYAs) initially deemed critical for Drosophila eye development, are now well known for a myraid of functions including DNA repair, innate immunity and organogenesis. The highly modulated domain structure of EYA proteins enable them to possess several functions that include phosphatase activity and transcriptional co-activation. However the role of EYA proteins in endocytic trafficking is unknown. Here we demonstrate that besides these actvities, EYA proteins form a complex that facilitates the retrograde trafficking of Wntless cargo from early endosomes to the trans-golgi thus regulating wnt-signalling. Mechanistically, EYA complex interacts with the retromer on the surface of wntless-enriched early-endosomes and coats them with SCAMP3 (Secretory Carrier Membrane Protein 3), a step necessary for their fusion with the Golgi membrane. The SCAMP3 coating on wntless endosomes act as molecular cues that distinguish between the recycling vesicles and the vesicles meant for lysosomal degradation. We also show that disintegration of EYA complex by depletion of any EYA component or SCAMP3 directs the vesicles to lysomes for degradation. This places the EYA complex at an important interface between the early endosomes and trans-golgi where it can both maintain the balance between wntles recycling and degradation and skew it towards any direction as per the cellular need. We also demonstrated that EYA mutations found in people that suffer from progressive sensori-neural hearing loss and craniofacial syndrome form a dysfunctional EYA complex, that either lacks several interactions between individual EYA members or fails to bind the retromer. The dysfunctional EYA complex doesn't induce wnt-signalling that is critical for the development of inner ear and other tissues including the lining of intestine and lungs. The dependence of wnt-signalling on EYA complex formation and lack thereoff in hearing-loss patients points to a causal relation between EYA expression and wnt-driven cell polarity in the hair cells of inner ear. The sequence of events, mechanistic details and significance will be discussed.

Key words: Eyes Absent Proteins (EYAS), Retromer, Secretory Carrier Membrane Protein 3 (SCAMP3), Wntless, Wnt3a

BCH-8 ORAL

Trophoblast Stem Cells and Blastoids Generation Follow Competing Molecular Trajectories

Debabrata Jana, Priya Singh, Purnima Sailasree, Mansi Srivastava, P Chandrasekhar
Centre for Cellular and Molecular Biology, Hyderabad

Early mammalian development comprises of two major processes: development of epiblast, and development of extraembryonic layers like trophoblast and hypoblast for providing support to the epiblast. I am particularly curious to understand how these very early cells of embryo decide to become foetus or supporting cells, using mouse as a model system. Developmental potential of Embryonic stem cell (ESCs) known to restrict to embryo proper and hypoblast but not trophoblast. However recent reports in the past one year have shown that ESCs cultured in extended potential media can form extraembryonic layers including trophoblast. However, mechanism of such process is still unknown. In this study we have identified one of the major signalling pathways and the molecular players essential for attainment of the extended pluripotent and differentiation to trophoblast lineage. We have also identified a complex interaction between three transcription factors regulated by small molecules leading to trophoblast differentiation of pluripotent cells. In addition, we have derived trophoblast cell lines and also show that the cells can contribute to trophoblast lineage when injected into 8-cell morula. With these mechanistic insights and few other perturbations, we were able to self-organise preimplantation embryo like structure solely from mouse embryonic stem cells in-vitro. We also show that these embryo-like structures can implant and develop till dpc 7.5.

Key words: Embryonic stem cells, Totipotency, Trophoblast stem cell, Blastoid

BCH-103 ORAL

Role of USP7 in DNA Damage Response

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USP7 is a multitasking deubiquitinase. It plays several roles in cellular physiology by regulating protein stability of multiple substrates. The canonical role of USP7 is stabilization of MDM2 oncogene which in turn degrades p53 tumour suppressor. USP7 has recently been implicated in DNA damage response (DDR). However, the molecular mechanism by which USP7 plays a role in DDR is not known. We have discovered that USP7 interacts with DDB1. DDB1 is a subunit of the multiprotein $CRL4^{Cdt2}$ E3 ubiquitin ligase complex. We show that USP7 deubiquitinates DDB1 both in vivo and *in vitro*, thereby promotes its stabilization. Overexpression or silencing of USP7 respectively increases and decreases half-life of DDB1. Silencing USP7 with shRNA or inhibiting USP7 deubiquitinase activity with p22077 impairs homologous recombination pathway. In conclusion, this study projects USP7 inhibition as a molecular mechanism to augment the positive outcome of radiation or chemotherapy in cancers.

Key words: Deubiquitinase, Ubiquitin Specific Protease, DNA Damage response, Homologous recombination repair

BCH-172 ORAL

The Emerging Role of Adamts4, A MMP and ECM Molecule as a Novel Cardiac Injury Biomarker with Implications in Patients with Cardiac Injury

Riffat Khanam, Arunima Sengupta, Dipankar Mukherjee, Santanu Chakraborty
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Pathological cardiac remodeling as an aftermath of a severe cardiac injury can lead to ventricular dysfunction and subsequent heart failure. Our study focuses on Adamts4, a matrix metalloproteinase (MMP) and extracellular matrix (ECM) marker following cardiac injury. Our *in-vivo* studies in mice model show widespread prevalence of Adamts4 throughout chamber myocardium in the embryonic stages but that its expression severely wanes and is only restricted to the edge of the Interventricular septum (IVS). However, reactivation of Adamts4 in LV of chamber myocardium post Myocardial Infarction (MI) induction in adult murine model is observed and interestingly, the expression of Adamts4 co-localised with cardiomyocytes as confirmed by MF20 co-labelling study. To further decipher the signalling, Adamts4 induction was induced by hypoxia and ROS stress treatment in H9c2, a rat cardiomyocyte cell line. In response to both the stress conditions, Adamts4 expression along with Tgf-B, a-SMA, Col-III and Periostin was significantly enhanced as validated by Western Blot, IF and qPCR data. Moreover, Tgf-B inhibition by ALKI treatment shows Adamts4 inhibition and thereafter inhibition of the above-mentioned ECM and fibrosis markers. However, Adamts4 loss of function by Adamts4 specific siRNA transfection showed no significant change in the expression of Tgf-B indicating the Tgf-B dependent Adamts4 functioning. Finally, Adamts4 and a-SMA expression was studied in clinical samples with a history of MI (Anterior wall MI, Inferior wall MI) and Dilated cardiomyopathy (DCM) where the expression of Adamts4 was significantly elevated as quantified by Western blot for Adamts4 and a SMA in addition to Adamts4 specific ELISA. Our work for the first time highlights the emerging role of Adamts4 as an alternative cardiac injury marker in addition to the routinely assessed cardiac biomarkers.

Key words: Cardiac remodeling, Adamts4, Tgf-B, Biomarker

BCH-195 ORAL

Early Activation of PARP1 Triggers HMGB1 Translocation and Mitochondrial Complex I Mediated Sterile Inflammation

Sourav Dutta, Ankita Sarkar, Piyali Mukherjee
Institute of Health Sciences presidency, University Kolkata

Proteins that function in the regulation of cellular maintenance and homeostasis have been shown to act as Damage associated molecular patters (DAMPs) under different stress conditions. High Mobility Group Box 1 (HMGB1), a non-histone protein that primarily acts in chromatin arrangement, stability and repair is now widely considered as an important nuclear DAMP, due to its ability to induce innate immune signalling and trigger heightened inflammation in both pathogenic and non-pathogenic inflammation. Different studies have shown HMGB1 gets post translationally modified in a wide range of stress conditions, from DNA damage to pathogenic infections. Oxidation, PARylation and acetylation have been shown to be the major driver of HMGB1 translocation. Once the HMGB1 gets poly(ADP-ribosylated), it loses its affinity to chromatin and leaks out of the nucleus. Rotenone has been reported to cause sporadic cases of PD, though the exact mechanism is still to be revealed, it has been shown to induce oxidative damage through complex I inhibition of mitochondrial ETC. As our previous findings have shown rotenone to cause induction in inflammatory responses, we further aimed to look into the exact mechanism of this heightened inflammation to counteract the progression of cell death. Our study focuses on the regulation of HMGB1 and its role in mitochondrial complex I mediated cell death. Our study first shows that rotenone induced complex I inhibition induces mitochondrial ROS mediated DNA damage and subsequent nuclear PARP1 hyper-activation that in turn depletes the intracellular NAD^+ pool. Rotenone further triggers the HMGB1 translocation from nucleus that may act as a prominent DAMP followed by heightened inflammation. Our data strongly suggests HMGB1 may interact with PARP1 in the nucleus prior to its translocation. Our data claims that oxidative stress triggered by complex I inhibition as not the sole mediator of rotenone induced HMGB1 translocation and cell death. Further replenishing NAD^+ levels by targeting NAD+ consuming enzyme PARP1 prevented these effects claiming an important role of PARP1 in complex I inhibition mediated inflammation and subsequent cell death. As well as our study indicated, increased HMGB1 expression and translocation to be involved in rotenone induced sterile inflammation and cell death.

Key words: Mitochondrial Complex I Inhibition, Neuroinflammation, Parylation, HMGB1 Translocation

BCH-211 ORAL

Cytoplasmic Capping Enzyme Mediates Cellular Recovery from Oxidative Stress by Alternation in Cap Homeostasis of Specific mRNA Transcripts

Anakshi Gayen, Avik Mukherjee, Shubhra Majumder And Chandrama Mukherjee
Institute of Health Sciences, Presidency University, Kolkata

mRNA Capping enzyme (CE) adds cap to the 5'-end of the nascent messenger RNA (mRNA). It plays a vital role on mRNA stability, transport from nucleus to cytoplasm and also in translation. Decapping has been thought to be an irreversible decay process until the identification of cytoplasmic pool of CE (cCE) that has changed the paradigm of mRNA decay. It has specific mRNA targets and maintains 'cap homeostasis' by a cyclic process of decapping and recapping in the cytoplasm. Inhibiting cytoplasmic capping reduces cell's viability when introduced to brief oxidative stress. During stress condition, non-translating mRNAs and proteins form aggregates termed as stress granules (SGs) and after the removal of stress, these granules disperse and the sequestered mRNAs and proteins modulate gene expression to enable the cells for growth and recovery from stress.

In our search to decipher the biological role of cCE, we identified localization of cCE in SGs by both confocal microscopy and biochemical purification method. Interaction of cCE with eIF3 is detected in non-stress and stress conditions using co-immunoprecipitation studies that indicates eIF3 may act as a cargo through which CE can be recruited to SGs. Depletion of CE using specific siRNA, does not alter SG assembly and has no effect on cell viability. However,

overexpression of cCE reduces the formation of SGs. In order to identify how cCE regulates cap homeostasis during stress and recovery, we measured the cap status of specific cCE targeted mRNA transcripts along with non- targeted transcripts during non-stress, stress and recovery phase using Xrm1 susceptibility assay. Our data show cCE targeted mRNA transcripts lost their caps in stress condition when cCE is sequestered in SGs. After removal of stress, when cCE is released from SGs, the cap status has been restored for these transcripts suggesting role of cCE in altering cap homeostasis and thus promoting cellular recovery from stress.

Key words: Capping Enzyme, Cytoplasmic Capping, Stress, Recapping

BCH-314 **ORAL**

Plasmodium falciparum Cullins form SCF and Cullin-4 Ubiquitin E3 Ligases, And Cullin-4 Ubiquitin E3 Ligase is Crucial for Parasite Development

Zeba Rizvi, Priyanka Pundir, G Srinivas Reddy, Somesh Gorde, Puran Singh Sijwali
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Malaria parasites undergo multi-stage development in diverse intracellular and extracellular environments, which necessitates timely turnover of both parasite and host cellular contents. Inhibitors of ubiquitin proteasome system (UPS), a major degradation machinery in eukaryotes, block parasite development, indicating that it has crucial roles during parasite development. The crux of UPS function is ubiquitination, which has key roles in diverse cellular processes, including cell cycle progression, differentiation, DNA repair and signalling. UPS comprises of ubiquitin, ubiquitin conjugation enzymes, and 26S proteasome. Ubiquitination involves sequential action of ubiquitin activating enzyme E1, ubiquitin-conjugating enzyme E2, and ubiquitin-ligase E3. Ubiquitin E3 ligases determine accuracy of UPS function by selecting substrates. The most abundant ubiquitin E3 ligases are cullin-RING ubiquitin E3 ligases (CRL), which contain a cullin scaffold for assembly of the complex, a RING-box protein as an E2 recruiter and a substrate adaptor/receptor for substrate recruitment. Skp1-Cullin 1-F-box (SCF) and anaphase promoting complex/cyclosome (APC/C) are the two most notable CRLs, which mediate timely degradation of cell cycle regulatory proteins. Despite conservation and drug target potential of UPS, CRLs have not been investigated in parasitic protozoa. Given the critical regulatory roles and possibility of exploitation in ongoing CRL-targeted drug discovery efforts, we investigated whether *Plasmodium* has CRLs with roles during parasite development. We demonstrate that *Plasmodium* and related Apicomplexan parasites code for 1-3 cullin homologs. Immunoprecipitation and protein-protein interaction studies showed that *P. falciparum* cullins form functional SCF and cullin 4-like ubiquitin E3 ligases, which likely function both in the cytoplasm and nucleus. Knock-down of cullin 4-like ubiquitin E3 ligase protein increased susceptibility to endoplasmic reticulum stress and DNA damaging chemicals, which were in agreement with significantly altered levels of proteins associated with endoplasmic reticulum and DNA repair/replication pathways, suggesting a role for the ligase in these pathways. Parasites with knock-down of cullin 4-like ubiquitin E3 had disrupted morphology, which was corroborated by altered levels of membrane and lipid biosynthesis pathways. Taken together, we for the first time, show that *P. falciparum* contains two functional CRLs, cullin 4-like ubiquitin E3 ligase is critical for parasite development and it regulates endoplasmic reticulum and membrane biosynthesis pathways.

Key words: Ubiquitin Proteasome System, Cullin-Ring Ubiquitin E3 Ligase, CRL, SCF, Malaria, Plasmodium

BCH-2 **POSTER**

Identification of Novel Regulators of Mitochondrial Fusion through Genetic Screens in Drosophila

Rajit Naraynan[1], Tarana Anand[1], Priyanka Pandey[2], Sonal N Jaiswal[2], Manish Jaiswal[1]
[1]*Tata Institute of Fundamental Research, Hyderabad, India*
[2]*CSIR-Centre for Cell and Molecular Biology, Hyderabad, India*

Mitochondria undergo fission and fusion to maintain their health and size. We performed a genetic screen in *Drosophila* to identify novel players involved in mitochondrial fusion. Through this screen, we identified mutations in bendless causing increased levels of mitochondrial fusion protein Mitofusin/Marf. Bendless is a K63-ubiquitin-conjugating enzyme. We found Bendless is essential for the activity of the Pink1/Park pathway to degrade Mitofusin/Marf by the ubiquitin proteasome system. Younus
Mutations in PINK and PARK in humans are known to cause. Further, we also found that Ben is required for Marf regulation to inhibit mitochondrial hyper-fusion under stress conditions and hence it is crucial for mitochondrial size and quality control mechanism. Finally, we also found that under mitochondrial stress conditions, Bendless is neuroprotective.

Key words: Mitochondrial dynamics, Mitofusin, Parkonson's disease

BCH-3 **POSTER**

A Comparative Study on the Non-Enzymatic Antioxidant Status of Cancer Patients (Exposed or Unexposed to Pesticides) of the Eastern Uttar Pradesh Region

Anupama Ojha and Sarad Kumar Mishra
Deen Dayal Upadhyay Gorakhpur University, Gorakhpur

Oxidative stress is implicated in various carcinogenesis and has been found to be aggravated gradually in individuals exposed to pesticides. A great deal of attention has been focused on the antioxidant status of cancer patients. Non-enzymatic antioxidants interrupt the chain reaction induced by free radicals. The major non-enzymatic antioxidants include vitamin C, vitamin E, a plant polyphenol, thiol, carotenoids, and glutathione. In the present study, we determined the level of thiol and ascorbic acid in the serum of cancer patients (exposed or unexposed to pesticides) as compared to control to check the status of oxidative stress. We have found significant changes in the level of thiol content and ascorbic acid as compared to the control. However further study is needed on a large sample size to reach any conclusive findings on the involvement of non-enzymatic antioxidants in the removal of oxidative stress observed in process of carcinogenesis

Key words: Oxidative Stress, Pesticides, Non-Enzymatic Antioxidants, Thiol and Ascorbic Acid

BCH-4 **POSTER**

Nuclear Envelope Protein LBR Protects the Genome from Chromosomal Instability and Tumorigenesis

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Lamin B Receptor (LBR) is an inner nuclear membrane protein that assembles the nuclear envelope post mitosis. Here we show that LBR depletion induces mitotic defects accompanied by recurrent chromosomal losses. In addition, LBR knockdown results in nuclear aberrations such as nuclear blebs and micronuclei, with chromosomes showing a higher frequency of losses, being enriched within the micronucleus. Furthermore, doxycycline-induced conditional depletion of LBR significantly increased tumor volumes that form within subcutaneous xenografts of mice. Of note, the tumor-

derived primary cells recapitulated chromosomal losses and gains, revealing a novel role for LBR as a tumor suppressor. Overexpression of full-length but not mutant LBR (LBRΔ1-89), increased chromosomal gains, implicating the Tudor and RS domains of LBR in modulating chromosomal instability. Co-immunoprecipitation (Co-IP) of LBR uncovered an association of LBR with telomere-associated factors. Interestingly, qPCR array-based gene expression profiling showed a significant upregulation of TRF1 upon LBR depletion. Remarkably, TRF1 knockdown in the background of LBR depletion maintains chromosomal stability, unraveling a novel mechanism involving LBR and TRF in the maintenance of chromosomal stability in colorectal cancer cells.

Key words: Nuclear Envelope, Lamin B Receptor (LBR), Chromosomal Instability (CIN), Aneuploidy, Telomere

BCH-6 POSTER

Impact of Pigmentation Levels in the Regulation of Melanoma Responses

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Skin pigmentation is very important phenotypic trait whose regulation, despite of several advances, has not yet been fully elucidated. Melanin pigment is produced in a membrane bound subcellular organelle called melanosomes inside melanocytes by a complex process known as melanogensis. Melanocyte interacts with inflammatory, immune, endocrine and central nervous systems and its activity is regulating by intrinsic as well as extrinsic factors including drugs and UV radiations. Melanoma is the most aggressive among all skin cancers arising from pigment producing melanocytes, accounts for about 1% of all skin cancers and about 80% mortality among various dermatological cancers. Melanoma has very lethal consequences in advanced stages and has very poor prognosis once it starts metastasizing due to the multidrug resistance exhibited by malignant melanomas. However the multidrug resistance mechanisms underlying the intractability of melanomas remain elusive. As known, the active process of melanogensis is associated with generation of mutagenic and immunosuppressant field which can augment the melanoma resistance to varioustreatment regimes, including chemotherapy, radiotherapy and photodynamic therapy. In this study, we demonstrate that the development of multidrug resistance in melanomas partly involves altered melanogensis, which significantly increases the intracellular pigmentation levels acting as a shield against various treatment regimes. We observed that indeed, inhibition of melanogensis / depigmentation by Kojic acid (KA) sensitizes the melanoma cells (B16F10) towards the chemotherapeutic agents such as Dacarbazine (DTIC) increasing its cellular toxicity. Therefore inhibition of melanogensis/depigmentation will facilitate in understanding the pathogenesis and the development of potential therapeutic options.

Key words: Melanoma, Melanogenesis, Drug Resistance

BCH-7 POSTER

Mir-34a Negatively Regulates Cell Cycle Factor Cdt2/DTL in HPV Infected Cervical Cancer Cells

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MicroRNAs have emerged as an important regulator of cell cycle and various other cellular processes. Aberration in microRNAs has been linked with development of several cancers and other diseases but still very little are known about the mechanism by which they regulate these cellular events. High risk human papilloma virus (HR HPV) is the causative agent of 99% of cervical cancer cases which attenuates multiple tumor suppressors and checkpoint factors of the host cell. The viral proteins also stabilize many oncogenic factors, including an essential cell cycle regulator Cdt2/DTL which in turn promotes cell transformation and proliferation. In this study, we report that a micro-RNA, miR-34a by suppressing HPV E6 protein, destabilizes Cdt2/DTL protein level in HPV infected cervical cancer cell lines. Destabilization of Cdt2 stabilizes pro-apoptotic and onco-suppressor proteins like p21 and Set8 and suppresses cell proliferation, invasion and migration capabilities of the HPV positive cervical cancer cells. Overexpression of either HPV E6 or Cdt2

genes along with miR-34a restored back the suppressed proliferation rate. This study is the first-ever report to show that miR-34a regulates cell cycle factor Cdt2 by suppressing viral E6 protein level, thus opening up the possibility of exploring miR-34a as a specific therapy for cervical cancer treatment.

Key words: Cervical Cancer, High-Risk Hpv, Cdt2, Mir-34a, Hpv E6

BCH-9 POSTER

A NANOG-pERK Reciprocal Regulatory Circuit Regulates Nanog Autoregulation and ERK Signaling Dynamics

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The self-renewal and differentiation potential of Embryonic stem cells (ESCs) is maintained by the regulated expression of core pluripotency factors. The expression level of core pluripotency factor Nanog is tightly regulated by a negative feedback autorepression loop. However, it remains unclear how the ESCs perceive the NANOG levels and execute autorepression. Here, we show that a dose dependent induction of Fgfbp1 and Fgfr2 by NANOG activates an autocrine-mediated ERK signaling in high-Nanog cells to trigger autorepression. pERK recruits NONO to the Nanog locus to repress transcription by preventing POL2 loading. The Nanog autorepression process establishes a self perpetuating NANOG-pERK reciprocal regulatory circuit. We further demonstrate that the reciprocal regulatory circuit induces the pERK heterogeneity and ERK signaling dynamics in pluripotent stem cells. Collectively our data suggest that NANOG induces Fgfr2 and Fgfbp1 to activate ERK signaling in Nanog-high cells to establish a NANOG-pERK reciprocal regulatory circuit. This circuit regulates ERK signaling dynamics and Nanog autoregulation in pluripotent cells.

Key words: Nanog, Reciprocal regulatory loop, FGFR2, FGFBP1, ERK1/2, Embryonic stem cells

BCH-10 POSTER

Regulation of Autophagy by the Annulate Lamellae-Resident Nucleoporin Nup358

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Annulate lamellae (AL) are subdomains of endoplasmic reticulum (ER) characterized by stacked membranes containing a subset of nucleoporins including Nup358. The cellular functions of AL are relatively unknown. ER also makes physical connections with mitochondria through ER-mitochondria contact sites (ERMCS). Recent studies have shown that ERMCS is important in regulating many of the functions mediated by ER and mitochondria such as inter-organelle calcium and lipid transfer, apoptosis, mitochondrial energetics and autophagy. We find that Nup358-positive AL are present at the ERMCS and depletion of Nup358 results in induction of autophagy. Mechanistically, we show that Nup358 interacts with the ER-resident calcium channel IP3R and negatively regulates the calcium release into the cytoplasm. Consequently, depletion of Nup358 leads to calcium-induced autophagy through activation of CaMKKβ/AMPK axis. Our results uncover an unexpected role for AL, and particularly for Nup358, in cellular homeostasis by regulating functions governed by ERMCS.

Key words: Nucleoporin, Nup358, Ermcs, Autophagy, Calcium, Ampk, Camkkbeta

Rab11 Rescues Muscle Degeneration in Parkinson Model of *Drosophila Melanogaster*

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Mutation in *parkin* and *pink1* are associated with Parkinson's disease (PD), the most common movement disorder characterized by muscular dysfunction. In another study, we observed that Rab11, a member of small Ras GTPase family regulates the mitophagy pathway of Parkin and Pink1 in the larval brain of the *Drosophila* PD model. Here, we describe that the expression and interaction of Rab11 in PD model of *Drosophila* is highly conserved across different phylogenic groups. The loss of function in these two proteins, i.e., Parkin and Pink1, leads to the mitochondrial aggregations and Rab11 loss of function results into muscle degeneration and movement defects. We report that overexpression of Rab11 improves muscle organization and movement disorder by reducing mitochondrial aggregations, cytoskeleton structural organization and ameliorates Parkin and Pink1-mediated defects in adult flies. In conclusion, this work emphasizes the importance of Rab11 in rescuing of muscle degeneration and movement dysfunction by preserving mitochondrial function in PD model of *Drosophila.*

Key words: Neurodegeneration, Parkinson's disease, Vesicular-trafficking, Rab11, Mitochondria

Combinatorial Impact of Dmyc and Dfoxo in Mitigating Human Poly(Q) Toxicity in Drosophila Disease Models

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Polyglutamine disorders, such as Huntington's Disease (HD), Spinocerebellar Ataxia (SCA) etc. are neurodegenerative disorders characterized by abnormal expansion of the polyglutamine tract in respective proteins, leading to their misfolding and subsequent formation of neurotoxic inclusion bodies. It has been noted earlier that tissue-specific overexpression of *dmyc* (*Drosophila* homologue of human *cmyc* proto-oncogene) suppresses pathogenesis of poly(Q) disorders in *Drosophila*. However, a single modifier is inefficient to provide complete rescue owing to the wide range of phenotypic outputs and complexity of the disease aetiology. Thus, a combinatorial approach has been proposed to deliver additive rescue against these disorders. In view of the above, our initial observations suggest that downregulation of *dfoxo* (*Drosophila* homologue of human *foxo3a*) along with overexpression of *dmyc* in poly(Q) background delivers significant additive rescue as compared to their independent rescue efficiencies. This indicates that *dfoxo* is a potent modifier and can be utilized along with *dmyc* against poly(Q) disorders in a combinatorial manner. Subsequent experiments are expected to generate novel insights about the interaction dynamics of *dfoxo* and *dmyc* in mitigating poly(Q) disorders.

Key words: Neurodegeneration, Polyglutamine disorders, Drosophila melanogaster, Dmyc, Dfoxo

BCH-13 POSTER

Inhibition of a Tau-Specific Kinases Ameliorates Human Tau Mediated Neurotoxicity in Drosophila Disease Models

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Tauopathies are a group of human neurodegenerative diseases characterized by the formation and accumulation of hyperphosphorylated tau containing neurofibrillary tangles (NFTs) in the brain neurons. Tau, a microtubule-binding protein requires a basal level of phosphorylation to bind and stabilize the neuronal microtubules. The optimal level of tau phosphorylation is maintained by a fine balance between tau kinases and phosphatases. A distressed balance between kinases and phosphatases due to genetic and/or epigenetic factor(s) may cause tau hyperphosphorylation, which subsequently results in its disintegration from microtubules and activation of a pathogenic cascade. Following an evidence-based drug screening, we have identified a chemical inhibitor that significantly mitigates human-tau (h-tau) mediated neurotoxicity by restricting pathogenic tau hyper-phosphorylation in *Drosophila* disease models. Subsequent investigation is expected to generate interesting mechanistic insights about this newly identified molecule in restricting h-tau toxicity in *Drosophila* disease models.

Key words: Tauopathies, Tau-Specific kinase inhibitors, Tau hyperphosphorylation, Drosophila delanogaster

BCH-14 POSTER

Investigating the Mechanism of Binding of β-resorcylic acid with Serum Albumin by Spectroscopic and Computational Approaches

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β-resorcylic acid (BR) is a phytochemical widely distributed among the angiosperms. BR has been found to have antibacterial activity against various types of bacteria. Drug-protein interaction studies are of great significance as serum albumin is a principal extracellular protein present in high concentration in blood plasma and carrier for many drugs to different molecular targets. Interaction studies of BR with bovine serum albumin (BSA) were performed using various spectroscopic techniques in combination with *in silico* studies. UV-visible absorption and fluorescence spectroscopy confirmed the formation of BR-BSA complex. The binding constant calculated was in the order of 10^3 M^{-1}. Changes in BSA conformation induced by BR were confirmed by circular dichroism and 3D fluorescence. Furthermore, the synchronous fluorescence spectra showed microenvironmental alterations near the tyrosine and tryptophan residues. Competitive site marker assays revealed the binding of BR at site-II of BSA. Finally, the binding details between BR and BSA were further confirmed by molecular docking and molecular simulation analysis.

Key words: β-Resorcylic acid, Bovine Serum Albumin, Spectroscopic, Fluorescence, Competitive displacement, Molecular simulations

BCH-23 POSTER

Rosmarinic acid Exhibits Anticancer effects via MARK4 Inhibition

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Microtubule affinity regulating kinase (MARK4) is a potential drug target for different types of cancer as it controls the early step of cell division. In this study, we screened a series of natural compounds and finally identified rosmarinic acid (RA) as a potential inhibitor of MARK4. Molecular docking and 500ns all-atom simulation studies suggested that RA binds to the active site pocket of MARK4, forming enough non-covalent interactions with critical residues and that the MARK4-RA complex is stable throughout the simulation trajectory. RA shows an excellent binding affinity to the MARK4 with a binding constant (K) of 10^7 M^{-1}. Furthermore, RA significantly inhibits MARK4 activity (IC_{50} = 6.204 µM). The evaluation of enthalpy change ($\Delta H°$) and entropy change ($\Delta S°$) suggested that the RA-MARK4 complex formation is driven by hydrogen bonding, and thus complexation process is seemingly specific. Cell-based tau-phosphorylation studies suggested that RA inhibited the phosphorylation of tau. Treating cancer cells with RA significantly controls cell growth and subsequently induces apoptosis. Our study provides a rationale for the therapeutic evaluation of RA and RA-based inhibitors in MARK4-associated cancers and other diseases.

Key words: Natural products, Rosmarinic acid, Molecular dynamics simulation, Kinase inhibitor, Drug discovery, MARK4

BCH-27 POSTER

Inhibition Of PDK3 by Artemisinin, A Repurposed Antimalarial Drug in Cancer Therapy

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Cancer has emerged as a global concern, claiming one-sixth of lost total lives. Despite advancements in technologies and cancer therapy, there is still a need for easily available novel therapies. In recent years, drug repurposing has gained popularity as it accelerates the selection of new candidates for anticancer therapeutics. One such repurposed candidate is the antimalarial drug artemisinin (AMS), which has anticancer potential. AMS is known to work against the major hallmarks of cancer. The compound halts some of the major signalling pathways involved in cancer, such as Wnt/β-catenin and PI3K signalling pathways. Pyruvate dehydrogenase kinase 3 (PDK3) is overexpressed in many cancer types and thus is considered an attractive drug target for cancer therapy. We investigated the binding and PDK3 inhibitory potential AMS in the current study using computational and spectroscopic methods. We observed a significant binding affinity of AMS for PDK3. In addition, the kinase activity of PDK3 is significantly inhibited by AMS. We further complemented our findings with molecular docking and MD simulation studies. After getting the required clinical validation, artemisinin may be explored as an anticancer therapeutic

Key words: Drug repurposing, Cancer therapeutics, Kinase inhibitors, Molecular dynamics Simulation, Isothermal titration calorimetry

BCH-28 POSTER

Exportin-1 Mediates Conserved Nuclear Export Signal Dependent Nuclear Export of the Mammalian mRNA Capping Enzyme

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The N^7-methylguanosine (m^7GpppN) cap structure (where 'N' denotes the first transcribed nucleotide) was identified as a common feature of every RNA polymerase II transcript which includes all pre-mRNAs, miRNA precursors, long noncoding RNAs (lncRNAs), small nucleolar RNAs (snoRNAs), and small nuclear RNAs (snRNAs). This cap structure is synthesized co-transcriptionally in the nucleus by mRNA Capping Enzyme (CE) and is involved in many aspects of RNA metabolism including nuclear export of RNA to the cytoplasm, protein synthesis, and turnover. The earlier belief of mRNA degradation post decapping is changed after the identification of stable uncapped transcripts and cytoplasmic capping in eukaryotic cells. Cytoplasmic capping machinery, composed of cytoplasmic Capping Enzyme (cCE), a 5'-monophosphate kinase, an adaptor protein Nck1, and RNA methyltransferase were found to recap 5'-monophosphate RNAs and thus maintain the cap status of the transcript. Since no other sequence homologs of CE are reported, this led to the belief in the active nucleo-cytoplasmic shuttling of CE. Transport between the nucleus and the cytoplasm takes place through different nuclear pore complexes (NPCs). Recently nucleo-cytoplasmic shuttling of CE has been found in Drosophila, but no information exists about the molecular mechanism of mammalian CE shuttling. Herein, we show mammalian CE shuttles between the nucleus and cytoplasm. We also demonstrate nuclear export of mammalian CE is facilitated by the Exportin-1 pathway and through a conserved Nuclear Export Signal (NES) sequence of CE.

Key words: Capping enzyme, Cytoplasmic capping, Nuclear export, Exportin-1, Nucleo-cytoplasmic shuttling, Nuclear export signal

BCH-29 POSTER

KIF1A Neurodegenerative Disease Mutations Modulate Motor Motility and Force Generation

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The Kinesin family members (KIFs) are microtubule-based, ATP-driven molecular motors involved in the anterograde transport of cellular cargoes. Defects in these motor proteins can lead to various disease conditions including polycystic kidney, neurodegenerative diseases and cancer. KIF1A, a founding member of the Kinesin-3 family motor, is a neuron-specific motor protein involved in fast axonal transport of synaptic vesicle precursor, neurofilament, and dense-core vesicle, important for the development and maintenance of neuronal cells. Point mutations in the motor domain of KIF1A are associated with various motor neuron diseases, which can be autosomal dominant or recessive like Hereditary Spastic Paraplegia (HSP) and Hereditary sensory autonomic neuropathy type-2 (HSAN-II). In-silico modeling has shown that some of these mutations affect the motor's microtubule-binding or ATP binding ability, rendering it inactive. In the present study, we analyzed the effect of 19 point mutations on the KIF1A motor activity, force generation and cellular cargo transport. These mutants showed diffused, microtubule bound or peripheral accumulation in COS-7 cells. The high load (Golgi) and low load (peroxisome) dispersion assay showed complete, partial or no dispersion by the mutants as compared to wild-type motors. Correspondingly, in vitro single molecule motility analysis of diffused and peripherally accumulating mutants revealed slow velocity, decreased landing and low processive motion along the microtubule. However, the microtubule-binding mutants showed strong rigor-like confirmation on the microtubule. Furthermore, live-cell cargo transport analysis of mutant motors showed defects in cargo transport properties compared to wild-type motors.

Key words: Kinesin-3, Superprocessive, Neurodegenerative Diseases, Point Mutation, Cargo Transport

Subtilisin Secreted by Bacillus Amyloliquefaciens Induced Tubulin Degradation and Apoptosis in Breast Cancer Cells by Ubiquitin-Proteasome Mediated Pathway

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Cancer continues to be a global threat and one of the main causes of death worldwide. Though several approaches have developed, due to the limitation of current therapeutics option, one of the aims is to search for effective anti-cancer drugs. Microbial proteases are commonly used industrial enzymes, also act as therapeutics against cancer cells. In this study, we have purified subtilisin from Bacillus amyloliquefaciens and studied its anti-cancer properties. Flow-cytometric analysis showed purified subtilisin induced apoptosis in MCF-7 breast cancer cells but showed no effect on mouse peritoneal macrophage and normal breast cells (MCF10A). Wesern blot analysis showed subtilisin could not induce the intrinsic pathway of apoptosis rather it induced tubulin degradation in MCF-7 cells. Pathway analysis revealed subtilisin induced tubulin degradation through ubiquitination and proteasomal activation. We further observed PARKIN, one of the known E3-ligase, is overexpressed and interacts with tubulin in subtilisin treated cells. Knockdown of PARKIN effectively inhibit tubulin ubiquitination. Activation of ER-stress, caspase-7, PARP cleavage and nuclear DNA degradation was also observed in MCF-7 cells after subtilisin treatment.

Key words: Subtilisin; Apoptosis; Tubulin degradation; Cancer

Repurposing of DPP4 Inhibitor Vildagliptin in Glioma: A Potential Temozolomide Sensitizer

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Background: Gliomas have variable, clinical courses that are difficult to predict, prompting studies to identify prognostic biomarkers. The main challenge in devising a therapeutic regimen for glioma is the inability of drugs to cross the blood-brain barrier (BBB). Previous studies indicate the criticality of peptidases in glioma and found that dipeptidyl peptidase 4 (DPP4) is expressed abnormally. Under normal physiological conditions, cleaves a variety of substrates such as growth factors, cytokines and neuroactive peptides. A number of drugs with DPP4 inhibitory activity and ability to cross BBB have been used clinically as hypoglycemic agents. Interestingly, DPP4 plays a crucial role in proliferation and migratory ability in several aggressive cancers, including glioma. Therefore, the potential repurposing of DPP4 inhibitors for cancer therapy has attracted great interest. This study aims to examine the detailed molecular and clinical context of DPP4 expression in gliomas. In addition, we are inclined to determine the potential of a DPP4 inhibitor, vildagliptin, as a chemotherapeutic agent for GBM by examining the cellular response of this drug on temozolomide-resistant and temozolomide-sensitive Glioma cell lines. **Method**: Gene expression data from glioma patients from The Cancer Genome Atlas (TCGA) and Chinese Glioma Genome Atlas (CGGA) studies were utilized to determine the expression pattern and prognostic significance of DPP4 in glioma. The effect of DPP4 inhibitor vildagliptin on temozolomide (TMZ)-resistant (U87-MG) and temozolomide-sensitive (LN229) glioblastoma (GBM) cell lines was assessed using cell-based assays, such as cell proliferation assay, migration assay, invasion assay, and drug sensitivity assay. **Result**: It was found that DPP4 expression was significantly higher in grade IV gliomas compared to lower grades. Gliomas with IDH mutation showed a lower expression of DPP4. Survival analysis suggested that higher DPP4 expression was associated with poorer overall survival in lower-grade gliomas, particularly on astrocytic histology. Vildagliptin alone and in combination with low-dose temozolomide reduced glioma cell proliferation even after drug discontinuation. Vildagliptin alone and in combination with TMZ inhibit the colony-forming ability of TMZ-resistant U87-MG cells. However, vildagliptin enhanced cell migration in both cell lines. **Conclusion**: The current data suggest that DPP4 is a potential prognosticator in glioma and vildagliptin may prove useful to counter drug resistance in glioma cells.

Key words: DPP4, Vildagliptin, Glioma, Glioblastoma

Prognostic Utility of Key Copy Number Alterations in T Cell Acute Lymphoblastic Leukemia

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Background: T-cell acute lymphoblastic leukemia (T-ALL) is molecularly heterogeneous disease, and comprises distinct subtypes defined by the chromosomal rearrangements that usually involve one of the T cell receptor (TCR), but non TCR driven translocation, including whole chromosome and subchromosomal gain and loses are the common contributors of disease progression and have demonstrated its utility for patient prognosis in T-ALL. **Methods:** Multiplex ligation-dependent probe amplification (MLPA) reactions were performed on 128 newly diagnosed pediatric T-ALL patients using the SALSA P383-A2 MLPA probemix, containing 56 probes, for detection of deletion and duplication in 13 different chromosomes regions affected by recurrent CNAs in T-ALL: STIL-TAL1, LEF1, CASP8AP2, MYB, EZH2, MLLT3+MTAP+CDKN2A/B, NUP214-ABL1, PTEN, LMO1, LMO2, NF1+SUZ12, PTPN2 and PHF6. For this 100 ng input genomic DNA was denatured and hybridized. The reactions, including 12 negative control samples, were performed according to the instructions. The amplified probes were analyzed using Coffalyser.net software. After intrasample and intersample normalizations, copy number status at each locus was estimated. Relative peak ratios between 0.8 and 1.2 were considered normal, while values below or above indicated losses or gains of genetic material, respectively. **Results:** Highest percentage of deletion events were observed in PHF6 (69.53%), ARHGEF6 (69.28%), SH21A (60.15%) and CDKN2A (46.87%), while PTPN2 (10.15%), NUP214 (5.46%), EZH2 (6.25%) exhibited highest duplication events. Out of 128 T-All patients 88.28% patients exhibited at least one deletion events, while 73.43% patients exhibited at least one duplication. A total 92.96% patients exhibited CNAs (either deletion or duplication). STIL-TAL1, NUP214-ABL1, and LMO2-RAG2 fusion were observed in 3.90%, 2.34%, and 0.78% of T-ALL patients respectively. **Conclusion**: The observed molecular heterogeneity in T-ALL may provide molecular basis for variations observed in clinical response in T-ALL.

Key words: Leukemia, T-ALL, MLPA, Copy Number Alterations, CDKN2AB

In Vitro and In Silico Analysis Reveal Glycosylation Association to the HER2 Status of Breast Cancer

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Breast cancer (BC) HER2 status determines the severity and aggressiveness of tumors in patients. Various studies have highlighted the role of HER2 in BC, with less emphasis on correlating it to glycosylation. Herein, *in silico* and *in vitro* analysis identified the role of important glycosyltransferases namely ST3GAL1 and GCNT3 in BC HER2 pathogenesis. Initially, survival plots were determined for ST3GAL1, GCNT3 and ERBB2/HER2 along with their differential expression in normal versus tumor samples. The immunohistochemical analysis validated higher expression of ST3GAL1 and GCNT3 in higher stages and grades of BC human tissues. To identify any functional relevance, correlational analysis was carried out between ST3GAL1 and HER2 which exhibited a positive correlation between the two. Gene Set Enrichment Analysis (GSEA) on the HER2 low versus high BC samples resulted in overexpression of several glycogenes in HER2 high samples. GSEA also depicted higher expression of ST3GAL1 on HER2 high BC samples whereas GCNT3 was non-significantly related to HER2 status. Wound healing and colony formation assays using talniflumate determined the oncogenic role of GCNT3 in BC cell lines. Global GSEA analysis on normal versus tumor samples predicted higher

expression of MUC1 and β-catenin. These proteins were validated along with Cyclin D1 in BC and were found to be expressed increasingly from Stage I to III of grade 2 and grade 3 tissues.

Key words: Glycosylation, Breast Cancer, GCNT3, *In Vitro, In Silico*

BCH-58 POSTER

In-Silico Analysis of the Phytocompounds of *Nigella Sativa L.* in terms of Human Cancer by Targeting Pyruvate Kinase-M2

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Cancer is a multifactorial disease which leads to altered gene expression in humans that changes the overall activity of cells and tissues. Several proteins are switched on or off in cancer to ungoverned tumour growth that dramatically changes the overall activity of the cell. Overexpression of cancer protein may give a piece of wide information about the specific type of tumour. Pyruvate kinase-M2 (PK-M2) is the most important oncogenic ATP-producing glycolytic enzyme that is upregulated in most cancer cells. The higher expression of PK-M2 tends to accumulate glycolytic metabolites, enhancement of glucose uptake, and reprogramming of metabolism in cancer cells. The phytocompounds of medicinal plants such as Nigella sativa L. exert potent pro-apoptotic, anti-proliferative, cytotoxic, anti-metastatic, and anti-mutagenic effects that inhibit the proliferation and activity of tumour cells. This study anticipated the pharmacokinetics, toxicity, and anticancer properties of phytocompounds through in-silico tools like SwissADME, pkCSM, and PASS-Way2Drug. Moreover, the CLC-Pred web server provided the cytotoxicity prediction of chemical compounds against several human cancer cell lines. Moreover, molecular docking, and molecular dynamic (MD) simulations study optimized the conformational changes, intermolecular interaction, and stability of lead phytocompounds such as Epicatechin, Apigenin, and Kaempferol against PK-M2.

Key words: Cancer; Toxicity, Drug-likeness, Pharmacokinetics, Molecular docking, MD Simulation

BCH-59 POSTER

Hesperetin Modulates TGFβ-Induced Migration and Invasion of Prostate Cancer Cells

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Cancer metastasis is the process by which malignant cancer cells spread throughout the body resulting in organ dysfunction. About 90% of cancer-related deaths are attributed to cancer metastasis. It is therefore important to come up with treatment strategies that target cancer metastasis. Prostate cancer is among the top ten leading sites of cancer in India and about 85% of cases are diagnosed in the later stages (III and IV). Phytochemicals are being deeply researched as cancer drugs as they are protective to normal cells and have lesser side effects. In our study, we used Hesperetin, a citrus bioflavonoid to target the process of Epithelial to Mesenchymal Transition (EMT) in prostate cancer cells. We found that hesperetin can significantly inhibit the cell proliferation of PC3 cells and arrest the cells in the S and G2M phase of the cell cycle. The invasion and migration assay results decipher the inhibitory effect of hesperetin on TGFβ-induced invasion and migration of prostate cancer cells. Our results confirmed that hesperetin also acts through the canonical TGFβ-signalling pathway as we observed a significant decrease in the expression of pSmad3. Hesperetin can inhibit the TGFβ induced EMT by increasing E-cadherin expression and decreasing N-cadherin expression. Hesperetin could modulate the TGFβ-induced histone methylation marks like H3K4me3, H3K9me3, and H3K27me3. Further investigation is required to understand the role of hesperetin in modulating these marks and thus inhibiting TGFβ-induced EMT. Hence, the results of our study identified the potential of hesperetin to modulate TGFβ-induced cell proliferation as well as invasion and migration of prostate cancer cells which may help inhibit the metastatic growth of prostate cancer cells.

Key words: Metastasis, EMT, TGFβ, Hesperetin, Histone Modifications

BCH-63 POSTER

Protective Effect of Rutin Against Thiram-Induced Cytotoxicity and Oxidative Damage in Human Erythrocytes

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Thiram is a fungicide that is used to prevent fungal diseases in seeds and crops and also as an animal repellent. The pro-oxidant activity of thiram is well established. Rutin is a flavonoid glycoside present in many fruits and plants and has several beneficial properties, including antioxidant effects. We have previously shown that thiram causes oxidative damage in human erythrocytes. The present study was designed to evaluate the protective effect of rutin against thiram-induced damage in human erythrocytes. Treatment of erythrocytes with 0.5 mM thiram for 4h increased the level of oxidative stress markers, decreased antioxidant power and lowered the activity of antioxidant and membrane bound enzymes. It also enhanced the generation of reactive oxygen and nitrogen species (ROS and RNS) and altered the morphology of erythrocytes. However, treatment of erythrocytes with rutin (0.5, 1 and 2mM) for 2h, followed by 4h incubation with 0.5mM thiram, led to decrease in the level of oxidative stress markers in a rutin concentration-dependent manner. A significant restoration in the antioxidant power and activity of antioxidant enzymes was observed upon the treatment of erythrocytes with 1 and 2 mM rutin. Pre-incubation with rutin lowered the generation of ROS and RNS which will reduce oxidative damage in erythrocytes. The thiram-induced changes in cell morphology and activity of membrane-bound enzymes were also attenuated by rutin. These results suggest that rutin can be used to mitigate thiram-induced oxidative damage in human erythrocytes.

Key words: Rutin, Thiram, Oxidative stress, Antioxidant, Human erythrocytes

BCH-64 POSTER

IP6K1- A Regulator of Digestion Physiology in Mammals

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Inositol hexakisphosphate kinases (IP6Ks) catalyse the synthesis of the inositol pyrophosphate 5-IP7 (5-diphosphoinositol pentakisphosphate) from IP6 (inositol hexakisphosphate). Mice lacking the IP6K1 enzyme show different physiological defects including male infertility, delay in blood clotting, reduced insulin levels, and lower body weight compared to wild type mice. The expression of IP6K1 is conserved throughout the gastrointestinal tract epithelium, including stomach, ileum, colon, and rectum. We have observed that IP6K1 is highly expressed in isolated mouse gastric glands. Immunofluorescence studies show that IP6K1 is localized to chief cells in the gastric gland – these cells secrete enzymes like pepsin and gastric lipase that help in the digestion of protein and lipid ingested in food. IP6K1 knockout mice display a reduction in the number of chief cells in their gastric glands. In knockout mice, the gastric chief cells show a reduction in the number of secretory granules and defective Golgi morphology. Analysis of gastric secretion from IP6K1 knockout mice following pyloric ligation and carbachol stimulation revealed reduced levels of pepsin and an absence of gastric lipase. We used the AGS gastric cancer cell line as a model system to explore the mechanism by which IP6K1 regulates secretory enzymes in gastric chief cells. CRISPR-mediated knockout of IP6K1 in AGS cells led to altered Golgi morphology and reduced granular intensity of pepsinogen C, which may be a reason for the reduction in secretory granules. We propose that IP6K1 expression in gastric chief cells plays an important role in the regulation of secretory granule formation and digestion physiology in mammals.

Key words: Chief Cell, Pyloric Ligation, Secretory Granules

Detection of Resistance against the 'last Resort' antibiotic colistin in Indian Hospital Sewage: a metagenomic Surveillance Approach

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Antimicrobial resistance (AMR) is a 'silent pandemic' creating a global public health hazard for years. The global mortality due to AMR rose to approximately five million in 2019, and ten million mortalities are expected by 2050. The reckless and rampant consumption of antibiotics, 'over-the-counter' availability of drugs, and inadequate quality checks during antibiotic manufacturing contribute extensively to AMR. Colistin is the last resort antibiotic administered against multi-drug resistant (MDR) and extremely drug-resistant (XDR) infections. India is a hotspot for AMR. The detection of colistin resistance in Indian hospital sewage is problematic and reflects its dissemination in hospital settings. In this study, we identified the *mcr*-5.1 gene, a mobile colistin resistance gene, for the first time in Indian hospital sewage using shotgun metagenomics. The sewage sample was collected from Domkal Super Specialty and Sub-divisional Hospital, Domkal, Murshidabad, West Bengal, India. Murshidabad is a poverty-stricken area with a low literacy rate of 63.88%, 80.22% rural population (as per Census 2011), and open drainage. After DNA extraction and quality check, the DNA was sequenced by Illumina HiSeq, 2X150 bp paired-ends run. FastQC and MultiQC checked the data quality, Megahit v1.1.3 assembled the data into contigs, and Bowtie2 checked the quality. The contigs homology was checked against the NCBI nucleotide database, and the TaxonKit v0.2.3 identified the taxonomic distribution. Prokka v1.14.6 annotated the assembled data after removing eukaryotic contigs. The Resistance Gene Identifier (RGI) detected antibiotic resistance genes (ARGs) using the Comprehensive Antibiotic Resistance Database (CARD). ABRicate v1.0.1 using CARD, NCBI, and Resfinder database confirmed ARGs' presence. PlasFlow and PlasClass identified the plasmids. We detected plasmid-mediated *mcr*-5.1 (1644 bp) in contig k141_458493. The nucleotide BLAST search listed *E. coli* strain ENV103 plasmid pSGMCR103 (MK731977.1) as the best result with 99% identity, 0% expected value, and 0% gaps. A truncated mobile element protein, a ChrB domain protein that confers resistance to chromate, a putative major facilitator superfamily type transporter, and a hypothetical protein was also detected. The emergence of *mcr*-5.1 in Indian hospital settings is of urgent clinical concern. The lack of a closed drainage system and inefficient wastewater treatment strategies may disseminate the colistin resistance to drinking water leading to an XDR outbreak.

Key words: Antimicrobial Resistance, Colistin, Metagenomics, Bacteria

BCH-66 POSTER

A Computational, Biophysical, and Biochemical Study Identified Flavone and Coumarin-Based Isoxazole Derivatives as Broad-Spectrum Inhibitors of Serine β-Lactamases and Metallo β-Lactamases

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The most effective drugs for treating bacterial infections are β-lactam antibiotics. The challenge to their future usage comes from resistance to them, particularly from the development of β-lactamases, which can hydrolyze all varieties of β-lactams. There are several inhibitors against serine-β-lactamases (SBLs). Metallo-β-lactamases (MBLs) are Zn(II)-dependent enzymes able to hydrolyze most β-lactam antibiotics, and no clinically useful inhibitors against them have yet been approved. There is an urgent need for effective inhibitors that can restore the activity of β-lactams.It may be possible to use the synthetic flavone and coumarin-based isoxazole derivatives as broad-spectrum inhibitors of the mechanistically distinct serine-(SBL) and metallo β- lactamases (MBL). Molecular docking and in silico pharmacokinetic studies were used to identify the synthesised compounds as powerful β-lactamase inhibitors. We used biophysical, biochemical, and computational methods to investigate the interactions of chemically synthesised inhibitors with clinically important β-lactamases of classes A, B, and C. These molecules are acceptable in terms of solubility,

permeability, and oral bioavailability and adhere to Lipinski's rule of five. These compounds were discovered to be non-toxic or non-carcinogenic. According on MIC data, these compounds are thought to improve antibiotic effectiveness against class A, B, and C β-lactamases. Kinetic results demonstrated that these compounds decrease the the catalytic efficiency of clinically significant class A, B, and C β-lactamases. The class A/B/C β-lactamases and these flavone/coumarin based isoxazole derivatives interacted significantly, according to a fluorescence research. This investigation demonstrated the broad-spectrum β-lactamase inhibitory potential of these next generation drugs against both SBLs and MBLs.

Key words: ESBL, XDR, MDR, β-Lactam Antibiotic, β-Lactamases, β-Lactamase Inhibitors

BCH-67 POSTER

Bioactivity-Guided Isolation, Identification and In-Depth Evaluation of the Anticancer Properties of the Compounds Isolated from *Garcinia cowa* Leaf Extract

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Introduction: Among the several ethnic communities, *Garcinia cowa* (Clusiaceae) is very popular for its ethnomedicinal properties. In this study, we have isolated and identified the lead fraction from different isolated fractions through Bioactivity-guided isolation. Anticancer properties of the lead fraction were evaluated thoroughly on human lung cancer cells A549 and its cytotoxic effect was evaluated on normal cells. **Material and Methods:** Fresh leaves of *G. cowa* were collected in July 2017 from Tripura, India (23°45'43.4" N 91°15'39.7" E). The voucher specimen (Specimen number 2724) was deposited in the Tripura University Herbarium. Leaf methanolic extract was separated by column chromatography and preparative TLC. The bioactivity of the fractions was checked by MTT assay. Identification of the compounds has been performed by GC-MS analysis. Apoptotic effects of the lead fraction were assessed by Annexin V/PI, AO-EtBr staining, DAPI staining, cell cycle analysis through PI staining, and spectrophotometric measurement of caspase activity. The effects of the lead fraction on intracellular redox balance were assessed using fluorescent probes like H_2DCFDA and JC1. **Results:** Bioactivity-guided isolation leads to the identification of the lead fraction. GCMS analysis reveals the presence of diterpenoid and phytosterol groups of compounds in the lead fraction. A significant decrease in anti-proliferative activity with a concomitant increase in apoptosis and arrest of the cell cycle at the Go/G1 phase was observed in lead fraction treated A549 cells. Apoptotic effect was visualized through AO-EtBr staining and consequent nuclear fragmentation was visualized through DAPI staining. The lead fraction-induced apoptosis was associated with the generation of intracellular ROS, loss of mitochondrial membrane potential and upregulation of caspase-3 and caspase-9. In normal cells, nominal apoptosis and very low cytotoxicity were recorded. **Conclusion:** As the lead fraction induces programmed cell death in lung cancer cells with a very minimal effect in normal cells, it holds great therapeutic potential as a future drug in combating human lung cancer.

Key words: Garcinia cowa, Lung cancer, Apoptosis, ROS

BCH-68 POSTER

Podocyte Derived TNF-α Mediates Monocyte Differentiation and Contributes to Glomerular injury and Diabetic Nephropathy

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Diabetes shortens the life expectancy by more than a decade, and the excess mortality in diabetes is correlated with the incidence of kidney disease. Diabetic kidney disease (DKD) is the leading cause of end-stage kidney disease. Macrophage accumulation predicts the severity of kidney injury in human biopsies and experimental models of diabetic nephropathy (DN). However, the mechanism underlying macrophage recruitment in diabetes glomeruli is unclear. Elevated plasma growth hormone (GH) levels in type I diabetes and acromegalic individuals impaired glomerular biology. In this study, we examined whether GH-stimulated podocytes contribute to macrophage accumulation. RNA-seq analysis revealed elevated TNF-α signaling in GH-treated human podocytes. Conditioned media from GH-treated podocytes (GH-CM) induced differentiation of monocytes to macrophages. On the other hand, neutralization of GH-CM with the TNF-α antibody diminished GH-CM's action on monocytes. The treatment of mice with GH resulted in increased macrophage recruitment, podocyte injury, and proteinuria. Furthermore, we noticed activation of TNF-α signaling, macrophage accumulation, and fibrosis in DN patients' kidney biopsies. Our findings suggest podocytes could secrete TNF-α and contribute to macrophage migration, resulting in DN-related renal inflammation. Inhibition of either GH action or TNF-α expression in podocytes could be a novel therapeutic approach for DN treatment.

Key words: Podocytes, Diabetic Nephropathy, Macrophages, Inflammation

BCH-69 POSTER

Knockdown of Sperm Associated Antigen 11A (SPAG11A) Enhances the Susceptibility of Epididymis and Prostate to Chemically Induced Carcinogenesis

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Sperm-associated antigen 11a (Spag11a), an epididymis specific gene, is expressed in the principal cells of the caput. Our recent studies report that the ablation of SPAG11A protein by active immunization promotes oncogenesis in rats. This study aims to determine the changes in the epididymal transcriptome that is related to oncogenesis in Spag11a knockout mice. Further, we investigated the susceptibility of Spag11a knockout mice to chemically induced carcinogenesis. Spag11a knockout mice were administered a very low dose (0.05 ppm) of N, N-diethylnitrosamine (DEN) via drinking water for 12 weeks. A comparison of the caput transcriptomes of wild type and Spag11a knockout mice revealed that 601 genes were differentially expressed, of which 280 and 321 were up-regulated and down-regulated respectively. Interestingly, 2090 genes were uniquely present in the caput of Spag11a knockout mice (not detected in wild type) and 1700 genes that were not detected in the Spag11a knockout mice. Processes related to cell cycle and cell division-related genes were dysregulated. The KEGG pathway analyses suggested that the absence of Spag11a may activate microRNAs associated with cancer, chemical carcinogenesis-receptor activation and chemical carcinogenesis-DNA adducts pathways, which may contribute to the promotion of oncogenesis in the epididymis. Further, the epididymis and prostate of Spag11a knockout mice appeared to be more susceptible to DEN induced carcinogenesis compared to wild type mice, which is evident by histopathological examination. Hyperplasia, anaplasia, dysplasia, neoplasia, and inflammation in the epididymis and prostate of Spag11a knockout mice, while that of wild type mice displayed normal anatomical structure. Our results provide concrete evidence that the loss of Spag11a makes the epididymis and other tissues more susceptible to chemical carcinogenesis. The involvement of an epididymal gene in carcinogenesis is being demonstrated for the first time and also provides possible answer to the complex question of as to why epididymal cancers are rare.

Key words: SPAG11A, Diethylnitrosamine, Epididymis, Oncogenesis, Hyperplasia

Examining the Role of IP7-Mediated Pyrophosphorylation in Nucleolar Function

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The inositol pyrophosphate IP_7 is an energy-rich, water-soluble small signalling molecule, containing five monophosphate and one pyrophosphate moieties. IP_7 is synthesized from IP_6 by IP6 kinases. IP_7 regulates protein function either by direct binding to proteins or by protein pyrophosphorylation- a unique post-translational modification where the β-phosphate moiety of IP_7 is transferred to a pre-phosphorylated serine residue lying in an intrinsically disordered region (IDR) of the substrate protein. Analysis of the IP_7 interactome revealed an enrichment of several nucleolar proteins, including TCOF1, NOLC1, NCL, NPM1, DDX21, DKC1, NOP58, and UBF1. Using radiolabelled IP_7, we observed that TCOF1, NOLC1, NCL, and UBF1 undergo IP_7-mediated pyrophosphorylation. We found that IP6K1, the enzyme that synthesizes IP_7, colocalizes with UBF1, a nucleolar fibrillar centre (FC) marker, in an rDNA transcription-independent manner. In addition to this, we have observed that upon co-overexpression, IP6K1 colocalizes with DDX21, UBF1, and NOLC1 in a kinase activity dependent manner, indicating that the synthesis of IP_7 is necessary for the nucleolar localization of IP6K1. Pulldown studies revealed interactions of IP6K1 with FC proteins (NOLC, TCOF, UBF, and RPA194), which are involved in rDNA transcription. We found lowered pre-rRNA transcripts in cells with reduced IP_7, suggesting a role for IP_7 in rDNA transcription. We also found that the loss of IP6K1 leads to an increase in nucleolar number and a decrease in nucleolar volume, indicating a role for IP6K1 or its product IP_7 in nucleolar assembly. We are currently investigating the effect of pyrophosphorylation on the liquid-liquid phase separation behaviour of these nucleolar proteins in cells with varying levels of IP_7, and its contribution towards nucleolar assembly and function.

Key words: Inositol Pyrophosphate, Nucleolus, Phase Separation, rDNA Transcription

BCH-78 POSTER

Deciphering the Transcriptional Regulation of GM2-Synthase Gene in Cancer

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We ask the "WHY" and "HOW" of Ganglioside over-expression in cancer. "Why" select gangliosides are aberrantly over-expressed in many cancers? And "How" do this over-expression influence the process of tumorigenesis? In an attempt to address these key questions, our laboratory identified ganglioside GM2, which is over-expressed in a number of cancers to play a critical role in the tumorigenic process, and that targeted genetic knockout of GM2-synthase, the critical gene regulating GM2 synthesis could inhibit AIG, and metastatic induction. However, the underlying mechanism of the over-expression of GM2-synthase in several cancers (Renal Cell Carcinoma-RCC, Glioblastoma multiforme-GBM) was still elusive. We showed for the first time that the GM2-synthase gene is epigenetically regulated at the level of transcription. Here, we demonstrate that increased acetylation of the chromatin environment near the Transcription Start Site (TSS) of the GM2-synthase gene in cancer, leads to acetylation of the transcriptional repressor Sp1 resulting in its proteasomal degradation and consequent decreased binding of the repressor HDAC1, leading to overall de-repression of the GM2-synthase transcription in RCC. Currently, studies are underway to identify the proteome associated with the regulation of GM2-synthase transcription. Identification of the proteome will help to achieve a clear understanding of the mechanism of GM2-synthase transcription, and may eventually be strategically exploited to interfere and reverse GM2 over-expression observed in many cancers.

Key words: Gangliosides, Transcription, Epigenetics, Chromatin, Cancer, Metastasis

BCH-79 POSTER

Targeted Reduction of Toll Pathway Confers Rescue against h-Tau Mediated Neurotoxicity in Drosophila Disease Models

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Processes like inflammageing (heightened innate immune response) and neurodegeneration are both age-onset phenomena which can be attributed to the dwindling adaptive immune response and heightened neurotoxic activities in the system. Several studies have reported characteristically high levels of immune-specific markers in the brain tissues and cerebrospinal fluid of patients suffering from neurodegenerative disorders such as Alzheimer's, Parkinson's disease and Amyotrophic Lateral Sclerosis. While most of these studies highlight increased cell death response, the mechanism underpinning the induction of immune response, the sequelae of neuroinflammatory event(s) and other molecular details in neurodegenerative condition are still enigmatic. *Drosophila*, a well-established model system for the study of neurodegenerative disorders is armed with a sophisticated innate immune system and extensive genetic toolkit that can help in dissecting the enigma behind this scientific conundrum. In the present study, we observed that reduced expression of various immune response genes can mitigate *h*-Tau-mediated toxicity in *Drosophila* disease models. Furthre, the immune pathway(s) were found to alleviate wide range neurotoxic manifestations both structurally, molecularly and functionally. Further investigations are expected to generate interesting molecular insights about involvement of various immune response pathways in tau etiology.

Key words: Drosophila, Neurodegeneration, Neuroinflammation, Immune Response

BCH-80 POSTER

Leishmania Donovani Sphingosine-1-Phosphate Kinase (Sphk) Represents a Druggable Target to Limit Leishmania Growth by Inducing Autophagy and Apoptosis in Macrophages

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Sphingosine-1-phosphate (S1P) is a crucial regulator of a wide array of cellular processes, such as apoptosis, cell proliferation, migration, and differentiation. The role of S1P in Leishmania donovani phagolysosomes has recently been studied both *in vitro* and *in vivo* however there is no study addressing the role of SphK in management of lysosome stress in human macrophages *infected with L. donovani.* To address this, here we have cloned the leishmania SphK1 gene, followed by the molecular and enzymatic characterization of SphK1 from L. donovani. To establish the role of SphK, we took pharmacological inhibitors. We *show that SphK1 inhibitors;* PF-543, DMS and SKI-5C inhibit Leishmania within a range of IC_{50} of 5μM- 500μM however ABC294640; a SphK2 inhibitor did not kill the parasite but was toxic to THP-1 macrophages at an IC_{50} of 60μM. Sphingokinase assay was performed in the presence of these inhibitors using NBD-SIP Assay to determine sphingosine levels. The fluorescence Intensity of upper aqueous phase containing NBD-SIP was found to be significantly reduced in L. donovani promastigotes cells treated with PF-543, SKI-5C and DMS. For molecular characterization, the level and activity of SphK-1 were measured in vitro in both untreated and SphK inhibitor treated macrophages infected with L. donovani. We found that 48 h post infection, SphK1 level was predominantly reduced to ~50% in infected compared to uninfected macrophages and was further downregulated in SphK inhibitor treated infected macrophages. We next analyzed the phosphorylation status of SphK-1, where ~50% and ~70% decrease in p-SphK-1 was observed respectively in infected and treated cells that could be corroborated with significant reduction in the production and release of S1P in inhibitor treated infected macrophages. To gain further insight, cytokines levels were determined in the treated and untreated infected samples. We show that SphK1 inhibition by PF-543 and SphK2 inhibition by *ABC294640* decreased IL-12 and parasite load while increased IL-10 expression at mRNA level and increased LC-III, Beclin1, Cytochrome-c, Caspase-3 and Caspase-9 expression at protein level in infected THP-1 cells. Our overall study not only reports the significant role of S1P signaling during L. donovani infection but also provides a novel platform for the development of new drugs against Leishmaniasis.
Key words: Leishmania donovani, Sphingosine kinase, SIP, SPHK Inhibitors, THP-1

BCH-83 POSTER

Nickel (II) Chloride Generates Reactive Oxygen Species, Impairs Antioxidant Defense System And Alters Metabolic Pathways in Human Red Blood Cells

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Nickel is a heavy metal that is recognized as a possible hazard to living beings due to its genotoxicity, immunotoxicity, mutagenicity and carcinogenicity. Nickel chloride ($NiCl_2$) has been shown to generate oxidative stress by altering the redox balance in cells. We have explored the effect of $NiCl_2$ on isolated human red blood cells (RBC) under in vitro condition. RBC were treated with different concentrations of $NiCl_2$ (25-500 µM) for 24 h at 37 ºC. This increased the formation of reactive oxygen species (ROS) within the cells. A significant increase in oxidation of proteins and lipids was seen accompanied by a reduction in levels of glutathione and total sulfhydryl groups. $NiCl_2$ treatment dramatically increased ROS generation and the development of oxidative stress in RBC. The specific activity of the primary (SOD, catalase, GP) and secondary (GR, TR, GST) antioxidant enzymes were decreased with increase in $NiCl_2$ concentration. In addition, $NiCl_2$ treatment inhibited the activity of enzymes of the two glucose metabolic pathways in RBC (glycolysis and pentose phosphate shunt). Treatment with $NiCl_2$ resulted in severe morphological changes converting normal discocytes to echinocytes. All changes were seen in a $NiCl_2$ concentration-dependent manner. Thus, $NiCl_2$ generates cytotoxic ROS in RBC, causing oxidative damage that might reduce the oxygen carrying capacity of blood and life span of RBC leading to hypoxia and anemia.

Key words: Nickel, Oxidative stress, Human Red Blood Cells; Antioxidant, Enzymes, Echinocytes

BCH-84 POSTER

Vanillin Attenuates Cadmium Chloride-Induced Oxidative Stress on Human Erythrocytes

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Cadmium is a ubiquitous environment pollutant that causes several health problems in humans and animals. Cadmium exposure leads to multi-system disorder. Here, we have investigated the potential role of vanillin in mitigating the cytotoxic effect of cadmium chloride ($CdCl_2$) on human erythrocytes. Erythrocytes were isolated from young healthy donors. They were treated with $CdCl_2$ (0.5 mM), either alone or in presence of varying concentrations of vanillin. Incubation of erythrocytes with $CdCl_2$ alone increased formation of protein carbonylation and lipid peroxidation with simultaneous decrease in reduced glutathione (GSH) and total sulfhydryl group and free amino group content. $CdCl_2$ treatment showed enhanced superoxide and reactive oxygen species generation. Downregulation of most antioxidant and metabolic enzymes was also observed. However, prior treatment of erythrocytes with vanillin, significantly attenuated $CdCl_2$ induced oxidative damage to proteins and lipids and also restored the activity of major antioxidants and metabolic enzymes. A significant decrease in the formation of reactive oxygen species was also observed. Our result suggests that vanillin protects human blood cells from $CdCl_2$-induced oxidative damage.

Key words: Cadmium chloride; Vanillin; Erythrocytes; Reactive Oxygen Species; Antioxidant Enzyme

BCH-87 POSTER

MAO-A Promotes Cancer Aggressiveness by Activating PI3K/AKT/mTOR Signaling Pathway

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Monoamine oxidase-A (MAO-A), a pro-oxidative enzyme catalyzes the oxidative deamination of biogenic amines to produce corresponding aldehydes and reactive oxygen species (ROS). MAO-A has already been shown to be involved in depression, neurodegenerative diseases, and many neuropsychiatric disorders. Compelling evidence has reported the function of MAO-A in promoting the progression of prostate cancer, lymphoma, renal cell carcinoma, etc, but the role of this oxidative enzyme in non-small cell lung cancer and several other cancers remains unclear. Here, we identified the role of MAO-A in promoting cancer in several tumor cells. We investigated that Janus kinases (Jak2 and Tyk2) and transcription factor Stats (Stat1, Stat3, and Stat6) are the key regulators of MAO-A gene expression/activity in A549 cells. Pharmacological inhibition and siRNA-mediated knockdown of MAO-A causes reduction of aggressiveness in several cancer cells including lung, prostate and colon cancer cells. In addition, CRISPR-Cas9 mediated MAO-A knockout causes a significant reduction of lung cancer cell proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT). Furthermore, we explored that MAO-A is involved in promoting aggressiveness in cancer cells via the PI3K/AKT/mTOR signaling pathway. Altogether, these results suggest MAO-A as a potential therapeutic target in the treatment of lung cancer.

Key words: Monoamine Oxidase-A (MAO-A), Lung cancer, EMT, CRISPR-Cas9, Cancer aggressiveness

BCH-88 POSTER

Unveiling the Dopamine-Replenishment Potential of the Principle Bioactive Component of *Garcinia Sp.*

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Introduction: Parkinson's disease (PD) affecting mainly the elderly population occurs due to the progressive degeneration of dopamine containing cells in substantia nigra pars compacta region of the midbrain. Loss of dopaminergic neurons results in significant depletion of dopamine levels in the striatum thereby leading to motor abnormalities in PD. Despite intensive research, the exact aetiology of disease still remains obscure, while the therapies provide only symptomatic relief. Replenishment of dopamine by oral supplementation of its precursor, the levodopa (L-DOPA), remains the principal mode of treatment of PD. Regardless of being associated with potential side-effects, inhibitors of dopamine catabolizing enzymes, particularly monoamine oxidase-B (MAO-B), are prescribed to reduce the daily dosing of L-DOPA in PD patients,. Studies brought to light the efficacy of different phytoconstituents of *Garcinia sp.*, in different neurodegenerative diseases including PD. Garcinol-one of the principle bioactive molecule of *Garcinia sp.* is recently reported to have beneficial effect in different diseases, however, its role in dopamine upregulation in Parkinson's disease is yet to be revealed. **Main methods:** To test the efficacy of this bioactive compound-garcinol, it was administered into the neurotoxin-induced PD mice as well as naïve animals. Mice were than sacrificed to test the ability of garcinol to prevent the degradation of dopamine levels as well as to analyse the efficacy of this biomolecule against the loss of dopamine containing cells in brain. To determine the potential of Garcinol to prevent dopamine degradation its MAO-B inhibiting potential was analysed. While the status of dopaminergic neurons was assessed by immunohistochemistry. **Results:** This biomolecule-garcinol was found to enhance dopamine bioavailability in brain due to its significant MAO-B inhibiting potential comparable to the known inhibitors of this dopamine degrading enzyme. Further, garcinol administration in the parkinsonian mice significantly prevented the degeneration of dopaminergic neurons in brain. **Significance of the Study:** The findings of this study for the first time highlighted the efficacy of the bioactive component garcinol, to replenish dopamine levels as well as to attenuate the degradation of dopaminergic cells in the brain of neurotoxin-induced mice model of PD. Thus, the present study puts forward a

plausible anti-parkinsonian bioactive molecule garcinol, which might serve as a potent drug candidate in Parkinson's disease therapeutics in the near future.

Key words: Parkinson's disease, Dopaminergic cells, L-DOPA, Monoamine oxidase-B, Garcinol

BCH-89 POSTER

Polyoma Small T Antigen promotes DBC1 Protein Degradation to Antagonize AKT Signaling via Activation of LKB1

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Deleted in Breast Cancer 1 (DBC1) is a transcriptional factor that controls cell proliferation, apoptosis, histone modification, adipogenesis and cellular metabolism. DBC1 is also critical for cell proliferation, cell cycle and apoptosis and plays an important but paradoxical role in tumorigenesis. We were, therefore, interested in studying the role and activity of DBC1 during the cell cycle and in tumorigenesis. We found that under condititions of cellular stress induced by polyoma small T (PyST), the expression of DBC1 is decreased. Ectopic expression of DBC1 under conditions of mitotic arrest allows the cells to overcome this arrest. In part, this effect could be explained by our observation that DBC1 localizes at spindle during mitosis, implying that it plays a critical role in mitosis. In agreement with these observations, we found that over-expression of DBC1 promotes cell growth in soft agar and is thus oncogenic. In addition, we also show that cellular DBC1 is downregulated by LKB1 in an AMP kinase independent manner. LKB1 negatively regulates the phosphorylation as well as activity of AKT1 through DBC1 and TRB3. In conclusion, our results elucidate a signaling mechanism that connects LKB1, DBC1, TRB3 and AKT1. Thus, our results suggest that DBC1 may provide a link between metabolism, cell proliferation, cell growth and tumorigenesis.

Key words: Mitosis, Cell Cycle, Tumorigenesis, Dbc1, Cancers, Dbc1, Lkb1, Akt, Polyoma Small T

BCH-96 POSTER

LncRNA PVT1 May Play A Regulatory Role In Pan-Cancer Gene Expression Regulation

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Cancer is among the deadliest diseases, killing thousands of people worldwide, both through emergence as well as relapse owing to chemo-resistance. Recent studies have highlighted the roles several long non-coding RNAs (lncRNAs) are found to play in cancer progression. LncRNAs, with a length of >200 nucleotides, have been shown to function either as oncogenes or tumor suppressors. One of the several mechanisms through which lncRNAs function is through their interaction with DNA, RNA and proteins. From our laboratory studies, a model has been deduced wherein lncRNA *PVT1* as well as few other molecules can act as a pan-cancer master regulator of key coding genes (1, 2). This function can be attributed mainly to the complex secondary and tertiary structures of these lncRNAs. Further understanding of the interaction between these lncRNAs and their interacting partners will give us an insight on the exact regulatory role of these lncRNAs in pan-cancer gene expression regulation. We performed siRNA knockdown experiments to knock down *PVT1* and assess the expression levels of the predicted interacting genes after the knockdown. We also performed structural analyses of lncRNA *PVT1* and coding genes to study their interactions at a structural level. From our experiments, we expect to find a difference in the expression levels of the genes interacting with or regulated by *PVT1* indicating an interaction and a possible regulatory function, which we aim to discuss further. Structural studies using predicted structures of *PVT1* and proteins encoded by coding genes as analyzed by an interaction map will be presented as well.

Key words: Long Non-Coding Rnas (LNCRNAS), Pan-Cancer Gene expression, Structural studies

BCH-97 POSTER

Exploring the Cell Death Mechanism Induced by Vibrio Parahaemolyticus Thermostable Direct Hemolysin

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Thermostable Direct Hemolysin (TDH) is the key virulence factor secreted by the marine bacterial pathogen *Vibrio parahaemolyticus*, which is one of the major causal organisms for the human gastro-enteric diseases. It is a potent pore-forming toxin and can damage cellular homeostasis, presumably due to its ability to form pores on the plasma membrane of the target cells. TDH exhibits potent cytotoxicity against the nucleated mammalian cells. However, the mechanism of the TDH-mediated cell death pathway is yet to be elucidated. Here, we show that TDH evokes features of apoptosis-like programmed cell death, such as phosphatidylserine flipping and a laddering pattern of DNA fragmentation. However, we have observed that unlike apoptosis, TDH-induced cell death is independent of any caspase activation. Thus, a caspase-independent programmed cell death is induced by TDH in the nucleated mammalian cells. Further, our results have revealed that TDH causes mitochondrial membrane permeability transition (MMPT) resulting into the release of important mitochondrial factors that take part in subsequent execution of the caspase-independent cell death pathway and apoptosis-like DNA laddering pattern induced by TDH. Interestingly, TDH alone fails to induce MMPT in isolated mitochondria suggesting involvement of other cytoplasmic factors in the process. We have observed that TDH shows a remarkable ability to translocate to the mitochondria of the target cells. Furthermore, we have observed interaction of TDH with the pro-apoptotic molecule Bax. Thus, we speculate that TDH and Bax together possibly constitute a functional mitochondrial permeability transition pore (MPTP)-like structure that may result into MMPT induction. In sum, our study elucidates a novel mechanism of cell death induction by TDH that, to the best of our knowledge, has not been documented earlier for any other PFT family member. Our study adds valuable new insights regarding the role of TDH in the bacterial pathogenesis and host-pathogen interaction processes.

Key words: Pore-Forming Toxin, Thermostable Direct Hemolysin, Caspase-Independent Cell Death, Mitochondrial Membrane Permeability Transition, Bax

BCH-102 POSTER

Formulation and Characterization of Chrysin Loaded Phytosomes and its Cytotoxic effect against Colorectal Cancer Cells

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Chrysin is a phytoconstituent which has anticancer activity. The study aims to formulate, characterize and evaluate the cytotoxic effect of chrysin loaded phytosomes against HT29 cells. Materials and Methods: Antisolvent precipitation technique was employed to prepare phytosomes. Particle size, polydispersity index, zeta potential, entrapment efficiency, scanning electron microscope and Fourier transform infrared spectroscopic analysis were carried out for the characterization of chrysin loaded phytosomes. Cell viability was done to evaluate the cytotoxic effect of developed phytosomes comparing with plain chrysin. Results: The developed chrysin loaded phytosomes showed the particle size of 94.40nm, polydispersity index of 0.31, and zeta potential -1.33 mV. The entrapment efficiency was 74.28 %. Chrysin loaded phytosomes showed increased cytotoxic effect on HT-29 cells. Conclusion: This research work produces confirmative indication for the use of Chrysin loaded phytosomes in experimental animals to further gain in depth analysis for anticancer activity of chrysin loaded phytosomes against colon cancer.

Key words: Chrysin, Phytoconstituent, Nanoformulation, Colorectal Cancer, Cytotoxicity.

BCH-104 POSTER

Singed, a Multirole Player in Cell Migration

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Cell migration is vital to a variety of biological processes, ranging from normal embryonic development to adult wound healing. While most studies have focused on single cell migration, cells *in vivo* are capable of migrating singly, in sheets, or in cohesive (collective) groups. To better understand how collective cell migration is regulated at the molecular and cellular level, we have turned to the genetically tractable *Drosophila* border cell migration model. Border cells are a group of epithelial cells in the ovary that undergo specific morphological changes to form a cluster. The cluster of 6-10 cells detaches from a polarized epithelium and migrates ~150 µm to reach the oocyte, its final migratory target. Singed (mammalian Fascin) is an actin binding protein that express abundantly in border cell seemingly without any role. Although overexpression of singed leads to higher rate of metastasis. We hypothesized that; redundancy can be a factor. Our search for redundant factors led us to find quite a few genes and we will focus only on two of them, *vinculin* and *Arp2/3*. Both seems to work with singed to regulate total F-actin level and therefore protrusion characteristics. Vinculin, not a canonical actin bundling protein, works with singed in three different tissues; border cell, brush border and follicle cell rotation. Arp2/3, on the other hand, uses non-canonical pathways to regulate border cell migration. We like to think that singed play significant roles in controlling F-actin during border cell migration, albeit redundantly.

Key words: Collective Cell Migration, Border Cell Migration, Drosophila, Singed, Vinculin, ARP2/3

BCH-108 POSTER

Prognostic Relevance and Therapeutic Potential of Targeting Cyclin D1-CDK 4 Axis in Breast Carcinomas

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Cyclin D1-CDK 4 axis is a critical junction where most cell signaling pathways converge with the cell cycle machinery leading to proliferation. This axis has particularly gained significance since the introduction of CDK4/6 inhibitors as a new class of drugs in breast carcinomas. The present study aimed to analyze the expression pattern of Cyclin D1 and CDK 4 by immunohistochemistry in 60 pathologically confirmed formalin fixed paraffin embedded breast tumor tissues and relevant controls for determining the prognostic relevance of these markers based on their expression. Here, Cyclin D1 was expressed in 63.3% and CDK 4 in 43.3% of the breast cancers. Correlation analysis revealed significant association of positive cyclin D1 expression with SBR Grade and positive estrogen and progesterone receptors, however CDK4/6 expressing tumors did not show any significant association with any of the traditional prognostic factors. Survival analysis of these patients revealed Cyclin D1 overexpression to be a good independent prognostic factor with more favorable impact on the overall survival (OS) and CDK 4 overexpression to be a poor prognostic factor with a decreased OS. Contrary to Cyclin D1, CDK 4/6 overexpression is a tumor-specific event and therefore, routinely checking for expression of CDK 4/6 in breast cancer patients of all molecular subtypes may help identify the subset of patients that may actually get benefited from CDK4/6 inhibitors.

Key words: Breast Cancer, Cyclin D1, CDK 4, Immunohistochemistry, Survival Analysis

BCH-122 POSTER

Tbx20 Transcription Factor Function in Adult Cardiac Fibrosis Process

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Cardiovascular disease is one of the main cause of death worldwide and nearly all etiologies of cardiovascular disease associated with activation of adult cardiac fibroblasts. After adult cardiac injury such as myocardial infarction, these resident cardiac fibroblasts proliferate and differentiated into activated myofibroblasts with production of excessive amount of fibrous collagens and subsequent fibrotic scar formation. This pathological myocardial remodeling associated with cardiomyocyte hypertrophy and death that leads to overall cardiac dysfunction and progression towards heart failure. Despite prevalence of cardiac fibrosis downstream of many cardiac injuries, we have a little understanding about its transcriptional regulation *in vivo*. T-box transcription factor, Tbx20 has role in heart development and also play important role in embryonic, foetal and neonatal cardiomyocyte proliferation and cardiac chamber maturation but it's role in cardiac fibrosis process is unknown. Here, we have generated a cardiac fibrosis model in adult male rats by isopreterenol treatment. Treatment of isoproterenol induces hypertrophic response along with increased expression of activated myofibroblasts and collagen type III associated with active fibrosis. To our surprise, preliminary experiment also detected increased number of Tbx20 positive activated myofibroblasts in isoproterenol treated adult hearts. Overall, this study for the first time, exploring the Tbx20 function in adult fibroblasts post-injury with possible therapeutic intervention in near future.

Key words: Hypertrophy, Cardiac Fibrosis, Fibroblast, Myofibroblast, Collagen Type Iii, Tbx20

BCH-130 POSTER

Epigenetic Control over Centrosome Duplication and Spindle Bipolarity

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Histone synthesis and nucleosome assembly occur in the S phase of the cell cycle. Histone chaperones are histone escort proteins that facilitate all facets of histone metabolism. Hence, the enrichment of the histone chaperones in the S phase is quite apparent. However, we observed the expression of a core histone chaperone and NHEJ repair factor, Aprataxin PNK-like Factor (APLF), peaks at the G1/S phase of the cell cycle, which coincides with centrosome duplication. Centrosome duplication is a tightly regulated process controlled by the coordinated interplay of multiple proteins. Having observed the localization of APLF in centrosomes and its profound expression at G1/S, we were intrigued to understand the possible function of APLF in centrosome duplication in mouse embryonic stem cells. We observed an elevated level of APLF results in supernumerary centrosomes due to centrosome amplification or overduplication. Consequently, mitotic cells formed defective spindles, impairment in chromosome segregation. Interestingly, this phenotype coincides with a significant increase in the expression of serine-threonine kinases, Polo-like kinases, and their activation. APLF is a multidomain protein having Forkhead Association (FHA) domain in N-terminus, which is responsible for DNA repair activity, whereas the Acidic domain (AD) in C-terminus has its histone chaperoning function. We speculate that the interaction and regulation of polo-like kinases by APLF is through the FHA domain of APLF, which is a phosphoprotein binding domain. Here we provide an evidence for an epigenetic factor as one of the crucial players in the surveillance of centrosome integrity and genomic stability.

Key words: Histone Chaperone, Aplf, G1/S Phase, Centrosome Duplication, Polo-Like Kinases

BCH-131 POSTER

Increased Peroxisome Proliferation is Associated with Early Replicative Ageing in Yeast

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Ageing is an inevitable degenerative cellular process characterized by progressive decline in the optimum functioning of a cell ultimately resulting in cell death. *Saccharomyces cerevisiae* has emerged as an interesting model organism for studying the hallmarks of cellular ageing, as yeast ageing phenomenon is comparable to the ageing in higher eukaryotes. In yeast, there are two models of ageing termed as replicative and chronological ageing. Reactive oxygen species is one of the primary causes of ageing. Peroxisomes are single membrane-bound organelles ubiquitously present in several cell types and are one of the major contributors of reactive oxygen species in the cells. Peroxisomes also play important role in scavenging the cellular reactive oxygen species as they contain antioxidant enzymes like catalase. In this study, we aimed at understanding how peroxisome dynamics change upon early replicative ageing in yeast. We investigated the alterations in peroxisome number in the replicatively aged cells under peroxisome inducing oleic acid and non-inducing glucose media. An increase in the number of peroxisomes was observed with replicative ageing. Induced activity of the antioxidant enzyme catalase and reduced accumulation of reactive oxygen species was reported in all studied strains in oleic acid medium. Replicatively aged cells also displayed reduced mitochondrial function and fragmentation in all the strains studied. In conclusion our data suggests a correlation between increase in peroxisome number and replicative ageing in yeast. Interestingly this increase seems to be partly dependent on the fission proteins and partly due to mitochondrial dysfunctioning in the aged cells.

Key words: Yeast, Replicative Ageing, Peroxisome, Biotinylation, Reactive Oxygen Species

BCH-132 POSTER

Anti-Glycation Potential of β-Glucogallin from Asparagus Racemosus Contribute to Management of Metabolic Disorder

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Diabetes is a metabolic disorder characterized by the presence of persistence hyperglycemia resulting in chronic complications such as neuropathy, retinopathy and nephropathy. Hyperglycemia plays an important role in the development of diabetic complications by increasing the rate of protein glycation. Increased formation and accumulation of advanced glycation end products (AGEs) has been implicated in the pathogenesis of chronic affliction, including diabetes associated secondary complication, ageing, inflammatory and neurodegenerative disease. Therefore, inhibition of AGEs formation is a critical strategy for the reduction of various pathologies. Here, we have demonstrated the AGEs inhibitory activity of β-glucogallin, isolated for the first time from the roots of *Asparagus racemosus*. *In-vitro* antiglycation activity of β-glucogallin was evaluated in fructose, glucose, methylglyoxal and glyceraldehyde induced glycation of BSA. β-glucogallin also decreased the level of carbonyl content, fructosamine level and increased thiol group content of protein in fructose incubated BSA. These activities of β-glucogallin from *Asparagus racemosus* underscore its likely pharmacological potential for impeding metabolic disorders.

Key words: *Asparagus racemosus*, Hyperglycemia, Metabolic Syndrome, Inflammation, Ageing

BCH-133 POSTER

Implication of PRMTs in Diabetes-Associated Skeletal Muscle Atrophy

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Diabetes mellitus is a multifactorial metabolic disease characterized by insulin resistance, hyperglycemia with systemic low grade, chronic inflammation that manifests as a number of secondary complications, including microvascular complication, macrovascular complication, locomotor dysfunctions, etc. Skeletal muscle atrophy characterized by decline in mass and functions of skeletal muscle, is a disorder of the locomotor system that causes pathologically profound alterations in a patient's quality of life. Skeletal muscle atrophy can be triggered by various insults, including prolonged disuse, ageing and diabetes mellitus. Multiple mechanisms, such as the IGF1-Akt, inflammation, TGFβ/BMP-Smad, etc. have been reported to participate in the regulation of protein degradation machineries, but a defined mechanism for skeletal muscle atrophy under diabetes is still remains poorly understood. Protein arginine methyltransferases (PRMTs) are family of enzymes that catalyze the posttranslational methylation of arginine on target proteins, thereby altering their stability, localization, and activity. PRMTs play an important role in regulation of diverse cellular processes such as signal transduction, gene transcription, protein subcellular localization, and cell cycle progression. The role of PRMTs in metabolic disorders is increasingly recognized. Here, we explore the role of PRMTs in diabetes-associated skeletal muscle atrophy. Incubation in high glucose (30mM) medium upregulated the gene expression of atrophy markers (Atrogin1 and MuRF1) in L6 skeletal muscle cells, associated with increased expression of PRMT1, 4 and 5. Results were further validated in STZ-induced hyperglycemic rats, where we also observed higher expression of PRMTs along with atrophy markers in gastrocnemius muscle. Pharmacological inhibition of PRMTs abolished hyperglycemia-induced expression of the atrophy marker, indicating the potential involvement of PRMTs in pathogenesis of diabetes-associated skeletal muscle atrophy.

Key words: Diabetes Mellitus; Skeletal Muscle Atrophy; Protein Arginine Methyltransferases (PRMTs)

BCH-134 POSTER

Activation of NOD1 in Adipocytes Induces Features of NAFLD in Hepatocytes

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Non-alcoholic fatty liver disease (NAFLD) is a most common chronic liver disorder considered as hepatic manifestation of metabolic syndrome characterised by excessive fat accumulation in the hepatocyte of an individual. Over the past few decades, non-alcoholic fatty liver disease has become a major health problem worldwide due to diet and lifestyle modification. Despite the rising incidence, definitive treatment for NAFLD, specifically non-alcoholic steatohepatitis (NASH), has not yet been established. NAFLD is strongly associated with insulin resistance, metabolic syndrome and activation of pro-inflammatory response. However, emerging evidence indicates that innate immune signalling is also a driving force in NAFLD progression. It directly regulates all key pathogenic features of the disease processes, including metabolic dysregulation, inflammation and fibrosis. NOD proteins are intracellular pattern recognition receptors of the innate immune system that sense specific peptidoglycan moieties of microbial pathogens and trigger inflammatory response. NOD1/2 activation in metabolic tissues has been linked with induction of inflammatory response, insulin resistance and oxidative stress. Given the association of these factors with development of insulin resistance and inflammation, we hypothesized that NOD1/2 activation signalling may contribute to development and progression towards NAFLD. In this study, we have found that activation of NOD1 in adipocyte causes development of NAFLD in liver cell. Further, NOD1 mediated lipolysis and inflammation in adipocyte together contribute in induction of NAFLD features in liver cell. The liver lipid metabolism pathways including fatty acids transporters and the triglyceride synthesis pathway are the major contributor for the lipid accumulation in liver cell. This study suggests that NOD1 activation plays a significant role in pathogenesis of NAFLD and may act as a new therapeutic target for NAFLD, which may open new avenues for the rational design of novel therapies for NAFLD.

Key words: NAFLD, Inflammation, Innate Immunity, NOD1, Fat, Adipocyte, Hepatocyte

BCH-135 POSTER

Minimal In Vitro Microtubule-Motor Systems Mimicking Flagellar Beating

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Cilia and flagella play an important role in cellular locomotion and sensing. The structural unit of flagella i.e. axoneme consists of microtubules, linkers and dynein, whose interplay mediates conversion of dynein stepping to flagellar beating. However the minimal structural components driving the beating are yet to be studied in detail due to high structural complexity of the system. Single as well as bundled microtubules have been shown *in vitro* to mimic patterns resembling ciliary beating. Most of the studies lack specificity in MT immobilization or use kinesin, a motor that does not drive flagellar mechanics *in vivo*. Here we report a minimal MT-motor system mimicking beating *in vitro* that we use to study the role of MT geometry and motor type on the beating mechanics. The setup is an extension of previously described *in vitro* gliding assay, with a key modification being MTs pinned at their plus ends. This relatively simple system demonstrates flagella-like beating and matches predictions from simulations. We demonstrate that motors are essential for this mobility, density and MT length affect the nature of dynamics and the proportion of the filament pinned can lead to distinct phases. These results can provide a system for bottom up reconstitution of flagella and help better understand more complex *in vivo* scenarios such as Leishmania motility and ciliary transport.

Key words: Flagellar Beating, Microtubule, Dynein, Reconstitution, Buckling

BCH-136 POSTER

Understanding the Role of Scavenger Receptor CD36 in Modulation of Dendritic Cell Responses upon Activation with *V. cholerae* OmpU

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Dendritic cells (DCs) are professional antigen presenting cells (APCs) that play a central role in immunity, acting as a point of convergence of innate and adaptive arm of the immune system. DCs, like other immune cells usually relies on various germline encoded pattern recognition receptor (PRRs) to recognize some of the conserved patterns, called pathogen associated molecular patterns (PAMPs), on microbes. In our lab, we have explored the role of innate immune cells (monocytes and macrophages) against an outer membrane porin protein, OmpU of gram-negative human pathogenic bacterium, *Vibrio cholerae*. Further, towards exploring how OmpU modulate DC responses, we have observed that TLR2-MyD88 pathway is involved in OmpU mediated pro-inflammatory responses in DCs. In addition to classical PRRs such as TLRs, in the recent times, scavenger receptors (SRs) are emerging as a distinct class of PRRs. Although the role of scavenger receptors is well established in sterile inflammatory disorders like atherosclerosis, their role in infection scenario is still less understood. Our lab has reported the involvement of CD36, a class- B scavenger receptor in recognition of OmpU in macrophages and its crucial role in induction of pro-inflammatory responses via ROS-mediated MAPK (JNK) activation. Towards exploring its role in DCs, we have observed that CD36 co-operate with TLR2 in NOX2-mediated ROS generation which contribute to OmpU-mediated pro-inflammatory responses in DCs. However, experiments involving DCs from $CD36^{-/-}$ transgenic mice suggested that there is an increase in pro-inflammatory cytokine production in absence of CD36, suggesting that CD36 down-regulates OmpU-mediated pro-inflammatory cytokine (IL-1β and IL-6) production in DCs. Therefore, it seems that CD36 play a paradoxical role in DCs. We are trying to elucidate the mechanism by which CD36 play a regulatory role for OmpU mediated pro-inflammatory responses in DCs.

Key words: Dendritic Cells, Immune Cells, Scavenger Receptors, Inflammation, CD36, TLRs, V. Cholerae, Porin, OmpU

BCH-140 POSTER

Singed and Arp2/3 Complex Regulates F-actin Dynamicity in Drosophila Border Cells: An in Vivo Approach to Study Collective Cell Migration

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Cell migration (CM) is imperative during vertebrate development, wound healing, and tissue homeostasis. CM studies have been crucial for cancer metastasis since decades. It can be studied very well in single cell as well as collective cell migration (CCM). The leading cells in the CCM cohort create forward protrusions and lagging cells make backward retractions, in a synchronized and collaborative manner. Essentially, it is the actin cytoskeleton which stands as the primary driver of protrusion formation and retractions. During migration, F-actin folds are generally arranged as branched filaments in sheet-like protrusions called 'lamellipodia' and parallel bundles in finger-like 'filopodia'. However, these F-actin bundles are strongly controlled by sequential feat of plethora of actin-interacting proteins, the utmost crucial contestants through our findings are lamellipodial Arp2/3 complex, filopodial fascin, NPFs like WASP and elongators like Ena. We have chosen Border cell (BC) migration in *Drosophila melanogaster* egg chamber as genetically tractable model to study CCM. We have found that, two key players, singed (vertebrate homolog fascin) and Arp2/3 complex genetically interact with each other to control F-actin architecture in BC. Depletion of both have not only impeded migration considerably but also significantly reduced the cortical F-actin level in migrating cluster. The consequence of this F-actin alteration is manifested upon various aspects of protrusion morphology. Henceforth, we have tried to understand and verify the protrusion classification in BC cluster. We have also tried to design a signaling pathway owing to non-canonical genetical crosstalk that can regulate the robust protrusion dynamicity during BC migration.

Key words: Collective cell migration, Drosophila border Cells, F-actin signaling

BCH-141 POSTER

Characterising the Functional Role of Lis1 With COP9 Signalosome in Mammalian Cells

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Protein-protein interactions are essential for various cellular processes, which are mediated by conserved domains. These domains impart a peculiar function to a protein. LisH domain is known to form protein-protein interactions which are conserved across species. We have identified 28 LisH domain-containing proteins found in humans. However, the functional relevance of the LisH domain is unknown. We have purified the protein complexes associated with LisH domain-containing proteins. Among these 28 LisH domain-containing proteins, Lis1, a LisH domain and WD repeats containing protein, interacts with various higher-order multi-protein complexes, such as COP9 Signalosome (CSN).
CSN is known to deneddylate the Cullin-RING E3 ligases (CRLs) to regulate their ubiquitination activity. However, the mechanism for regulating CSN and its ability to decide its substrates are unknown. Here, we report that Lis1 functions as a regulator for CSN. We have identified a new substrate of CSN, such as Triad1, an RBR-E3 ligase. Functionally, Lis1 is required to maintain the assembly of CSN, thereby regulating its deneddylation activity on Triad1. Together, our data suggest that Lis1 acts as a molecular scaffold for multi-protein complex CSN and plays an essential role in its deneddylation activity on Triad1.

Key words: COP9 Signalosome, Lis1, Triad1, Neddylation, Ubiquitination, Lish Domain

BCH-142 POSTER

Novel Role of Tbx20 and Bmp2 Signalling in Regulating Cardiac Remodelling Post Endoplasmic Stress (ER) Induced Cardiomyopathy

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Adult cardiomyocytes in mammals fails to retain the proliferative capacity exhibited by neonatal cardiomyocytes prior to birth. An insult to Endoplasmic reticulum (ER) machinery often results in the development of ER stress mediated cardiomyopathy. There is a very fine balance between pro-survival and pro-apoptosis during ER stress induced cardiomyopathy. Tbx20 is a cardiogenic pro-proliferative T-box transcription factor that plays a cardinal role in both embryonic as well as adult cardiac function. In this study we are investigating the novel role of Tbx20 and Bmp2 signalling in imparting this pro-survival response in the milieu of ER stress. We observed increased expression of Tbx20 and Bmp2 with increased cardiomyocyte proliferation and decreased apoptosis upon ER stress induction. Their expression decreased with increased intensity and duration of ER stress with concomitant increase in cardiomyocyte apoptosis, hypertrophy and fibrosis. Administration of Recombinant Bmp2 protein resulted in restoration of cardiomyocyte proliferation even during chronic ER stress in vitro. Knockdown of Tbx20 and use of Bmp2 inhibitor Noggin showed Bmp2 to be downstream of Tbx20. In mice, sustained ER stress resulted in drastic increase in Bmp2 expression which is attributed to the heterogeneity of heart tissue. Sustained ER stress also results in increased inflammation which in turn increases Bmp2 expression. Thus, Bmp2 imparts protection post ER stress by augmenting cardiomyocyte proliferation, however it's drastic increase during chronic ER stress is due to factors like inflammation and other cell types of the heart thus, making it a suitable candidate for a novel biomarker for early detection of ER stress mediated cardiomyopathy. Prolonging the expression of Tbx20 could tilt the balance towards pro-survival even during acute ER stress Therefore, identification of the unknown regulatory mechanism imparted by Tbx20 and Bmp2 signalling in reactivating proliferation of adult cardiomyocyte during ER stress could open new therapeutic approaches in treating ER stress induced cardiomyopathies.

Key words: Tbx20, Proliferation, Apoptosis, Cardiomyocyte

BCH-143 POSTER

Understanding Role of HSP70 in Regulating Autophagy Observed in GNE Defective Cells: Pathological Relevance to Rare Genetic Disorder

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GNE myopathy is a rare autosomal recessive neuromuscular disorder caused due to biallelic mutations in sialic acid biosynthetic enzyme, GNE (UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase). One of the characteristic features of the GNE Myopathy is presence of rimmed vacuoles in anterior tibialis muscle biopsy samples of patients[1]. The pathomechanism of the disease is poorly understood with no effective treatment to cure the disease. Besides hyposialylation, other cellular abnormalities such as ER stress, protein aggregation, autophagy, apoptosis and mitochondrial dysfunction have also been observed in muscle biopsy samples suggesting alternate roles of GNE[2]. Recently HSP70 chaperone was identified as a binding partner of GNE in HEK cell based model for GNE Myopathy. Also treatment of cells with BGP-15, an activator of HSP70, reduced the phenotypic cellular effects such as protein aggregation due to various GNE mutations. In the present study, we aim to understand how GNE affects HSP70 function, particularly, protein folding and autophagy. We studied the refolding activity of HSP70 *in vitro* by Luciferase based luminescence assay. Our study indicated approx. 50% reduction in HSP70 refolding activity of GNE mutant cells compared to wild type GNE cells. Treatment of GNE mutant cells with BGP-15 resulted in 80% increase in HSP70 refolding activity. The increase in refolding activity of HSP70 resulted in reduced protein aggregation as observed in

GNE mutant cells. The cryo-protective role of HSP70 is regulated by calcium homeostasis in the cells. The cytosolic calcium levels were found to be elevated in GNE mutant cells by Fluo-4AM. Increased expression of autophagic marker such as LC3, p62 in GNE mutant cells indicated increased autophagic flux. The number of autophagic punctae were also increased in GNE mutant cells compared to wild type GNE control as measured by confocal microscopy. The results were validated in L6 skeletal muscle based GNE knock out cell line. Our study indicates altered HSP70 function in absence of functional GNE and proposed HSP70 activator as potential therapeutic targets for restoring GNE function in affected cells.

Key words: GNE, Myopathy, HSP70, Autophagy, BGP-15, Refolding activity

BCH-164 POSTER

Identification of Small Molecule Based Inhibitor of SphK1 Targeting Lung Cancer

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Sphingosine kinase 1 (SphK1) is responsible for the conversion of sphingosine to its phosphorylated form which is known to participate in cell proliferation, migration, anti-apoptosis, angiogenesis, allergic and immune responses. The upregulation of SphK1 has been associated with tumor angiogenesis, lymph angiogenesis and radiation or chemotherapy resistance and sensitivity. Overexpression of SphK1 results in enhancement of tumor metastatic potential and neovascularization across a variety of human tissues. The three-dimensional structure of SphK1 is better understood and has served as a target for inhibition by small molecules. Small molecule inhibitors of SphK1 are purported as potential therapeutic agent for various cancers and inflammatory diseases. Nevertheless, isoform selectivity of such small molecules remains to be addressed. Lead molecules based on the triarylbenzenesulfonamide scaffold have been previously reported from our research group that indicated attractive scope of refinement based on the substitution patterns. Here, we have synthesized and characterized para-substituted thiazole-based triarylbenzenesulfonamides as prospective SphK1 inhibitors. The binding affinity of these compounds was measured by fluorescence-binding assay and isothermal titration calorimetry. Compounds 1, 2 and 5 showed excellent binding affinity to the SphK1 in the 10^5-10^7 M^{-1} range and significantly inhibits the activity of SphK1 with IC_{50} values in the micromolar range. Molecular docking studies revealed that these compounds fit well into the sphingosine binding pocket of SphK1 and could be implicated in therapeutic management of SphK1 associated diseases.

Key words: Sphingosine kinase-1, Sphingosine-1-phosphate, Cancer therapy, Enzyme inhibition, Kinase inhibitors, Molecular docking, Drug Design and Discovery

BCH-175 POSTER

Role of Inorganic Polyphosphate in Mammalian Granule Biology

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A polymer of orthophosphates formed by high-energy phosphoanhydride bonds was first reported in prokaryotes and was named polyphosphate or polyP. Later, this biopolymer was identified across all taxonomic kingdoms, but with lower abundance in higher eukaryotes. PolyP performs some vital functions in bio-energetics, stress response, pathogenicity, cell signalling, seed germination, blood coagulation and immune response. In Bacteria, Protista and Fungi, polyP synthesis, function and storage are well explored and understood. In mammals, lysosome-related organelles (LROs) store polyP but its synthesis machinery and its regulation remain enigmatic. PolyP synthesis in budding yeast is allosterically regulated by diphosphoinositol pentakisphosphate (IP7). Our lab has shown that mice lacking the IP7 synthesizing enzyme IP6K1, show low platelet polyP levels, slower platelet aggregation, lengthened plasma clotting time and altered clot ultrastructure compared to wild-type mice. To investigate the relationship

between IP6K1 and polyP, we selected a rat mast cell model that is rich in LROs. We detected polyP and found its co-localisation with the specific granule mediator, serotonin. To study the synthesis and storage of polyP inside these LROs we isolated various organelle fractions and examined their polyP synthesis potential. We are attempting to identify the proteins that may be involved in polyP synthesis or its regulation. Additionally, we have generated a list of human proteins interacting with polyP and possessing potential sites for polyphosphorylation. Protein polyphosphorylation has been recognised as a post-translational modification (PTM) and its targets have been reported in eukaryotic systems. Our interest lies in investigating the polyphosphorylation of granule proteins found in our polyP interactome list. This will give us an insight into the granule-mediated processes that rely on polyphosphorylation for their function. Largely, this study will highlight the proteins involved in the synthesis of polyP and the cellular processes mediated by this biopolymer in the cell.

Key words: Polyphosphate, Inositol hexakisphosphate, Lysosome-related organelle

BCH-176 POSTER

Sesn2: An Attractive Novel Drug Target in Colorectal Cancer

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Sestrins are a family of proteins with profound biological importance owing to their antioxidant properties and regulation of metabolic pathways. Sestrin2 (Sesn2) is a novel redox regulating protein with multitude of functions driving cellular homeostasis. Nrf2 acts as a regulator of Sesn2 along with p53 and Activator Protein -1. Mitogen activated protein kinase (MAPK) is a key signalling cascade and plays a seminal role in plethora of extracellular stress mitigation. Phosphorylation of key MAPK's is precursor of many diseases including cancer. Caffeic acid phenethyl ester (CAPE) a major active component of honey bee propolis. In this study, colon cancer HT29 cells were treated with CAPE and its anticancer effect was tested. Cell migration assay reveal that CAPE could ominously inhibit the cell migration. Cell cycle analysis revealed that CAPE could arrest the cancer cell cycle progression in G_2-M phase. Since, Sesn2 plays a major role in cancer progression, the expression of Sesn2, Nrf2 and heat shock proteins was evaluated using immunofluorescence and Western blotting. Western blot analysis of MAPK pathway proteins like p38α, ERK and JNK and Heat Shock Proteins (Hsp90, Hsp70 and calnexin) reveal that under tumour milieu, CAPE could significantly inhibit the aberrant expression of these proteins. The process of epithelial to mesenchymal transition (EMT) in CAPE treated HT29 cells was also evaluated. EMT markers (E-Cadherin, N-Cadherin, Vimentin, Slug and Snail) reveal that CAPE has significant role in modulating EMT. The data generated from this study implicate that CAPE has strong affinity to induce Sesn2 response and modulate MAPK/HSP/EMT axis.

Key words: Sesn2, Mapk, Hsp70, NRF2/KEAP1, CAPE, EMT, Apoptosis

BCH-177 POSTER

Inorganic Polyphosphate in Mitochondrial Energy Metabolism

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Inorganic polyphosphate (PolyP) is a biopolymer composed of long chains of phosphate residues linked by phosphoanhydride bonds. The enzymes responsible for polyP synthesis have been identified in prokaryotes and unicellular eukaryotes, but the machinery involved in polyP biosynthesis in mammals is unknown. PolyP synthesis in budding yeast is allosterically activated by the inositol pyrophosphate IP7. Our lab has reported that mice lacking the IP7 synthesising enzyme IP6K1, have lower levels of platelet polyP, indicating that IP7 also upregulates polyP synthesis in mammals. To further explore the relationship between IP7 and polyP in mammals, we identified proteins from

HEK293T cells that interact with IP7 or polyP immobilised on agarose beads. Interestingly, the IP7 and polyP interactome contain several mitochondrial proteins, suggestive of a cross-talk between IP7 and polyP in the regulation of mitochondrial energy metabolism. Mitochondria isolated from human cell lines or mouse liver depleted for IP6K1 show reduced PolyP levels compared to their respective wild type controls. We have also observed that the polyP levels in mitochondria are dependent on its activity. *IP6K1*$^{-/-}$ cells have reduced mitochondrial respiration which correlates with their reduced polyP levels. We are focusing on understanding the mechanism underlying reduced respiration and its effect on polyP levels. We are also conducting assays to examine the dependence of mitochondrial polyP synthesis on orthophosphate, ATP, and IP7 levels. These investigations may reveal the direct and indirect phosphate sources for polyP synthesis in mammalian mitochondria. We are presently exploring the effect of altering intra-mitochondrial levels of IP7 or polyP on mitochondrial function.

Key words: Mitochondrial metabolism, Polyphosphate, IP7

BCH-178 POSTER

Inhibition of Amyloid Fibrillation of Human Serum Albumin by 6, 7-Dihydroxycoumarin: An Implication in Protein Misfolding Disorders

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Till date around more than 50 proteins are involved in amyloid related disorders, a condition characterized by deposition of insoluble cross beta-sheet rich protein aggregates intracellularly or extracellularly. Therefore, scientists are actively involved in searching for therapeutics that can prevent the disease occurrence. In this study, we have used human serum albumin as a model protein for amyloid fibrillation and screened 6, 7 dihydroxycoumarin (6, 7-DHC), a fluorescent coumarin derivative, for its amyloid inhibitory potency through various biophysical methods. The tested compound displays both primary and secondary inner filter effect in rayleigh light scattering (RLS) which is corrected and after IFE correction it is found that 6, 7-DHC is an aggregation inhibitor. 6, 7-DHC is also a fluorophore whose fluorescence overlaps with that of Thioflavin T (ThT), therefore high concentration of ThT is used to quench 6, 7-DHC fluorescence and it is established as a true amyloid inhibitor. Other assays such as Congo Red assay, Nile Red assay, dynamic light scattering, far-UV circular dichroism and transmission electron microscopy also established the same. In all the assays a dose dependent inhibition is observed. Kinetics is done through far-UV CD that showed a decrease in rate of HSA fibrillation in a dose dependent manner. Finally, it was concluded through MTT assay that the aggregates formed in presence of 6, 7-DHC are less toxic than the amyloid fibrils. This study has clinical significance in designing inhibitors to combat protein misfolding disorders.

Key words: Inner Filter Effect, Tht Biasing, Nile Red, Chromophore, Fluorophore

BCH-179 POSTER

Identification of an Allosteric Inhibitor Binding Pocket in IGF1R for the Development of Novel Anti-Cancer Agents

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Insulin receptor (IR) and insulin like growth factor receptor (IGF1R) are receptor tyrosine kinase that shows high degree of sequence and structural homology. While the IR is involved in regulating metabolic activities in the cell like glucose homeostasis, IGF1R is involed in regulating mitogenic activites to promote cell growth, proliferation and differentiation. Unlike IR, IGF1R is dysregulated in many cancers, therefore, IGF1R is pursued as a therapeutic target for the development of anticancer drugs. Since IGF1R and IR show nearly 100% homology in their ATP binding region, kinase inhibitors developed against IGF1R are inevitably targeting IR as well. This is one of the primary reasons why IGF1R

specific small molecules fail to reach to advanced clinical stages. Scientists believe that when the natural active sites of a target protein are not amenable to drug development, allosteric inhibitor binding pockets provide the most tenable alternative to perturb the function of target protein. Recently, we identified a novel allosteric inhibitor binding pocket in IGF1R. Moreover, we identified a stretch of four discontinous residues within this pocket involved in regulating kinase activity of IGF1R. During in-silico analysis, we observed many structural changes occurring in different conserved regions particularly in the activation loop of these mutants. As a result of these structural changes critical active site tyrosine residues (1161, 1165, and 1166) present in the activation loop showed altered orientation when compared with wild type protein. These structural changes may be contributing to the abrogation of auto-phosphorylation as well as downstream activities of IGF1R. Presently, we are screening compound libraries for the identification of small molecules that can fit into this pocket and specifically target IGF1R only.

Key words: Insulin Signalling, IGF1R, Allosteric Inhibitors, PI3K Signalling

BCH-180 POSTER

Elucidating the Effect of Modulating Cellular Ageing on Intestinal Tissue Homeostasis in Drosophila

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Tissue homeostasis entails a balance between stemness and differentiation. Stem cells employ cytoprotective and regenerative strategies to maintain tissue homeostasis. Ageing results in a gradual decline in cellular and molecular functions leading to derogatory effects on stem cell and tissue homeostasis. Ageing may induce aberrant cell proliferation, apoptosis and skewed differentiation having far ranging effects on the organ system contributing to age-associated disorders like cancer. Our study aims to understand the mechanistic basis of how ageing impacts at the cellular level. Here, using *Drosophila* larval midgut stem cells, we have either accelerated or stalled ageing using genetic approaches or by chemical interventions. Genetically, we have over-activated the inflammatory pathways namely Toll and Imd or have induced reactive oxygen species (ROS) generation to accelerate ageing; and overexpressed Atg8, a key molecular player in autophagy or FOXO, a transcription factor that functions downstream of Insulin signalling to stall ageing in different cellular populations of the larval intestine. In chemical treatment, we have used paraquat, hydroxyurea to accelerate ageing and rapamycin to stall ageing. Our results indicate that induction of ageing leads to increased proliferation, DNA damage, increased differentiation of the entero-endocrine lineage and decreased levels of septate junction molecule, Coracle. While stalling ageing results in reduced entero-endocrine differentiation and DNA damage. Furthermore, we find that there is a consistent upregulation in the transcript levels of genes belonging to DNA damage response and apoptosis upon activation of IMD pathway or ROS generation. Whereas in guts where ageing is stalled, there was a differential profile observed for DNA damage response and pro-apoptotic genes. Chemically induced ageing resulted in altered cellular differentiation, elevated DNA damage and levels of pro-apoptotic genes whereas rapamycin induced stalling showed similar profile as FOXO overexpression with decreased proliferation and increased levels of Coracle. Further, we have also modulated ageing specifically in the intestinal stem cells, entero-endocrine cells in order to delineate cell autonomous vs non-autonomous effects. Taken together, our findings reveal that modulating ageing at the cellular level specifically in the stem cell and progenitor cell population has an overall impact on tissue homeostasis in the *Drosophila* larval midgut.

Key words: Drosophila, Ageing, Stem cells, Drosophila, Larval Midgut, Genetic approaches, Chemical intervention, Proliferation, Differentiation, DNA Damage, Apoptosis

BCH-181 POSTER

Vibrio cholerae Cytolysin activates Dendritic Cells through Engagement of a Novel Assembly of Pattern Recognition Receptors

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Vibrio Cholerae cytolysin (VCC) is a major pore-forming toxin secreted by the cholera-causing bacteria Vibrio cholerae. Upon interaction with the target cells, VCC forms oligomeric pores in the membrane lipid bilayer and and causes cytotoxicity. Apart from serving as a cell-killing exotoxin, soluble monomeric form of VCC and its oligomeric assembly generated in the membrane lipid bilayer can modulate immune responses. Previous study from our lab has shown that preformed VCC oligomer acts as a pathogen-associated molecular pattern (PAMP) and activates the pathways involved in triggering innate immune responses in monocytes and macrophages via engagement of the TLR2/6-MyD88-dependent signalling cascades. In this direction, our present study explores the possibility whether VCC can activate dendritic cells (DCs) as DCs are the most important cell type for modulation of both innate and adaptive immunity. Consistent with the membrane-damaging pore-forming activity of the soluble monomeric form of the toxin, we have observed that VCC monomer is more cytotoxic towards the bone marrow-derived DCs (BMDCs) as compared to the pre-formed VCC oligomer incorporated in the lipid bilayer. Further, we have discovered that both VCC monomer and oligomer could activate BMDCs in terms of production of the pro-inflammatory cytokines. Towards exploring the pattern recognition receptors (PRR) involved in the recognition of VCC, we have demonstrated that in DCs both forms of VCC are not recognised by TLR2/6 hetero-dimer, as observed in monocytes and macrophages. Rather, they engage a unique TLR hetero-dimer that, to the best of our knowledge, is not documented so far for any other ligand recognition. The downstream signalling is propagated via adaptor molecule MyD88. Scavenger receptor CD36 plays an important role in recognition and augmenting the signalling via both the VCC forms. Thus, our study reveals that still a lot to explore in understanding the inflammation in terms of receptor co-operation.

Key words: Vibrio cholerae, Cytolysin, Dentritic Cells, PRR, CD36, Receptor Co-operation

BCH-182 POSTER

MAP/Microtubule Affinity Regulating Kinase 4 Inhibitory Potential of Irisin: A New Therapeutic Strategy to Combat Cancer and Alzheimer's Disease

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Irisin is a clinically significant protein playing a valuable role in regulating various diseases. Irisin attenuates synaptic and memory dysfunction, highlighting its importance in Alzheimer's disease. On the other hand, Microtubule Affinity Regulating Kinase 4 (MARK4) is associated with various cancer types, uncontrolled neuronal migrations, and disrupted microtubule dynamics. In addition, MARK4 has been explored as a potential drug target for cancer and Alzheimer's disease therapy. Here, we have purified the irisin and MARK4 proteins and studied the binding and subsequent inhibition of MARK4 by irisin. Irisin binds to MARK4 with an admirable affinity ($K = 0.8 \times 10^7\ M^{-1}$), subsequently inhibiting its activity (IC_{50}=2.71 µm). *In vitro* studies were further validated by docking and simulations. Molecular docking revealed several hydrogen bonds between Irisin and MARK4,including its active site residues Lys38, Val40 and Ser134. Further, molecular dynamic simulation revealed that the binding of irisin resulted in enhanced stability of MARK4. This study provides a rationale to use irisin as a therapeutic agent to treat MARK4-associated diseases.

Key words: Irisin, Alzheimer's disease, Molecular docking, Molecular dynamics simulation

BCH-183 POSTER

Studies on the Interaction of Mancozeb with Human Hemoglobin by Spectroscopic Analysis and Molecular Docking

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Mancozeb is a fungicide widely used to protect crops from numerous fungal diseases. Human hemoglobin (Hb) is an abundantly present metalloprotein in erythrocytes and is responsible for transporting oxygen from the lungs to various tissues. Exposure of human erythrocytes to mancozeb has been reported to cause hemolysis. In this study, the interaction of mancozeb with Hb was investigated using multi-spectroscopic techniques and molecular docking to elucidate the effect of such interaction on Hb structure and function and ascertain the biological toxicity risk of mancozeb. UV-visible spectroscopy studies suggested intimate binding of mancozeb to Hb. The intrinsic fluorescence of Hb was observed to be quenched by mancozeb, and Stern-Volmer plots revealed that the quenching mechanism was of static type. The negative values of the thermodynamic parameters (ΔG, ΔH, ΔS) indicated that the binding of Hb to mancozeb was spontaneous, with van der waals forces and hydrogen bonding playing a major role in the binding reaction. Synchronous fluorescence experiments showed that mancozeb disturbed the microenvironment around tryptophan residues. Circular dichroism studies revealed that the α-helical content of Hb decreased upon interaction with mancozeb. The inhibition of esterase activity suggested that mancozeb can have a detrimental effect on the enzymatic functions of Hb. Molecular docking study further confirmed that a strong binding affinity exists between mancozeb and Hb. To conclude, the findings of this study show that mancozeb binds strongly to Hb, induces conformational changes, and adversely affects its function.

Key words: Human Hemoglobin, Mancozeb, Spectroscopy, Molecular Docking.

BCH-184 POSTER

Differential Gene Expression and Weighted Correlation Network Dynamics in High-Throughput Datasets of Prostate Cancer

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Precision oncology is an absolute need today due to the emergence of treatment resistance and heterogeneity among cancerous profiles. Target-propelled cancer therapy is one of the treasures of precision oncology which has come together with substantial medical accomplishment. Prostate cancer is one of the most common cancers in males, with tremendous biological heterogeneity in variable molecular and clinical behavior. The spectrum of molecular abnormalities and varying clinical patterns in prostate cancer suggest substantial heterogeneity among different profiles. We performed a state-of-the-art bioinformatics study to identify novel therapeutic targets and precise biomarkers implicated with prostate cancer, beginning with analyzing high-throughput genomic datasets from the Cancer Genome Atlas (TCGA). Weighted gene co-expression network analysis (WGCNA) suggests a set of five dysregulated hub genes (MAF, STAT6, SOX2, FOXO1, and WNT3A) that played crucial roles in biological pathways associated with prostate cancer progression. Among them, we found overexpressed STAT6 and SOX2 and proposed them as candidate biomarkers and potential targets in prostate cancer. Furthermore, the alteration frequencies in STAT6 and SOX2 and their impact on the patients' survival were explored through the cBioPortal platform. The Kaplan-Meier survival analysis suggested that the alterations in the candidate genes were linked to the decreased overall survival of the patients. Altogether, the results signify that STAT6 and SOX2 and their genomic alterations can be explored in therapeutic interventions of prostate cancer for precision oncology, utilizing early diagnosis and target-propelled therapy.

Key words: Prostate cancer; Precision oncology; Target-propelled therapy; The Cancer Genome Atlas; Weighted Gene Co-expression, Network Analysis

BCH-185 POSTER

Expression, Purification and Characterization of Alpha-Synuclein Protein

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Parkinson's disease (PD) is the second most common neurodegenerative disease, characterized by tremor, rigidity, and bradykinesia, with postural instability. α-synuclein (α-syn) is an intrinsically disordered protein (IDP) that plays a crucial role in the pathogenesis of (PD). The pathological hallmarks of PD are intraneuronal inclusion, i.e., Lewy bodies and Lewy neurites, mainly composed of α-syn protein. Many *in-vitro* and *in-vivo* studies suggested that alpha-syn misfolding and aggregation is a major pathogenic event in PD. Herein, we have expressed full-length alpha-syn in BL-21(DE3), and purified the protein using the non-chromatographic method. Further, various biophysical techniques such as UV-Vis, fluorescence and circular dichroism (CD) spectroscopies were employed to elucidate the structural information of α-syn protein. The underlying mechanism behind alpha-syn aggregation remains unknown. Therefore, developing an invitro model of alpha-syn aggregates formation and it inhibition using osmolytes would be advancement in biomedical research.

Key words: Parkinson's disease, Fluorescence, Circular dichroism, Lewy bodies

BCH-186 POSTER

MTG3 Coordinate's Mitoribosome Assembly with mRNA Loading During Translation Initiation in *Saccharomyces cerevisiae*

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Mitochondrial diseases are hereditary with a prevalence of greater than 1 in 5000 adults. Mitochondrial biogenesis requires coordinated expression from two genetic sources, one in mitochondria, and another in the nucleus. Thus, this requires coordination of protein synthesis from two independent translation machineries. The mitoribosomes that synthesize proteins from mRNA encoded by the mitochondrial genome is made up of proteins encoded by the nuclear genome which are separate than those that makeup the cytosolic ribosomes. Assembly of mitoribosome requires a number of auxiliary proteins which includes RNA helicases, modifying enzymes, GTPases, and kinases. These auxiliary factors are nuclearly encoded and guide the processing, and modification of mitoribosome prior to monosome formation during translation initiation. Any mutation in genes encoding for these auxiliary factors leads to an aberrant OXPHOS subunit expression and subsequent assembly, which is an underlying cause in many pathological conditions. *MTG3* belongs to the circularly permuted family of GTPases in which the nucleotide-binding/hydrolysis domain organization is G4-G1-G2-G3 instead of G1-G2-G3-G4. It has been implicated to regulate small mitoribosome subunit (37S) assembly. Herein we show that the putative GTPase activity of Mtg3 is essential for its *in vivo* function. Contrary to its bacterial orthologue YqeH, Mtg3p associates with ribosomal subunits on a sucrose density gradient independent of its nucleotide occupancy state. Furthermore, we show that the C-terminus of Mtg3p has an independent binding site on the ribosome. The putative RNA binding domain at the N-terminus associates with 15S rRNA and a subset of mitochondrial mRNAs *in vivo*. Consistent with a model for ribosome biogenesis whereby individual mitoribosome subunit levels are synergistically coordinated *in vivo*, we observed a specific reduction in levels of mitochondrial large subunit compared to small subunit in cells expressing *mtg3ts*. Taken together these results implicate the role of Mtg3p to coordinate mitoribosome subunit maturation for optimal protein translation.

Key words: MTG3, Mitochondrial diseases, Mitoribosme assembly, GTPases, Auxillary factors, Mitochondrial biogenesis

Cholesterol Biosynthesis Pathway is Down Regulated by Influenza a Virus by Targeting HMGCR Enzyme In A549 Cell Line

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Influenza is one of the major respiratory virus disease caused by influenza virus that comprises of negative sense single stranded RNA as genome. This virus causes epidemic and infrequent pandemic imposing impact on the health and global economy. In the enveloped virus life cycle like influenza cholesterol is considered as one of the major component. However, its function in virus infection and fitness is still not cleared. Different viruses modulates the rate limiting enzyme of the cholesterol biosynthesis pathway HMGCR in both ways either negatively or positively. In our study we have observed the HMGCR modulation by Influenza virus. It was found that Influenza virus decreases total cholesterol. HMGCR protein is down regulated which is mainly due to proteasomal degradation. Further it is also found that virus inactivates HMGCR enzyme by its phosphorylation since Phospho - HMGCR was found to be up regulated at different time post infection. This phosphorylation is bought about by the phosphorylation of AMPK which is one of the major phosphorylating enzyme of HMGCR. Enzyme activity of HMGCR was also measured by HMGCR enzyme activity assay kit and a significant decrease in activity was found. Therefore this study reveals the mechanism involve in host virus interaction with special emphasis on HMGCR the rate limiting enzyme of the cholesterol biosynthesis pathway. This finding may also help in better understanding of pathogenesis of Influenza virus. Further this study reveals that down regulation of HMGCR may be an antiviral response from the host side as cholesterol biosynthesis down regulation can activate innate immunity via STING mediated activation of IRF3 and NLRP3.

Key words: Influenza Virus, HMGCR, Cholesterol, Proteasomal degradation, AMPK

Cracking the whip to Impair Pace-Restoring Primary Cilia Assembly to Attenuate Tumorigenesis

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Primary Cilia (PC) are microtubule-based organelle that protrude out of the membrane, which perform sensory function and transduce physiological and developmental signals such as Shh, Wnt etc. The mother centrioles of vertebrate centrosome transform into basal body that assemble PC during cellular quiescence or interphase, while the PC disassemble before mitosis allowing cells to proliferate. Aggressively proliferating cells from human cancers frequently lack PC. We hypothesize that restoring ciliogenesis in epithelial tumor cells may reduce aberrant proliferation and restore PC-driven signal transduction, and thereby attenuate tumorigenic potential. Voltage Dependent Anion Channel (VDAC) is mitochondrial outer membrane channel proteins that allow movement of ions and small molecules between mitochondria and cytoplasm thereby regulating cellular bioenergetics. VDAC1, the most studied VDACs, is critical in regulating metabolism and inhibiting apoptosis and is an attractive anti-tumorigenesis target. Importantly, our lab has previously identified novel functions of two VDACs, VDAC3 and VDAC1 in negatively regulating ciliogenesis, which is a) to suppress PC assembly in growing hTERT-RPE1 (or RPE1) cells, and b) to promote serum-induced PC disassembly. Here, we tested if VDAC1 depletion in pancreatic ductal adenocarcinoma Panc-1 cells that commonly assemble very few PC may restore ciliogenesis. Our study indicated that VDAC1 depletion not only increases ciliation in growing Panc-1 cells but also results in remarkably long PC. Though VDAC1 depletion does not significantly decrease cell viability, the proliferation index as judged by BrdU incorporation drastically decreased in these cells. Tumorigenic potential of Panc-1 cells as measured by colony formation in a limiting dilution assay also decreased upon VDAC1 depletion. Data suggest that increased ciliation and aberrant elongation of PC likely contributed to the observed anti-proliferative effect of VDAC1 depletion that attenuates metabolic activities. Indeed, co-depletion of TTBK2 that is required for PC formation in siVDAC1 depleted cells, removed almost all PC and cellular proliferation is significantly restored. Thus, our study

reiterates the importance of VDAC1 as the pharmacological target in solid tumors due to its additional function in ciliogenesis. Future research in this aspect will identify the molecular pathways of VDAC1-regulated PC length, and how PC-mediated signaling is modulated upon VDAC1 depletion.

Key words: Primary Cilia, Epithelial Tumor cells, Voltage Dependent Anion Channel (VDAC), Pancreatic Ductal Adenocarcinoma

BCH-190 POSTER

Mps1 Kinase Activity Protects Sas6 at Centrioles and Thereby Promotes Centriole Reduplication

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Centrosomes contain two centrioles surrounded by g-tubulin rich pericentriolar material. Centrosomes serve as the major microtubule organizing centers during interphase and spindle poles during mitosis. Canonical centriole assembly is initiated during S-phase, predominantly by Plk4 kinase, via recruitment of Sas6 to the proximal end of a mother centriole. Sas6 is the key protein of the 9-fold symmetrical cartwheel structure onto which other centriolar proteins are gradually stacked during procentriole formation. Sas6 needs to be maintained at the centrioles during the tenure of centriole assembly and is degraded during mitosis. Notably, supernumerary centrioles are often associated with majority of the tumor cells and tissues. These excess centrioles often form pseudo-bipolar spindle leading to merotelic attachment of kinetochores to spindle microtubular fibers that may lead to aneuploidy, a hallmark of many cancers. Excess centrioles may be generated via cytokinetic failure, or through centriole reduplication during an extended S-phase. The field is actively searching various strategies to prevent excess centriole numbers to inhibit tumorigenesis. Mps1 is a prominent cell cycle kinase that is often overexpressed in cancers. In addition to its critical role in spindle assembly checkpoint activation, Mps1 also plays important role in centriole assembly. It phosphorylates at least two bona fide centriolar proteins Centrin 2 (Cetn2) and Centrin 3 (Cetn3). Mps1 phosphorylation sites in Cetn2 are important for its centriolar recruitment that happens during the new centriole assembly. Hyperactivation of Mps1 during extended S-phase gives rise to supernumerary centrioles in almost all cell types. Here we found that depletion of Mps1 attenuates centriole reduplication, though Sas6 recruitment in S-phase cells was not affected. Interestingly, we found that Mps1 is critical for maintaining Sas6 at the centrioles during an extended S-phase. Evolutionarily phosphorylated Sas6 is protected at centrioles. Our study indicates that Mps1 phosphorylates Sas6 in vivo, and thus likely protects Sas6 at centrioles during extended S-phase. Thus, our study indicated a novel mechanism of regulating Sas6, thereby controlling centriole reduplication. Our ongoing study will likely identify the mechanism of Sas6 degradation during extended S-phase.

Key words: Centrosome assembly, Centriole reduplication, Mps1 kinase, Tumorigenesis, Cell cycle

BCH-191 POSTER

Investigating the Impact of Naturally Occurring Mutations in Tumor Suppressor Protein TIP60 on its Structure and Function

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TIP60 is an epigenetic regulator that possesses histone acetyl transferase activity and thus plays a crucial role in chromatin modifications and regulating gene transcription. TIP60 is also known as a tumour suppressor and it is shown to be downregulated in many cancers, including breast, colorectal, and cervical cancer. Mutation in a protein can impair its function, localization, stability, and many important proteins including tumour suppressors required for normal functioning of the cell are known to be mutated in many cancers. Although many mutations are reported in TIP60 in

multiple cancers, their impact on TIP60's structure and functions are not known. In the present study, we have analysed mutations reported in various cancers in the TIP60 protein and identified that several of these missense mutations are deleterious and destabilizing. We further subjected to structural analysis of these selected mutations to determine for any alterations in the TIP60 structure and also performed molecular dynamics simulation. Structural and MD simulation data revealed changes in TIP60 protein conformational stability and its radius of gyration due to some of these mutations, which is further supported by the significant changes observed in TIP60 protein solvent accessibility and its intramolecular hydrogen bonding. Furthermore, docking studies of TIP60 wild-type and its mutants with acetyl Coenzyme-A revealed a significant change in the interaction energy with the ligand, suggesting that selected mutations induce structural changes in the binding pocket of the protein, which can impact its catalytic activity. Additionally, localization studies of generated mutations in TIP60 protein by live cell imaging showed altered localization of the TIP60 mutant inside the cell. Overall, our study identified mutations in the TIP60 protein reported in cancer that can disrupt its structure and function and thus adds to our understanding of abnormal functioning of cells due to these mutations that might play a role in cancer generation and progression.

Key words: Mutation, Cancer, TIP60, Molecular Dynamic Simulation

BCH-192 **POSTER**

Journey of *Vibrio cholerae* Outer Membrane Protein OmpU to The Host Cell Mitochondria

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Mitochondriais central to caspase-dependent and -independent programmed cell death processes. Various bacterial toxins target host cell mitochondria to cause cell death. Our lab has previously shown that *V. cholerae* porin OmpU induces target cell death in a programmed manner in which mitochondria play a central role. Translocation of OmpU into the host cell mitochondria causes mitochondrial membrane permeability transition leading to caspase-independent cell death. In this study, we aimed to investigate how OmpU trafficking happens inside the host cell leading to its translocation to the host cell mitochondria and triggering cell death. We observed that recombinantly purified OmpU translocates to the mitochondria of THP-1 monocytes via the clathrin-dependent actin-mediated pathway. However, in HEK293 epithelial cells, mitochondrial translocation of purified OmpU happens via the caveolin-mediated pathway. Further, we have observed the involvement of endosomal and lysosomal compartments in the trafficking of purified OmpU in HEK293 epithelial cells. Towards checking the translocation of OmpU in a more physiological scenario, we have used outer membrane vesicles (OMVs), naturally secreted by *V. cholerae*. We have purified and probed the presence of OmpU in the OMVs isolated from *V. cholerae* culture. Further, we observed that in OMV-treated THP-1 monocytes and HEK293 epithelial cells, OmpU takes the clathrin-mediated endocytic pathway.

Key words: Mitochondria, OmpU, *V. Cholerae*, Endocytosis

BCH-193 **POSTER**

Modulation of Intestinal Epithelial Cell Responses and Tight Junction by *Vibrio cholerae* OmpU

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Mammalian gut is believed to be the largest immune organ comprised of cells from both hematopoietic and non-hematopoietic origin. It harbours abundant immune cells, neurons and microorganisms which help in training and maintenance of immune homeostasis. Intestine, being the residence for plethora of microorganisms need a tightly regulated immune system and a strong barrier to prevent the breach. Cells in the intestinal epithelial layer are tightly packed with help of cell-cell junctions called tight junction. Enteric pathogens infecting the intestine produce several

factors causing disruption of these junctions which help them to breach the intestinal epithelial layer to gain access to the systemic circulation. *Vibrio cholerae* is one such an enteric pathogen. OmpU is one of the major outer membrane proteins present in *Vibrio cholerae*. We wanted to check the effect of OmpU on intestinal epithelial cells. Our observations suggest that OmpU can activate intestinal epithelial cells in terms of the production of IL-8 and increased expression of several cytokine and chemokine genes which help in the recruitment and activation of dendritic cells, T-cells and neutrophils. Further, we observed that OmpU can disrupt tight junctions of the intestinal epithelial monolayer. We also observed that both activation of intestinal epithelial cells and disruption of tight junction depend on MAPKs (mitogen activated protein kinases) activation. We are further exploring the underlying mechanism of the OmpU-mediated disruption of the tight junctions.

Key words: Vibrio cholerae, Tight junction, Chemokines, Intestinal Immune System

BCH-194 **POSTER**

Understanding the Role of Scavenger Receptor LOX-1 in *Vibrio cholerae* OmpU-Mediated Inflammatory Responses in Macrophages

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OmpU is one of the major outer-membrane porin protein of *Vibrio cholerae* which is a gram-negative enteric pathogen and the causative agent for human disease cholera. OmpU plays a significant role in the survival of the bacterium in the host's gut. Previous reports from our lab have established that *V. cholerae* OmpU can activate immune cells such as macrophages and monocytes to produce pro-inflammatory mediators. OmpU by acting as pathogen associated molecular pattern (PAMP) activates both monocytes and macrophages via pattern recognition receptor (PRR) TLR1/2 hetero-dimer. Our lab has also reported that in macrophages in addition to TLRs, OmpU is recognized by CD36, a scavenger receptor (SR) which contributes to OmpU-mediated pro-inflammatory responses. Earlier, scavenger receptors (SRs) were majorly known for sensing endogenous ligands and damage-associated molecular patterns (DAMPs) and their role was majorly appreciated in sterile inflammatory diseases and clearing debris. However, SRs are currently emerging as a new class of PRRs. Some of them can even act as co-receptors to TLRs. There are a large number of receptors present among different groups of SRs. Their role as PRR and in receptor co-operation in response to microbial ligands are still not fully elucidated. Here we report that in addition to CD36, another scavenger receptor, LOX-1, participates in OmpU-mediated pro-inflammatory responses. LOX-1 generally recognizes endogenous ligand oxLDL, which is reportedly involved in the inflammatory disease atherosclerosis. However, LOX-1 is not well studied for its role as a PRR against an exogenous ligand. Our study aims to characterize the role of LOX-1 in macrophages in presence of exogenous ligand *V. cholerae* OmpU. We observed that in response to *V. cholerae* OmpU, there is an upregulation of LOX-1 gene expression both at mRNA and protein level. We have further observed that upon knock-down of LOX-1, there is a decrease in pro-inflammatory cytokine (IL-6, TNF-α) production in response to OmpU in macrophages. Furthermore, we explored different signaling molecules and adaptors associated with LOX-1-mediated signaling in OmpU-activated macrophages.

Key words: Macrophages, PRRS, SR, LOX-1, Inflammatory Responses, Signaling

BCH-196 POSTER

Pex30 Undergoes Phosphorylation and Regulates Peroxisome Number in *Saccharomyces cerevisiae*

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Pex30 is a dysferlin domain-containing protein whose role in peroxisome biogenesis has been studied by several research groups. Notably, recent studies have linked this protein to peroxisomes, endoplasmic reticulum and lipid bodies in *Saccharomyces cerevisiae*. Phosphoproteome studies of S. cerevisiae have identified several phosphorylation sites in Pex30. In this study we expressed and purified Pex30 from its native host. Analysis of the purified protein by circular dichroism spectroscopy showed that it retained its secondary structure and revealed primarily a helical structure. Further phosphorylation of Pex30 at three residues, Threonine 60, Serine 61 and Serine 511 was identified by mass spectrometry in this study. To understand the importance of this post-translational modification in peroxisome biogenesis, the identified residues were mutated to both non-phosphorylated (alanine) and phosphomimetic (aspartic acid) variants. Upon analysis of the mutant variants by fluorescence microscopy, no alteration in the localization of the protein to ER and peroxisomes was observed. Interestingly, reduced number of peroxisomes were observed in cells expressing phosphomimetic mutations when cultured in peroxisome-inducing conditions. Our data suggest that phosphorylation and dephosphorylation of Pex30 may promote distinct interactions essential in regulating peroxisome number in a cell.

Key words: Peroxisomes, Phosphorylation, Er, Pex30, Mass Spectrometry

BCH-197 POSTER

Injury-Induced Activation and De-Differentiation of Epicardial Cells Towards Early Cardiomyocyte Lineage *In-Vitro* And *In-Vivo*

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Adult heart failure is a major public health issue and its prevalence is increasing in recent post-pandemic times at an alarming rate. The pathophysiological effect of oxygen depletion during heart failure leads to the massive loss of cardiomyocytes which are ultimately replaced by permanent scar tissue. Unlike zebrafish or neonatal rodent hearts with limited cardiac regenerative capability, adult mammalian hearts with terminally differentiated cardiomyocytes cannot repair or regenerate damaged cardiac muscles post-injury. Here in this study, we have used avian embryonic epicardial cells which are an important source for both cardiomyocytes and non-cardiomyocyte cell lineages, and subjected to oxidative stress by generation of ROS and hypoxia. To our surprise, an increased number of Nkx2.5 and Mf20 positive cells, which marks early and late cardiomyocytes respectively, indicate possible de-differentiation of epicardial cells towards cardiomyocyte lineage post-injury. An epithelial to mesenchymal transition (EMT) marker Twist1, showed to be upregulated in cells following injury induction. This suggests that EMT might be responsible for epicardial cell de-differentiation. We also found that Bmp2 and pSmad1/5/8 expressions are elevated, which might be the possible molecular signaling pathway for Twist1-dependent EMT induction and cardiomyocyte de-differentiation. Furthermore, we also checked the effect of ROS in the isoproterenol-mediated cardiac injury model in adult rats *in-vivo*. We have observed increased number of Wt1 positive cells suggesting activation of epicardial cells following ROS-mediated oxidative stress. In addition, in consistent with the *in-vitro* data, increased number of Nkx2.5 and Twist1 positive cells are also detected in treated adult hearts *in-vivo*. Overall, all these findings suggest that de-differentiation of activated epicardial cells post-injury towards cardiomyocyte lineage might compensate for the lost cardiomyocytes during heart failure, which will open up new research avenues in the field of cardiac repair and regenerative therapeutics.

Key words: ROS, De-differentiation, Cardiomyocyte, EMT, Bmp2-Smad1/5/8

Novel Complex of TIP60-PXR Regulate Genes involved in Actin Reorganization & Filopodia Formation and Promotes Wound Healing

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Wound healing process is characterized by a series of precisely regulated programmed events (haemostasis, inflammation, proliferation, and tissue remodelling) and requires coordination of numerous molecular and cellular changes to facilitate timely and efficient repair of the damaged tissue. Thus it is necessary to characterize the course of these events at higher resolution to thoroughly understand the complex aspects and molecular machineries involved. Research work from our lab had identified that TIP60 (an essential lysine acetyltransferase) interact with unliganded PXR (class II nuclear receptor) and form nuclear foci by modulating PXR's intranuclear dynamics. Domain analysis showed that TIP60 interact with LBD region of PXR through its NR box region and acetylate PXR at lysine 170. Interestingly, PXR augments the catalytic activity of TIP60 for histones substrates and together this complex induces cell migration and adhesion properties of the cell for faster wound healing under wound generated conditions. Further, to dissect the mechanism by which TIP60-PXR complex promote wound healing, our results showed that in response to a wound injury, TIP60-PXR complex promotes rapid formation of filopodia in the cells at the wounded cell front. qPCR analysis of genes showed heightened expression of *Cdc42* and *ROCK1* genes, key regulators involved in filopodia formation and actin reorganization, by TIP60-PXR complex under wound generated conditions. We also showed context-specific binding of TIP60 on the *ROCK1* promoter and demonstrated that the TIP60's chromodomain is essential for loading of the TIP60-PXR complex onto the chromatin. Further, we also identified that TIP60 specifically acetylate histones H2B and H4 during wound generated conditions and thus alters the chromatin microenvironment thereby modulating the expression of targeted genes. Overall, findings from our studies showed that TIP60 is a important regulator of the wound healing process which plays important role in filopodia formation and cell migration during wound generated conditions. In future, identification of downstream signalling pathways targeted by this complex will improve our understanding of wound healing phenomenon. Besides, identification of novel drugs/compounds that could enhance/disrupt TIP60-PXR interaction may provide opportunities for therapeutic interventions for wound healing related diseases.

Key words: Wound healing, TIP60, PXR, Cdc42, Rock1

Cellular Mechanisms of Diabetic Foot in Diabetic Patients

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Diabetic foot ulcers (DFUs) are one of the most common and serious complications of diabetes and affects 15% of all diabetic patients. According to the International Diabetic Federation, 9.1–26.1 million patients get DFU each year and results in a high financial burden. Neuropathy, peripheral vascular disease, and reduced resistance to infection are recognized risk factors leading to the development of DFUs, which have all the characteristics of a chronic wound. Diabetic foot ulcers can lead to amputation causing misery to the patient. It is known to cause increased morbidity and mortality. The continuously increasing worldwide prevalence of diabetes will be accompanied by a greater incidence of diabetic foot ulcer, a complication in which many of the morphological processes involved in normal wound healing are disrupted. The diabetic foot syndrome represents a major problem in the health care of diabetic patients.

Understanding the molecular basis of this disease is an important step toward a rational treatment. Due to the systemic character of diabetes, disturbances in several basic cell functions appear to contribute to impaired wound healing It not only occurs as a typical complication in the late stages of diabetes but also in patients with newly diagnosed diabetes.

Key words: Diabetic foot ulcers, Chronic wounds, Amputations, Diabetes, Rational treatment

BCH-200 POSTER

Evaluation of *Curcuma amada* Rhizome Fractions and In-Silico Molecular Docking Study Reveals that Androstene May be an Important Antidiabetic Bioactive Molecule

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Introduction: *Curcuma amada* commonly known as Amada has been widely used as medicinal plant in Asia. In this study antidiabetic properties of the crude ethyl acetate extract of *Curcuma amada* was evaluated. **Material and Methods:** The rhizomes of *C. amada* were subjected to serial extraction by Hexane, Ethyl acetate and Methanol. The Ethyl Acetate crude extract was further subjected to column chromatography. Fifty fractions were obtained and they were subjected to enzyme inhibition analysis. Fraction 43 was further subjected to glucose uptake potential assay in 3T3-L1 cells. The *Curcuma amada* ethyl acetate was subjected to GC MS analysis for the estimation of probable compounds present in it. *In-silico* molecular docking studies were also performed against receptors alpha amylase, alpha glucosidase, GLUT4 and IRS-1 using the compounds obtained from the GC MS analysis as ligands. **Results:** Fraction 43 showed the lowest IC_{50} value against both alpha amylase and alpha glucosidase enzymes. Fraction 43 showed enhanced glucose uptake potential using 2NBDG for analysis. The compounds obtained from the GC MS analysis are known for their antidiabetic potential. Androstene is a compound of recent interest for its link with diabetes in Men especially. The *in-silico* molecular docking analysis showed a strong binding affinity of the compounds against the chosen receptors. **Conclusion:** The enzyme inhibition and Glucose uptake analysis reveal that *Curcuma amada* is a potent upcoming solution for Diabetes Mellitus.

Key words: *Curcuma amada*, Bioactivity guided fractionation, In-Silico molecular docking, Glucose uptake, Enzyme inhibition

BCH-201 POSTER

Role of YAP1 and FOXM1 in Hyperglycemia Stress Mediated Cardiac Hypertrophy and Fibrosis in an AKT-GSK3β Dependent Signaling

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Cardiac diseases are one of the most common complications with higher susceptibility in diabetic patients. Hypertrophy of cardiomyocyte and fibrosis of heart muscle often lead to structural and functional abnormalities leading to risks of heart failure in diabetic individuals. YAP1 and FOXM1 are recently being investigated for their role in hypertrophic and fibrotic disorders. However, while the expression of FOXM1 has been found to be significantly up regulated in several diabetic cardiomyopathy patients, but how it is regulated or how it interacts with other molecules to induce high glucose mediated cardiomyopathies is still unclear. In this study we have observed high glucose mediated upregulation of FOXM1 induces hypertrophy and increased fibrotic response of cardiomyocyte. As the underlying mechanism, we have further observed that improper glucose metabolism activates YAP1, a key organ size regulatory molecule that

further acts to activate AKT-GSK3ß signaling in cardiomyocyte. Suppression of GSK3ß mediated FOXM1 inactivation results in imbalanced expression and accumulation of FOXM1 within cardiomyocyte leading to hypertrophic enlargement and fibrosis. Further YAP1 and AKT manipulation has been resulted in reduced expression of FOXM1 pointing to a possible interaction of YAP1 and FOXM1 in the cardiomyocyte. Modulation YAP1, AKT and FOXM1 also decreases the overexpression of hypertrophic and fibrotic markers of high glucose stimulated cardiomyocyte. In the control cells, FOXM1 overexpression alone has also been observed to have a profound effect on the induction of hypertrophy of H9c2 and fibrosis. Further, our study aim to observe the role of YAP1 in EMT mediated fibrogenesis of cardiac cells under hyperglycemic stress. Altogether the present study suggests an upregulated YAP1, FOXM1 expression in the adult cardiac myocyte cells may be a potential marker of cardiomyocyte pathogenesis.

Key words: Diabetes, Cardiomyopathy, YAP1, FOXM1

BCH-202 POSTER

Arsenic Induced Cardiotoxicity and its Effect on Adult Epicardium Activation and Differentiation of Epicardium Derived Cells or EPDCs

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The basis of cardiovascular diseases upon arsenate exposure leads to an increase in morbidity and mortality worldwide. But the detailed molecular insight towards arsenic mediated cardiotoxicity in adult heart homeostasis and function is largely unknown. Therefore, our current study is exclusively focused on determining the effects of arsenate upon adult cardiac cell types specifying cardiomyocytes and fibroblasts originating from the epicardial cells through epithelial to mesenchymal transition via epicardial derived cells in utero. While conducting the Wheat germ agglutinin staining, commonly used to label the glycoproteins for plasma membrane, an increase in the cell surface area of arsenate exposed samples is being observed compared to the control ones, indicating hypertrophic response. Changes in expression level of β-MHC have clearly supported the observed phenomenon. Moreover, analysis of lineage specific marker expression level of α-SMA, have established a significant increase in the expression of activated fibroblasts within arsenic exposed hearts compared to control samples. Studies have shown that, Yap molecule of the Hippo-Yap signalling pathway is connected to cellular hypertrophy as well as proliferation leading to proper organ size development in embryonic condition. Based upon observation and previous studies so far, there might be a possibility of Yap getting activated upon arsenate exposure which in turn activates the EMT mechanism in adult heart leading to myofibroblast (activated fibroblast) generation from the adult epicardial cells. Preliminary data has been obtained in order to support epithelial to mesenchymal transition mechanism in adult heart by checking the expression level of EMT specific marker Twist1 upon chronic arsenate exposure. Furthermore, *in-vitro* studies have also being introduced using H9c2, a cardiomyocyte specific cell line from embryonic rat myoblast origin in order to support the preliminary observations of Hippo-Yap signalling pathway *in-vivo*. Overall, we are trying to explore the arsenate dependent affected signalling pathway and its manipulation in the adult heart to reduce the burden of cardiac pathological hypertrophy and fibrosis *in-vivo* with future therapeutic implications.

Key words: Arsenate, EPDC, EMT, Myofibroblast, Hippo-Yap Signaling, Twist

BCH-206 POSTER

The Bipartite Approach of Ankzf1 to Overcome the Mitochondrial Proteotoxic Stress

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Accumulation of misfolded or aggregated proteins is one of the main factors that govern mitochondrial damage and dysfunction. Proteotoxicity is known to cause mitochondrial damage, and these damaged mitochondria are destined for clearance by several pathways, mainly via mitophagy to keep the cell healthy and alive. Mitophagy is an extensively studied pathway, however more intricacies in the process are being elucidated continuously. We have recently shown the modulatory role of yeast Vms1 (VCP/Cdc48-associated mitochondrial stress-responsive) protein during mitochondrial proteotoxic stress. Vms1 is known to participate in two divergent pathways, MAD pathway (Mitochondria associated degradation) and RQC pathway (Ribosome quality control) to protect mitochondria from proteotoxicity. As major component of MAD pathway Vms1 recruits VCP (Valosin-containing protein) on damaged mitochondria to facilitate the clearance of damaged mitochondria via ubiquitin proteasome machinery. While as a component of RQC pathway Vms1 by antagonizing the CAT-tailing activity of Rqc2, protects mitochondria from CAT-tailed-precursor mediated proteotoxicity. In an attempt to understand the role of AnkZF1 (Ankyrin repeat and zinc finger peptidyl tRNA hydrolase 1) (mammalian ortholog of Vms1) during mitochondria proteotoxic stress, we are studying the role of this protein during proteotoxic stress in human cells. Our ongoing study shows that, during mitochondrial proteotoxic stress, AnkZF1 is recruited to mitochondria, indicating its role during mitochondrial proteotoxic stress. We further found that, AnkZF1 and VCP are co-localizing on over the damaged mitochondria, this suggests similar pathway like MAD, in higher eukaryotes. Furthermore, we checked the AnkZF1 localization during chemical stress (H_2O_2, CCCP and Rapamycin)-induced damage of mitochondria. Only during rapamycin treatment, we found the recruitment of AnkZF1 on mitochondria, and it co-localizes with Parkin indicating the role of AnkZF1 in mitophagy. Interestingly, in our model of mitochondrial proteotoxic stress, AnkZF-1 similarly co-localized with Parkin and mitochondrial localization was significantly higher in presence of overexpressed Parkin. These findings together indicate a two tailed approach (MAD pathway and Mitophagy) of AnkZF1 to cope up the mitochondrial proteotoxic stress.

Key words: Mitochondrial Diseases, Mitochondrial Damage, Mitophagy, Proteotoxic Stress

BCH-210 POSTER

Efficiently Spread of Carbapenem-Resistant NDM-Producing Gram-Negative Bacilli Isolated from NICU of an North Indian Hospital

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The emergence of *bla*$_{NDM}$ particularly in Gram-negative bacteria is a burden on the healthcare system in developing countries. Hence, this study was initiated to screen New Delhi Metallo-β-lactamase (NDM) producing Gram-negative bacterial strains from NICU of Indian Hospital. A total of 18 *bla*$_{NDM}$ producing isolates were detected in the present study. Out of 18 *bla*$_{NDM}$ variants isolates, 6 were *Klebsiella pneumoniae*, 4 *Escherichia coli*, 2 *Enterobacter aerogenes*, 1 *Acinetobacter lwoffii*, 1 *Enterobacter cloacae*, 3 *Acinobacter baumannii* and 1 *Cedecea davisae* from NICU, showing resistant against all antibiotics except colistin and polymixin. The transferability of resistance determinants was tested by conjugation. Transfer of *bla*$_{NDM}$ producing strains was successful in all 18 strains. In the case of transconjugants, the MICs values were found to decrease. The *bla*$_{NDM}$ producing isolates contained detectable plasmids of size 66kb, 38kb, and 6kb. Plasmid-based replicon typing revealed the incompatibility types Inc (A/C, FIIA, FIC, K, F, W, FIA, P, X, FIB, B/O)

in bla_{NDM} carrying isolates. This study revealed the outbreak of multiple variants of bla_{NDM} (13 NDM-1, 4 NDM-5 and 1 NDM-7). Moreover, other resistance markers, viz. bla_{OXA-1}, bla_{CMY-1}, bla_{VIM-1}, bla_{SHV-1} co-associated with bla_{NDM} were also found. Here, we reported NDM-1 producing *Cedecea davisae* as a first report to the best of our knowledge. This study is an attempt to reveal the dissemination of bla_{NDM} isolated from neonates in NICU and their efficiently transferability among Gram-negative bacilli via horizontal gene transfer.

Key words: Carbapenem-resistant, Gram-negative bacilli, NDM

BCH-212 POSTER

PCTAIRE1 and FAK as novel regulators of mitosis and their relevance to drug resistance in cancer

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PCTAIRE1 (PCT1) is a cyclin-dependent kinase (CDK) that belongs to the family of serine-threonine kinases. It is highly expressed in terminally differentiated tissues, including the brain and testis, and it is important for neuronal cell differentiation, intercellular vesicular transport, and spermatogenesis. However, its role in cell cycle regulation, particularly mitosis, is not well understood yet. Here, we report that PCT1 is regulated by several serine-threonine and tyrosine kinases within the cell and also plays an important role in mitosis. In our previous study, we have screened a library of 200 serine-threonine kinases using an inducible overexpression cell line that expresses Polyoma virus small T (PolST) as a tool. **We** identified PCT1/CDK16 and FAK as a potent kinases that overcomes PolST induced mitotic arrest, thereby promoting cell survival against apoptotic stimuli. Interestingly, this survival by PCT1 and FAK was also seen when cancer cell lines were grown in presence of anti-mitotic/anti-cancer agents like paclitaxel. We also observed that PCT1 protein levels are quite high in various cancer cell lines. Moreover, PCT1 protein levels changed steadily during the course of the cell cycle and reached their maximum during mitosis. Our findings have also revealed that some prominent players of mitosis, including PLK1 and AurB, regulate PCT1. Further, we show that two that the tyrosine kinases FAK and Src1, which are well-known for their involvement in cancer, also regulate PCT1. We also report that PCT1 and FAK1 colocalize at the spindle poles and midbody along with SRC. Furthermore, we also observed that PCT and its target PRC1 colocalize at midbody with PLK1. Interestingly, we found that PCT1, FAK and SRC are overexpressed in ovarian tumors, thereby suggesting their importance in tumorigenesis. Together, our results show that PCT1 along with FAK is a highly expressed and regulated protein of the cell cycle and has a role in cancer and drug resistance.

Key words: PCTAIRE1, SRC, FAK, Mitosis, Cancer, Cell Cycle, Kinases

BCH-213 POSTER

Non-Canonical Sonic Hedgehog Signaling Amplifies Platelet Reactivity and Thrombogenicity

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Sonic hedgehog (Shh) is a morphogen in vertebrate embryos that is also associated with organ homeostasis in adults. We report here that human platelets, though enucleate, synthesize Shh from pre-existing mRNAs upon agonist stimulation, and mobilize it for surface expression and release on extracellular vesicles, thus alluding to its putative role in platelet activation. Shh, in turn, induced a wave of non-canonical signaling in platelets leading to activation of small GTPase RhoA and phosphorylation of myosin light chain (MLC) in AMP-activated protein kinase (AMPK)-dependent

manner. Remarkably, agonist-induced thrombogenic responses in platelets, which include platelet aggregation, granule secretion and spreading on immobilized fibrinogen, were significantly attenuated by inhibition of Hedgehog signaling, thus implicating inputs from Shh in potentiation of agonist-mediated platelet activation. In consistence, inhibition of Shh pathway significantly impaired arterial thrombosis in mice. Taken together, above observations strongly support a feed-forward loop of platelet stimulation triggered locally by Shh, similar to ADP and thromboxane A2, that contributes significantly to stability of occlusive arterial thrombus and that can be investigated as potential therapeutic target in thrombotic disorders.

Key words: Platelet Activation, Sonic Hedgehog, Thrombosis, Antiplatelet Drugs

BCH-214 POSTER

Mimicking Human Drp1 Disease-Causing Mutations in Yeast Dnm1 Reveals Altered Mitochondrial Dynamics

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The dynamin-related protein 1 (Drp1) and its homologs in various eukaryotes are essential to maintain mitochondrial morphology and regulate mitochondrial division. Several mutations in different domains of Drp1 have been reported, which result in debilitating conditions. Four such disease-causing mutations of the middle domain of Drp1 were mimicked in the yeast dynamin-related GTPase (Dnm1) and were characterized in this study. Mitochondrial morphology and protein function were observed to be altered to a variable extent in cells expressing the mutated variants of Dnm1. Several aspects related to the protein such as punctate formation, localization to mitochondria, dynamic behavior and structure were analyzed by microscopy, biochemical studies and molecular dynamics simulations. Significant effects on the protein structure and function were observed in cells expressing A430D and G397D mutations. Overall, our data provide insight into the molecular and cellular alterations resulting from middle domain mutations in Dnm1.

Key words: Mitochondria, Neurodegenerative Diseases, Dynamin-like GTPase, Yeast, Drp1, Dnm1

BCH-215 POSTER

The Nexus between Peroxisome Abundance and Ageing in *Saccharomyces cerevisiae*

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Ageing is characterized by changes in several cellular processes, with dysregulation of peroxisome function being one of them. Interestingly, the most conserved function of peroxisomes, ROS homeostasis, is strongly associated with ageing and age-associated pathologies. Previous studies have hinted towards a role for peroxisome function in the regulation of replicative and chronological lifespan in yeast. However, no detailed analysis of the effect of number of peroxisomes an ageing has been studied. For this, we have investigated in detail three mutants, *pex11*, *pex25* and *pex27,* defective in peroxisome fission for both replicative and chronological lifespan. Interesting difference between

the mutants and on the growth conditions on yeast ageing was observed. Increased ROS accumulation and reduced catalase activity was exhibited by aged mutant cells. Interestingly, mutants with a reduced number of peroxisomes concomitantly also exhibited an accumulation of free fatty acids and increased number of lipid droplets. We also report for the first time that increased peroxisome number can be a marker for early replicative ageing in yeast. Taken together, our results reveal a previously unrealized effect of fission proteins in the lifespan of yeast.

Key words: Aging, Peroxisome, Yeast, ROS

BCH-216 POSTER

EGF and IGF-1 signaling Cross-talk enhances Expression of EMT Promoting Genes: Implications on Morphology and Proliferation in Breast Cancer Cells

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Breast cancer (BC) is one of the most prevalent cancer-related deaths, and it continues to pose a severe threat to women's health and well-being around the world. Despite significant advancements in breast cancer treatment, metastatic breast cancer remains a fatal disease. To produce next-generation therapies, a thorough understanding of the mechanism of systemic cancer cell dissemination is necessary. A slew of experimental evidence suggests that an epithelial to mesenchymal transition (EMT) plays a crucial role in the multistep process of metastasis development. Epithelial-mesenchymal transition (EMT) is a prerequisite step in various aggressive malignancies, including breast cancer, that aids in invasion and metastasis. In the present study, we evaluated the effect of epidermal growth factor (EGF) and insulin-like growth factor (IGF-1) on breast cells (MDA-MB-468, MDA-MB-231 and MCF10A). It was found that IGF-1 enhances EMT stimulated by EGF. Also, expression of EMT inducing transcription factors viz, snail, slug, zeb1, and zeb2 were found enhanced in breast cells exposed to EGF or IGF-1. In addition, we also found that cell proliferation in metastatic breast cancer cell lines increases substantially in response to EGF and IGF-1 treatment. Interestingly, this increase in cell proliferation was not observed in normal breast cells. We also observed that the morphology of breast cancer cell lines changes when exposed to EGF and IGF-1, whereas in normal breast cells morphology remains unchanged, indicating that growth factors viz EGF and IGF-1 stimulate EMT in breast tumor cells.

Key words: Breast Cancer, EMT, Metastasis, EGF, IGF-1, QPCR, Western blotting, Cell proliferation, Cell morphology

BCH-229 POSTER

Kinase Dependent and Independent Functions of IGF1R

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IGF1R is a widely distributed receptor tyrosine kinase that is essential for cell growth, proliferation, and survival. Clinical investigations have demonstrated that IGF1R-mediated signalling is upregulated in a variety of cancers, including colon, breast, and lung tumours. In certain cancers, overexpression of the IGF1R is linked to a poor prognosis and overall survival. IGF1R has recently been demonstrated to translocate into the nucleus and carry out different functions. In this study, we generated IGF1R kinase mutants to examine kinase dependent and independent functions of IGF1R. We showed that IGF1R kinase activity is critical for its conventional cytoplasmic activities whiles as the kinase independent roles impact its nuclear functions. We also generated a library of IGF1R deletion and point mutants to examine the impact of these mutants on subcellular localization of IGF1R and it was observed that cytoplasmic domain is primarily responsible for the nuclear localization of IGF1R. Furthermore, we also identified a cross-talk between IGF1R and Wnt/β-catenin signaling pathways and showed, for the first time, that IGF1R is associated with upregulation of TCF-mediated β-catenin transcriptional activity.

Key words: IGF1R Signaling, Subcellular Localization, Wnt/β-Catenin signaling, Nuclear functions

BCH-230 POSTER

Curcumin Inhibits the Pore-Forming Function of *Vibrio cholerae* Cytolysin (VCC)

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Plasma membrane and its integrity is crucial for the functioning of the life. Therefore, many pathogenic organisms target plasma membrane to disrupt the cellular integrity and cause infections. Pore-forming toxins (PFTs) are one of the assets used by many pathogens to attack and rupture the target cell membrane by forming pores. *Vibrio cholerae* cytolysin (VCC) is a prominent member in the class of β-PFTs, and it is secreted by bacterial pathogen *Vibrio cholerae*. It interacts with the target membrane and forms heptameric β-barrel pores causing membrane permeabilization and osmotic lysis. VCC exhibits potent cytotoxic activity against a wide range of eukaryotic cells including erythrocytes and intestinal epithelial cells. Apart from its membrane- damaging activity, VCC also induces several signaling pathways in the target cells that lead to varied responses including programmed cell death. Despite the extensive studies on structure-function mechanisms of VCC, no natural inhibitor for VCC has been reported yet. Our study reveals, that curcumin, a small molecule extracted from the roots of *Curcuma longa* (turmeric), effectively compromises the pore-forming activity of VCC. Owing to its extraordinary biological and pharmacological properties, curcumin is an extensively-studied molecule reported to modulate a wide range of biological processes. Curcumin is also shown to inhibit the membrane-damaging activity of certain other PFTs. Curcumin is a hydrophobic molecule and therefore remains almost insoluble in the aqueous solvents leading to extremely poor bioavailability. Our study demonstrates that the insoluble fraction of curcumin in the aqueous medium associates with the VCC and decreases its availability to the target membranes, blocking its membrane damaging activity. Further, we have observed that the soluble aqueous extract of curcumin, also causes a severe reduction in the pore-forming activity of VCC. However, the properties of VCC to bind and oligomerize on the target membrane remain unaffected by such treatment. Overall, our work reports curcumin as the first ever natural inhibitor of the pore-forming membrane-damaging activity of VCC. In addition, our work highlights that curcumin employs two different mechanisms to inhibit the toxin activity in different solvent environments depending on its mode of preparation.

Key words: *Vibrio cholerae* Cytolysin, Membranes, Curcumin, Oligomerization, Pore-Forming Toxin

BCH-231 POSTER

G6PD: The Connecting Link Between Metabolism and Cancer

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Cancer cells alter their metabolic requirements needed for their replication and survival in an inappropriate and unusual environment. In order to meet their high energy and metabolite demands, cancer cells make use of glycolysis (by phenomenon called Warburg effect) and Pentose Phosphate Pathway (PPP). As PPP is an alternative pathway of glycolysis, therefore it is easy for cancer cells to use this pathway to meet their surplus demands of lipids and nucleotide precursors, which ultimately leads to their uncontrolled proliferation under stress conditions. Furthermore, Glucose 6-phosphate dehydrogenase (G6PD) catalyzes the first rate-limiting step of the PPP and has been found to be overexpressed in various cancers. In this study, we have shown that G6PD is highly expressed in cancer cells. Its high expression in cancers is associated with growth, proliferation and survival of cancer cells. Furthermore, we have also observed that G6PD protein expression doesn't change with an increase in the expression of two prominent oncogenes that is NFκB and RelA.but there is a change in its activity in their presence. Moreover, we have also found that a notable tumor suppressor of the cell p53 decreases the activity of G6PD. Together, our results suggest that G6PD activity can be regulated through a complex of NFκB, RelA and p53 induced mechanism, which can ultimately lead to the control of cell division or the tumor growth.

Key words: G6PD, Rela, P53, NFκB, Cancer, Metabolism

BCH-232 POSTER

Cholesterol and TRPM8 Crosstalk: An Overview

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TRPM8 is a thermosensitive cation channel belongs to the transient membrane potential family. TRPM8 is activated by low temperature (less than 23°C) as well as by different cooling compounds such as menthol and icilin. The role of membrane lipids including PI_2P and cholesterol is known to be necessary for functional regulation of transmembrane proteins. In this work we explored the evolutionary conservation and interaction of cholesterol with TRPM8 by using sequence analysis and molecular docking. The *in-vitro* dynamics of TRPM8 on the neuronal cell membrane in cholesterol-reduced condition was performed by immunostaining. The study suggests that reduction of cholesterol on the membrane interfere with the TRPM8 localization on the membrane micro-domain. TRPM8 modulation by pharmacological agents and/or reduction of cholesterol, both cause altered localization of TRPM8 in membrane micro-domains at different efficiency. The results indicate that TRPM8 favors lipid raft localization preferably in ligand-bound state, especially in cholesterol reduced condition. This findings indicate the involvement of membrane cholesterol in TRPM8 structure-function and regulation. These findings may also be important for patients undergoing long-term cholesterol reducing medication and other related disorders.

Key words: TRPM8, Cholesterol

BCH-233 POSTER

Functional Aspects of Wingless Signalling in Drosophila Ovarian Follicle Cell Migration

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From gastrulation to organogenesis, as well as being connected to morphogenesis and wound healing, collective cell migration (CCM) is essential for several developmental processes. On the contrary, erroneous cell motility might accelerate the spread of metastatic cancer and inflammatory illnesses. The *Drosophila* egg chamber (EC) starts as a spherical tissue structure that elongates to create an oval egg shape as it matures. The *Drosophila* EC, a genetically tractable model to study CCM, is a multicellular structure made up of 16 germ line cells, ringed by an epithelial layer of follicle cells (FC). A sheet-like, direction-independent, specialised migration of the outer FCs creates the molecular corset that gives a mature egg chamber its elliptical form. The fundamental molecular process of FC migration, which ultimately mediates the rotation of the egg chamber, is largely unknown. FCs migrate by forming protrusions, much like any other migrating cell but unlike other CCM, neither a leader cell nor a known source of cues for guidance are shown to exist. The primary focus of this research is on the function of canonical wingless (mammalian wnt) signalling in this atypical follicle cell rotation. A number of biological processes, such as embryonic development, cell division, cell adhesion and migration, and planar cell polarity, are already known to be regulated by wingless signalling. Our genetic screening data revealed some potential candidates for wingless signalling regulator genes that alter the aspect ratio, or shape, of the mature egg by obstructing FC migration.

Key words: Collective cell migration, Drosophila, Ovarian follicle, Cell migration, Molecular corset, Egg shape, Wingless signalling

BCH-234 POSTER

Role of Deubiquitination in Vesicular Trafficking in *Schizosaccharomyces pombe*

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Deubiquitination is a process that trims off the covalently conjugated ubiquitin proteins either from the substrates or from the long polyubiquitin chains by a group of enzymes known as deubiquitinases (DUBs). USP7 (Ubiquitin specific protease 7) is a human DUB that regulates the stability of the tumor suppressor p53 and many other proteins. Two orthologs of USP7 are known in *Schizosaccharomyces pombe,* namely- Ubp5 and Ubp15**.** A study from our lab had shown that in addition to its deubiquitinase activity, these two DUBs play an unconventional role in processing the ubiquitin-like fold of an intron-specific splicing factor-Sde2. Earlier work had demonstrated that Ubp5 localizes to the Golgi via its interacting partner Ftp105, but the functional relevance of such localization was unknown. Using the whole-cell proteomics analysis, we have identified a list of hyper-ubiquitinated proteins in the ubp5 mutant. We consider this set of proteins as the substrates of Ubp5, which includes a few plasma membrane transporters. Further experiments were performed to show that the absence of Ubp5 affects the protein level and the trafficking of the transporters to the plasma membrane. However, it was previously known that the protein level of the plasma membrane transporters is regulated by vacuolar degradation machinery. Thus, the reduced protein level of a transporter intrigued us to investigate whether there is any change in the vacuole morphology or activity. We found that cells lacking ubp5 showed smaller vacuoles than wild-type cells. Abnormal vacuoles or lysosome-related organelles lead to several diseases, including Chediak-Higashi syndrome (CHS) type I, lysosome storage disorders, inflammatory disorders, and cancer. This study may reveal a novel regulatory player for vacuole biogenesis that can give us a better understanding of the vacuole/lysosome-related disorders.

Keywords deubiquitinating enzymes, Golgi, transporter trafficking, vacuolar abnormalities

BCH-235 POSTER

Reactivation of Silenced Tumor Suppressors Through an Activation of DNA Methylation Dependent On/Off Mechanism Leads to Reduction in Growth of Head and Neck Squamous Cell Carcinoma

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Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide with high mortality and poor prognosis for patients, associated with smoking and excessive alcohol consumption, major known risk factors for the development of HNSCC. Despite advances in diagnostic and therapeutic methods, survival of HNSCC remains unchanged over the last 30 years. Epigenetic alterations are commonly associated with several types of cancers including HNSCC. Thus, epigenetic changes are considered as promising therapeutic targets for chemoprevention. In the present study, we investigated the effect of epigallocatechin 3-gallate (EGCGs) on DNA methylation and growth of HNSCC. First, we checked the expression levels of global DNA methylation in HNSCC cells and found enhanced as compared with normal human bronchial epithelial cells. Treatment of EGCGs to HNSCC cells (FaDu and SCC-1) significantly inhibits global DNA methylation upto 70-80% after 6 days. To confirm the findings, 5 AzaDc, an inhibitor of DNA methylation was used as control. Inhibition of DNA methylation in HNSCC cells was further confirmed by the conversion of 5-methylcytosine to 5-hydroxymethylcytosine. DNA methylation is regulated by DNA methyltransferases. Next, we checked the effect of EGCGs on the expression levels of DNMT activity and DNMT protein (3a and 3B). Treatment of EGCGs to HNSCC cells significantly reduces DNMT activity upto 60% in SCC-1 and 80% in FaDu cells. The protein levels of DNMT 3a and DNMT 3b were down regulated after EGCGs treatment in the both cell lines.

EGCGs treatment to HNSCC cells reactivates tumor suppressors and caused decreased cell proliferation. Our in vivo study demonstrated that administration of EGCGs (0.5%, w/w) as a supplement of an AIN76A control diet resulted in inhibition of tumor growth of FaDu xenografts in athymic nude mice (80%; P<0.05-0.01) compared to non-EGCGs-treated controls. The growth inhibitory effect of dietary EGCGs on the HNSCC xenograft tumors was associated with the inhibition of DNA methylation, DNMTs, and reactivation of silenced tumor suppressors. Together, this preclinical study provides evidence that the EGCGs act as a DNA demethylating agent and able to reactivate an epigenetically silenced tumor suppressors to inhibit growth of HNSCC cells.

Key words: Epigenetics, DNA methylation, Growth, HNSCC, EGCGs

BCH-236 POSTER

Evaluation of Potential Inhibition of HCV Entry Derived from Natural Sources-An In-Silico Study

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Hepatitis C virus (HCV) is a blood-borne disease that progresses slowly. It is the most common cause of several liver related diseases such as fibrosis, cirrhosis, steatosis, which left untreated can severely damage liver and lead to the development of hepatocellular carcinoma (HCC). Although there are several drugs available for treatment for over 25 years, high mutation rate in the virus makes few drugs pangenotypic. Furthermore, all drugs come with side effects and are very expensive. Till date HCV has 8 identified genotypes of which, genotype 1 is most prevalent and extensively studied followed by genotype 3 which is common in South-East Asia. Tetraspanin protein CD81 is a potential therapeutic target as it is one of the key receptors mediating HCV entry by interacting with the envelope glycoprotein E2. This study is aimed to investigate effective natural entry inhibitors against CD81 and HCV genotype1 , and 3. Literature survey revealed a list of 83 compounds which have been reported to restrict entry of HCV. The structure of these inhibitors were either generated using Marvin's sketch tool or downloaded from PubChem. Docking studies were performed using these inhibitors against CD81 and HCV E2 1a by using AutoDock tool, Galaxy web, PatchDock and SwissDock servers. Potent inhibitors were selected based on their Pose score and binding affinity against their receptors. Non bonded interactions such as hydrogen bonds, hydrophobic interaction were calculated between inhibitors and the proteins CD81 and HCV E2 1a. Inhibitor Eugenin gave the best result against CD81 whereas Oleanolic acid derivative 70, Laccase, Punicalagin, and Imidazole derivative 5 showed to be binding effectively with t HCV E2 1a,1b, 3a and 3b respectively. Further work is ongoing to identify the exact interaction residues and to find compounds that could inhibit E2 of other genotypes as well. Inhibitor studies will also guide us to generate potential preventives with pangenotypic activity and less side effects.

Key words: HCC, CD81, HCV E2

BCH-239 POSTER

ALIBY: ALFA Nanobody-Based Toolkit for Imaging and Biochemistry in Yeast

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Specialized epitope tags continue to be an integral component in various biochemical and cell biological applications such as fluorescence microscopy, immunoblotting, immunoprecipitation, and protein purification. However, until recently, no single tag could offer this complete set of functionalities on its own. Here, we present a plasmid-based toolkit named ALIBY (ALFA Toolkit for Imaging and Biochemistry in Yeast) that provides a universal workflow to adopt the versatile ALFA tag/NbALFA system within the well-established model organism Saccharomyces cerevisiae. The kit comprises of tagging plasmids for labelling a protein-of-interest with the ALFA tag, and detection plasmids encoding a

fluorescent protein-tagged NbALFA for live-cell imaging purposes. We demonstrate the suitability of ALIBY for visualizing the spatiotemporal localization of yeast proteins (i.e., cytoskeleton, nucleus, centrosome, divisome and exocyst) in live cells. Our approach has yielded an excellent signal-to-noise ratio without off-targeting or effect on cell growth. In summary, our yeast specific toolkit aims to simplify and further advance the live-cell imaging of differentially abundant yeast proteins while also being suitable for biochemical applications.

Key words: ALFA, TAG ALFA, Nanobody, Live-cell imaging, Biochemistry, Cell biology, Yeast

BCH-244 POSTER

Elucidation of Changes in Cellular Metabolic Profile and Modulatory Role of Vms1 during Mitochondrial Proteotoxic Stress

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Vms1 (VCP/CDC48 associated Mitochondrial Stress responsive 1), a ~72.7 kDa protein that was first discovered in yeast Sachharomyces cerevisiae. It resides in the cytosol in normal condition but during certain stresses like oxidative stress, the protein is localized in mitochondria. Vms1's translocation to stressed mitochondria is protein-independent and depends on sterol oxidation of mitochondrial membranes. It is a key component of a ribosome quality-control pathway (mitoRQC) and MAD (Mitochondria associated Degradation) as a component of a Cdc48p-complex. Vms1 antagonizes CAT tailing by Rqc2, thereby avoiding aggregate formation and protects mitochondria from proteotoxicity. We have recently shown that VMS1 deletion specifically aggravates the proteotoxicity in mitochondrial matrix in yeast, Saccharomyces cerevisiae. VMS1 deletion leads to more aggregation of mitochondrial chaperones like Hsp60 which is an essential protein to maintain mitochondrial proteostasis and yeast viability. We will discuss the possible mechanisms of Vms1's role to protect mitochondria from proteotoxic stress.

Key words: Protein Homeostasis, Mitochondria, Protein Folding

BCH-245 POSTER

Deciphering the Molecular Interaction of isochroman with Haemoglobin from Bovine Blood

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Under hyperglycemic conditions, non-enzymatic protein glycation gives rise to advanced glycation end-products (AGEs). The AGEs produce free radicals which stimulate the development of diabetes and its complications. Inhibition of glycation is expected to play a significant role in controlling diabetes. Isochroman, a phytocompound obtained from *O. europaea* has been shown to exhibit several beneficial pharmacological activities. It has also been shown to exhibit anti-glycating activity. The mechanism of interaction between isochroman and haemoglobin from bovine blood (BHb) was investigated using various biophysical techniques, i.e. UV-visible absorption spectroscopy and fluorescence spectroscopy, circular dichroic spectroscopy. The value of the binding constant was found to be in the order of 10^3 M^{-1}. Conformational and microenvironmental changes in BHb were confirmed by circular dichroism and synchronous fluorescence spectroscopy after the addition of isochroman, respectively. The above experimental results further corroborated with molecular docking studies. These studies have given insight into the types of interaction and binding of isochroman with target protein.

Key words: Isochroman, Haemoglobin from Bovine Blood (Bhb), Spectroscopy, Computational Modelling

BCH-246 POSTER

Antibacterial Activity and Characterization of Ag/Ag-Cl Nanoparticles Biosynthesized from Rhodiola

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Green synthesis of metal nanoparticle using plants has been recognized as a non-toxic and efficient method for applications in biomedical field. In this regard, silver nanoparticles with diameter ranging from 1 to 100 nm are considered to be important due to their unique properties, extraordinary range of bactericidal and other therapeutic abilities. The aim of this study is to investigate the role of different parts of medicinal plant *Rodiola* on biological synthesis of silver nanoparticles, characterization and evaluation of their antibacterial and cytotoxic activity. Our results showed that the biosynthesis of AgNPs/AgCl NPs, mediated by the aqueous extract of *Rhodiola,* in the range from 20 to 50 nm showed significantly higher antibacterial activity on both gram-negative bacterium *Escherichia coli* and gram-positive bacterium *S. aureus*. FTIR analysis revealed the elemental units of the sample responsible for bio-reduction and capping. The biosynthesized silver nanoparticles were evaluated further for their cytotoxicity to determine percent viability of cells using MTT assay. Our study showed that silver nanoparticles (AgNP) synthesized via whole plant extract exhibited a blue shift in UV-Vis absorption spectra and showed its characteristic XRD pattern as reported in the literature. Moreover, Field Emission Scanning Electron Microscopy (FESEM) was performed which revealed spherical morphology of biosynthesized AgNPs. Our study indicates the possibility of using special *Rhodiola* plant organs in biological/green synthesis of silver nanoparticles and development of nano-based antibacterial drugs.

Key words: Green Synthesis, Rhodiola, Silver nanoparticles, Nanobased antibacterial drugs

BCH-247 POSTER

OmpU Protein of Vibrio Vulnificus Engages various PRR to Induce Heightened Pro-Inflammatory Responses in Murine Macrophages

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Vibrio vulnificus is a human pathogenic gram-negative bacterium. It is known to cause severe wound infection and gastrointestinal diseases. The outer membrane of *V. vulnificus* contains a major outer membrane protein known as VvOmpU. Immunization with VvOmpU has been reported to elicit protective antibodies in murine model, which suggest a probable virulence action of the protein. We wanted to check how VvOmpU activates the innate immune cells. Towards that we have observed that VvOmpU induces huge production of various pro-inflammatory mediators, such as, cytokine (IL-6 and TNFa), reactive oxygen species (ROS), nitrous oxide (NO) in macrophages. For production of different pro-inflammatory mediators VvOmpU engages various innate immune receptors such as, Toll like receptors (TLR2 and TLR4) and scavenger receptor CD36. We observed that both TLR2, TLR4 are involved in pro-inflammatory cytokine production, however, TLR4 is involved in ROS generation. CD36 is also partially involved in ROS generation. Further, we tried to elucidate the underlying signalling mechanism of pro-inflammatory cytokines and ROS production in VvOmpU-activated macrophages. Our study reveals that owing to the various innate receptor co-operation, VvOmpU is capable of production of a huge amount pro-inflammatory responses.

Key words: Vibrio vulnificus, Macrophages, Reactive oxygen species, Toll like receptors, Cd36

BCH-250 POSTER

Erythritol, A Safe Natural Sweetener Exhibits Multi-Stage Anti-Malarial Activity By Permeating into *Plasmodium falciparum* through Aquaglyceroporin Channel

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The increased resistance of human malaria parasite *Plasmodium falciparum* to currently used drugs necessities the development of novel anti-malarials. Here, we examine the potential of erythritol, a sugar substitute for therapeutic intervention. Erythritol is a permeant of *Plasmodium falciparum* aquaglyceroporin (*Pf*AQP) which is a multifunctional channel responsible for maintaining hydro-homeostasis. We show that erythritol effectively inhibited growth and progression of asexual blood stage malaria parasite, and effect invasion and egress processes. It also inhibited the liver stage (sporozoites) and transmission stage parasite (gametocytes) development. Interestingly, erythritol inhibited *in vivo* growth of malaria parasite in mouse experimental model. It was more effective in inhibiting parasite growth both *in vivo* and *in vitro* when tested together with a known anti-malarial 'artesunate'. Additionally, erythritol showed cytokine-modulating effect which suggest its direct effect on the host immune system. Ammonia detection assay demonstrated that erythritol uptake effects the amount of ammonia release across the parasite. Our functional complementation assays suggest that *Pf*AQP expression in yeast mutant restores its growth in hyperosmotic conditions but showed reduced growth in the presence of erythritol. Osmotic lysis assay suggests that erythritol creates osmotic stress for killing the parasite. Overall, our data bestow erythritol as a promising lead compound with an attractive antimalarial profile and could possibly be combined with known drugs without losing its efficacy. We propose the use of erythritol based sweet candies for protection against malaria specially in children living in the endemic area.

Key words: Plasmodium falciparum, Malaria, Aquaglyceroporin, Erythritol, Artesunate

BCH-251 POSTER

Genetic Polymorphism of IL-1 Beta (-511C/T & +3953C/T) and Il-10 (-1082A/G & -819C/T) with Cervical Cancer Susceptibility

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Cervical cancer (CC) is one of the most destructive disease caused by persistent HPV infection which affects women worldwide, especially in developing countries. The genetic basis of host immune response especially cytokine function has been shown to influence CC susceptibility. Though, aim of our study to investigate the association between IL-1 beta (-511C/T & +3953C/T) and IL-10 (-1082A/G & -819C/T) promoter polymorphism and CC susceptibility. This study comprised 192 women with CC and 200 controls. HPV detection was done by RT-PCR and genotyping was assessed through PCR-RFLP method. Findings of our study revealed that incidence of HPV 16 positivity (65.62%) was more common as compared to HPV 18 (19.8) in cases. Also, significant difference was found in the CC, CT and TT genotype frequency of IL-1 beta -511C/T in cases (16.67%, 45.31% and 38.02%) as compared to controls (41%, 31% and 28%). Similarly, difference was found with AA, AG and GG of IL-10 -1082A/G genotype (38.54%, 55.73% and 5.73%) as compared to controls (56%, 34.5% and 9.5%). But there was no significant association was found with genotype frequencies of IL-1 beta +3953C/T and IL-10 -819C/T as compared to controls. Women with CT and TT genotypes of IL-1 beta -511C/T had 3.3-3.6 folds higher risk of cervical cancer (P= <0.001). The -511T allele was significantly linked with susceptibility to cervical cancer (P=0.0001). Individuals with AG and AG+GG genotypes of IL-10 -1082A/G had two-fold increased risk of CC [OR, 2.35 (95% CI, 1.54-3.58), p = 0.005], [OR, 2.03 (95% CI, 1.36-3.04), p = 0.0005] compared to controls. Women with G allele of -1082A/G polymorphism had linked with CC susceptibility [OR, 1.39 (95% CI, 1.02-1.88), p = 0.036] compared to controls. No significant difference was found between patients and controls in the

genotype or allele frequencies of IL-10 -819C/T polymorphism [OR, 1.00 (95% CI, 0.63-1.58), p = 0.99] and IL-1 beta +3953C/T polymorphism (P >0.05). These findings help to understand that polymorphism of IL-1 beta -511C/T and IL-10 -1082A/G gene is associated with increased risk of CC development and can serve as a marker of genetic susceptibility to CC.

Key words: Hpv, Cervical Cancer, Gene Polymorphism, PCR-RFLP

BCH-252 POSTER

Encapsulated Silibinin in Bovine Serum Albumin Nanoparticles Shows Increased Cytotoxicity and Anti-EMT Capacity in Lens Epithelial Cells

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Background: Silibinin (SIL) has demonstrated potential as the inhibitory agent for TGFβ-induced cell migration and epithelial-mesenchymal transition (EMT) of lens epithelial cells (LECs). However, there is a range of challenges to SIL's use in therapeutic contexts. Being natural protein bovine serum albumin (BSA) nanoparticles are good drug delivery carriers. In this study, we optimized BSA nanoparticles (BNPs) for the encapsulation and delivery of SIL to the LECs. **Methods:** The variables for protein desolvation were optimized by three factorial response surface methodology. The prepared SIL-loaded BNPs (SIL-BNPs) were characterized for size, shape, surface morphology (Field emission- scanning electron microscopy), zeta potential, polydispersity, attenuated total reflectance- Fourier transformed infrared spectroscopy, encapsulation efficiency, loading capacity, and *in vitro* release kinetics. Cytotoxicity and anti-EMT capacity of SIL-BNPs in HLE B-3 cells were investigated by MTT assay, wound healing assay, quantitative real-time PCR, western blotting, and immunofluorescence analysis following their incubation in the presence or absence of TGFβ2 for 24 hours. **Results**: Optimal BNPs and SIL-BNPs showed spherical shapes with a diameter of ~107 nm and ~158 nm respectively. Characterization methods indicated stable formulation and successful encapsulation of SIL into BNPs. SIL-BNPs showed encapsulation efficiency of 77% and release of SIL for 96 hours following quasi-Fickian diffusion. SIL-BNPs reduced the viability of HLE B-3 cells dose-dependently and reduced IC_{50} 5 times compared to that of free SIL. SIL-BNPs also inhibited TGFβ2-induced migration and expression of mesenchymal markers (vimentin, fibronectin, α-SMA, N-cadherin) and elevated the expression of epithelial markers (E-cadherin, Pax6) at a lower concentration than that of free SIL. **Conclusion:** Collectively, the results from this study demonstrated that SIL-BNPs have potential application for drug delivery and EMT inhibiting capacity in lens epithelial cells and other ocular cells.

Key words: Silibinin nanoparticles, Response surface methodology, TGFβ2, Bovine serum albumin nanoparticles, Epithelial-mesenchymal transition, Lens epithelial cells

Synthesis of 3-N-/O-/S-Methyl-Imidazo [1, 2-A] Pyridine Derivatives for Caspase-3 Mediated Apoptosis Induced Anticancer Activity

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CSIR-IIIM Jammu

A library of 49 analogs of imidazo[1,2-a]pyridine with 2-halo, aryl, styryl and phenylethynyl-substitution at C-2 position and N-/O-/S-methyl linkage at C-3 position, have been synthesized and evaluated for their anti-proliferative activity against breast (MCF-7, MDA-MB-231), pancreatic (MiaPaca-2), lung (A549), prostate (PC-3) and colon (HCT-116) cancer cell lines and normal cells (HEK-293). Among the screened compounds, 5b exhibited best anticancer potential in all tested cancer cells with IC_{50} ranging from 3.5 to 61.1 μM and no toxicity in normal cells. Studies have confirmed that 5b is increasing ROS generation with concentration dependent way. Besides, after inhibiting ROS by NAC, there is

significant decline in cell death. Further 5b has reduced mitochondrial membrane potential (MMP), which is strengthened via expression of key proteins of intrinsic pathway of apoptosis. DAPI staining of nucleus showed the apoptotic bodies and nuclear fragmentation after treatment with 5b. Western blot results had shown that the cell death in HCT-116 colon cancer cells was achieved through the induction of apoptosis via upregulation of the PTEN gene and downregulation of AKT pathway. Molecular docking and binding energy (ΔG) studies of hit 5b with respect to three important cancer targets (EGFR, mTOR and PI3Kα) revealed strong binding of inhibitor with PI3Kα (docking score − 6.932 and ΔG − 56.297). Cell cycle analysis of 5b, arrest the HCT-116 in G1 phase.

Key words: Imidazo[1,2-A]pyridine, HEK-293, ROS, NAC, MMP, PTEN

BCH-254 POSTER

Starvation Induced Tbx20 Function in Promoting Cardiomyocyte Progenitor Cell Formation with Novel Implication in Cardiac Regenerative Therapy

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Due to very limited proliferative and regenerative capacity of adult myocardium, myocardial infarction associated cardiomyocyte loss results in substantial morbidity and mortality in higher mammals including humans. Therefore, a large number of studies have been directed to explore the possibility to generate cardiac progenitor cells or to mobilize resident cardiac stem cells for better cardiac repair and/or regenerative therapeutics. On the other hand, autophagy is an intracellular bulk degradation process, where cytosolic, long-lived proteins and organelles are degraded and recycled to generate free fatty acids and amino acids and promote cell survival. In cardiac biology starvation induced autophagy plays an important role both during development and in disease. In disease, autophagy is also commonly observed in the adult heart with acute and chronic ischemia, heart failure and aging as a cardiac protective mechanism against injury/age induced cardiac cell deaths. Several T-box transcription factors play an important role in the cardiogenesis process in utero, but the involvement of any such T-box transcription factor gene in the naturally occurring starvation induced autophagy process in adult hearts are unknown. Our *in-vitro* data showed enhanced expression of Tbx20 along with autophagy markers like Lc3b, Gabarapl-1, Beclin-1 as quantified by qPCR and immunostaining/Western blot (WB). Likewise, similar results are seen with our *in-vivo* murine models subjected to either starvation or Rapamycin (administered via intraperitoneal injection) treatment. In-silico work showed Nkx2.5, Gata4 and Sirtuin1 as potential binding partners of Tbx20. As anticipated, levels of Nkx2.5, a marker related to and expressed in cardiac progenitor cells was also found to be upregulated significantly as quantified by IHC and WB, so was the expression of Sirtuin1 and Gata4 hinting at the possibility that the induced levels of Tbx20 mediates the expression of Nkx2.5, Gata4 and Sirtuin1 to maintain the cardiac progenitor like characteristics in cardiac myocytes as a way to regulate autophagic flux besides reducing apoptosis and cellular senescence under these stress conditions. Overall, this work demonstrated that starvation induced Tbx20 function in promoting cardiomyocyte progenitor cell formation with novel implication in adult cardiac regenerative or reparative therapeutics.

Key words: Transcription factor; Tbx20; Cardiomyocyte; Progenitor cells; Starvation; Autophagy; Bmp-Smad signaling

Discovery of a Novel Cell Wall Hydrolase of *E. Coli* that Cleaves the Linkages Between Braun's Lipoprotein, Lpp and the Peptidoglycan

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Gram-negative bacteria are covered by an integral three-layered cell envelope which is made up of an outer membrane (OM), an inner membrane (IM) that encloses the cytoplasm, and a periplasmic space between the two membranes containing peptidoglycan (PG or murein). PG is an elastic polymer that forms a mesh-like sacculus around the IM. PG protects cells from turgor and environmental stress conditions and defines the cell shape. In several bacteria including *E. coli*, the OM is covalently anchored to PG by a numerically abundant OM lipoprotein, Lpp (or Braun's lipoprotein) which functions to maintain the structural and functional integrity of the cell envelope. Lpp has been studied extensively, and PG-Lpp cross-links are known to be synthesized by members of an L,D-transpeptidase family, LdtA, LdtB, and LdtC. Although the formation of PG-Lpp cross-links by L,D-transpeptidases has been studied earlier, how these linkages are modulated is unknown. Using genetic and biochemical approaches, here, we show that LdtF (formerly *yafK*), a newly-identified paralog of L,D-transpeptidases in *E. coli* is a hydrolytic enzyme that catalyses the cleavage of Lpp from the PG sacculus. We also show that LdtF is a glycine-specific carboxypeptidase that cleaves terminal glycine residue from muropeptides of the PG sacculi. Overall, our study describes the discovery of a murein endopeptidase which cleaves the PG-Lpp cross-links suggesting a role for LdtF in regulating PG-OM linkages to maintain the structural integrity of the bacterial cell envelope.

Key words: Cell Envelope, Lipoprotein (Lpp), L, D-Transpeptidase, LDTF

BCH-258 POSTER

Cdk5 and Primary Cilia Disassembly: Insights into Rare Ciliopathies

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Ciliopathy is a term given to group of multisystemic diseased condition that occur due to dysfunctional cilia that are either motile or non-motile, which confer to its motility or sensory functions. Motile cilia that are found in multitude at specialized epithelial layers such as trachea, oviduct or ependyma regulate directional fluid flow, while sperm flagellum provide swimming ability. On the other hand, non-motile primary cilium is present in majority of human cells, where it functions as sensors or transduces signalling pathways like that of hormones, growth factors, Ca^{2+} response or developmental morphogens. Thus, primary cilia are critical during development, in maintaining homeostasis of adult tissue, and also has an impact on memory and learning. Therefore, defects in its structure and function that mostly occurs due to genetic abnormalities lead to a wide spectrum of ciliopathies, among which several are considered to be rare. There is no standard definition for rare disease, every country defines rare disease depending on its health care system, resources present and the prevalence of the disease in terms of total number of people having the disease per 10,000 people in the population. Ciliopathies that are considered rare, globally, are: Alström Syndrome, Bardet-Biedl Syndrome, Jeune Asphyxiating Thoracic Dysplasia (JATD), Joubert Syndrome (JBTS), Autosomal Recessive Polycystic Kidney Disease (ARPKD), and Oral-facial-digital syndrome type 1 (OFD1). Our preliminary studies to tabulate ciliopathies that are rare diseases in India suggests that 'Nephronophthisis' may be considered rare ciliopathy. It can be characterized in three clinical subtypes based on age: Infantile, Juvenile and Adolescent/adult nephronophthisis. Although, in most of the cases it is presented with- reduced renal concentrating ability, chronic tubulointerstitial nephritis, cystic renal disease, and progression to end-stage renal disease (ESRD) before age 30 years. We want to explore how Cdk5, a critical post-mitotic kinase which was recently found to be mutated in nephropathies, in regulating primary cilia length and cilia disassembly.

Key words: Primary Cilia, Ciliary disassembly, Ciliopathies, Rare diseases, Cdk5

BCH-259 POSTER

Understanding the Role of a Glycan Hydrolase, MltD in Expansion of Peptidoglycan In *Escherichia Coli*

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Peptidoglycan (PG) is a unique and essential component of bacterial cell walls. PG forms a sac-like exoskeleton to protect bacteria from lysis due to turgor and from harsh environmental conditions. It is a single, large, elastic polymer which is composed of linear glycan strands cross-linked by short peptide stems to form a net-like sacculus around the bacterial cytoplasmic membrane. Since the PG encases the bacterial cytoplasm, its expansion is tightly coupled to bacterial growth. We earlier showed that a set of redundant endopeptidases, MepS and MepM are required for cleavage of peptide cross-links for incorporation of new material thus helping in PG expansion. Here, we find that overexpression of MltD, a PG hydrolase that cleaves the glycan strands compensates the absence of MepS and MepM. Using genetic and biochemical approaches, we established that MltD contributes to PG enlargement along with the endopeptidases, MepS and MepM. In addition, using spectinomycin-chase experiments and *in-vitro* degradation assays, we show that MltD is regulated post-translationally by a periplasmic proteolytic machinery comprised of an adaptor-protease complex, NlpI-Prc. Overall, our results suggest that coordinated cleavage of glycan strands and peptide cross-links is required to open the PG mesh for insertion of nascent material for successful expansion of bacterial cell wall.

Key words: Bacterial Cell Wall, Peptidoglycan, Glycan Hydrolase, Endopeptidase, MltD

BCH-260 POSTER

Inter-Relationship of Pro- and Anti-Inflammatory Biomarkers with the Development of Type 2 Diabetes Mellitus: A Case Control Study.

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Background and Aims: There has been growing evidence that inflammatory markers play a role in the development as well as severity of Type 2 diabetes mellitus (T2DM). This study has been designed to decipher the involvement of C-Reactive Protein (CRP), Tumor Necrosis Factor (TNFα), Interleukin-6 (IL-6) and Interleukin-10 (IL-10) in the etiopathogenesis of T2DM. **Methodology**: A total of 480 T2DM cases and 540 healthy controls were recruited for the study. Blood samples were collected from each study subject to measure the serum levels of CRP, TNFα, IL-6 and IL-10. **Results and Discussions:** We found that serum levels of CRP in mg/dl (4.2±0.9), TNFα in pg/ml (34.5±8.8), IL-6 in pg/ml (19.2±7.2) in T2DM patients were significantly high as compared to control participants (CRP; 1.4±0.6, TNFα; 12.7±3.4, IL-6; 3.1±1.4; P<0.0001). The serum levels of IL-10 in pg/ml were lower in T2DM cases compared to controls (4.35±1.2 vs. 9.6±1.2). In addition, we observed a significant association of CRP levels with insulin resistance, obesity and dyslipidemia. Increased TNFα levels were strongly associated with female gender, Poor glycemic control and strong family history of diabetes. Poor glycemic control was significantly associated with elevated IL-6 levels. Moreover, significantly reduced IL-10 levels were found in T2DM patients with sedentary lifestyle; low educational and rural

background. **Conclusions:** This study showed a strong relationship between TNFα, IL-6, CRP, IL-10 and T2DM patients of Kashmiri ethnicity, treated at SMHS and Super specialty hospital. Thus, supporting other studies and showing that cytokines may be good markers for T2DM development.

Key words: Type 2 Diabetes mellitus, C-Reactive protein, Tumor Necrosis Factor

BCH-261 POSTER

The Interplay of Cholesterol and Membrane Dynamics in the Pore-Formation Mechanism by Listeriolysin O

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Listeriolysin O (LLO) is an essential virulence factor secreted by *Listeria monocytogenes,* which is the causative agent of listeriosis, a serious food-borne disease that severely affects pregnant women and immunocompromised individuals. LLO assists the bacteria in phagosomal escape and modulation of several cellular pathways. LLO-mediated pore-formation induces a wide range of effects, which help in the establishment of pathogenesis in the host cells. LLO belongs to the family of CDCs (cholesterol-dependent cytolysins), which homo-oligomerize exclusively on the cholesterol-containing cellular membranes to perforate and make aqueous pores of up to 300 Å in diameter. Cholesterol is known to play an indispensable role in the pore-formation mechanism of CDCs. Studies on CDCs like perfringolysin O (PFO), intermedilysin (ILY), and streptolysin O (SLO) revealed that cholesterol is required for the binding of monomers and membrane-insertion of the oligomeric assemblies. However, implication of cholesterol in the pore-formation mechanism of LLO is not fully explored. In our study, we aimed to investigate the role of cholesterol in the pore-formation mechanism of LLO. We employed the liposomes-based model membranes to study the LLO-cholesterol interactions. We further explored the effect of cholesterol in erythrocytes and T84 epithelial cell lines. Based on our results, LLO displayed a different mechanism of cholesterol interaction during pore-formation as compared to that of the other members of the CDC family. Cholesterol was found to enhance the binding of LLO to the membranes and was crucial for the oligomerization process. Next, we investigated the molecular mechanism responsible for the LLO-cholesterol interaction. We characterized the cholesterol recognition motif (CRM) and its role in the pore-formation mechanism. Our results also layed a hypothesis regarding the effects of membrane dynamics and heter ogeneity during the mechanism of pore-formation by LLO. Overall, we established the effects the membrane cholesterol in the pore-formation mechanism by LLO and provided critical insights into the effects of cholesterol-induced membrane organization in the activity of LLO.

Key words: Pore-forming toxins, Cholesterol, Membrane dynamics, Listeriolysin O

BCH-262 POSTER

Synergistic Effect of Flavonoids Bergapten and Myricetin Enhances Apoptosis in Non-Small-Cell Lung Cancer Cell Lines: Potential for Development of Anticancer Nutraceuticals Byusing In-Silico Andin-Vitroapproaches

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Background: Cancer is one of the top global causes of mortality and morbidity. Despite the development of various anti-cancer drugs and treatment modalities, the global burden of cancer-related mortalities has been expected to mount to over 13.1 million by 2030. One of the major drawbacks of current anticancer treatment therapies includes a lack of specificity toward the cancer cell and their side effects. Lung cancer is one of the most widespread types of adenocarcinoma. Non-small cell lung cancer is responsible for 80% of all lung cancer cases.Actin and other cytoskeletal proteins play important roles in maintaining cell shapeand may serve as important therapeutic targets for potential anticancer candidates.Flavonoids have been shown to have anticancer effects against cancer cell proliferation **Aim**: To

investigate the cytotoxic potential and the mechanism(s) of action of Myricetin and Bergapten on human cancer cells by using *in silico and in vitro* approaches. **Materials and Methods:** *Insilico* data was analyzed byautodock 4.2.6, Molinspiration, Osiris software, swissADME, and LARMDv1.0 software.*In vitro* anticancer activity was determined by MTT,DPPH, DCFDA, and Hoechst 33342, AO/EtBr, and Annexin V/ PI assay.Chou-Talalay'sapproachwas used to determine the effect of the combination. **Results**-*Insilico* data demonstrated that Myricetin and Bergapten haveshownthe best binding energy and dissociation constants (Kd) with gelsolin and Myricetin following four parameters while Bergapten follows five parameters of Lipinski's rule.Myricetin displayedgood stability of complex and RMSF showed flexibility in all regions of the protein. Myricetin and Bergapten showed the best docking score by analysis with Schrödinger release2020-4. A combination of Myricetin and Bergapten was obtained at 16+16µM on the A549 cell line. The combination of Bergapten and Myricetin leads to significant ROS generation in the A549 cell line. Hoechst staining indicated nuclear condensation in the A549 cell line. AO/EtBr staining and flow cytometry resultsindicated early and late apoptosis in the A549 cell line. **Conclusion-** Based on the above investigation, the results indicated that the selected flavonoids can be used to formulate novel drugs in the future.

Key words: Myricetin, Bergapten, Flavonoids, Anticancer, Nutraceuticals, Potential, Apoptosis

BCH-263 POSTER

Human Carboxylesterase 1 (CES1)/Triacylglycerol Hydrolase (TGH) Reduces Triacylglycerol Turnover and Fatty Acid Oxidation through the Inhibition of Autophagy

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Non alcoholic fatty liver disease (NAFLD) is a clinicopathological condition that results due to the intracellular accumulation of lipids in hepatocytes and is considered to be the leading cause of chronic liver injury. Mouse ortholog of human carboxylesterase1 (CES1) known as Triacylglycerol hydrolase (TGH) has been shown to play an important role in NAFLD. However the direct effect of human CES1 on triglyceride (TG) turnover and fatty acid oxidation (FAO) and its mechanism of action are yet to be elucidated. We elucidated the effect of CES1 on TG turnover and FAO and attempted to understand its mechanism of action. McArdle rh7777 cells stably transfected with human CES1 (hTGH) show decreased TG turnover and FAO as compared to cells stably transfected with empty vector (Pci Neo) in a pulse chase experimental setup. Inhibition of ATGL by Atglistatin reduced the FAO. Blocking the lysosomal function by NH_4Cl reduced both FAO and TG turnover. The reduction in TG turnover was more drastic in hTGH as compared to Pci Neo. Combination of Atglistatin and NH_4Cl reduced TG turnover and FAO in both the cells. Again the effect on TG turnover was more in hTGH35. Liver specific TGH knockout mice when fed with a high fat diet show decreased LC3II and SQSTM1. Interestingly, wild type mice and TGH KO mice when fed with a normal chow diet did not show any difference in pAMPK and SQSTM1 after fasting. However, pAMPK was significantly higher and SQSTM1 was lower in TGH KO mice after refeeding. Our results suggest that human CES1 or TGH reduces autophagy that results in reduced TG turnover and FAO. Therefore, targeting CES1 could provide us with a possible therapeutic strategy for reducing the lipid burden in NAFLD.

Key words: Non-alcoholic fatty liver disease, Carboxylesterase, Triacylglycerol hydrolase, Triacylglycerol, Turnover, Fatty acid oxidation, Autophagy

BCH-264 POSTER

Identification of Degs as Potential Biomarkers through Transcriptome Profiling of Epithelial Ovarian Cancer

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Background: Among all gynaecologic malignancies, ovarian cancer stands out with the highest mortality rate. The asymptomatic nature and non-specific symptoms of ovarian cancer makes it difficult to diagnose at early stage. This study aimed towards the identification of hub genes and potential pathways that could help in understanding the molecular mechanisms involved in ovarian cancer progression. **Method and Material:** We performed expression profiling of four tumor and two normal samples through RNA-sequencing on NGS platform. Functional analysis and PPI network analysis of DEGs was conducted followed by verification of RNA-sequencing results through QRT-PCR. Correlation studies were performed between gene expression and clinical characteristics of ovarian cancer followed by survival analysis and expression validation on TCGA database. **Results:** Through RNA-sequencing, a total of 141 upregulated and 79 downregulated DEGs were obtained. Gene ontology analysis showed the enrichment of DEGs in basal cell carcinoma, cell cycle, FoxO signalling pathway, GPCR signalling, and glycolysis in senescence. Interaction analysis identified 10 DEGs involving upregulated CDKN1A, BCL6, PFKFB4, CDC45 and downregulated WNT2, TLR5, NKILA, CSN1S1, PL2R1, AQP5. The expression of obtained 10 DEGs were validated by qRT-PCR and by TCGA database. Finally, the above DEGs were correlated with clinical characteristic and survival analysis. Among all, BCL6, CSN1S1 and AQP5 showed significant correlation with overall survival. **Conclusion:** This work highlighted eight DEGs (CDKN1A, BCL6, CDC45, WNT2, TLR5, AQP5) including two novel DEGs (CSN1S1 and NKILA), that were significantly associated with the features of epithelial ovarian cancer. These may serve as useful biomarkers and potential therapeutic targets for EOC.

Key words: Epithelial Ovarian Cancer, Differentially Expressed Genes, Rna-Sequencing, Qrt-Pcr, Gene Expression, Biomarker.

BCH-265 POSTER

Molecular Targets of Genistein in Cancer

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Genisteinchemically known as 4', 5, 7-trihydroxyisoflavone is an isoflavones that is originate in varied soybeans and soy products. Genistein has potential beneficial effects on human grave diseases, such as cancer. Mechanistic vision of genisteindivulges its potential for cell cycle arrest, apoptotic induction, anti-angiogenic, anti-metastatic, and anti-inflammatory effects. The molecular mechanism of action of genistein as a chemotherapeutic agent has been expansivelyconsidered in diverse types of cancers. Genisteinmoderatesnumerous steps of apoptosis, cell cycle, angiogenesis, and metastasis. The main molecular targets of genistein include Bcl-2-associated X protein (Bax), caspases, B-cell lymphoma 2 (Bcl- 2), nuclear factor-κB (NF-κB), inhibitor of NF-κB, phosphoinositide 3-kinase/Akt (PI3K/Akt), extracellular signal-regulated kinase 1/2 (ERK 1/2), mitogen- activated protein kinase (MAPK), and Wingless and integration 1/β-catenin (Wnt/β-catenin) signaling pathway.

Key words: Apoptosis, Cancer, Cell cycle; Estrogen receptor; Genistein

Elucidating the Role of EGFR Pathways in Liver Cancer Cells

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The epidermal growth factor receptor (EGFR) is a transmembrane tyrosine kinase receptor of the ErbB family of receptors. EGFR (also known as ErbBI or HER) gets activated by a specific growth factor (EGF) and transforming growth factor alpha (TGF-α) that binds to its extracellular domain. Upon ligand binding, EGFR undergoes a transition from an inactive monomeric form to an active homodimeric state. EGFR undergoes dimerization and its intrinsic intracellular protein-tyrosine kinase activity that causes phosphorylation of several tyrosine residues in the C-terminal domain.EGFR is involved in regulating cell proliferation, differentiation, and survival. EGFR is actively pursued as a therapeutic target because its aberrant expression or activity has been reported in several cancers. Several studies have reported the nuclear localization of the EGFR in various cell types. However, its exact nuclear functions are unclear. In this study, we have generated GFP fusion constructs of EGFR and its mutants to analyze their subcellular localization in normal and cancer cells and the impact of its sub-cellular location on its various activities using immunoblotting confocal microscopy, reporter assays, loss-of-function EGFR mutants, and EGFR specific small molecule inhibitors. We show that EGFR is involved in modulating TCF-dependent β-catenin transcriptional activity in HepG2 cells similarly to IGF1R tyrosine kinase.

Key words: EGFR, ERBB Family, Tgf-A, HEPG2, IGF1R, β-Catenin

BCH-267 **POSTER**

Design and Synthesis of Nitrogen Containing Heterocyclic Analogs to Cure Inflammatory Disorders

Sadaf Fatima

Jamia Millia Islamai

Systemic inflammation, is triggered by microbial infection are the result of release of the pro-inflammatory cytokines from immune-related cells and the chronic activation of the innate immune system and often leads to impaired function of the lungs, kidneys or other vital organs and leads to death. uncontrolled, inflammation may arise numerous diseases like rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, psoriasis, immune-inflammatory ailments, and neoplastic transformations. Despite recent advances in the approaches to cure condition of inflammation, there are still problems in managing patients with this condition. A novel series of nitrogen bearing heterocyclic derivatives were designed, synthesized and characterized via different techniques like H^1 NMR, C^{13} NMR and mass spectrometry. Docking and scoring were used for design inflammatory inhibitors and show their binding affinity with active site key residues of receptor. The different new heterocyclic molecules were synthesized via multiple step reaction. Physical parameters such as Rf values, LogP values, Mpts were also determined and purification of compounds was performed using Column chromatography. All the synthesized compounds were evaluated for their drug like properties using Lipinski's rule of five and also the pharmacokinetics studies were performed. The elucidated synthesized target compounds can be subjected to the biological evaluation as anti-inflammatory candidates because such scaffold have been reported as therapeutically important anti-inflammatory agent.

Key words: Heterocyclic, Anti-Inflammatory, Design, Docking

BCH-268 POSTER

Intrinsic Dynamics of ISWI and its Modulation during Nucleosome Sliding

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Multi-scale folding of chromatin from nucleosomes to chromosomes ensures packaging of chromatin within the nucleus. At the primary level, 147 bps of DNA are wrapped around an octamer of histone proteins forming a nucleosome, but their assembly, disassembly, occupancy and accessibility, as well as inter-nucleosome spacing, is regulated by ATP-dependent chromatin remodeling factors. Chromatin remodeling factor, Imitation Switch (ISWI), utilizes the energy of ATP hydrolysis to slide nucleosomes in order to maintain proper nucleosome spacing. The catalytic activity of ISWI is autoinhibited by the binding of it N- and C- terminal regions to its ATPase domain. This inhibition is relieved in presence of nucleosomes, a highly conserved mechanism. But the mechanism by which ISWI switches between auto-inhibited and sliding-competent states and the conformation(s) it attains during nucleosome sliding remain elusive. We are using Hydrogen/Deuterium exchange coupled to mass spectrometry (HDX-MS), to monitor the conformational dynamics of ISWI while resting and during nucleosome sliding. Our results show that several regions of ISWI are inherently dynamic in nature. During nucleosome sliding ISWI attains an "open" conformation with enhanced dynamics at certain regions fluctuating intrinsically and involved in inter-domain interactions. We suggest that intrinsic conformational dynamics of ISWI may have evolved to optimize its activity. This study has implications in understanding the mechanics of several protein families containing Rec-A like domains like ISWI.

Key words: Nucleosomes, Chromatin remodeling, Hydrogen/Deuterium Exchange coupled to Mass Spectrometry (Hdx-Ms)

BCH-269 POSTER

Protective Role of N-Acetylcysteine on Monocrotophos-Induced Inflammation in Rats

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Monocrotophos (MCP) is a systemic organophosphate pesticide with well-known persistence in environmental resources and toxicity in mammals. Exposure to MCP is associated with altered molecular physiology at the sub-cellular level. The present study examined the effects of N-acetylcysteine (NAC), a natural antioxidant, on MCP exposure-induced biomolecular alterations, inflammatory response and histopathological changes. Monocrotophos exposure (0.9 mg/kg b.wt) caused peroxidation of lipids and proteins and significantly up-regulated the mRNA expression of TNF-α, IL-1β, IL-6 and IL-12, suggesting oxidative damage and inflammation after MCP exposure. The histopathological analysis also showed congestion of the central vein, sinusoidal broadening, pyknotic nuclei and inflammatory cell infiltration in MCP-exposed rats. Supplementation of NAC (200 mg/kg b.wt) prevented lipids peroxidation and protein oxidation and down-regulated the gene expression of pro-inflammatory cytokines. Additionally, NAC also prevented histopathological changes in co-treated groups. The findings indicate that NAC's anti-oxidative and anti-inflammatory properties are responsible to prevent MCP-induced hepatic oxidative injury and inflammatory response in rats.

Key words: N-Acetylcysteine, Monocrotophos, Inflammation, Histopathology

BCH-270 POSTER

Berberine Regulates the Transcriptional Expression of Mitochondrial Complex Subunits to Attenuate Mitochondrial Dysfunction in Acetamiprid-Exposed Rat Liver

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Acetamiprid is a new generation neonicotinoid insecticide widely used to control sucking and chewing insect pests. Acetamiprid primarily causes oxidative stress, mitochondrial dysfunctions, genetic damage and imposes non-target toxicity on humans. Berberine is a plant-derived alkaloid possessing several therapeutic and pharmacological properties. This study aimed to evaluate berberine's role against acetamiprid-induced mitochondrial dysfunctions in rat liver. Biochemical analysis showed restoration of acetamiprid exposure (21.7 mg/kg b.wt) reduced complex I, complex II and complex IV activities on berberine treatment (150 mg/kg b.wt). Semi-quantitative RT-PCR revealed that berberine treatment elevated the acetamiprid exposure mediated depletion in the mRNA expression of ND1 and ND2 (subunits of complex I), COX1 and COX4 (subunits of complex IV), along with MnSOD. The result of the current study highlights the anti-oxidative and modulatory properties of berberine against acetamiprid-induced hepatic mitochondrial dysfunctions. In conclusion, our findings indicate berberine as a promising therapeutic agent against acetamiprid-mediated hepatic mitochondrial dysfunctions.

Key words: Acetamiprid, Berberine, Mitochondrial dysfunctions, Liver

BCH-271 POSTER

Investigating the Role of Mir-198 in Oral Squamous Cell Carcinoma Pathogenesis

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Oral Squamous cell carcinoma (OSCC) is a cancerous growth encompassing the epithelial lining of oral cavity. Around 75 % of OSCC are linked to excessive consumption of tobacco and alcohol. It is the most common cancer in males and fourth most common cancer in females in India, highlighting the grave condition in our country. Despite technological advances, the five-year survival rate for advanced stage OSCC has not changed. The treatment is still limited to radiotherapy, chemotherapy, surgery or their combination and more recently targeted immunotherapy. MicroRNAs are non-coding, single-stranded endogenous RNAs of ~22 nucleotides length. They play an important role in RNA silencing and post-transcriptional regulation of genes. Multiple studies now correlate miRNA dysregulation to several diseases including cancers, Alzheimer's and cardiovascular diseases. Several reports observed the role of miRNA dysregulation as a causal factor for OSCC pathogenesis. They can be broadly classified as tumour suppressors (TSs) and oncomiRs. The downregulation of TSs and activation of oncomiRs play a critical role in tumorigenesis. We hypothesized that TS miRNAs, just like TS genes, might be under the promoter hypermethylation silencing in certain cancers. This could be one of the mechanisms, which provide aggressiveness to the disease, and it could be directly targeted for the cure. With this background, we theorised that 5-Azacytidine (DNA hypomethylating drug) treatment of oral cancer cells would lead to global hypo methylation, which when compared with control-treated cells could identify the silenced TS miRNAs. This study focuses on the identification of miR-198 as a TS miRNA after 5-Azacytidine treatment of SCC131 cells (OSCC). We have explored the tumor suppressor potential of this miRNA. We have identified a direct target of miR-198 and the effect of miR-198 mediated regulation of the target gene on cell proliferation, apoptosis and anchorage-independent growth. The detailed analysis of the findings will be presented and discussed.
Key words: Oral Squamous Cell Carcinoma (OSCC), MicroRNAs (MiRNAs), Tumour Suppressor

BCH-272 POSTER

Elevated Cholesterol Levels in Brain Potentiates Dopaminergic and Cholinergic Dysfunctions in Mice: Relevance to Parkinson's Disease and Alzheimer's Disease

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Cholesterol and its metabolites have been suggested as putative contributors of the pathogenesis of Alzheimer's disease (AD) and Parkinson's disease (PD). Previous studies highlighted the strong link of elevated plasma cholesterols and neurodegenerative changes in PD patients. However, the direct linkage of high fat diet with dopaminergic and cholinergic functions in brain is not yet properly elucidated. The present study hypothesized that high-fat diet and consequent elevation of cholesterol levels in brain causes neurobehavioral and neurodegenerative changes in experimental animal models. To determine the effect of hypercholesterolemia on brain, mice were administered with high fat diet and its effect on cholinergic and dopaminergic neurons were assessed respectively, along with cognitive and motor behavioral performances. The findings of our study revealed that hypercholesterolemia in mice caused significant cholinergic and dopaminergic dysfunctions in discrete brain regions. Thus, the present work emanates a direct relationship between hypercholesterolemia and neuronal functions in brain.

Key words: Cholesterol; Parkinson's disease, Alzheimer's disease, Dopamine, Acetylcholine, Hypercholesterolemia

BCH-273 POSTER

Inhibitory Effect of Chlorogenic acid and Cholecalciferol on Glycated HSA (Human Serum Albumin) in Polycystic Ovarian Syndrome (PCOS)- A Biophysical and Biochemical Study

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Glycation is a non-enzymatic reaction which forms Advanced Glycation End products (AGEs) through the formation of Schiff's base between carbonyl group of carbohydrates and free amino group of lipids, protein and DNA. AGEs accumulation in serum and body tissues is associated with pathogenesis of several diseases including polycystic ovarian syndrome (PCOS). HSA is an essential protein involved in several functions like transport of drugs, fatty acids, hormones and other macromolecules; and it also helps in maintaining blood osmotic pressure. HSA is the serum protein which is the most abundant protein in blood plasma. Concentration of albumin is also high within follicular fluid of females. As previous studies suggest that AGEs concentration increases in serum as well as follicular fluid of PCOS women, this study aimed to evaluate the antiglycation potential of chlorogenic acid (CGA) and cholecalciferol (vitamin D3) on AGEs formation *in-vitro,* which might be helpful in the treatment of PCOS. The antiglycation activity was studied by assessing fructosamine content, protein carbonyl content, free lysine, free arginine, free thiol, AGEs specific fluorescence, Bilirubin binding capacity and intrinsic fluorescence. Combination of CGA with cholecalciferol showed decrease in fructosamine, protein carbonyl content, AGEs specific fluorescence was also quenched while free lysine, free arginine, free thiol concentration was increased; Bilirubin binding capacity and intrinsic fluorescence of HSA was also restored. ANS fluorescence decreased as compared to glycated-albumin which indicates shielding of hydrophobic patches. Glycation also induces cross-linking and aggregation in HSA which was assessed by Thioflavin-T fluorescence assay. Further, Dynamic light scattering and scanning electron microscopy confirmed decrease in aggregate formation in treated samples. Far-UV circular dichroism spectroscopy showed increase in alpha helicity of treated samples. Secondary structure was further evaluated by fourier transform-infrared spectroscopy (FT-IR). Electrophoretic mobility was also restored in case of treated samples as depicted by SDS-PAGE. This study deciphers the antiglycation potential of CGA and cholecalciferol given in combination.

Key words: Glycation, Polycystic ovarian syndrome (PCOS), Chlorogenic acid, Cholecalciferol, Methylglyoxal, Human serum albumin (HSA)

BCH-274 POSTER

Forkhead Transcription Factor FOXO1/NFATc3 Functions in Stress-Induced Cardiomyocyte Hypertrophy and Calcification: Therapeutic Targets in Treating Cardiovascular Diseases.

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The aim of this work is based on mainly two important aspects of cardiovascular disorders (CAVDs), cardiomyocyte hypertrophy and cardiomyocyte calcification. Chronic exposure to toxic metals like cadmium, mercury, lead, arsenic and many such metals induces various cardiac problems. Several previous studies have been done on the effect of these metals in inducing cardiac damage but very few cellular and molecular studies have been done. It is known that arsenic causes oxidative stress, cardiomyocyte apoptosis, reduces cell proliferation causing cardiac damage. According to our studies, arsenic increases heart weight / body weight ratio in mice along with increased expression of cardiac hypertrophy markers. Moreover, arsenic also reduces AMPK (a known anti-hypertrophic agent) expression and reduces nuclear localization of FoxO1 (a Forkhead box transcription factor and an antioxidative agent) along with increased expression of NFATc3 (a known cardiac hypertrophy inducer). Interestingly, we have observed that oleic acid (OA), a monounsaturated fatty acid helps in ameliorating cardiac hypertrophy in arsenic exposed mice. Our studies on OA mediated protection from arsenic induced cardiac hypertrophy in H9c2 cells shows that OA upregulates AMPK activity along with increased nuclear FoxO1 localization, thereby reducing NFATc3 expression and attenuating cardiomyocyte hypertrophy. We have further extended our study of FOXO/NFATc3 signaling pathway to investigate its role in cardiomyocyte calcification. A number of investigations and research work have been done previously on the molecular mechanism of vascular and heart valve calcification but the mechanism of myocardial and cardiomyocyte calcification has remained uninvestigated. Our studies in H9c2 cardiomyocytes show that calcific deposition in cardiomyocytes does not occur in 15 days but upon osteogenic induction for one month where FoxO1 expression gets reduced thereby increasing the expression of its downstream target NFATc3 thus increasing the expression of the osteogenic marker Runx2. Overall, our studies show that FoxO1/NFATc3 signaling pathway plays important role not only in cardiomyocyte hypertrophy but also in cardiomyocyte calcification. Analyzing the detailed molecular mechanism involved in cardiac hypertrophy and calcification as well as the interrelation between the two may help in finding out new avenues in the treatment of cardiac hypertrophy and calcification and other related cardiac problems.

Key words: Cardiovascular, Cardiomyocyte, Hypertrophy, Calcification, FOXO1, NFATc3

BCH-275 POSTER

Microtubule Regulation by Par-1 and Sgg During Collective Cell Migration: A Drosophila Border Cells Perspective

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Cell migrations, whether single or in group, are important for various biological aspects like remodeling of tissue, homeostasis and diseases. Various aspects of single cell migration has been fairly studied over last few decades but how cells move in a coordinated manner, especially *in vivo,* is less explored. During *Drosophila* oogenesis, 6-8 epithelial-derived migratory cells, known as border cells (BCs) and a pair of central non-motile anterior polar cells (PCs) form a cohesive cluster, detach from epithelial layer of anterior follicle cells (FCs), migrate between germline nurse cells (NCs) to reach the oocyte border. This BC migration is an excellent model to study the conserved molecular and cellular pathways that govern collective cell migration (CCM) *in vivo*. In various cellular functions, a well-known cytoskeleton component microtubule (MT) plays important role but limited knowledge is available till date regarding how MT stability and dynamics regulate CCM. On that context, our focus is to study MT stability, dynamics and it's regulation by two serine/threonine kinases – Par-1 and Shaggy (Sgg) during BC migration. Par-1/MARK is known to phosphorylate microtubule-associated proteins (MAPs) including Tau and can regulate MT stabilization. On the other hand, wingless signaling component Shaggy (mammalian GSK-3β) can phosphorylate Tau. Here, we show both Par-1 and Sgg can affect

stable MT structure and BC migration. We also observed *par-1* and *sgg* show genetic interaction and can regulate few MT binding proteins, thus might regulate MT stabilization and dynamics, during BC migration as well as in other CCM.

Key words: Collective Cell igmration, Drosophila, Border cells, Microtubule, PAR-1, SGG

BCH-276 POSTER

Crosstalk between Phospholipid Synthesis and Peptidoglycan Enlargement is Mediated via Cell Wall Hydrolase Regulation

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The cell envelope of a Gram-negative bacterium consists of the inner membrane (IM), outer membrane (OM), and an in-between periplasmic space containing peptidoglycan (PG) layer, with an essential structure-function relationship. During cell expansion, a coordinated synthesis of each layer is required to maintain cell envelope integrity, which is a challenging task since these envelope components are synthesized by distinct protein complexes. Currently, how such coordination is achieved is unclear. We find that unregulated PG hydrolytic activity of an elongation-specific PG hydrolase, MepS in *E. coli* is lethal when cellular fatty acid (FA) synthesis is inhibited. Further, using genetic and biochemical methods, we demonstrate cellular availability of FA or phospholipid controls the activity of a periplasmic protease complex NlpI-Prc towards MepS degradation. Overall, our results suggest a coordinated expansion of the PG sacculus with that of plasma membrane results in balanced triple-layered envelope biogenesis in Gram-negative bacteria.

Key words: Peptidoglycan, PG Hydrolase, MePs, NLPI, PRC

BCH-277 POSTER

Interaction of Citrus Flavonoid Naringenin with Major Anti-Proteinase Human Alpha-2-Macroglobulin: Biophysical and Molecular Docking Approach.

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Naringenin is a natural phytochemical that belongs to the flavanones subclass. It is a vital component of many fruits including citrus fruits, tomatoes, bergamot, and grapes. It is crucial in the treatment or prevention of a wide range of ailments, including obesity, heart disease, diabetes, and metabolic syndrome. The biological effects of this phytochemical include antioxidant, anticancer, antiviral, and anti-inflammatory. Through their multitude pharmacological properties, naringenin offer great therapeutic potential in a number of disorders. In the present study, we explored the interaction of human alpha-2-macroglobulin (α2M) with naringenin and determined the structural and functional alterations brought about in α2M structure. α2M is a highly prevalent multifunctional, homo-tetrameric antiproteinase and carrier glycoprotein present in blood and other body fluids with a multitude functions. According to our findings, functional assays indicate that α2M antiproteolytic potential is reduced when it interacts with naringenin. The formation of a complex between the naringenin and protein is suggested by changes in the UV-visible spectra. Fluorescence quenching demonstrated that the naringenin-α2M complex forms as a result of a static process of binding. Secondary structure perturbations in α2M are unveiled by circular dichroism and FTIR. The Stern-Volmer was used to calculate binding constant and the number of binding sites (N) of alpha-2-macroglobulin-naringenin binding in solutions as well as other thermodynamic parameters like entropy, enthalpy, and Gibb's free energy changes were calculated. It was discovered that the interaction between naringenin and alpha-2-macroglobulin was exothermic.

Synchronous fluorescence studies suggest alteration in the microenvironment of both tyrosine and tryptophan residues. Furthermore, molecular docking illustrates the major key residues involved during the interaction process. The structural changes in the conformational state of alpha-2-macroglobulin induced by naringenin interactions could result in its functional inactivation. This study investigated the possible relationship between the therapeutic potential of ingested bioactive compounds and the effectiveness of plasma protein binding.

Key words: Naringenin, Alpha-2-Macroglobulin, Anti-Proteinase, Anti-Inflammatory, Anti-Cancerous, Antioxidant.

BCH-278 **POSTER**

Repurposing Nitrofurantoin, an FDA Approved Anti-Microbial, as Plasmodium Redox Homeostasis Disruptor

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The emergence of resistance as well as decreasing clinical efficacy to first line anti-malarials signifies the need for discovery of alternative therapeutic options to combat malaria. One of the novel approaches for speedy drug development is repurposing of clinically approved therapeutic. The present study evaluates the anti-plasmodial activity of Nitrofurantoin (NTF), a clinically used anti-bacterial drug for treating urinary tract infections. NTF exhibited potent growth inhibitory effect against asexual intra-erythrocytic stages of drug sensitive (3D7) and artemisinin-resistant (R539T) strains of *Plasmodium falciparum (Pf),* alone and/or in combination with artesunate (ART). NTF treatment increased the reactive oxygen species (ROS) and reactive nitrogen species (RNS) levels as well as induced mitochondrial membrane depolarization in malaria parasites (*Pf*3D7 strain). Concomitantly, ring survival assay revealed synergistic association of NTF with ART in ART-resistant strain. Further, *in vivo* administration of NTF, alone as well as in combination with ART, to *P. berghei* ANKA infected mice significantly decreased parasitemia as well as increased mean survival time, compared to mono-therapies. A computational protein target identification approach identified a putative *P. falciparum* anti-oxidative protein *Pf* Glutathione Reductase (*Pf*GR), involved in maintaining parasite redox homeostasis, as a potential NTF target. Target validation experiments showed that exposure of infected RBCs (iRBCs) to NTF disrupted the parasite redox balance by modulating the enzyme activity of *Pf*GR, thereby decreasing glutathione levels and inducing parasite death due to elevated oxidative stress. Overall, our results indicate NTF as a promising repurposable drug with therapeutic potential against parasites resistant to current antimalarials.

Key words: Malaria, Plasmodium Falciparum, Resistance, Drug Repurposing, Nitrofurantoin, Glutathione Reductase, Anti-Plasmodial, Reactive Oxygen Species, Oxidative Stress

BCH-279 **POSTER**

Putative Role of JAK/STAT Modulator Maheshvara in Dpp Signaling

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Maheshvara (*mahe*) is a novel conserved DEAD-box RNA helicase, which regulates Notch signaling and neuronal development in *Drosophila melanogaster*. Mutants of *mahe*, like that of its human orthologues *DDX59*, display impaired central nervous system development, which parallels neurological defects of patients harbouring *DDX59* mutation. Overexpression of *mahe* in *Drosophila* eye tissue induces eye roughness with fused ommatidia. To get a better understanding of the mechanisms and pathways involved with *mahe* associated phenotypes, we utilized eye and wing tissues and performed a genetic modifier screen to identify novel interactors of *mahe*. RNAi screen was performed in *mahe* overexpression background. A number of modulators of *mahe* phenotype were identified. The two prominent candidates uncovered were Chaperonin containing TCP1 subunit7 (*CCT7)* and *Tkv*, which showed a significant modification in *mahe* phenotype. *CCT7* is a negative regulator of *upd1,* a JAK/STAT pathway ligand and downregulation

of *CCT7* with overexpressed *mahe* leads to enhancement of *mahe* induced apoptotic phenotype. Our proof of principle for the modifiers identified is further strengthened, since we have observed that *mahe* induces apoptosis in the photoreceptor neurons via activation of JAK/STAT signaling in *Drosophila*. The second candidate identified through the same RNAi screening, *tkv*, is the type I receptor of product of *dpp* and thus regulates the DPP siganling pathway. It is well established that JAK/STAT pathway positively regulates DPP signaling in germline stem cell niche. *Mahe*, a known regulator of JAK STAT when overexpressed with tkv RNAi resulted in rescue of the eye phenotype due to reduced *tkv*. Interestingly, overexpression of *mahe* in the eye-antennal discs with depleted *tkv* resulted in suppression of *tkv* phenotype. Thus, our study provides a crosstalk of *mahe* with JAK/STAT and DPP pathway. It would be interesting to explore the role played by *mahe* in *CCT7* mediated activation of JAK/STAT pathway. We need to explore further the molecular mechanisms of *mahe* and *tkv* interaction and their regulation of two important signaling pathways, JAK/STAT and DPP. This will further provide us a better understanding of the role played by these factors in disease and development.

Key words: JAK/STAT, Maheshvara, Apoptosis, DPP Signaling

BCH-280 POSTER

Anti-Glycating Effect of Crocin on Glycated Low Density Lipoprotein

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Human low-density lipoprotein (LDL) is known to have a role in coronary artery diseases when it undergoes modification due to hyperglycaemic conditions. Plant products like crocin play an essential role in protecting against oxidative stress and in the production of advanced glycation end-products (AGEs). In this study, the anti-glycating effect of crocin was analyzed using various biochemical, spectroscopic, and *in silico* approaches. Glycation-mediated oxidative stress was confirmed by carbonyl content and lipid peroxidation assays, and it was efficiently protected by crocin in a concentration-dependent manner. ANS fluorescence and electron microscopy confirmed that the structural changes in LDL during glycation lead to the formation of fibrillar aggregates, which can be minimized by crocin treatment. Moreover, secondary structural perturbations in LDL were observed using circular dichroism (CD) and Fourier transform infrared spectroscopy (FTIR), where crocin was found to prevent the loss of secondary structure in glycated LDL. Spectroscopic studies like UV absorbance, fluorescence spectroscopy, CD, FTIR, and *fluorescence resonance energy transfer* (FRET) provided insights into the interaction mechanism between LDL and crocin. Molecular docking supports these results with a highly negative binding energy of -10.3 kcal/mol, suggesting the formation of a stable LDL-crocin complex. Our study indicates that crocin may be a potent protective agent against coronary artery diseases by limiting the glycation of LDL in people with such disorders.

Key words: Anti-glycation; Oxidative stress; Advanced glycation end-products; Molecular docking

BCH-281 POSTER

Spoonbill a Novel Modulator of JNK Signaling In *Drosophila melanogaster*

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Spoonbill is a putative protein kinase A anchor protein which is homologous to human AKAP1. Spoonbill has been identified from large-scale genetic screens, implicating it to be involved in multitudes of processes in *Drosophila*. We have recently attributed novel functions associated with this protein. Spoonbill was identified as a novel suppressor of Spinocerebellar Ataxia 8 (SCA8) associated neurodegeneration that acts via its KH domain to suppress

neurodegenerative pathogenesis. Further, we have also reported that Spoonbill is a crucial interacting partner of Prospero, a cell fate-determining factor that has a vital role in the development of *Drosophila* neurons. In the present study, we are proposing Spoonbill as a novel regulator of JNK signaling pathway. In the current study we have observed that Spoonbill expression is partially required for JNK mediated cell death triggered either by extrinsic or intrinsic signals. Epistatic genetic studies analyzed through imaging, immunostaining and RT-PCR indicates Spoonbill to be a positive regulator of JNK mediated cell death in *Drosophila*, that acts downstream to the kinases of JNK. We observed colocalization between active JNK and Spoonbill in the photoreceptors, suggesting that perhaps Spoonbill facilitates localization of pJNK to a particular cellular niche that is critical for its activation and function that culminates into apoptosis. Mammalian JNK is reported to require scaffold protein-dependent phospho-regulation on the outer mitochondrial membrane which is a critical endpoint for therapeutic intervention for neurodegenerative diseases. Our study opens up a possibility that association of Spoonbill with JNK signaling may have some manifestation in neurodegenerative disorders like Parkinson's Diseases, which will help us to understand the disorder better and find novel therapeutic solutions for such diseases. In a nutshell, studies in our lab have expanded the understanding of Spoonbill protein, a unique *Drosophila* AKAP whose functions remain largely unknown.

Key words: JNK Signaling, Spoonbill, Apoptosis, Eiger, Drosophila

BCH-282 POSTER

Characterization of Fibrinogen Modified by the Synergistic Action Of Methylglyoxal and Peroxynitrite: A Multi-Technique Approach

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Oxidative stress plays a major role in various human pathologies. Earlier evidences suggest that glycation and nitro-oxidation modify proteins irreversibly and contribute to the accumulation of damaged proteins that are resistant to lysis. Therefore, increased production and accumulation of advanced glycation end products (AGEs) under hyperglycemic condition, might lead to the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Fibrinogen, a plasma protein is the main protein involved in blood coagulation cascade. This study aims to reveal the glyco-nitro oxidative profile of fibrinogen in the presence of peroxynitrite (PON) and methylglyoxal (MG) simultaneously. We performed different biophysical and biochemical investigations for the insight look of glyco-nitro oxidatively modified fibrinogen using various approaches, including UV-Vis spectrophotometry, AGE specific fluorescence, tryptophan and tyrosine specific fluorescence to detect the changes in the protein's micro-environment, Carbonyl content (CC) and Nitroblue tetrazolium (NBT) assays for the estimation of ROS. Secondary structural changes were investigated using circular dichroism and FT-IR. Formation of aggregates were confirmed by ThioflavinT assay and electron microscopy. We further performed the *in silico* study with AutoDock to evaluate the potential modification sites on fibrinogen. The role of glycol-nitro oxidatively modified fibrinogen in disease pathogenesis has been suggested. Further studies are being conducted to evaluate the role of modified fibrinogen in diabetes mellitus and its secondary complications.

Key words: Fibrinogen; Glycation; Oxidative Stress; Advanced Glycation End Product; Diabetes Mellitus

BCH-283 POSTER

Interleukin-6 Serum Levels in Age-Related Macular Degeneration Patients in North-Indian Population

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Age-related macular degeneration (AMD/ ARMD) is the 3rd leading cause of blindness in people >60 years of age, impacting ~200 million people worldwide and accounting for 6–9% of legal blindness globally. Interleukin-6 (IL-6) have been found to be elevated in the serum/ocular tissue/fluids of patients with AMD, either systemically or locally. This study has determined blood serum levels of IL-6 a north Indian cohort of AMD patients and age match controls. **Methods**: Concentration of IL-6 in fifty unrelated AMD cases and fifty controls serum samples have been determined with the help of commercially available ELISA kits (Cayman chemicals IL-6 ELISA kit [human], Catalogue No. PG-2010H). **Results:** The mean concentration of IL-6 levels in AMD patients and age match controls were 27.4 (SD=18.993) and 17.5197 (SD= 2.8323) respectively. **Conclusion**: The results showed that IL-6 levels in AMD patients were significantly elevated as compared to those of controls.

Key words: AMD, IL-6, ELISA

BCH-284 POSTER

Functional Characterization of a Novel Co-Chaperonin Prefoldin Complex in Proteostasis of Artemisinin-Resistant *Plasmodium falciparum*

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The fundamental research on Prefoldin subunits has demonstrated their enormous potential and importance in maintaining cellular proteostasis and survival. However, the complete lack of understanding of the prefoldin complex in malaria parasites remains a big void in understanding of functional chaperones and co-chaperones. This study on *Plasmodium falciparum* PFD (*Pf*PFD) subunits characterizes the functional and biochemical roles of this complex. We demonstrate that the six subunits of *Pf*PFD are expressed as a complex in the cytoplasm of the trophozoite and schizont stages of *P. falciparum*. Further, molecular interactions within the complex were investigated using microscale thermophoresis and demonstrated that the orchestrated organization of *Pf*PFD subunits forms the active PFD complex. Additionally, *Pf*PFD complex was found to interact with α-tubulin-I through *Pf*PFD2 both *in vivo* and *in vitro* indicating *Pf* α-tubulin-I as one of the substrates of *Pf*PFD complex. Interrogation of chemotypes from FDA against *Pf*PFD, identified Biperiden (BPD) as a potential inhibitor of the complex. BPD restricts the formation of *Pf*PFD complex *in vitro* and demonstrates potent anti-malarial activity. Treatment with BPD disrupted the PFD complex and induced degradation of α-tubulin-I. Owing to the fact that PFD interacts with unstructured proteins, and merozoite surface proteins (MSP) are highly rich in intrinsically unstructured regions, we demonstrate that BPD treatment leads to degradation of *Pf*MSP1 *in vivo*. Interestingly, we observed upregulation of all PFD subunits in R539T artemisinin-resistant line. This study describes that the fundamental functions of *Pf*PFDs are conserved with other PFDs however, the *Pf*PFDs have diverged and specialized themselves to interact with the unique substrates present in the *P. falciparum* proteome. Thus, *Pf*PFDs provide a unique opportunity for drug development against the malaria parasite.

Key words: Malaria, Prefoldin, Cytoskeletal Proteins, Merozoite Surface Protein, Biperiden.

BCH-285 POSTER

A Novel Cannabidiol Derivative, CS-20, Exerts Antitumoral Activity against Colorectal Cancer via ERK-Mediated Autophagy/ER-Stress Axis

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Cannabidiol (CBD), a major nonpsychoactive constituent of cannabis, is considered an antineoplastic agent based on its in vitro and in vivo activity against tumor cells. Here, we have shown that CS-20, a novel semi-synthetic derivative of CBD, induced cell death of colorectal cancer cells more effectively than CBD, independent of cannabinoid and vallinoid receptor activation. Western blot analysis revealed the coexistence of autophagy and apoptosis. We demonstrated that CS-20 activates autophagy through ERK1/2 activation. Additionally, CS-20 elicits an endoplasmic reticulum (ER) stress response, characterized by the initiation of inositol-requiring ER-to-nucleus signal kinase-1 (IRE1), eIF2α, and CHOP-mediated signaling cascades. Furthermore, CS-20 induces downstream activation of the pro-apoptotic c-Jun N-terminal kinase (JNK) pathway, leading to HCT-116 death. In addition, we showed that CS-20 reduces mitochondrial membrane potential and activates the intrinsic apoptotic pathway in colorectal cancer cells. CS-20 increased the generation of reactive oxygen species (ROS). Our study revealed an intricate interplay between apoptosis and autophagy and ER-stress in CS-20 -treated colorectal cancer cells and highlighted the value of the potential use of CS-20 as an antineoplastic agent.

Key words: Cannabidiol, C-Jun, N-terminal kinase, Endoplasmic reticulum, Reactive Oxygen Species, Autophagy

BCH-286 POSTER

Myocilin and Cytochrome P450 Gene Screening in North-Indian Juvenile Open-Angle Glaucoma Patients

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The goal of this research was to look for *MYOC* and *CYP1B1* gene variations in individuals with juvenile open-angle glaucoma (JOAG) from northern India. We used Sanger sequencing to examine the coding areas of *MYOC* and *CYP1B1* genes in 80 non-related patients with JOAG and 100 controls. PCR-direct DNA sequencing discovered eleven missense variants, one frameshift variant, and five synonymous or neutral variants inside the *MYOC* gene, and eighteen missense, three nonsense, and two synonymous variations inside the *CYP1B1* gene. Five novel sequence changes (p.G122A, p.R136I, p.S173T, p.K216I, and p.R200KTer*15) in the *MYOC* gene and twelve novel sequence changes (p.S131I, p.R183P, p.S206T, p.D218H, p.E220*, p.S226T, p.E230*, p.S282I, p.A295S, p.D316Y, p.E318K, and Q20=) in the *CYP1B1* gene have been registered at the National Center for Biotechnology Information (NCBI). Pathogenic MYOC variations were reported in 6.25% (5/80) cases and pathogenic *CYP1B1* variations were reported in 32.5% (26/80) cases. Digenic representation of JOAG was observed in 1.25% (1/80) of the cases. Pathogenic *CYP1B1* variations are the major cause of juvenile open-angle glaucoma in our study population, while pathogenic *MYOC* variations are responsible for a minor fraction of JOAG. This study augments the mutation spectrum of the *MYOC* and *CYP1B1* genes, provides population-specific information, and aids in better understanding the underlying lesions of the disease.

Key words: Juvenile Open-Angle Glaucoma, Glaucoma, Myocilin, Cytochrome P450

BCH-287 POSTER

To Determine the Efficacy of Some Common Agrowaste for Arsenic Removal from Water

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Arsenic is a metalloid that induces a number of harmful effects on both plant and animal system. The primary route of exposure of arsenic is through drinking contaminated ground water. Therefore, a sustainable method of eliminating arsenic is required. In the present study eight different types of easily accessible agricultural waste from plant source that can be used for the removal of arsenic from aqueous media is tested for its efficacy. The genotoxicity and cytotoxicity caused by arsenic in plant and animal test models both before and after the bio-sorption procedure by organic adsorbents has been evaluated. ICP-OES was used to quantify arsenic. *Allium cepa*, a robust plant test system, was used to determine the chromosomal aberration and mitotic index (MI) before and after the bio-sorption process. The root length inhibition were investigated over a period of 14 days. Furthermore, in order to determine the degree of biosorption and its impact on survivality and reproductive potentials in the animal test model, acute toxicity tests in the zooplankton *Daphnia magna* were carried out. The findings demonstrates that efficiency and time of exposure dependents on the type of agricultural waste. In the case of citrous agrowastes, the highest adsorption of 94–95 percent was attained after 15–30 min, for other adsorbents equilibrium was attained after 60 mins. The results also showed that arsenic-exposed *A. cepa* roots had increased chromosomal aberration and a significantly lower mitotic index than the control. The prevalence of different chromosomal anomalies was found to be rather high in arsenic treated roots.These observation could be reverted after bio adsorption of arsenic. The results of the acute toxicity test in *Daphnia magna* also reveal the hazardous effect of arsenic after a period of 48 hours. However, the dapnids exposed to a solution treated with citric agricultural waste shown significantly lower survival rates compared to other treatment groups. The findings suggested that agricultural waste with citric properties removes arsenic more effectively. However, in contrast to other chosen adsorbents, citrus agrowaste do not promote Daphnia magna survivility.

Key words: Bio-Sorption, Allium cepa, Mitotic index, Chromosomal aberrations, Daphnia magna

BCH-288 POSTER

In vitro and In vivo Evidence of Olea Ferruginea Ameliorating $AlCl_3$-Induced Cognitive Impairment in Rats

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Olea ferruginea, also known as Khao, is being used traditionally by the tribals for inflammation, fever, epilepsy, and for enhancing memory. Our study aims to assess the antioxidant and anti-Alzheimer activity of *Olea ferruginea* using *in vitro*, *in silico*, and *in vivo* approaches. We have evaluated the *in vitro* free radical scavenging and phenolic content assays of aqueous (OF-W) and methanolic (OF-M) extracts of *Olea ferruginea*. Moreover, the inhibitory activities of enzymes [acetylcholinesterase, butyrylcholinesterase, glycogen synthase kinase-3-beta (GSK-3-β), Rho kinase (ROCK II), and lipoxygenase (LOX)], and oxidative stress parameters (malondialdehyde, nitric oxide levels, and catalase activity) was also studied in the hippocampus and cerebral cortex regions. Histopathological changes in the hippocampus and cerebral cortex regions of the rat's brain were also evaluated. OF-W fraction of *Olea ferruginea* demonstrated substantial radical scavenging activity as compared to OF-M. The phytochemical analysis showed more flavonoid and phenolic contents in OF-W and OF-M extract as compared to other fractions. GC-MS analysis of OF-W and OF-M fractions shows multiple compounds. Based on *in vitro* data, the OF-W and OF-M fractions (50 and 100 mg/kg, p.o.)

were selected for *in vivo* study in $AlCl_3$-induced cognitive impairment in male Wistar rats. Morris water maze test was used for the assessment of cognitive function on the 5th, 16th, 26th, and 42nd day of the experiment. OF-W and OF-M fractions inhibited dose-dependently the $AlCl_3$-induced cognitive impairment by decreasing the oxidative stress, enhancing cholinergic function, and inhibiting the expression and activity of GSK-3-β, ROCK II, and LOX enzymes. Thus, the results suggest an anti-Alzheimer ability of OF-W and OF-M fractions of *Olea ferruginea*.

Key words: Olea Ferruginea, $AlCl_3$, Oxidative Stress, Cholinesterase, Histopathology

BCH-289 **POSTER**

Vibrio cholerae Cytolysin: Potential Connection between Lipid Metabolism, Cell Death and Cell Survival

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Pore-forming protein toxins are membrane-damaging cytolytic proteins, which are expressed by a wide range of organism. These proteins have the ability to make pores in their target cell membrane and thus they alter the permeability of the cell membrane, which generally leads to cell death. Autophagy is the process by which sometimes cell try to survive. We are working with one of the major pore-forming toxins, *Vibrio cholerae* cytolysin (VCC). It has already been reported that upon VCC treatment, autophagy is getting activated, which helps the cell to survive from the damaging effect of the toxin. However, how the autophagy has been triggered is not known yet. One of the PFTs, aerolysin, activates inflammatory mediator caspase-1, which can lead to the activation of lipid metabolic pathways and it eventually helps the cell to survive from damage caused by PFT. In our study also we are interested in looking at whether inflammatory mediator and lipid metabolism play any role in induction of autophagy in VCC-treated cells. Our study is mainly focused on intestinal epithelial cells, as the primary infection site of *Vibrio cholerae* is intestine. We observed that upon pre-treatment of cells with caspase-1 and NLRP3 inflammasome inhibitors, there is a significant decrease in cell death caused by VCC, suggesting that NLRP3 inflammasome and caspase-1 are playing a significant role in VCC-mediated cell death. Further, we have seen a clear reduction in cholesterol biosynthesis in VCC-treated cells. We are further exploring how the cholesterol-depletion and inflammasome activation is related and whether they are instrumental to activate autophagy in VCC-treated cells.

Key words: Pore-Forming Toxin, VCC, Autophagy, Inflammatory Mediators

BCH-290 **POSTER**

Lateral noncanonical E-Cadherin associated Basal Supra-Cellular Actomyosin Cortex Contributes to Tissue Compression in Drosophila Pupal Tracheal Epithelium

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Epithelia is the most common tissue type in animals that compose the primary organs, and the mechanisms involved in the formation and maintenance of a polarized epithelium are tightly regulated. However, the mechanisms of organ degradation are least studied at the cellular level. We believe that the signals involved in organogenesis are down-regulated during organ disassembly. Changes in all three layers of epithelium are crucial as they trigger the degeneration process, leading to organ degradation. We mainly focus on the cellular and supra cellular mechanisms involved in tissue degeneration by using Drosophila trachea as our model. In the Drosophila trachea, in addition to the classical zonula adherens (ZA), we have discovered a novel non-canonical belt of lateral punctate E-cadherin (LA). The LA molecules are present below the septate junction close to the basal edge of the Dlg domain. The belt of LA is functional and shows enrichment of all the ZA components such as α, β, and p120 Catenin. We found two distinct actomyosin cortices present in the ZA and LA. Actin organizers Rho1 and CDC42 are present at LA and regulate the

initiation of basal actin cortex in the third instar larval trachea (L3). In Mid L3(110h), actin bundles start from the LA and the cytoplasm. In wandering L3(115h), thick lateral F-actin belt forms at LA, which provides a scaffold for cytoplasmic actin incorporation. The F-actin belt disappears and the supra cellular actin cables form in 2h pupa. Reduced basal F-actin in Rho1, CDC42, ROK, and MRLC knockdown suggests that the basal actomyosin cortex is mediated by the Rho1-ROK-MRLC pathway. Alternate bands of α -actinin and phospho-myosin accumulate on the cables confirming the formation of stress fibers in 2h pupal trachea which contribute to force generation and transmission that lead to tissue compression in the posterior pupal trachea. The loss of basal actomyosin cortex leads to a partial loss of tissue compression in the posterior pupal trachea thus suggesting its supporting role in tube compression. Currently, we are focusing on the other physiological aspects of the basal actomyosin cortex with respect to the ECM of the pupal trachea.

Key words: Organ Degradation, Epithelia, Zonula adherens, Lateral E-Cadherin, Actomyosin cortex, Stress fibers, Small GTPases

BCH-291 **POSTER**

Improved Assay Design to Match the Constantly Evolving Cancer Genetic Landscape: A BCR-ABL1 Story

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Chronic myelogenous leukemia (CML) is a myeloproliferative neoplasm that is associated with the BCR-ABL1 fusion gene located in the Philadelphia chromosome. We report the case of a 28-year-male who was diagnosed with CML based on his physical examination and peripheral blood smear test indicative of hypercellular marrow with myeloid hyperplasia including 1.4% blasts and 5.2% basophils. Molecular testing of BCR-ABL1 fusion using qPCR based on Europe Against Cancer (EAC) assay showed the absence of fusion even after repeating it twice. On the contrary, cytogenetic G-band karyotyping analysis identified a shorter 22 chromosome showing 46, XY, t(9;22)(q34;q11.2). Fluorescence in situ hybridization (FISH) analysis also showed BCR/ABL1 fusion positivity in 98% of the interphase cells indicating the presence of t(9;22). Sanger sequencing analysis of that region revealed the deletion of 34 nucleotides that included the forward qPCR BCR primer annealing site from EAC design and an insertion of 13 nucleotides. Similar cases have been reported earlier also wherein Philadelphia (Ph+) CML patients with a major breakpoint cluster region (M-BCR) rearrangement was detected by FISH and classical RT-PCR but not with qRT-PCR using the standardized EAC protocol. To quantify BCR-ABL1 levels in this patient, we used the TRUPCR kit specifically designed to identify the presence of the inframe fusion caused by the rare phenomenon of deletion at the EAC primer binding site. BCR-ABL1 level was found to be 47% on IS Scale using the kit. The variants of BCR-ABL1 are an important factor to determine whether the first line TKI is receptive to CML patients or not. Thus we recommend the use of the TRUPCR kit in cases where negative results are obtained with the EAC protocol and are positive with FISH to avoid reporting any false-negative case which may have an impact on deciding treatment for the CML patients.

Key words: CML, BCR-ABL1, Mutation, Europe against Cancer, Molecular diagnostics

BCH-292 POSTER

Crosstalk between Phospholipid Synthesis and Peptidoglycan Enlargement is mediated via Cell Wall Hydrolase Regulation

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The cell envelope of a Gram-negative bacterium consists of the inner membrane (IM), outer membrane (OM), and an in-between periplasmic space containing peptidoglycan (PG) layer, with an essential structure-function relationship. During cell expansion, a coordinated synthesis of each layer is required to maintain cell envelope integrity, which is a challenging task since these envelope components are synthesized by distinct protein complexes. Currently, how such coordination is achieved is unclear. We find that unregulated PG hydrolytic activity of an elongation-specific PG hydrolase, MepS in *E. coli* is lethal when cellular fatty acid (FA) synthesis is inhibited. Further, using genetic and biochemical methods, we demonstrate cellular availability of FA or phospholipid controls the activity of a periplasmic protease complex NlpI-Prc towards MepS degradation. Overall, our results suggest a coordinated expansion of the PG sacculus with that of plasma membrane results in balanced triple-layered envelope biogenesis in Gram-negative bacteria.

Key words: Peptidoglycan, Pg Hydrolase, Meps, Nlpi

Modulation of Hedgehog Signalling Pathway By C-AMP-Dependent Phosphodiesterase 4 in Breast Cancer

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Relapse and recurrence of breast cancer makes the treatment of the same challenging, requiring new strategies and approaches for local and systemic therapy. Understanding different signalling pathways that play pivotal role in tumorigenesis and disease progression might bring in treatment options that can deal with the relapse of the cancer. One such important pathway in tumorigenesis is the Hedgehog (Hh) signaling pathway that also plays crucial role in maintenance of cancer signaling. Researchers have demonstrated that the use of traditional inhibitors of the Hh pathway like cyclopamine, is limited due to the gain of function mutations in the Smoothened (Smo) binding pockets. Altering the function of the GLI transcription factors bypassing the upstream regulators is therefore of key importance. In this study, we have observed the how cyclic nucleotide signaling is associated with Hh signaling and how its downstream modulation by phosphodiesterase (PDE), modulated Hh signaling. Our study reflected that PDE4 expression is dominant in the breast tissues and Rolipram, a PDE 4 inhibitor increased the intracellular level of cAMP and Protein Kinase A, modulating the ubiquitination of GLI transcription factors, key effector of the Hh signalling pathway, thereby altering the activator-repressor function of the GLI transcription factors. PDE4 inhibitor not only modifies the activator-repressor function of GLI transcription factors, but also provides a way to modulate Hh signalling pathway bypassing key upstream regulators.

Key words: Phosphodiesterase 4, Hedgehog Signalling, Gli, Breast Cancer

BCH-294 POSTER

Pin4, a Homolog of Human Parvulin Pin4, may be Required for Growth and Development Processes in *Dictyostelium discoideum*

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Parvulins belong to the family of peptidyl prolyl *cis/trans* isomerases (PPIases) which regulate various cellular processes by recognising proteins/peptides with non-phosphorylated or phosphorylated Ser/Thr-Pro moieties and accelerate *cis/trans* interconversion. Human parvulin having a numerous role in biological processes has shown that its dysregulation has growing number of pathogenesis and diseases. A range of developmental and differentiation abnormalities are found associated with human parvulin either directly or indirectly. *Dictyostelium discoideum*, a unicellular haploid amoeba which can develop into multicellular fruiting body upon starvation, has two parvulins, PinA and Pin4. Towards investigating the function of Pin4, bioinformatic analysis showed Pin4 has similar domain architecture and amino acid sequence with human parvulin Pin4 which is known for its diverse role in transcription, ribosome biosynthesis and chromatin remodeling etc. Pin4 has charged amino acids at N-terminal followed by PPIase domain. Temporal and spatial mRNA expression analyses showed that *pin4* is expressed throughout growth and development and are localised only in the prestalk region of developed structures. Overall, based on functional analysis using mutants of *pin4* showed that *pin4*mutants exhibited decreased growth rate, low germination rate and developmental defect such as delayed aggregation, small slug formation, delayed fruiting body formation with abnormal spore morphology suggesting that Pin4 may be important in growth, development and cellular differentiation.

Key words: Peptidyl Prolyl Cis/Trans Isomerases, Parvulins, Pin4, *Dictyostelium discoideum*

BCH-295 POSTER

Characterization of Calcium Binding C2 Domain Containing Merozoite Surface Antigen of *Plasmodium falciparum* mediating Red Blood Cell Invasion

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Invasion of red blood cells by *Plasmodium falciparum* merozoites is governed by multiple receptor-ligand interactions which are critical for bridging the two cells together. The critical function of these ligands for invasion and their direct exposure to the host immune system makes them a lucrative vaccine candidate. However, the polymorphic and redundant nature of crucial invasion ligands has road blocked the development of an effective blood stage malaria vaccine. This necessitates the discovery of new adhesins with less redundancy, involved in the binding of merozoite to the red blood cell and mediate invasion into it, that can serve as promising vaccine candidates. Here we have identified a novel C2 domain containing membrane antigen (*Pf*C2DMA) that is conserved throughout the *Plasmodium* species and has a membrane targeting C2 domain at its extreme N-terminal region. Recombinant C2 domain ($C2_{dom}$) was expressed heterologously in E. coli and purified to homogeneity using affinity chromatography. $C2_{dom}$ exhibited specific binding to Ca^{2+} ions but not to Mg^{2+} ions. *Pf* C2DMA is localized to the surface of merozoite and recombinant $C2_{dom}$ binds to the surface of human red blood cells in the calcium dependent manner. RBC receptor modifications by treatment with trypsin, chymotrypsin and neuraminidase showed that binding of $C2_{dom}$ to RBC surface is neuraminidase sensitive. Mice antibodies raised against $C2_{dom}$ of *Pf* C2DMA showed invasion inhibitory effects. In the presence of specific antisera against merozoites were found attaching to RBCs which failed to invade successfully. Thus, our findings suggests that $C2_{dom}$ of *Pf*C2DMA binds to surface of red cell in a calcium dependent manner, advocating a plausible role in invasion and can serve as a potential novel blood stage vaccine candidate.

Key words: Malaria, Merozoite, Invasion, Calcium, Vaccine, C2 Domain

BCH-296 POSTER

Elucidating the Mechanism of TDH-Mediated Immunological Responses

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Vibrio parahaemolyticus is a major food-borne pathogen and a leading cause of several life-threatening diseases, primarily causing acute human gastroenteritis. There have been several disease outbreaks of this pathogen in the past, which makes studying this pathogen and its associated virulence mechanisms more important. Among several virulence determinants, thermostable direct hemolysin (TDH) is the major factor involved in its pathogenesis. TDH belongs to a class of pore-forming toxin. It has been known that TDH induces potent cytotoxicity in diverse cell types. However, role of TDH in modulation of other cellular responses were not explored yet. In this study we are interested in exploring the immunological aspect of TDH in modulation of innate immune cells, such as in macrophages. We have observed that TDH can bind to the surface of macrophages and induce production of various pro-inflammatory mediators excluding nitric oxide in macrophages. This suggests possible involvement of a pattern recognition receptor (PRR) for binding of TDH on macrophage cell surface. Among all the PRRs, Toll-like receptors (TLRs) are one of the most important PRRs for the recognition of bacterial ligands. Therefore, we started exploring whether TLR(s) are responsible in TDH recognition. We observed an upregulation of expression of TLR2 and TLR4 at the gene level as well as in protein level in TDH -treated RAW264.7 macrophages, suggesting that TLR2 or TLR4 could be important for TDH recognition. Further, we also observed that TDH can induce pro-inflammatory cytokine production in vivo. We administered TDH to BALB/c mice intra-peritoneally and observed a high pro-inflammatory response generation in mice with even small doses of TDH. Apart from that, our preliminary observation suggest that TDH probably affect polarization of macrophage from M1 to M2 state. Further, we are probing the underlying signalling mechanism for modulation of macrophage responses by TDH.

Key words: Pore-Forming Toxin, Tdh, Macrophages, Toll-Like Receptors, Innate Immune Response, Pro-Inflammatory Responses

BCH-297 POSTER

Incidence of Hypovitaminosis D In PCOS Kashmiri Women

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Polycystic ovary syndrome PCOS is a common endocrine disorder in reproductive women with an incidence of up to 10%. PCOS is a disease characterized by ovulatory dysfunction, hyperandrogenism and polycystic ovaries. PCOS is a complex syndrome often leading to infertility. Vitamin D deficiency has been found of being significantly associated to a surfeit of many diseases including PCOS. Studies related to vitamin D and PCOS are less in Kashmir valley and more less is known about the association of PCOS and Vitamin D. Hence in the present study we sought to explore the incidence of hypovitaminosis D in Kashmiri PCOS women. In this study 385 Kashmiri PCOS women who met the inclusion and exclusion criteria were included. All the PCOS patients were outpatients of GMC associated LD hospital Srinagar. The PCOS patients visiting the OPD of Obstetrics and Gynecology in LD hospital were recruited in the study. Diagnosis of PCOS was made as per the revised Rotterdam PCOS consensus criteria. Ethical approval and written informed consent of all participants was obtained before the initiation of study. From Dec 2020 to October 2021, 385 patients at OPD of LD hospital were diagnosed with PCOS. The incidence of hypovitaminosis D which includes both vitamin D deficiency and vitamin D insufficiency in PCOS Kashmiri women was found to be in a higher proportion of about 65.6%. Most of the PCOS patients visiting GMC associated LD Hospital were diagnosed with PCOS according to Rotterdam criteria. Most of PCOS patients were young school going girls. Stress was found to be the main factor contributing to

the development of PCOS symptoms. Lack of education and unawareness about the menstrual irregularities was found to be important contributing factors to PCOS. Among the 385 processed blood samples it was concluded that nearly 65% PCOS Kashmiri women under study at LD Hospital were vitamin D deficient which represents an active area of energetic research. High prevalence of hypovitaminosis D in PCOS Kashmiri women indicated that impaired vitamin D status may act as an important risk factor in the development of PCOS and its metabolic and hormonal abnormalities.

Key words: PCOS, Vitamin D, Hypovitaminosis

BCH-298 POSTER

Understanding the Contribution of Liquid-Liquid Phase Separation in 3d Chromatin Organization

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Compartmentalization of the cell nucleus plays an important role in the regulation of genome function by sequestering the molecular machinery in the form of transcription factories, cajal bodies, polycomb bodies, nuclear speckles etc. Recent findings have implicated the role of liquid – liquid phase separation (LLPS) in nuclear compartmentalization. LLPS is driven by molecular crowding and multivalent interaction of proteins and DNA. Chromatin, being polymeric in nature and having the ability to form multivalent interactions, can also undergo LLPS. But it remains to be elucidated how phase separation property of chromatin modulates its 3D organization. Here we used perturbation in molecular crowding as a tool to understand the role of LLPS in chromatin organization using high throughput chromosome conformation capture, HiC. We found that genome organization gets altered upon increasing the molecular crowding. On reversing the crowding conditions the genome organization gradually reverts to the normal, implying that genome organization is regulated by LLPS.

Key words: Compatmentalization, LLPS, Molecular Crowding, 3D Genome Organization

BCH-299 POSTER

Genome Editing By in Vitro Reconstituted CRISPR Cas9 System

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The CRISPR-Cas9 system is the most remarkable recent breakthrough in modern biology. An advantage the CRISPR-Cas9 system offers over other techniques like ZFN and TALEN is the relative simplicity in design and construction of vectors. CRISPR technologies are now considered more accurate, easy to use, and multi-potential. Despite the remarkable advances in CRISPR, several limitations and concerns still exist. Integration of plasmid encoding Cas9 and guide RNA into genome can result in off-target effects, which is still a major concern. Here we have reconstituted an in-vitro CRISPR-Cas9 system for desirable genome editing to minimize off-target effects. The study involves the reconstitution of Cas9-SgRNA complex in vitro and estimation of its cutting efficiency on DNA and nuclei by PCR based assay. The amplification around the target sites is inversely proportional to the efficiency of in vitro reconstituted CRISPR Cas9 system. We observed that Cas9-SgRNA complexes used in study cleaved the respective target efficiently. The distinctive feature of these complexes is they do not last longer within the cells, hence, minimizes off-target effects. In future, this system will be used to edit different genomic regions of interest within cells.

Key words: CRISPR Cas9 System, Genome Editing

BCH-300 POSTER

Functional Profiling of Pharyngeal Microbiome in Respiratory Tract Infections

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Human microbiome has gained much attention recently due to its extensive involvement in infections and other pathogen-related diseases in addition to its significant role in the maintenance of overall health. Additionally, probiotic supplementation as an adjuvant treatment against infections has been momentous in current clinical research and practice because the overall effectiveness of antibiotics continues to decrease due to the emergence of drug-resistant pathogens. Studies have reported approximately 25-40 families of bacteria, archaea, fungi inhabiting the human nasal, oral and pharyngeal cavities. Although the number is ever increasing owing to the recent advances in metagenomic research techniques especially high-throughput sequencing technology. Due to rapid urbanization, both upper and lower respiratory tract complications are becoming increasingly prevalent in the Asia-Pacific region and account for one third of patient attendance in a general hospital. Multiple social and environmental factors found to be associated with RTI morbidity and mortality like poverty, malnutrition, low birth weight, inadequate breast feeding, poor housing conditions, indoor and outdoor air pollution, seasonality, and lack of access to preventive (including immunization) and curative services. A study from Assam identified soaring incidence of ARI among under-fives and indicated specific socio-demographic, nutritional and environmental features as the modifiable risk factors. Another study from Delhi also reported high prevalence of RTI in the population and that the severity declined with increasing age (Gupta et al., 1999). A cross sectional study from Ahmedabad reported that the age group of 4-5 years were mostly affected (47.3%). A community-based study from Karnataka and Tripura reported high incidence of pneumonia among infants. Statistically significant association was found between social class and ARI. High-throughput DNA sequencing of the 16S rRNA gene followed by composition and diversity analysis has been utilized to decipher the microbial content in the collected clinical samples (Jovel et al., 2016). Another similar analysis suggests that the changes in the lower respiratory tract microbiome are correlated with age.

Key words: Microbiome, Respiratory tract infections

BCH-301 POSTER

Quantitative Real-Time Analysis and Risk Factor Determination among Patients with Active Hepatitis C Virus Infection

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Introduction: Infection with Hepatitis C virus (HCV) is a major cause of liver disease eventually leading to liver cirrhosis and hepatocellular carcinoma in about 15% to 30% of chronic cases. Worldwide 58 million people have chronic hepatitis C virus infection and 1.5 million new infections appear every year. It is utmost important to know the disease prevalence and transmission model to design specific preventive measures and deduce the biology and interaction pattern of pathogen. **Methods:** The present study aimed towards the determination of seroprevalence and viral load among HCV patients attending the Medicine Out Patient Department (OPD) of Government Medical College (GMC), Jammu. The patients were enrolled in the study after obtaining their consent. About 16315 patients were screened for anti-HCV antibodies using third-generation ELISA. Viral RNA was extracted and quantified from the positive samples and viral load analysis was done. We also administered a self-designed questionnaire to collect all the relevant details like age, gender, mode of transmission, medical condition etc., for risk factor analysis. **Results:** Out of 16315 patients screened, 142 were reported to be positive amounting to seropositivity of 0.8%. The viral RNA was detected in 37 patients stating an active infection in 26% of positive patients. Among the 37 HCV RNA positive patients, the average age was reported to be 44 years with male preponderance (2.4:1). 23 patients were categorised under high viral load while 14 under low viral load. The major cause of HCV transmission appeared to be surgery and intravenous drug use (IVDU). **Conclusion:**

The present study spans a period of two years and five months testifying a seropositivity of 0.8 % and 26% active infection cases. The IVDU and surgery appears to be the predominant cause of transmission. Thus, it is very important to conduct routine blood tests for HCV especially of those which belong to high-risk group like IVDUs. We also recommend regular counselling, community surveillance and periodic epidemiological studies to prevent HCV.

Key words: Hepatitis C Virus, Viral Hepatitis, Active Infection, Mode of Transmission, Seroprevalence

BCH-302 POSTER

Genetic analysis of Fragile-X-Syndrome from an Intellectual Disability Cohort

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Fragile–X-Syndrome (FXS) is the most common inherited form of ID and the second most common cause of comorbid autism. It is a loss-of-function neuro-developmental disease, wherein expansion of CGG/CCG trinucleotide repeats in exon 1 of the X-linked *FMR1* gene reach above 200 in number, a diseased threshold hallmark of FXS. Expansion causes epigenetic alterations in DNA methylation, histone markers, and chromatin remodelling, which all leads to the heterochromatin-mediated transcriptional silencing of *FMR1* and loss of the gene product fragile X mental retardation protein (FMRP). Most of the symptoms of FXS overlap with the associated symptoms of other neuropsychiatric diseases such as ASD, epilepsy, ADHD, Soto's syndrome, Prader-Willi syndrome etc. Thus, the diagnosis of FXS patients on the basis of their physical and behavioral manifestation is very difficult. In order to avoid false positive diagnosis, preliminary testing for the detection FXS is very important. In the present study, molecular diagnostic tools are used for a better detection of FXS, and to estimate the prevalence of FXS in subjects with intellectual disability from the region Kashmir. In this study, 1135 individuals with irregular physical manifestations and behavioral symptoms, were assessed for neuropsychological evaluation including IQ assessment and ASD criteria. Based on low IQ scores and ASD questionnaire tools, 300 subjects were found intellectually disabled (ID). Conventional-PCR and triple-primer PCR followed by capillary electrophoresis were used to measure the CGG trinucleotide length in the gene. Methylation specific-PCR (MSP) was used to determine the methylation status of the fmr1 gene. Here, we report 4 females and 3 males were premutated, 5 males and one female were fully mutated (FXS), 1 male subject showed mosaicism and 2 females were in grey zone. Remaining subjects were normal, usually with an average of ~30 CGG trinucleotide repeats. The outcome of this study was to evaluate a cost effective molecular diagnosis of FXS and move it to public health action in Kashmir, important for better understanding the genetic history of FXS and its recurrence risks to their families, reproductive counseling, neurological and endocrine follow-up, and treatment for female carriers due to the increased risk of primary ovarian insufficiency.

Key words: Fragile X Syndrome, Intellectual Disability, Autism, Trinucleotide Expansion, DNA Methylation

BCH-303 POSTER

Unravelling Anti Apoptotic Role of BAG3 in Malignant Phenotypes

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Impaired apoptosis is a predominant cancer cell hallmark that not only aids in attainment of higher grades of malignancy but also aids resistance against available radio or chemotherapies. Therefore, it's mandatory to gain in depth knowledge of anti apoptotic strategies displayed by cancer cells to improve prognosis in cancer patients Curtailment in apoptosis is predominantly achieved by over expression of anti apoptotic proteins & one such protein is BAG-3. BAG-3 or Bcl 2 associated athanogene 3 is an anti apoptotic/pro cancerous protein characterized by presence of various domains motifs (WW domain, PXXP motif BAG domain) that allows it to play pivotal pro cancerous roles in

signaling pathways. encompassing proliferation, apoptosis, survival, metastasis so forth. While as anti apoptotic activity of BAG-3 pertaining to BAG domain has been well documented, this protein still is under research vigilance considering its massive anti apoptotic potential, suggesting its putative involvement in multitude of apoptotic pathways via its other two domains. With regard to this, we hypothesize BAG-3 via its WW domain can be a putative partner of proline rich p66shc that plays indispensable role in oxidative stress mediated apoptosis.(It is noteworthy to mention interaction between WW domain proline rich motifs is well documented operating numerous signaling cascades in normal diseased phenotypes p66shc upon sensing oxidative stress in the cell gets phosphorylated at serine located at position 36 causing its mitochondrial translocation culminating in release of cytochrome c. Since BAG-3 is anti apoptotic we anticipate via its interaction with p66shc must be curtailing apoptosis initiated under oxidative stress conditions. Mechanistic study in this regard can bring to light one anti apoptotic strategy adopted by cancer cells to curtail apoptosis initiated under oxidative stress conditions that can bear fruitful therapeutic intervention.

Key words: BAG-3, P66SHC, Apoptosis

BCH-304 POSTER

The Role of Pura Binding Protein in Fragile X Premutation rCGG Mediated Neurodegeneration

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Fragile X-associated tremor/ataxia syndrome (FXTAS) is a recently recognized neurodegenerative disorder in fragile X premutation carriers with *FMR1* alleles containing 55-200 CGG repeats. Various studies including our own, found that fragile X rCGG repeats are sufficient to cause neurodegeneration and that the rCGG repeat binding proteins Purα and hnRNP A2/B1 can modulate rCGG–mediated neuronal toxicity. To explore the role of Purα in rCGG–mediated neurodegeneration further, a proteomic approach identified more than 100 proteins that interact with Purα. Of particular interest is Cdk5/p35 complex, a well established protein in various neurodegenerative diseases. While the need of such interaction has already been established in many processes and nervous system, the requirement for these interactions in mediating rCGG induced toxicity has yet to be clarified. Therefore, we asked whether Cdk5/p35 complex is able to modulate rCGG mediated toxicity. To confirm the association between Cdk5/p35 and Purα, we constructed GST tagged clones of Cdk5 and Dp35 genes respectively in pGEX4T2, a bacterial expression vector. In the present study, we performed a pull-down experiment in which we show that Cdk5 and not Dp35 interacts specifically with Purα. To further explore the role of Cdk5/Dp35 complex in mediating rCGG neuronal toxicity, we used *Drosophila* as a model organism and its eye phenotype as a measure of genetic interaction indicator. Interestingly, it is found that Cdk5 requires Dp35 for its functioning and this functional complex is able to modulate rCGG mediated neurodegeneration. In summary, through biochemical purification, we have identified fly Cdk5/Dp35 complex interaction with Purα is conserved between mammals and *Drosophila*. Furthermore, overexpression of Cdk5/Dp35 complex in *Drosophila* could suppress rCGG-mediated neurodegeneration. These findings strongly support a general mechanistic suggesting that aberrant activity of Cdk5/Dp35 complex as one of the contributor in the pathogenesis of FXTAS.

Key words: Neurodegeneration, FXTAS, Drosophila, CGG-Repeats, Neuronal toxicity

BCH-305 POSTER

Sequence, Structure, and Dynamics of P132H Mutant of Mpro from Omicron Variant

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Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a causative agent for COVID-19 disease. COVID-19 has a huge impact on global health and economic condition across the globe. SARS-CoV-2 is a single-stranded RNA virus, which has a high mutation rate due to the weak proofreading ability by its RNA dependent RNA polymerase (RdRp). As a result, new strains with higher virulence rates, transmissible potential, and the ability to evade existing therapy or vaccine are emerging. The main protease (M^{pro}) of the SARS-CoV-2, also known as 3 C-like protease ($3CL^{pro}$), is a crucial protease involved in digestion of polyprotein at eleven different sites and plays an important role on viral replication and its life cycle. M^{pro} is the only protease with FDA-approved drugs for COVID-19 treatment. Though the drugs that target M^{pro} appear to be effective, there is a possibility of mutations that may result in drug resistance. With that background, mutational scan for M^{pro} from Wuhan, Alpha, Beta, Delta, Kappa, Omicron and B.1.617.1 variants was performed. Among all the variants analyzed, P132H mutant of M^{pro} was observed to be predominant and specific to Omicron variant. Further modelling and Molecular Dynamics (MD) simulations of P132H M^{pro} revealed its significant impact on the dynamics of catalytic pocket, hence its possible role in the catalytic efficiency and drug binding.

Key words: Keywords: Sars-Cov-2, Main Protease (Mpro), Variants, P132h, Md Simulations.

BCH-306 POSTER

Pharmacological Investigation of Sesqueterpene Isoalantolactone as Potential Anticancer Chemotherapeutic Agent

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Sesquiterpenes are known to be the largest group of plant secondary metabolites.These compounds are prominently distributed in bryophytes, several angiosperms, a few gymnosperms and bryophytes. Sesquiterpenes and their derivatives are bio-synthesized in various plant parts including leaves, fruits and roots. These plant-based metabolites are mostly identified in the Asteraceae family. these are characteristically associated with plant self defence mechanisms having antiviral, antifungal and antibacterial activities. Past two decades, these compounds have been reported as health promoting compounds against a wide range of metabolic related diseases like diabetes hyperglycemia, neural disorders cardiovascular problems, and most importantly cancer. Here in this review article we have discussed the high of one sequiterpenes that is Isoalantolactone which is isolated from roots of Inula racemose which acts against various cancer and also has hepatoprotective, nephroprotective metabolic effects. It is highly potent against cancers like breast, lung, pancreatic, colorectal, brain and several others cancers. Predominantly, this review recapitulates the literature elucidating isoalantolactone while highlighting the mechanistic approaches associated with its potent anticancer activities such as modulating nuclear factor kappa (NF-kB) activity, inhibitory action against lipid peroxidation and retarding the production of reactive oxygen & nitrogen species (ROS&RNS).Non-communicable diseases (NCDs) are known as the main death cause worldwide.According to WHO ranking, 5 most prevalent killer cancers include breast, lung and bronchus, colon and rectum and uterine among women, and prostate, lung and bronchus, colon and rectum and urinary bladder among men. Increasing the awareness of basic causes of cancer and its risk factors can be effective in prevention of cancer. Based on researches over the past decades, cancer is explained as a multifactorial ailment and both environmental and genetics factors are involved in its occurrence and progression. Since past decade, the complex mechanism of cancer has been identified by advanced genetic techniques, proteomics, and bioinformatics. No significant success has been achieved in cancer treatment, and there is still a long way to cure cancer. Researchers are trying to find new therapeutic compounds with high efficiency and low side effects for fighting and defeating cancer.

Key words: Sesquiterpenes, Asteraceae, Hyperglycemia, Nf-Kb, ROS, NCDS

BCH-307 POSTER

Role of SATB Proteins in the Regulation of Intestinal Cancer Stem Cells

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The differential expression of chromatin organizers SATB1 and SATB2 has been reported in the development and progression of colorectal cancer (CRC). CRCs contain a rare population of cells characterized by self-renewal, multi-lineage differentiation, tumor-initiating capacity termed as cancer stem cells (CSCs) which constitute the regenerative fraction within the tumor. These are responsible for chemo- and radio-resistance culminating in disease relapse. It is widely known that the β-catenin/TCF-LEF pathway contributes to the development of CSCs and CRC carcinogenesis, however, the exact mechanism involving SATB family proteins is not known. The goal of the proposed study is to understand the role of SATB1/2 in regulation of pluripotency factors, CSCs and colorectal cancer progression by modulating SATB1/2 expression in organoids. It has been reported that SATB2 over-expression in normal colorectal epithelial cells induced stemness potential by altering the expression of CSC markers and can induce epithelial to mesenchymal transitions leading to metastasis. We show that SATB1 over-expression in colorectal cancer cell line modulates the expression of pluripotency factors. Further, a cholesterol-reducing drug, statin, is known to reverse the expression profile of SATB1 and SATB2 proteins in CRC cell lines. We show that rosuvastatin reverses the aggressive phenotype of CRC by affecting SATB protein expression *in-vitro* and *in-vivo*. Therefore, the study also aims to evaluate the effect of statin as an anti-cancer therapeutic agent and its effect on CSC markers.

Key words: Cancer Stem Cells, Colonoids, Satb Chromatin Organizers, Pluripotency Genes, Colorectal Cancer, LGR5 Stem Cell Marker.

BCH-308 POSTER

Understanding the Contribution of Liquid-Liquid Phase Separation in 3D Chromatin organization

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Compartmentalization of the cell nucleus plays an important role in the regulation of genome function by sequestering the molecular machinery in the form of transcription factories, cajal bodies, polycomb bodies, nuclear speckles etc. Recent findings have implicated the role of
Liquid-liquid phase separation (LLPS) in nuclear compartmentalization. LLPS is driven by molecular crowding and multivalent interaction of proteins and DNA. Chromatin, being polymeric in nature and having the ability to form multivalent interactions, can also undergo LLPS. But it remains to be elucidated how phase separation property of chromatin modulates its 3D organization. Here we used perturbation in molecular crowding as a tool to understand the role of LLPS in chromatin organization using high throughput chromosome conformation capture, HiC. We found that genome organization gets altered upon increasing the molecular crowding. On reversing the crowding conditions the genome organization gradually reverts to the normal, implying that genome organization is regulated by LLPS.

Key words: Compartmentalization, LLPS, Molecular Crowding, 3D Genome Organization

BCH-309 POSTER

Anti-osteoporotic activity and Phytochemical Screening of *Boerhavia Diffusa Linn.*

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Osteoporosis is a disease characterized by structural deterioration of bone, leading to bone fragility. It is commonly known as a silent disease because it does not manifest any symptoms in an individual until fractures are not reported. *Boerhavia diffusa* Linn. is a species of flowering plant pantropical in India and belongs to the family Nyctaginaceae. It is commonly known as Punarnava. The plant has immense therapeutic potential and has been typically used in various ailments like diabetes, syphilis, leukoderma, blood disorders, inflammation, liver-kidney disorders, and skin problems. The aim of this study is to find out the osteoanabolic activity of *B. diffusa* leaf extract and the phytochemicals promoting it *in vitro* set-up. For this study, MG-63, an osteoblast like cell line was considered. Ethanolic extract of *B. diffusa* leaves was prepared by using Soxhlet method. The cell proliferation was carried out through MTT assay and we calculated the effective concentration (EC_{50}) value of the phytochemicals. For the qualitative analysis of secondary metabolites, we performed Shinoda, Mayer's reagent, alkaline reagent and ferric chloride test to check the presence of secondary metabolites. For the quantitative analysis of phytoconstituents, we performed High-Performance Liquid Chromatography and estimation of the total flavonoids and phenolic contents was done using Aluminum chloride and Folin & Ciocalteu's phenol reagent method respectively. We found that the EC_{50} of ethanolic leaf extract of *B. diffusa* is 25µg. It promoted the cell proliferation of MG-63 cell line. We found the presence of secondary metabolites like flavonoids, alkaloids and phenolic compounds and observed the amount of flavonoids was maximum in the leaves of *Boerhavia diffusa*. Flavonoids and phenolic compounds have great assurance in the treatment of osteoporosis and improvement of bone health. Further, mechanistic understanding of anabolic action of secondary metabolites from *B. diffusa* on osteoblasts at gene expression level is underway.

Key words: Osteoporosis, Boerhavia Diffusa, Proliferation, Secondary Metabolites, Osteoblast, MG-63.

BCH-310 POSTER

Role of Neurodevelopmental Protein WDR62 in Neural Cancer

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Genes regulating early embryonic development are increasingly shown to play roles in diseases such as cancer and are also utilised by pathogens for their sustenance. In this context, our lab studies the roles of certain neurodevelopmentally important genes, called Microcephaly genes (MCPH genes), the loss of which leads to small brain phenotype in humans. Considering that the MCPH genes display low tissue specificity, it is unclear as to how the loss of function primarily results in brain developmental defects, whereas dysregulation of these genes is associated poor prognosis of cancers of various tissue origins. Moreover, the allelic heterogeneity of these genes, lack of correlation between phenotypic continuum and the severity of mutations alludes to additional non-mitotic roles for these proteins. In this regard, my work will demonstrate the novel role of one of the most commonly mutated MCPH gene WDR62 in glioblastoma (emphasis on neural cancer stem cells). For this, I have undertaken a systematic approach that employs quantitative methods in different model systems ranging cancer cell lines, glioma spheres and brain organoid.

Key words: Cancer, Neurodevelopment, WDR62, Brain Organoid

BCH-311 POSTER

Purification and Characterization of a 30 kDa Anticancer Protein from a Medicinal Plant of the Kashmir Himalayas: Towards Exploration of Therapeutically Active Proteins

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The conventional drugs used to cure various diseases have deleterious effect on normal cells and tissues of body along with increased chances of resistance and recurrence which discourage their further use. Thus, motivate researchers to look for some alternative treatment strategies. From antiquity, medicinal plants have been used to treat various diseases and thus improve human health. In fact, these are still in use for prevention and treatment of various ailments ranging from mild infections to severe diseases like cancer. The medicinal plants own this importance due to the presence of active molecules in them which mostly include secondary metabolites, peptides and proteins. Although secondary metabolite-based drugs have been very effective but severe unavoidable snags associated with these drugs like toxicity, improper metabolism and limited availability have paved way for proteins and peptides, being highly specific in action with negligible toxicity, to be explored as potent therapeutic agents. In this context, extensive research has been diverted towards exploration of medicinal plants for potentially active therapeutic proteins and peptides to be used or developed as potent protein/peptide-based drugs. Keeping this in consideration, the study was designed to explore and characterize bioactive protein(s) from a medicinal plant of the Kashmir Himalayas. For this, a protein fraction from the rhizome of this plant was prepared which on SDS-PAGE analysis indicate the presence of major protein bands in the range of 16kDa to 29kDa, 29kDa to 33kDa and some light intensity bands. Interestingly, fraction observed anti-proliferative activity on MDA-MB231 cell line with IC_{50} value ~18.01µg/ml. Subsequent fractionation of the active fraction was carried out using 60% salt precipitation followed by ion-exchange and gel filtration chromatographic techniques. So far, we have been able to purify a 30 kDa protein and the purity of the protein was confirmed by SDS-PAGE. As intended the purified protein was also observed to exhibit anti-proliferative activity. Future studies are warranted to carry out detailed mechanistic activity studies followed by its structural characterization.

Key words: Medicinal Plant, SDS-PAGE, Anticancer Activity, Ion Exchange Chromatography, Gel Filtration Chromatography

BCH-312 POSTER

Future Prospect of Non-Coding RNAs in HNSCC

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Head and neck squamous cell carcinoma (HNSCC) stands sixth among various cancers worldwide and is one of the most disastrous and deathly diseases battled by clinicians worldwide. According to GLOBOCAN 2020, the number of incidence and deaths in India has more or less doubled in last four years. According to data released by ICMR, it is the most common type of cancer in males in India. The escalating incidence is attributed to poor nutrition, bad oral hygiene, risk factors and lack of early diagnosis methods. Identified risk factors incorporate consumption of alcohol, smoking and smokeless tobacco, betel-quid with or without tobacco, viral infections (Human papillomavirus and Epstein barr virus). In a developing country like India, the health burden posed by rising cases of HNSCC is having an impinging effect on the quality of life. The gold standard for detection of oral cancer includes tissue biopsy and visual inspection. Majority of carcinoma cases remain unknown until it reaches advanced stages. Treatment options for HNSCC include chemotherapy, radiotherapy, surgical resection and combination of all three. Despite advancements in clinical care, the survival rate of affected patients remained relatively unaffected. Ongoing research in the last couple of decades have pondered the role of non-coding RNAs in the increased pathogenesis, resistance to treatment and invasiveness in HNSCC. They have become the favorite candidate to serve as potential early biomarkers, targeted treatment and better management of disease, thus increasing overall survival of affected.

Key words: HNSCC, Tobacco, Non-Coding RNAs, Biomarkers, Targeted Treatment

BCH-313 POSTER

Structural-Functional Integrity of Oxidoreductase Enzyme, Catalase: Towards Identification of Small Molecule Modulators of Cellular Redox Status

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Cells under stressful conditions accumulate small molecular weight organic compounds called as osmolytes primarily regulating cell volume homeostasis along with protecting the structural-functional integrity of cellular macromolecules including proteins. Osmolytes prevent protein misfolding and even refold misfolded proteins, thus being able to modulate the cellular proteostasis. On the other hand, antioxidant enzyme systems also counteract various types of stresses experienced by the cells. For example, catalase neutralizes the H_2O_2 formed due to various physiological reaction that would otherwise cause the oxidative damage of proteins and other cellular macromolecules, resulting in oxidative stress. These antioxidant enzymes are differentially expressed in various neurodegenerative disorders and metabolic disorders as shown in many studies. Hence, the accumulation of osmolytes and differential expression of these enzymes in oxidative stress related disorders encouraged us to design the study regarding the structural and functional integrity of catalase under stress conditions. We have used methylamine class of osmolytes such as sarcosine, betaine and Trimethylamine-N-oxide (TMAO) in our study. Our findings revealed, methylamines decreased catalytic activity of enzyme due to reduced affinity for its substrate i.e., peroxide (enhanced K_m) with no change in V_{max}. This decrease in the enzyme activity is due to destabilization of heme region of catalase which is the active site of this enzyme. Similarly, methylamines were found to affect the tryptophan environment and hydrophobic patches of catalase. However, these osmolytes were found to reduce the aggregation propensity of catalase. In conclusion, these small molecular weight compounds (methylamines) have the capability to modulate the structural and functional integrity of oxidoreductase enzyme catalase.

Key words: Osmolytes, Methylamines, Oxidoreductase, Redox, Catalase, Sarcosine, Betaine, TMAO, Soret Region, Aggregation

BCH-315 POSTER

Role of Stem Cell RNA Binding Protein Musashi1 In SARS-CoV-2 Infection

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The Musashi (Msi) family of RNA binding proteins serve as important post transcriptional regulators of stem cell homeostasis in a variety of tissues, including intestine and central nervous system. In this study we show how Musashi RBPs can bind to SARS-CoV-2 3'UTR and influence the viral life cycle in host. We performed MD simulations, and *in-vitro* and *in-vivo* immunoprecipitation assays to demonstrate a novel direct binding of Msi1 to the SARS-CoV-2 UTR. Notably, both Msi1 and 2 can bind to the SARS-CoV-2, unlike the specific binding of Msi1 to Zika virus which we have previously demonstrated (Chavali et al., 2017). Using transient and stable Msi1 knockout cells, we show how the viral load and viral proteins are affected upon depletion of Msi1. This is an important finding since gut cells have been shown to be a reservoir for persistent SARS-CoV-2 and Msi1 is highly expressed in the intestinal cells as it helps in the regeneration of intestinal epithelia. Thus our studies reflect how such stem cell RBPs could aid in the maintenance of cell homeostasis after active viral infection.

Key words: Musashi, Stem Cells, SARS-CoV-2, RNA Binding

CS, Is A Potent Neuroprotective Agent That Attenuates Glutamate-Induced Excitotoxicity In Neuron-Like SHSY5Y Cells Via Cannabinoid Receptor 1 (CB1R) Signaling

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The most prevalent G protein-coupled receptor (GPCR) in the mammalian brain is the CB1 cannabinoid receptor, which is the primary biological target of endocannabinoids. Glutamate-mediated excitotoxicity contributes to the pathogenesis of a multitude of neurodegenerative diseases that are characterized by the progressive deterioration of neurons. Here, we examined the neuroprotective potential of CS, a THC-based semisynthetic molecule, against the excitotoxic effects of glutamate in differentiated SHSY5Y cells. The glutamate-induced activation of SHSY5Y cells triggers the release of cytokines and other inflammatory mediators, which subsequently activate the mitochondrial pathway of apoptosis and neuronal degeneration. Here, we report that the administration of CS attenuated the glutamate-treated cell death in SHSY5Y cells. The neuroprotective effects of CS in glutamate-treated SH-SY5Y cells are mediated, at least in part, by attenuating intracellular reactive oxygen species (ROS), increasing anti-oxidant defenses, and restoring calcium homeostasis and mitochondrial membrane potential ($\Delta\Psi M$). The neuroprotective effects of CS against the glutamate-induced excitotoxic effects in SHSY5Y cells also evident from a decrease in the cleavage of poly (ADP) ribose polymerase-1 (PARP-1) and an increase in Bcl-2 to Bax ratio. CS inhibited acetylcholinesterase (AChE) activity and modulated PI3K-Akt signalling to increase cell survival. CS possesses high total antioxidant capacity and was able to inhibit both LDH release and lipid peroxidation in glutamate-treated SHSY5Y cells. Since, CS is analogue of delta-9-tetrahydrocannabinol, we next assessed its effect on cannabinoid receptor-1 signalling and found that it enhanced the expression of CB1 receptor. Overall, our results suggest that CS is a potent CB1 agonist and can be used as a neuroprotective agent for the mitigation of neurogenerative manifestations

Key words: Excitotoxicity, Neuron, Neurodegeneration, Cannabinoid, Glutamate, Agonist

BCH-317 POSTER

Apocynin Alleviates Paraquat-Induced Dopaminergic Neurodegeneration in the Rat model of Parkinsonism

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Background: Parkinson's disease (PD) is the second most common progressive neurodegenerative disease after Alzheimer's disease characterized by the presence of intra- cytoplasmic inclusion bodies known as Lewy bodies having α- synuclein aggregate and the loss of dopaminergic neurons in the substantia nigra regions of the brain. This disease has prevalence of more than 1% globally among population of over age of 60 years. The exact cause of dopaminergic neuronal loss in PD remains unknown for a long time; however, recent studies report that oxidative stress plays a crucial role in the pathogenesis of PD. Paraquat (PQ), a widely used herbicide, is an oxidative stress inducer that has been implicated as a potential risk factor for the development of PD. To date, no complete cure is available for the disease. Pharmacological approaches targeting antioxidant machinery may have therapeutic value against PD. Flavonoids are naturally occurring polyphenolic compounds that display a variety of therapeutic properties against oxidative stress. Apocynin (4-hydroxy-3- methoxyacetophenone) is a natural flavonoid obtained from the medicinal plant Picrorhiza kurroa that exhibits neuroprotection against PD-related pathology. However, studies on its neuroprotective role and the underlying mechanisms are scarce. **Aim**: The proposed study will explore the effect of Apocynin on Paraquat-induced dopaminergic neurodegeneration in the rat model of Parkinsonism. **Methods:** As a part of preliminary study, we have developed PQ-induced Parkinsonism model in adult Wistar rats. We performed motor coordination-related

behavioral experiments and immunohistochemistry to validate the establishment of PQ-induced Parkinsonism. Then we determined the effect of Apocynin on motor function in the PQ-induced rat model of Parkinsonism. **Results:** Paraquat-induced nigro-striatal dopaminergic neurodegeneration in the rat model of Parkinsonism. Apocynin improved motor deficits in the PQ-induced rat model of Parkinsonism. **Conclusion:** Apocynin treatment alleviates PQ-induced dopaminergic neurodegeneration in the rat model of Parkinsonism. In the future, we will be assessing the neuroprotective effect of Apocynin in the developed model of Parkinsonism.

Key words: Parkinson's disease, Paraquat, Neuroprotection, Apocynin, Neurodegeneration

BCH-318 POSTER

A Multi-Spectroscopic and Computational Approach to Investigate the Binding Potential of Trans-Resveratrol to HSA for an Efficient Displacement of Aflatoxin B1

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Trans-resveratrol is the active and stable form of resveratrol present in good amount in grapes. Aflatoxin B_1 is a hepato-carcinogen, teratogen and mutagen, produced by *Aspergillus* species, and is classified as group 1 human carcinogen by the International agency for research on cancer. The study focuses on unraveling the interaction of *trans*-resveratrol with HSA using spectroscopic and computational approach followed by competitive dislodging of AFB_1 from HSA by *trans*-resveratrol. The UV-visible spectroscopic study showed hyperchromicity at 280 nm suggesting the ground state complex formation between HSA and *trans*-resveratrol. The binding constant of ~10^7 M^{-1} with a single binding site was obtained for *trans*-resveratrol and HSA complex. The Stern-Volmer quenching constant was calculated as 7.83×10^4 M^{-1} at 298.15 K, suggesting the strong fluorescence quenching ability of *trans*-resveratrol. Warfarin and ibuprofen site markers displacement assay indicated subdomain IIA as the binding site of *trans*-resveratrol to HSA. The computational approach like molecular docking and molecular dynamics simulation studies envisages the amino acid residues forming the binding pocket and stability of *trans*-resveratrol and HSA complex. As confirmed from the site marker displacement assays, both *trans*-resveratrol and AFB_1 binds to HSA in the same binding site, subdomain IIA. Trans-resveratrol was able to displace AFB_1 bound to HSA, nevertheless AFB_1 failed to displace trans-resveratrol bound to HSA. The study discovers the ability of *trans*-resveratrol to displace AFB_1 from the HSA-AFB_1 complex, consequently influencing the toxicokinetic behavior of AFB_1 associated with hepato-carcinoma.

Key words: Aflatoxin B1, Trans-Resveratrol, Fluorescence Spectroscopy, Circular Dichroism, Molecular Docking.

BCH-319 POSTER

Poly (C) Binding Protein Mediated Regulation of Utrophin-A in C2C12 Cell line

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Duchenne Muscular Dystrophy (DMD) is a genetic disorder characterized by muscle degeneration and weakness caused by the deficiency of dystrophin. Several therapeutic approaches have been tested to date but a successful treatment regimen is yet to achieve. Our study focused on the upregulation of utrophin, an autosomal homolog of dystrophin, which can compensate for dystrophin deficiency in DMD. Therefore, utrophin overexpression has long been considered as a potential therapeutic approach for DMD. In this study, we identified Poly (C) Binding Protein 2 (PCBP 2) as a post-transcriptional suppressor of utrophin-A. We also observed PCBP 2 mediated nuclear retention of utrophin-A mRNA in C2C12 cells, which makes utrophin-A transcripts less abundant for translation in the cytosol. Moreover, we have also studied the regulation of utrophin-A expression by Poly C Binding Protein 1 (PCBP 1), a retrogene of PCBP2. Through

overexpressing PCBP1 in C2C12 cell line, we have observed downregulation of utrophin expression. On the other hand, silencing of PCBP1 in the C2C12 cell line resulted in the upregulation of utrophin. PCBP1 and PCBP2, therefore, may be the targets to de-repress utrophin-A expression in DMD.

Key words: PCBP1, PCBP2, Utrophin-A, DMD

BCH-320 **POSTER**

Understanding the Functional Relevance of Homopolymer Repeats in Med21 Protein of Dictyostelium Discoideum

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Trinucleotide repeats are found in both expressed and silent regions of the genome. These repeats are known to arise from DNA replication slippage. When expressed, these repeats give long runs of single amino acid within a protein. Few of these repeats are known to give evolutionary advantage and perform species-specific function. In some cases, few amino acid repeats found in nature tend to aggregate once the repeat exceeds a critical length and often implicated in human diseases e.g., Poly Q diseases. Moreover, some of these single amino acid repeats are reported to function as activators or as facilitators of interactions between biomolecules. However, the functions of many such repeats in proteins are largely unknown. Towards understanding the role played by single amino acid repeats in protein and their regulation, we initiated our work on *Dictyostelium discoideum*, a cellular slime mould, offering a unique model system with large number of proteins containing homopolymer amino acid repeats. For our study, we have chosen *med21* gene encoding Med21 protein, a component of the mediator complex in RNA polymerase II transcription machinery. The complex helps in relaying signals from gene specific regulatory proteins to the transcription machinery formed by RNA polymerase II. Protein sequence alignment revealed *D. discoideum* Med21 has a unique stretch of glutamine repeats interrupted by a stretch of proline repeats but absent in its orthologues from human and yeast proteins. This study aims to find the relevance of amino acid repeats in Med21 function. For this, overexpression analysis of wild type or mutated protein will be done in wild type or *med21* null background and analyze the effect on growth and development compared to wild type protein. Additionally, confocal analysis will be done to check the cellular localization of the wild type and mutated protein in order to assess the role of these repeats in protein localization. Further protein-protein interaction studies by pull down will be carried out to assess the effect of deletion/replacement of these sequences on normal protein-protein interactions. Results from initial work involving both bioinformatics and molecular studies will be presented.

Key words: Med21, Homopolymer Repeats, *Dictyostelium discoideum*

BCH-321 **POSTER**

Identifying Specific Misfolded Protein Aggregates in Primary Mammary Tumor-Derived Exosomes in Mice

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The leading cause of death in most breast cancer patients is metastasis. Therefore, requisite understanding and targeting this process will have a significant outcome in patient prognosis. Exosomes, a subset of extracellular vesicles (average size 20 - 150 nm), which are released from primary tumor cells in the body fluids, arrive at future metastatic sites much before the circulating tumor cells and facilitate the pre-metastatic niche formation, which is a crucial step for metastasis. Among the various contents, one very interesting cargo of primary tumor-derived exosomes is "misfolded proteins" since specific misfolded proteins can induce endoplasmic reticulum (ER) stress, and subsequently unfolded protein response (UPR), which have a prominent role in tumorigenicity. Thus, specific misfolded protein aggregates within primary tumor-derived exosomes may play important roles in secondary tumorigenesis. To validate

this hypothesis, mammary tumors were induced in BALB/c mice by injecting 4T1 cells in the mammary fat pad of mice. Blood was collected at different time points. Exosomes were isolated from serum, and characterized by dynamic light scattering, western blot hybridization and scanning electron microscopy. Lung, liver and bone marrow cells of healthy BALB/c mice were treated with exosomes isolated from tumor-bearing mice. Increased tumorigenic activity of normal lung, liver and bone marrow cells was observed as the treated cells had higher expression of stemness markers ALDH1A1 and SOX2, proliferation marker cyclin D1 and oncogenic markers c-MYC and hTERT. Furthermore, it was observed that the amount of misfolded proteins within exosomes increased from 7 day-tumors to 21 day-tumors as observed by fluorescence microscopy and fluorescence spectrophotometry using the fluorescent dye, ANS. Additionally, a non denaturing polyacrylamide gel of exosomal proteins was run and misfolded aggregates of specific proteins were analyzed by mass spectrometry to identify which protein promotes tumorigenecity within pre-metastatic niche and facilitates secondary tumor growth.

Key words: Tumor-derived Exosomes; ER Stress; UPR; Misfolded Proteins

BCH-322 POSTER

Altered Microbiota-induced Neurological Disorders in Mice Exposed to Arsenic

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Arsenic, a potent ground water pollutant, is a threat worldwide due to its malefic manifestations. Several epidemiological and clinical studies reported arsenic-mediated learning and memory impairment, cognitive deficit and mood disorders. However, the molecular mechanisms behind arsenic-mediated neurotoxicity at the sub-chronic level have not been evaluated till date. Arsenic enters the body through gastrointestinal tract and alters the composition of the gut bacterial population, which are known to orchestrate brain functions, through the gut-brain axis. To delineate the effects of arsenic, mice were exposed to different doses of arsenic for 30 days. Significant arsenic deposition was found in brain of 100 ppm group by ICP-OES. Behavioural studies revealed onset of anxiety and depression in a dose-dependent manner. Altered neurotransmitter levels (serotonin, dopamine and norepinephrine) were also observed by ELISA. Histological study revealed appearance of pycnotic nuclei in the hippocampus. Deleterious effects were studied in the small intestine and colon where arsenic was observed to damage the tissue architecture. In addition, it increased the gram negative bacterial abundance in mice fecal pellets. Enhanced inflammation and down regulation of tight junction proteins rendered the intestine leaky and increased plasma LPS levels, which in turn may have a role in exerting ill effects in the brain. To assess whether the above neurotoxic effects are a direct consequence of modulations of gut microbiota, fecal microbiota transplantation was performed. Although deposition of arsenic in the brain of FMT mice was insignificant, similar changes in the gut and related alterations in behaviour were observed in these groups as seen in arsenic-treated groups. In addition, scanning electron micrographs depict epithelial cell extrusion in small intestine along with loss of goblet cells in colon of FMT mice which suggest appearance of compromised barrier function in mice gut. 16S rRNA gene sequencing revealed perturbations in gut microbial population which can be correlated with high LPS level in mice plasma and onset of neurological disorders. These results may establish arsenic-induced alterations of the gut-brain axis as a mechanism behind arsenic-mediated neurotoxicity in mice.

Key words: Arsenic; Gut Microbiota; Fecal Microbiota Transplantation, Leaky Gut; Brain

BCH-323 POSTER

Combination Studies of Meriolin (3-Pyrymidinylazaindole) Derivatives with Known Cytotoxic Agents against Non Small Lung Cancer

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Non-small cell lung cancer (NSCLC) is a challenging disease due to poor prognosis and lack of druggable targets where over half of the people diagnosed with this cancer die within one year, and the 5-year survival is less than 18%. Therefore, chemotherapy remains the standard of care, and identifying new targets is a high clinical priority. Aberrant cell cycle machinery is one of the key somatic events in non-small cell lung cancer (NSCLC) pathogenesis. The effect of a single agent is usually limited in cancer therapy, and using a single agent may mediate drug resistance. Therefore, in this direction, we explored the potential of combining 3-pyrimidinylazaindole derivative IIIM-368, a CDK-2 inhibitor, with Paclitaxel, a first-line chemotherapeutic drug for NSCLC. The simultaneous combination of IIIM-368 with paclitaxel exerted a synergistic effect that inhibited cell proliferation, increased cell death more efficaciously, and reduced drug dosage by half than single treatments. The superior efficacy of this combination was ascribed to its ability to downregulate CDK-2/Cyclin-E /Rb/E2f axis. The combination resulted in the alteration in the expression of the Bcl-2 family of proteins mediated by the upregulation of MAPK pathway proteins leading to the induction of apoptosis in the NSCLC cell line. Our results suggest that the efficacy of standard chemotherapy can be significantly improved by simultaneous treatment of IIIM-368 along with paclitaxel, thus offering a better therapeutic option for Non-small lung cancer.

Key words: Non-Small Cell Lung Cancer (NSCLC), Combination, CDK-2, Cell Cycle, MAPK

BCH-324 POSTER

Red Blood Cell-Derived Nanoerythrosomes Mediated Efficient Delivery of mRNA Vaccine Candidate against Covid-19

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The COVID-19 pandemic has been a major public health concern throughout the world. Various ventures of vaccine candidates are being studied rigorously in this regard and one such candidate is the receptor binding domain (RBD) of spike protein which interacts with angiotensin converting enzyme 2 (ACE2) on the host cell's membrane. Exploiting this interaction, many scientists across the world attempted to develop mRNA vaccine against SARS-CoV-2. A major lacuna associated with mRNA vaccines is their delivery through a suitable carrier, especially given the stability issues associated with mRNA vaccines. We have developed small vesicles from erythrocyte ghosts, known as nanoerythrosomes, which are in the nanometre range and focussed on development of nanoerythrosomes for delivery of mRNA-based vaccines. Self-amplifying RNA (saRNA) of RBD was synthesized through *in vitro* transcription. Simultaneously, nanoerythrosomes were prepared from erythrocytes using osmotic and ultrasonic frequency stress and loaded with saRNA vaccine candidate. Thereafter, the nanoerythrosomes were characterised using Dynamic Light Scattering (DLS) and Scanning Electron Microscopy (SEM) to confirm their homogeneity, integrity and size. The characterization of nanoerythrosomes using DLS and SEM revealed their size in the range of 100-200 nm. The carrier efficiency of the mRNA loaded nanoerythrosomes was evaluated by the delivery efficiency of the mRNA in Vero E6 cells and evaluated the expression of RBD domain of spike protein. Western blot data of VeroE6 cells demonstrated the expression of RBD domain of Spike protein confirming the efficient delivery of the RBD domain encoding saRNA by nanoerythrosomes. The delivery mediated by nanoerythrosomes was comparable to the Lipofectamine mediated uptake of saRNA indicating the excellent delivery efficacy of nanoerythrosomes. The added advantage of nanoerythrosomes mediated delivery is that they are rapidly taken up from blood by macrophages of the reticuloendothelial system (RES) that is present in liver,

lung, and spleen. Thus the combination of saRNA and nanoerythrosomes can accelerate the uptake and antigen presentation in reticuloendothelial system and will provide an outstanding platform for the development of SARS-CoV2 vaccine. Overall, we have successfully developed a new approach to deliver vaccine candidates using nanoerythrosomes and believe that this will surpass the limitations associated with vaccine delivery.

Key words: COVID-19, RBD, ACE, Nanoerythrosomes, mRNA, Vaccine

BCH-325 POSTER

Antimalarial and G6PD Deficiency Correction Potential of Melatonine and its Derivatives will Aid in Malaria Elimination

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G6PD deficiency is a genetic metabolic abnormality which is caused by deficiency of the enzyme G6PD. The gene encoding G6PD are found on the distal long arm of the X chromosome. It is a key and rate limiting enzyme in the pentose phosphate pathway (PPP). It contributes to many chronic diseases associated with the oxidative stress. Infection, certain foods, and medication cause oxidative stress. Broad beans eg. Fava bean contains high level of vicine, divicine, convicine and isouramil, all of which create oxidants. Thus before the person exposed to these, it is beneficial to cure this deficiency. Moreover, treatment of malaria eradication programme involves the generation of ROS, thus this knowledge/cure decreases the fatality risk rate. Approximately 400 million people are affected worldwide. Currently no medications are available to cure G6PD deficiency, thus in current study we seek to identify drug like small molecule that corrects it. Here we choose the G6PD wild type and variants prevalent in India like – Canton, A- and Mediterranean to study. Mutant variants were expressed and purified and steady state kinetic parameters were determined by fitting the data to Michaelis–Menten equation. Secondary structure and thermal stability of all four enzymes were analysed using circular dichroism (CD). Melatonin and its derivatives which were earlier reported to increase the activity of wild type G6PD enzyme were tested, if they increase the activity of the G6PD variants too and found to increase the activity of wild type and Mediterranean variant by 20 and 30 percent respectively. Interaction studies were performed using Microscale thermophorosis technique which indicated the binding of Mediterranean variant with melatonine with Kd value 3.14uM, and the derivatives 6- hydroxyl-melatonine 3-(N-acetylaminoethyl)-6-hydroxy -5-methoxy indole and N-butanoyl 2-(5,6,7- trihydro-11-methoxybenzo[c] cyclohept [2,1-a] indol-13-yl) ethanamine melatonine were showing binding with Kd values of 83.3uM and 104uM respectively. Preliminary antimalarial studies are also indicating the potency of molecules against the parasite. Thus our study suggest Melatonine and derivatives as a potent molecules for Malaria eradication since it take cares of G6PD deficient condition and antimalarial action both.

Key words: G6PD Deficiency, Antimalarial, Enzyme Activity

BCH-326 POSTER

XRCC1: A Novel Regulator of Cancer Cachexia

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Cancer cachexia is a wasting syndrome, characterized by loss of appetite, muscle mass leading to a life-threatening condition associated with metastasis. It is a multifactorial condition involving wasting of both adipose tissue and skeletal muscle thereby, negatively regulating different organs of the body. In colorectal cancer (CRC) patients, there is more than 15% of body weight loss in post cachexic condition. CRC arises as a consequence of the accumulation of

genetic and epigenetic alterations that transform colorectal epithelial cells into colorectal adenocarcinoma cells. The X-ray repair cross-complementation group 1 (XRCC1), is a scaffold protein, that plays important role in base excision repair and single strand base excision repair. XRCC1 works as an indispensable mediator of muscle differentiation process and modulates muscle atrophy. By using In-silico analysis and mechanistic studies we identified up-regulation of XRCC1 gene in clinical samples and delineated its role as a key regulator of cancer cachexia in CRC. XRCC1 is responsible for cancer cachexia condition that regulates muscle atrophy. Therapeutic inhibition of XRCC1 restored muscle function and structure, and reduced tumor size thereby underscoring it key role in cancer cachexia.

Key words: Cancer Cachexia, XRRC1, Base Excision Repair, Colorectal Cancer

BCH-327 POSTER

A Novel Triazine Analogue IIIM-873 Exhibits Antitumoral Potential Against Breast Cancer by Targeting The PI3K-mTOR Pathway

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A novel **triazine** analogue, IIIM873, showed antitumor properties against MDA-MB-231 (TNBC), MCF-7 (breast cancer), HCT-116(colon cancer), PC-3(prostate cancer), OVCAR 3,4,8 (ovarian cancer) cell lines using SRB assay. IIIM-873 exhibits good inhibitory activity against breast cancer cell line with no toxicity against normal counterpart HEK293 cells. DAPI staining shows nuclear degradation in MDA-MB-231 cells after treatment of IIIM-873. Colony forming and wound healing ability of MDA-MB-231 cells were inhibited after treating cells with IIIM-873. Furthermore, western blot analysis revealed that IIIM-873 showed considerable inhibitory action against PI3K110α and mTOR in triple-negative breast cancer MDA-MB-231 cells.

Key words: Antitumor, Triazine, SRB Assay, DAPI, PI3K110A

BCH-328 POSTER

Atypical Anoiksis: A Novel Mode of Cell Death is Induced by *Leishmania donovani* in Epithelial Cells During Traversal for Infection

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Leishmaniasis is the second largest parasitic infection exhibited in several forms among which visceral leishmaniasis (VL) is the most lethal form. Other than visceral form which is caused by *Leishmania donovani*, cutaneous (CL) and mucocutaneous (MCL) are additional clinical forms of leishmaniasis caused by *L.major* and *L. braziliensis* respectively. Despite different clinical manifestations, all forms of leishmaniasis transmitted to humans through the bite of sand fly. This leads to formation of skin lesions and inoculates promastigotes in the pool of blood. Further parasites get disseminated to deeper visceral tissues like spleen, liver and bone marrow for systemic pathogenesis as in the case of VL. Furthermore, *Leishmania donovani* infection leads to the formation of parasitized skin patches that is clinically manifested as VL induced CL and more aggressive form, known as PKDL. This patchy skin lesions are known to be the best route and reservoir for outward transmission through vector sandflies. However, paucity exists in understanding of cellular and molecular alterations in skin epithelial cells induced by *L. donovani* infection. This lack of knowledge restricts the researchers for designing of novel strategies to combat the disease and block the transmission. Herein, to understand the "*host-parasite*" interactions following the sandfly bite, we established an *in vitro* cellular model involving co-culture of *L. donovani* with epithelial origin MDCK cells. Upon co-culture of *L. donovani* parasites with

MDCK cells, we observed distinctive flipping in of plasma membrane followed by permanent distortion of cytoskeletal architecture with breaching of tight junction barrier and change in expression of extracellular matrix receptors. These phenomena lead to a unique kind of cell death, known as "homelessness" or atypical anoiksis apoptosis. Plausibly, this work provides novel insights into mode of parasite traversal through epithelial cells and the parasite-induced cellular and molecular alterations at the site of bite. This study has introduced a prototype co-culture model based on epithelia-*Leishmania* interaction mimicking the skin pathophysiological linked to *L. donovani* induced CL and PKDL. These observations suggested a new co-culture model for understanding host-parasite interactions in leishmaniasis, that can be used for screening and developing of novel antileishmanial and transmission blocking drug candidates.

Key words: Atypical anoiksis, *Leishmania donovani*, Traversal, Outward transmission

BCH-329 POSTER

Effect of Bioactive Compounds from *Alcea rosea L.* on Inhibition of Self-Renewal Properties of Colon Cancer Cell Lines

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Plant derived compounds modulate various molecular pathways involved in the initiation and progression of cancer. The present study aims to examine the effect of isolated compound(s) of ethyl acetate extract of *Alcea rosea* seeds on the progression of colon cancer cells, using various *in vitro* and *in vivo* assays. Hexane, ethyl acetate (E.A), ethanol, methanol, and aqueous extracts of Alcea rosea seeds were obtained using Soxhlet extraction. DPPH, Total phenolics, reducing power, DNA damage, Ferrozine assay, TBARS (Thiobarbituric acid reacting species assay), Protein denaturation, Anti-proteinase assay, Nitric oxide assay, HRBC assay and Lipoxidase assay confirmed that E.A extract has best anti-oxidant and anti-inflammatory potential compared to rest of the extracts. Upon investigating the effect of these extracts on HCT-116 and SW-480 cell lines, E.A extract showed chemo-preventive effects by inducing cell cycle arrest, apoptosis, decreasing cell proliferation and angiogenesis, inhibiting tumor cell invasion and metastasis. GC-MS analysis of E.A extract revealed different forms of high and low molecular weight chemical substances, among them the maximum area covered by 9,12-Octadecadienoic acid (Z, Z) (29.87 %) followed by Bis (2-Ethylhexyl phthalate (16.10 %), 9-octadecenoic acid (14.88%), Linoleic acid ethyl ester (10.31 %), n-Hexadecenoic acid (7.67 %) and AI3-09519(1%). Active compound like AI3-09519 is under clinical trials for the treatment of HIV-AIDS. We extracted seven main compounds from E.A extract using column chromatography. We are currently investigating the effect of these 7 isolated compounds from E.A extract on different pathways like Wnt/β-catenin, Notch, TGF-β and Hedgehog/Gli. Thus, effective bioactive constituent(s) from E.A extract of *Alcea rosea* will serve as the best anticancer compound(s) to block stem cell driven colon carcinogenesis in future.

Key words: Alcea rosea, Ethyl acetate, GC-MS Analysis, Phytoconstituents

BCH-330 POSTER

Anti-tubulin Compounds from MMV Pathogen Box Potentially Target Multiple Stages of Malaria Parasite

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The emergence of resistance to conventional antimalarial treatments continues to be a major cause of concern. To mitigate this danger, innovative Plasmodium parasite medication targets in diverse developmental stages are necessary. In the present investigation, we focused on *P. falciparum* Tubulin (*Pf*Tubulin) proteins, which are prospective therapeutic targets for malaria treatment. Plasmodium Microtubules (MTs) play an important role in parasite

proliferation, growth, and transmission, making them very desirable targets for the development of next-generation chemotherapeutics. To this end, we assessed the antimalarial activity of Tubulin targeting compounds obtained from the Medicines for Malaria Venture (MMV) " Pathogen Box " against the human malaria parasite, *P. falciparum*, including 3D7 (chloroquine and artemisinin sensitive strain), RKL-9 (chloroquine-resistant strain), and R539T. (artemisinin-resistant strain). At nanomolar concentrations, the filtered-out compounds displayed potent antimalarial activity against all stages of the parasite life cycle, including intraerythrocytic blood stages, liver stage parasites, gametocytes, and ookinetes. Concurrently, it was discovered that these chemicals inhibit male gamete ex-flagellation, demonstrating their transmission-blocking potential. Target mining of these potent compounds using a combination of in silico, biochemical, and biophysical experiments showed *Pf*Tubulin as their molecular target, which may impair MT assembly dynamics by binding at the interface of The Tubulin-dimer. In addition, the parent scaffold's favourable ADME profile encouraged its consideration as a lead compound for further research. Consequently, our research demonstrates the possibility of targeting *Pf*Tubulin proteins in the discovery and development of next-generation, multistage antimalarial medicines against Multi-Drug Resistant (MDR) malaria parasites.

Key words: Malaria, Plasmodium, Tubulin, Medicines for Malaria, Venture Inhibitor, Multistage

BCH-331 **POSTER**

Mitochondrial CI Evolution and Associated Deficiency Diseases: Is There a Connecting Link?

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Mitochondrial complex I (CI) is the largest among the respiratory complexes with 44 subunits in human. The 14 core subunits are conserved from prokaryotes. The accessory subunits are innovations to stabilize CI in eukaryotic mitochondria. Surprisingly, despite the conservation of the L-shaped structure distributed between the matrix and inner-membrane of mitochondria, cross-species substitution of subunits destabilize functional CI even within close metazoans. This suggests non-complementable evolution of CI-subunits which remain under-investigated. Here, we report that matrix arm CI-subunits are sequence-conserved throughout eukaryotes. Conversely, membrane arm subunits display mosaics of sequence conservation between core and accessory subunits in fungi, plants and metazoans. This does not alter the structure of the individual subunits but modulates their interaction chemistry with neighbouring conserved subunits. Accordingly, conserved accessory subunits of the matrix arm can be switched between eukaryotic kingdoms without affecting CI-assembly and function while unconserved membrane arm subunits are incompatible. Remarkably, the disease-associated CI-destabilizing mutations are often outside these protein-protein interaction surfaces and not well-conserved suggesting additional evolution of kingdom-specific membrane arm interactions beyond proteins. Therefore, we hypothesize that engineering the protein-protein interaction surfaces will not be sufficient to re-instate the structural or functional compatibility. Experiments in this direction are currently ongoing.

Key words: Mitochondrial complex I, Complex I deficiency disease, Sequenc evolution, Surface chemistry

BCH-332 POSTER

Limitations of Currently Available Therapeutic Regimes with respect to Host-Viral Interactions to Treat Chronic Hepatitis B

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Hepatitis B is a global public health threat, with about 296 million people living with chronic infection worldwide. Currently, seven antiviral therapies for clinical management of hepatitis B virus (HBV) are approved, which include nucleo(t)side analogues (NA) targeting viral DNA replication and interferons (IFN) modulating host immune response A major drawback of NAs is emergence of drug-resistant mutants with long-term therapy thus, they are safe for only short-term use. Use of IFNs have shown improved survival in responders, but it is limited to selected patients with compensated cirrhosis. Also, poor response in HBeAg-negative patients is reported. Furthermore, these treatments suppress but do not eradicate HBV. About 90% of people self-eliminate the virus, but 10% progress to chronic infection leading to fibrosis, cirrhosis, and hepatocellular carcinoma. Viral persistence depends on the crosstalk between viral and host factors Due to error-prone polymerase activity, HBV has a high mutation rate. Viral mutants are associated with unique clinical manifestations and can modify the pathogenicity and gives rise to a more aggressive course of the disease. Chronic hepatitis B infection leading to liver cirrhosis and carcinoma is due to inability of the host immune system to eliminate the virus in preliminary stage. Hepatocellular injury is due to the host immune response to the virus and not viral replication or cytopathic effect. It is accepted that virus clearance failure and liver inflammation is characterised by impaired innate immune response, dysfunctional T cells and T cell exhaustion. Thus, immunopathogenesis plays a critical role in the outcome and clinical progression of hepatitis B infection. But the mechanism of this immunopathogenesis is still not clearly understood. How host and viral determinants regulate the outcome of infection is unclear. Thus, we will try to summarize these viral and host factors in acute and chronic hepatitis B and update recent understanding on the mechanism of immunopathogenesis. This will help us to understand the mechanisms of chronic HBV infection and liver injury with more clarity and to develop combined treatment strategies of direct and indirect immunomodulatory antiviral drugs for HBV life cycle.

Key words: Hepatitis B, Antiviral Treatment, Immunopathogenesis, Viral Factors, Host Factors

BCH-333 POSTER

Cuminaldehyde induces Autophagy and Apoptosis in Non-Small Cell Lung Carcinoma

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Spices play an important role in human health and possess several medicinal properties. *Cuminumcyminum L.* also known as cumin is a spice that belongs to the Apiaceae family. It is used in the treatment of several diseases like Alzheimer's and cancer. Cancer is a disease that involves abnormal accumulation of cells, resulting from an imbalance in cell proliferation and impaired programmed cell death (PCD) pathways. PCD pathways play an important role in balancing cell death and survival of cells. PCD is divided into apoptosis, autophagy, and necrosis where autophagy plays a dual role in cancer. Thus, in our study we are trying to elucidate the effect of cuminaldehyde a major phytoconstituent present in cumin on the autophagy pathway in cancer.In our study we checked the interaction of cuminaldehyde with apoptotic and autophagic marker genesand found that cuminaldehyde shows good interaction with selected marker genes. Cuminaldehyde also shows cytotoxic effect against A549 lung cancer cell line.Cuminaldehyde also inhibits

proliferation and induces apoptosis in A549 cells, with increased *CASPASE-3* level. Moreover, ATG5 & LC3 levels were increased after cuminaldehyde treatment, indicating that cuminaldehyde could induce autophagy in A549 cells. Cuminaldehydesuppressed proliferation and promoted autophagy and apoptosis of A549 cells.

Key words: Spices, Apiaceae, Cancer, Programmed Cell Death (Pcd) Pathways, Apoptosis, Autophagy

BCH-334 POSTER

Role of Membrane-Cytoskeleton Interaction in Unicellular Tube Branching

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The development of epithelial tubes shaped the evolution of complex organs. They are critical for physiological functions in bilaterians. Processes such as sprouting angiogenesis, and kidney and lung tubule formation involve rapid cell shape alterations and branching. The fundamental cell biology behind the development of epithelial tubes is conserved between vertebrates and invertebrates. Here, we focus on the branching of a seamless unicellular tube using *Drosophila's* tracheal terminal cells as a model. Terminal cells start as a spherical structure in the embryonic stage. Each cell then elongates and invaginates its own membrane to form an intracellular tube. The inner (apical) membrane branching follows the branching of the outer (basal) membrane to form hollow tube branches. Membrane-cytoskeleton interactions generate the necessary pulling force required for the process. This tubular cell then attains a highly branched stellate architecture in the larva. Although, the branching program of the outer membrane is understood well, the same for the inner membrane remains to be understood. To visualize if cytoskeleton cables are pulling the tube membrane for branching, we performed timed imaging of fluorescently labeled fly embryos and larvae for cell-membrane and actin. We found that the site of filopodial activity in the outer membrane defines the location of kinks in the intracellular tubes. These kinks later serve as the branching point of the apical tube in the larval stage. We hypothesize that a mechanical connection and force transfer between the two membrane domains lead to branch initiation in the apical tube. Our future goal will be to capture the cytoskeleton components using live confocal microscopy and to model the forces involved to understand the process better.

Key words: Tubulogenesis, Morphogenesis, Unicellular tubes, Membrane-cytoskeleton interaction, Force generation, Branching, Tracheal system, Drosophila

BCH-335 POSTER

Mechanisms of Heat Shock Response Regulation By CGGBP1

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CGGBP1 is a repeat binding protein. It has multiple functions such as chromatin boundary regulation, binding to GC rich nucleosome poor regions, cell cycle regulation, mitigation of endogenous DNA damage and one such function is genomic repeat maintenance and stress response. Repeat activation is a stress response mechanism. Genomic repeats have changed in the course of evolution of mammals (homeotherms) from the poikilothermic ancestors. Changes in CGGBP1 from cold to warm blooded animals could have effects on cellular stress response. We want to address if heat shock response depends on homeothermic specific CGGBP1 or not. Can we rescue the absence of homeothermic specific CGGBP1 from human cells by overexpressing different forms of CGGBP1 from poikilothermic animals. How close or different the heat shock response resembles the canonical form of CGGBP1 in human cells when these different taxa CGGBP1 is overexpressed. We use human cells and overexpress CGGBP1 from different representative species and assay heat stress response in terms of (i) HSF1 occupancy (ii) CTCF occupancy. In addition, we

will establish the heat shock response by visualizing hsp markers such as XBP1 splice variants, HSP 70, HSP 90, HSF1, DDIT3 and CGGBP1.

Key words: CGGBP1, DNA Damage, Heat Shock Response, HSPS, HSF1, CTCF, XBP1

BCH-336 POSTER

Tributyltin Induced Toxicological Implications, DNA Damage in *Fejervarya limnocharis* Tadpoles

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Tributyltin (TBT), an organotin compound, is widely used in various commercial applications including pesticides, preservatives, glass coatings, heat stabilizers in PVC products and antifouling paints for boats, ships, etc due to its biocidal properties. Contamination of water by TBT with implications on environmental safety has been reported. Toxicological data involving TBT exposure to amphibians and its genotoxic potential are inadequate and inconclusive. Our study aimed to determine the genotoxic potential of TBT in *Fejervarya limnocharis* tadpoles. The LC_{50} for 24h, 48hr and 96hr was determined. Tadpoles of Gosner stage (26-30) were screened and exposed to different sub-lethal doses of TBT (10% and 20% of 96hr LC_{50} value) for the evaluation of its genotoxic potential by micronucleus and Comet assay. Results indicated significant induction of micronucleus (MN, $p<0.001$) and other nuclear aberrations (ONA, $p<0.01$) in the TBT-treated groups when compared to control group. Significant alteration in damage index in the TBT treated tadpoles were also observed. Other important TBT induced toxicological parameters that can adversely impact the anuran population, such as change in intestinal diameters, intestinal folds indicating pathological intestinal distension, hepatocyte heterotrophy, splenocyte viability were studied. This study also demonstrates that TBT exposure can have negative impact on survivability and metamorphosis for the anuran amphibian *Fejervarya limnocharis*. The result add to the fact that TBT induced toxicity as one of the cause of gradual decline in amphibian population.

Key words: Tributyltin, Fejervarya limnocharis, Genotoxicity, Micronucleus assay, Comet assay, Pathological intestinal distension, Immunotoxicity

BCH-337 POSTER

Metformin Protects Human Insulin against Fructosylation-Induced Biochemical, Biophysical and Structural Changes

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Objectives: The aim of this work was to investigate the protective effect of metformin against fructosylation-induced biochemical changes and structural alterations in human insulin using multi-spectroscopic, biochemical and biophysical procedures and electron microscopy. **Methodology:** Human insulin (56 µM) was incubated with D-fructose (25 mM), either alone or in presence of different concentrations of metformin hydrochloride (0.5 mM, 1 mM and 2.5 mM) in phosphate buffered saline, pH. 7.4, at 37°C for 10 days. Biophysical techniques performed included UV-visible spectroscopy, intrinsic fluorescence, advanced glycation end-products (AGEs) specific fluorescence and CD spectroscopy. Biochemical changes were measured by determining carbonyl and lysine contents of insulin. Fructosamine level was determined to find the extent of protection provided by metformin against fructosylation of insulin. Transmission electron microscopy was used to detect morphological changes in insulin. **Results:** UV-visible spectroscopy revealed that fructose-induced unfolding of insulin was less in the presence of metformin. Intrinsic fluorescence results showed that, in presence of metformin, there was less quenching of tyrosine residues compared to insulin samples incubated with only fructose. Treatment of insulin with fructose alone led to increase in carbonyl

content and decrease in lysine residues but these changes were restored in presence of metformin. CD spectroscopy revealed that alpha helix structure, which was reduced by fructosylation of insulin, was restored in the presence of metformin. Morphology of human insulin was examined by transmission electron microscopy. It showed that aggregation and fibril formation caused by fructosylation of insulin was greatly reduced by metformin. **Conclusion:** This study showed that metformin protects insulin against fructosylation and fructosylation-induced biochemical, biophysical, structural, and morphological changes. Since metformin is a very common drug that is given to patients with type II diabetes mellitus, this finding suggests that apart from controlling diabetes it can also provide protection against various AGEs related diseases and pathological conditions.

Key words: Fructosylation, Human Insulin, Metformin, Advanced Glycation End-Products

BCH-338 POSTER

Polycystic Ovary Syndrome Associated Infertility: A Link to be Uncovered

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Polycystic Ovary Syndrome (PCOS) is the most common cause of anovulatory infertility among the females of reproductive age group. Fertility is adversely affected by an individual being overweight, hyperandrogenism and having elevated serum concentration of luteinising hormone. This hormonal imbalance interferes with the growth and release of eggs from the ovaries resulting in anovulation. The association between these disorders is yet to be uncovered. The cross-sectional study was designed to assess the impact of PCOS on infertility by studying the various anthropometric, biochemical and hormonal parameters. The study included 30 subjects having PCOS women (diagnosed by Rotterdam criteria 2003), PCOS infertile, non-PCOS infertile, PCOS fertile women and healthy controls. After recruitment of participants for the study, assessment of clinical, biochemical and hormonal parameters was done. To assess whether PCOS could be the cause of primary infertility, the Rotterdam criteria was checked in different recruited groups. The results showed Ferriman-Gallwey (FG) score was found ≥8 in 11 subjects and ≤ 8 in 19 subjects. The testosterone was assessed as a biochemical parameter for hyperandrogenism in all the subjects. Compared to control the PCOS infertile (p=0.002), non-PCOS infertile (p=0.0002) showed significant increase in testosterone levels whereas PCOS group showed (p=0.07). Moreover, significant increase in testosterone levels was found while comparing PCOS group with PCOS infertile and non-PCOS infertile group (p=0.026), (p=0.01) respectively. Among the subjects the oligomenorrhea was predominant (n=10) followed by menorrhagia (n=1), where there was absence of anovulation (n=0). The ultrasonogram revealed polycystic morphology in (n=14) which also include (n=4) from non-PCOS infertile group. This is the preliminary work done so far, further subjects will be recruited in order to better understand the association between PCOS and infertility.

Key words: Keywords: PCOS, Infertility, Hyperandrogenism, Ferriman-Gallwey Score

BCH-339 POSTER

Synergistic Interaction of Notch and Neural Cell Adhesion Molecule Neuroglian Facilitates Eye Development in *Drosophila Melanogaster*

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Neural cell adhesion molecules are the glycoproteins present on the surface of neuronal cells that engage in homophilic or heterophilic interactions that tethers cells to cells or with the extracellular matrix (ECM) and help in neuronal development. Earlier studies in metazoans suggested the role of Notch as a cell adhesion molecule. Cell-cell interaction

is a prerequisite for the Notch signaling activation where Notch receptor upon binding with one of the ligands, Delta or Serrate on the adjacent cell leads to initiation of the signaling cascade that culminates in the translocation of Notch intracellular domain inside the nucleus thereby leading to transcription of the target genes. To identify cell adhesion molecules that might interact with Notch to regulate cell adhesion process, we carried out a large scale protein-protein interaction screen based on the identification of cellular protein complexes using co-immunoprecipitation followed by mass-spectrometry. Neuroglian (Nrg), a member of the Immunoglobulin superfamily of neural cell adhesion molecules, was identified as an interacting partner of Notch. This neural cell adhesion molecule is indispensable for the *Drosophila* nervous system development and plays a key role in several processes such as axonal growth and guidance, axon/dendrite morphogenesis, synaptic stability and function. We validated the physical association of Notch with Nrg using co-immunoprecipitation studies and their co-localisation on the cell membrane was determined by immunocytochemistry. The significance of this physical interaction was substantiated by genetic interaction studies between *Notch* and *nrg* mutants. Further, it was observed that Nrg gain-of-function phenotypes were identical to Notch gain-of function phenotypes which indicated a positive regulation of Notch signaling by Nrg. Additionally, we demonstrated that the synergistic effect of Notch with Nrg resulted in severe eye roughening, perturbed morphology of the eyes and delayed differentiation of the cone cells and the photoreceptor cells. Taken together, our results indicate that Notch plays a role in cell adhesion via interacting with the neural adhesion molecule, Nrg and this interaction may facilitate proper development and differentiation of the ommatidia in the *Drosophila* eye.

Key words: Notch, Neuroglian, Cell adhesion molecules, Drosophila melanogaster, Synergistic Interaction, Cell-Cell Interaction, Drosophila Eye Development

BCH-340 POSTER

G4 Quadruplex Landscape and its Regulation Revealed by a New Antibody Capture Method (Under Review: iScience)

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The human genome is packaged and maintained in the nuclei through higher-order chromatin conformations and orchestrated interactions between long-range genomic regions. The chromatin architecture proteins and their interacting partners ensure the ordered arrangement of the genome. Such constraints disallow the formation of DNA secondary structures, including DNA-G4 quadruplex. However, the DNA regulatory elements (enhancers and promoters) undergo strand metabolism and interactions with transcription factors. In addition, the G/C-richness of such regions allows the formation of DNA-G4 quadruplex. Though DNA quadruplex affects DNA-protein interactions, there is no known quadruplex-stabilizing mechanism in human cells reported. Chromatin constraints are further exerted by quadruplex-binding proteins binding to G/C-rich DNA and nucleosome depleted regions. The conventional G4-ChIP protocol drives understanding of the global G4 quadruplex profile *in cellulo*. This protocol involves formaldehyde crosslinking which creates a detection bias against the G4 quadruplexes not bound to proteins since formaldehyde passively denatures nascent DNA. Thus, an under-represented G4 landscape misleads our understanding of *in cellulo* quadruplex profile with *in vitro* artefacts. Our knowledge of the G4-quadruplex landscape and its regulation is hindered by multiple interrelated challenges. For example, does formaldehyde fixation truly capture the *in cellulo* quadruplexes only? Does G4 formation/stabilization depend on some regulatory protein(s)? Is there a chromatin constraint on G4 quadruplex forming sequences exerted by G4-binding proteins on G4 quadruplex formation? Here we have developed a DNA-G4 quadruplex ChIP-sequencing protocol in which we stabilize *in cellulo* quadruplexes and eliminate any quadruplexes formed due to formaldehyde treatment. A spike-in control DNA having the quadruplex

signature sequence is incorporated to quantitatively establish the extent of chromatin constraint on quadruplex formation by canonical sequences *in cellulo*. We have applied this protocol to understand potential chromatin constraints on G4 quadruplex forming sequences exerted by CGGBP1, a regulator of G/C-rich DNA sequences. We demonstrate that CGGBP1 exerts a selective chromatin constraint on quadruplex formation sequences with G/C-skew. Cells with depleted levels of CGGBP1 show enhanced quadruplex formation at CGGBP1-dependent non-canonical CTCF-binding sites with increased CTCF occupancy.

Key words: G4 Quadruplex, G4-ChiP, CGGBP1, CTCF

BCH-341 POSTER

Management of Aggressive Oral Cancer Through GR Mediated Targeted Therapeutics

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Acquisition of Epithelial Mesenchymal Transition (EMT) is the reason for conventional cancer related therapies such as surgical resection, chemotherapy and radiotherapy to be unsuccessful. Hence, targeting EMT to induce drug sensitivity and inhibit metastasis is significant for successful containment of aggressive oral cancers. Among the many cascades governing EMT, Steroid Hormone Receptors (SHRs) were found to be involved with malignant and aggressive property of cancer cells. To alleviate the treatment drawbacks, our group previously showed the EMT reversal of cancer cells through a Glucocorticoid Receptor (GR) mediated liposomal delivery system. In accordance with this, we are aiming to target Glucocorticoid Receptors (GR) of aggressive oral cancer to selectively co-deliver the chemotherapeutic drug along with pro-apoptotic gene, p53. The GR targeted cationic lipid formulations were formulated by simply associating cationic lipid, dexamethasone (a synthetic GR ligand), cholesterol, and an anticancer drug, Paclitaxel. There was significant lag in time to repopulate cells treated with GR-targeted formulations compared to non-targeted formulations in Cellular Scratch Assay. To further evaluate the mechanistic studies, Western blot analysis indicated the increased expression of epithelial marker protein, E-cadherin and decreased expression of mesenchymal marker protein, Vimentin in the aggressive oral cancer cells treated with GR-targeted liposomal formulations. The results from both scratch assay and western blots indicated the involvement of GR in EMT-reversal. To check whether the delivery system will be effective against 3D tumors, in vitro 3D tumor models (spheroids) were developed from aggressive cancer cell lines. The respective uptake of the EGFP plasmid delivered by GR-targeted and non-targeted liposomal formulations were analyzed by FACS. The GR-targeted liposome significantly increased EGFP expression in cancer spheroids when compared to its non-targeted equivalents. Further mechanistic and *in vivo* studies pertaining to EMT are currently in progress to broaden the role of delivery system in tumor regression.

Key words: OSCC, 3D Tumor Model, Liposomal Delivery System, Glucocorticoid Receptors, EMT-Reversal

BCH-342 POSTER

Augmented Level of Reduced Glutathione by Scopoletin Improves Form and Function of Dopaminergic Neurons in Parkinson's disease Model

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Parkinson's disease (PD) is a neuromuscular disorder clinically manifested in motor anomalies due to progressive loss of dopaminergic neurons and accumulation of alpha-synuclein proteins. Although alterations in genetic factors have been associated with the disease etiology, exponential accumulation of reactive oxygen species (ROS) initiates a chain reaction leading to mitochondrial dysfunctional, overwhelming of antioxidant system and cellular inclusions thereby

exacerbating disease progression. Implication of oxidative stress in PD is further supported with ROS induced Parkinsonian models and elevated oxidative markers in clinical PD samples thereby suggesting modulation of neuronal oxidative load as one of the major approaches in management of PD. Here we have found a potent antioxidant moiety Scopoletin (Sp), a common derivative in most of the nootropic herbs, with robust neuroprotective ability. Sp increased cellular tolerance to ROS through efficient recycling of GSH to prevent oxidative damage. The Sp treated cells showed higher loads of reduced glutathione making them resistant to perturbation of antioxidant machinery or neurotoxin MPP^+. Sp could restore the redox homeostasis, mitochondrial function, and prevented oxidative damage, leading to recovery of dopaminergic neural networks and motion abilities in Drosophila genetic model of PD. Our data also suggest that Sp, in combination increases the therapeutic potency of L-DOPA by mitigating its chronic toxicity. Together, we highlight the possible ability of Sp in preventing oxidative stress mediated loss of dopaminergic neurons and at the same time enhance the efficacy of dopamine recharging regimens.

Key words: Redox homeostasis, Antioxidants, Mitochondria, Parkinson's disease

BCH-343 POSTER

CGGBP1 and it's Direct and Indirect Interactions with the DNA

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The human genome contains CGG trinucleotide repeats, which are transcription- and translation-regulatory elements and also form secondary structures that hinder replication and give rise to sites of chromosome fragility. CGG trinucleotide repeats are highly rich in CpG sites which are present in gene-rich regions and can be methylated. CGG-trinucleotide repeat binding-protein 1 (CGGBP1) is a 20kDa protein which binds to such DNA sequences and is involved in multiple cellular processes such as transcription, DNA damage, and regulates epigenetic states. It is involved in several conserved processes such as endogenous DNA damage and repair, telomere integrity, cell cycle regulation, stress response, regulations of Alu and L1 repeats. These functions depend on the binding of CGGBP1 to its target DNA sequences. CGGBP1 is a C2H2 zinc-finger DNA-binding protein with its DNA-binding domain on the N-terminal end and its C-terminal end seems to be involved in its interaction with other proteins and also modulates its interaction with the DNA. We are attempting to study these interactions by using a system wherein the protein has been truncated to have either the N-terminal direct DNA binding domain or the C-terminal domain devoid of any known direct DNA interaction domains. To identify the indirect or direct interactions between CGGBP1 and DNA, we perform ChIP sequencing and global gene expression analyses. As an outcome we'll be able to elucidate its elaborate array of direct and indirect interactions with the DNA and its consequences on various cellular processes.

Key words: CGGBP1, DNA-Protein Interactions, CHIP sequencing

BCH-344 POSTER

Folate Receptor Targeting Biocompatible Nanospheres for Augmenting Drug Uptake in Oral Squamous Cell Carcinoma

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For the current work, we chose to target the Folate Receptor (FR) which is reportedly overexpressed on cancer cells. Previously, we developed a Folate based cationic lipid that shows its potent targeting ability while remaining associated with a variety of delivery systems. In here, we used carbon nanospheres (CSPs) as delivery system which is highly biocompatible and has the property to access multiple organs including brain when injected *in vivo*. These CSPs are

also resistant to the destabilizing effects of serum enabling efficient cellular internalization and nuclear targeting. The drug conjugated to our delivery system is Doxorubicin or Adriamycin, a popular topoisomerase inhibitor which is widely reported as an anti-cancer drug. Cancer cells often develop resistance to Doxorubicin due to a variety of mechanisms like EMT reversal, autophagy, the formation of vesicles or exosomes etc. Treatment of oral cancer cells with our FR-targeted system (ligand-conjugated), non-targeted system and free drug Doxorubicin for 6 hours showed significantly higher uptake of the targeted system indicating receptor-oriented delivery. We then conducted uptake assays for up to 24 hours and Doxorubicin uptake was found to be significantly higher in case of cells treated with our targeted system as opposed to those treated with free drug. Similar uptake studies conducted using non-cancerous cells showed significantly lower uptake and retention of our targeted delivery system, indicating commendable cancer cell targetability. To confirm FR mediated delivery, we pre-treated OSCC cells with Folate and found that it significantly reduced the uptake of our targeted system. Additional western blotting studies revealed a spike in the levels of circulating/soluble FRs immediately within 30 minutes of Folate treatment. These levels were then gradually seen to wane off within a matter of 2 to 3 hours, indicating that our delivery system would enter FR-overexpressing cancer cells quite rapidly while enabling re-circulation of circulating FRs to membrane. Further studies to investigate the therapeutic potential of our targeted system are ongoing.

Key words: Oral cancer, Targeted therapy, Folate receptor, Carbon nanosphere, Drug internalization

BCH-345 POSTER

Role of Cytoskeleton Proteins in Target Identification and Drug Discovery from *Withania somnifera* Using *In Silico* and *In Vitro* Bioprospecting Approaches

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The cancer burden continues to grow globally and is marked to be the world's second-largest cause of death. In the realm of breast cancer, recent breakthroughs in omics technology have focused on and enabled more precise treatments. In eukaryotic cells, the cytoskeleton is assumed to be a remarkable network of highly evolved cytoplasmic filaments. For a long time, plants with many nutritive and non-nutritive phytochemicals have been used in cancer therapy along with promising responses. Medicinal plant *Withania somnifera* (WS) possesses potent twenty-nine naturally occurring secondary metabolites. Therefore, the present study was designed to elucidate the interaction between WS phytoconstituents and the selected cytoskeletal proteins *viz.* actin, coronin, cofilin, gelsolin, vimentin, vilin, thymosin, and ezrin to perturb the initiation and differentiation of cancer cells using *in silico* and *in vitro* approaches. Docking analysis revealed that the phytoconstituents particularly withanolide A, B, D, M and O from WS displayed the greatest binding affinity towards the targeted cytoskeletal proteins. MD simulation results revealed that coronin-viscosalactone B complex showed maximum stability throughout the simulation run of 100ns. WS methanolic extract (WSME) exhibited potent cytotoxicity against MDA-MB-231 cells with an IC_{50} value of 66.2 µg/mL. The RT-qPCR analysis of WSME-treated cells revealed a decrease in the gene expression levels of mesenchymal markers *viz.* vimentin, N-cadherin, however, an increase in the levels of epithelial marker *viz.* E-cadherin was observed. To support the finding, an Annexin V/PI staining investigation revealed that early apoptotic cells were more prevalent in WSME-treated cells, possibly due to the drug's capacity to induce differentiation. The results indicate that the WS phytoconstituents can emerge as potential anticancer agents, if studied and screened further *in vitro* and *in vivo*.

Key words: *Withania somnifera*, Coronin, Cofilin, Molecular docking, Molecular dynamics Simulation, Epithelial-Mesenchyme Transition (EMT)

BCH-346 POSTER

Novel Sporadic SNCA Mutations Exhibit Variable Effects on Protein Aggregation, Cell Viability and Oxidative Stress

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α-synuclein aggregation is the hallmark feature of Parkinson's disease. Both familial and sporadic forms of the disease exhibit this feature. Several mutations have been identified in patients and are associated with the disease pathology. Interestingly, the localization, aggregation dynamics and toxicity observed is variable in these mutations. Hence, it is important to study every mutant variant in detail to understand the disease pathology. Our study aimed to characterize two less studied α-synuclein mutations in the well-established yeast model. To achieve this, we generated a yeast expression plasmid with α-synuclein tagged to GFP. Desired mutations were created and cells expressing the mutant variants of the protein were characterized for toxicity effects on cell growth, cell viability and oxidative stress. Additionally, we generated double mutants with A53T to analyze if this results in an additive effect. Our results provide a better understanding of the effects of α-synuclein mutations on the aggregation of the protein and cellular effects such as oxidative stress and cell viability.

Key words: A-Synuclein, Parkinson's disease, Yeast

BCH-347 POSTER

Evaluation of p53 and LIF Expression in Letrozole Induced Polycystic Ovarian Syndrome (PCOS) Rat Models in Relation to their Oxidative Stress Status

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Women with polycystic ovarian syndrome (PCOS) suffer from various serious health issues. It causes anovulatory infertility, menstrual cycle abnormalities and also increases the clinical risk of pregnancy complications. PCOS is multigenic disorder and its pathophysiology is not well understood. Recent studies related to extensive changes in DNA methylation and gene expression profiling (via Gene Ontology: GO analysis) and interaction of significant pathways (via Kyoto Encyclopedia of Genes and Genome: KEGG analysis) in PCOS patients suggested that the p53 pathway may potentially play a direct or indirect role in PCOS. p53 has been found as an significant gene involved in reproduction, in a gender-specific manner as p53 regulates maternal reproduction through leukaemia inhibitory factor (LIF). Also, Mdm2-p53-SF1 pathway in ovarian granulosa cells directs ovulation and fertilization by conditioning oocyte quality. Oxidative stress (OS) is increased in PCOS patients as compared to normal. OS induce infertility in women through a variety of mechanisms. Ovarian follicles experiencing OS can lead to direct damage to oocytes. OS also induces genetic variation, modifications of DNA bases and genetic mutations in numerous genes and these mutation in regulatory genes such as p53, mdm2 and LIF can affect their gene expression which might be an important factor affecting the reproductive health of PCOS patients. Increased oxidative stress and its effect on gene expression of P53 can be an imperative reason that affects oocyte quality and cause infertility and other complications in PCOS patients. The present study aims to elucidate the potential role of increased oxidative stress on p53 and LIF gene expression in PCOS rat models. Thus the study will provide an insight about the pathways that are disturbed in PCOS and will help in understanding its pathophysiology. We were successfully able to induce PCOS in different rat groups which included (control group, PCOS group, oxidative stress (OS) group, PCOS + OS group, Male group, Mated control group and mated PCOS group). We also found that there was increase in ovarian tissue specific levels of oxidative stress in different rat groups as compared to the normal.

Key words: PCOS, Rat models, P53, LIF

BCH-348 POSTER

Complementary Medicine: A New Therapeutic Approach for Treating PCOS

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PCOS is the common endocrine disorder in women of reproductive age, with prevalence of 6-20%. PCOS is a multifactorial disorder with genetic, metabolic and endocrine abnormalities. Women with PCOS suffer from serious health consequences such as infertility, type 2 diabetes, obesity and dyslipidemia. The central abnormality in PCOS is the excess ovarian androgen production. Women with PCOS also have increased oxidative stress. Hyperandrogenism might occur due to the inflammatory response of the abnormal ovarian theca cells to free oxygen radicals. Altered inflammatory response results in metabolic abnormalities such as insulin resistance and hyperinsulinemia. Hyperinsulinemia increases the secretion of androgens with different effects on ovary, adrenal, pituitary, LH receptor, sex hormone binding globulin etc. Conventional pharmaceutical treatment for PCOS addresses single symptoms like OCP (oral contraceptive pills), clomiphene citrate and anti-androgens but it is often associated with side effects and is not effective in most cases. So, women are now shifting to complementary medicine. Complementary medicine (CM) used by women has increased from the past ten years with rates of use ranging between 26% and 91%. One of the most popular type of CM is herbal medicine. Herbal medicines contain pharmacologically active constituents with effects on female endocrinology. *Nigella sativa used for present study is reported to modulate hormones related to fertility in dehydroepiandrosterone induced PCOS rats.* This study employs letrozole induced PCOS female wistar-rat models to evaluate efficacy of active-extracts of *Nigella sativa* on the expression of crucial inflammatory markers viz. TNF-α, NF-kB and INOS against the conventional drugs used for PCOS and we will try to find out the possible mechanism through which its active extract(s) exhibit such activity. Also, these observations will lead us to evaluate the formulation of same plants as a possible therapeutic agent to manage PCOS by targetting particular pathway involved.

Key words: PCOS, Inflammation, Hyperandrogenism, Rat model, Active extract

BCH-349 POSTER

Identification of Extraintestinal Pathogenic E. Coli (ExPEC) in Multiple Antibiotic Resistant (MAR) *Escherichia coli*

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Escherichia coli is a commensal bacterium that forms a part of the normal microflora of humans and various animals. *E. coli* strains can cause gastrointestinal infections as well as infections outside the gastrointestinal system. The later are caused by Extraintestinal pathogenic *E. coli* (ExPEC) variants. ExPEC strains are responsible for causing urinary tract infections (UTIs), adult bacteraemia and neonatal meningitis. Antimicrobial resistance, if present in such strains, can give them survival benefit and thus can severely hamper treatment options. Contaminated food & water are known to be major sources of pathogenic *E. coli,* many of them being Multiple Antibiotic Resistant (MAR). Several different types of virulence factors responsible for pathogenesis, like adhesins, invasins, toxins, capsules, siderophores etc. are associated with ExPEC strains. *E. coli* strains can be differentiated into seven phylogenetic groups- A, B1, B2, C, D, E and F. ExPEC variants are clustered mostly in B2 and D phylogroups. Many genes encoding for antibiotic resistance (ARGs) and virulence factors (VFs) are known to be present on mobile genetic elements and may get transferred to commensal bacteria together. Therefore, it is necessary to identify and perform molecular characterization of *E. coli* isolated from food and water bodies with respect to these genes.

Key words: E. Coli, EXPEC, Multiple Antibiotic Resistance, Virulence factors, Food and Water Bodies

BCH-350 POSTER

A Computational Approach from the Phytoconstituents of *Moringa oleifera* Targeting as an Antiviral Agents Against the SARS-CoV-2 Spike Glycoproteins

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Background: The rapidly spreading coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) accelerates the discovery of prophylactic and therapeutic drugs. Natural product based therapeutic drugs for the treatment of SARS-CoV-2 is currently unavailable.*Moringa oleifera* is a miracle plant with antibacterial, antiviral, and antioxidant properties having high content of flavonoids, glucosides and glucosinolates. Molecular docking can be used to predict the bound conformations and binding energies between ligands and macromolecular targetswhich could be implicated for structure-based drug design. **Aim and Objectives**: The present study was aimed to *in silico* evaluation of the antiviral potential of *M. oliefera* phytoconstituents against spike glycoprotein of SARS-CoV-2, as an herbal phytomedicine to face the urgent need for COVID-19 treatment. **Materials and Methods**: Molecular docking analyses elucidated the binding energies (BE) and dissociation constant (K_d) of ten selected potential phytoconstituents of *M. oliefera* against SARS-CoV-2 spike glycoproteins (PDB IDs: 6M0J, 6VXX, 6VYB and 6W41) through the AutoDock version 4.2.6 software. Further, these results were validated using AutoDock Vina. Bioactivity score and Prediction of Activity Spectra for Substances (PASS) analysis were also performed using chemoinformatic software Molinspiration and Osiris Data Explorer, respectively. **Results**:The results of the docking study showed that out of ten phytoconstituents,dihydroquercetin, kaempherol, quercetin and isorhamnetin displayed potent binding affinity with spike glycoprotein (6VYB) with B.E. -7.33,-7.87, -7.76 and -7.4 Kcal/mol and K_d 4.21µM, 1.71µM, 2.05µM, 3.73µM respectively in comparison with known SARS-CoV-2 inhibitor drug hydroxychloroquine (BE = –5.03andK_d = 206.99µM).Further these results were validated by Autodock Vina software which also showed good binding affinity. Drug likeness properties and ADMET prediction were analysed to determine the therapeutic aspect of these phytoconstituents. Interestingly, all four phytoconstituents displayed drug-likeness with no predicted toxicity and followed the Lipinski's rule with no violation andalso showed the highest gastrointestinal absorption. **Conclusion**: The current *in silico* studies showed that these four phytocontituents of *Moringa oliefera* could interact with the target spike glycoproteinof SARS-CoV-2 which would be adeveloped as promising prophylactic and therapeutic agentsagainst SARS-CoV-2.

Key words: SARS-CoV-2, Phytoconstituents, Spike Glycoprotein, Molecular Docking

BCH-351 POSTER

Outer Membrane Vesicles of *Campylobacter Jejuni:* A Defensive Custodian of the Host or an Offensive Striker for Microbes?

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Naturally secreted outer membrane vesicles (OMVs) from gut microbes carry diverse cargoes, including proteins, nucleic acids, toxins, and other intrinsic secretory components. As a generalized constitutive secretion system, bacterial OMVs hold the ability to establish cell-to-cell communication to facilitate bacterial self-survival and host pathogenesis during their gut transit. Although the harmonized secretion of major virulence factors is a shared mechanism of many mucosal pathogens, *Campylobacter jejuni* (*C. jejuni*) lacks classical virulence-associated secretion systems. As an alternative, *C. jejuni* often employs OMVs as a concerted strategy to deliver active toxins and secretory proteins into the target cells. Here we studied *C. jejuni* OMVs to venture their unique functional diversities and explore their potential

to influence immunological correlates of host protection. We performed mass spectrometry of in-solution trypsin digested OMVs protein and identified 237 proteins, including periplasmic, membrane-associated, and putative cytoplasmic virulence factors, including two key proteins of the bacterial Type VI secretion system, TssM and VgrG. To gain more insight into the OMVs mediated host-pathogen interaction, our study further suggests OMVs internalization of host cells is via membrane fusion and dynamin-independent endocytic *pathway*. Our final aim embodied to see the immunological effects of OMVs in host cells and carbohydrate mimicry of *C. jejuni* lipo-oligosaccharide (LOS) can induce anti-GM1 antibody, OMVs were treated with polymyxin B to minimize LOS-mediated endotoxicity. Interestingly, our *in vivo* chicken immunization study, confirmed that polymyxin B treatment of OMVs can retain its ability to confer significant immunoprotection against *C. jejuni* challenge.

Key words: Outer Membrane Vesicles, Campylobacter Jejuni, Lipo-Oligosaccharide (LOS), Immune-Protection

BCH-352 **POSTER**

T6SS-Dependent Dysbiosis as an Antibiotic Alternative for Improving Gut Health

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Campylobacter sp. is one of the four major global causes of diarrhoeal diseases, and is universal in early childhood, particularly in Middle and Low-Income group of counties (MLICs). Chickens remain the main source of *Campylobacter* infections, once colonizes, most of the birds remain reservoirs throughout their life and posing a potential risk for human transmission. Recent study suggest that chicken gut hosts a wide range of *C. jejuni* genotypes including those which harbour specialized secretion system, namely as Type VI Secretion System (T6SS). Bacterial T6SS, in general, secretes a vast range of effector molecules and facilitates bacterial predation, host cell adherence, and invasion, conferring a selective advantage to the predator over other prey bacteria. However we do not know how a functional T6SS of *C. jejuni* coexist with other resident microbes and whether they have any role in perturbation of gut homeostasis. Here we report a novel phenotypic difference among T6SS+ve and T6SS-ve *C. jejuni* in their predation abilities and response to the bile salt, a natural stressor present in the gut. We show that T6SS activity entails a cost during predation under environmental stress. Further, we confirmed that in the presence of bile salt and prey bacteria, T6SS+ve isolates displayed increased cell death exhibiting 'deflated' sac-like morphologies, and enhanced DNA damage. Together, we elucidate how T6SS-dependent predation can lead to self-killing under altered gut environment and highlight the prospect of using this unique attribute of T6SS-dependent "predation cost" as an "antibiotic alternative" approach for improving gut health.

Key words: *Campylobacter Jejuni*, Type VI Secretion system, Bile Salt, Gut Dysbiosis, Gut-Microbes

BCH-353 **POSTER**

Dissecting the Role of Camp Signaling Pathways in Cervical Cancer: A Target for Therapeutic Intervention

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Decreased cyclic nucleotide levels and increased expressions of various cAMP/cGMP-dependent phosphodiesterase (PDE) isoforms have been linked to several tumorigenesis including cervical cancer where increased expressions of PDE4 and PDE5 have been documented hinting towards the roles of cyclic nucleotide signaling pathways in tumorigenesis. Therefore, modulation of cyclic nucleotide signaling with selective in trial or market available PDE inhibitors might be a cost-effective therapeutic intervention against cervical cancer. Our study has shown that PDE4 and PDE5 inhibitors like rolipram and sildenafil can significantly increase cAMP and cGMP levels respectively in human

cervical cancer cell lines: Hela and SiHa (HPV $^{+}$ cell lines) but showed no modulation in C33A (HPV^{-}cell line). Cell proliferation study also revealed marked abrogation of cancer cell proliferation upon rolipram and sildenafil treatment in HPV $^{+}$ cell lines. It was therefore investigated whether such abrogation was the result of altered telomerase expression and activity. Taken together, these findings suggest that inhibition of PDE4 and PDE5 generate anti-proliferative effects in HPV^{+} cell lines but not in cell lines lacking HPV. These results clearly indicate towards the potential of rolipram and sildenafil as anti-cancer targets in HPV $^{+}$ cervical cell lines indicating an association of viral load with cAMP-PDE signaling modulation, while the precise mechanism of the same is yet to be unravelled.

Key words: cAMP, Phosphodiesterase, PDE Inhibitors, Cervical cancer, Rolipram, Sildenafil

BCH-354 POSTER

Impact of Protein Aggregation through Co-Solute Engineering Using Biophysical Approach: Theory To Therapy

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Protein misfolding and aggregation is one of the most exciting new frontiers in protein chemistry as well as in molecular medicine. Human insulin, a well-known model protein for understanding the development of amyloid formation since both are linked to insulin-injection amyloidosis in type II diabetes and are prone to the formation of amyloid fibrils in vitro. According to reports, the number of individuals with insulin-dependent diabetes is expanding at an alarming rate, with 366 million diabetics projected by 2030, up from 191 million in 2000. We aim to gain novel structural insights into insulin fibril production at physiological pH and temperature using a combination of fluorescent imaging dyes like thioflavin T (ThT) and ANS kinetics. Biophysical research with dynamic light scattering (DLS) and imaging with confocal laser scanning microscopy (CLSM) is followed by in-silico approaches such as molecular dynamics simulations. According to these investigations, recombinant human insulin (rHI) is adversely affected in the presence of sugar, with the maximum aggregation reported in 1M trehalose, indicating a novel path of information to hexameric insulin. As the concentration of trehalose rises, so does the level of aggregation. However, protein aggregation was inhibited comparatively at very low concentrations to trehalose using a combination of trehalose and co-solutes such as Arginine/CTAB/MSG, which decreased aggregation to that of the native protein. Amino acids, surfactants are expected to form bonding with the trehalose, thereby maintaining the integrity of insulin by inhibiting aggregation all at physiological conditions. Considerable effort are still required in maintaining the stability of the hexamer unit of Insulin, which is one of the most challenging issues in producing protein formulations and has been the focus of significant clinical, biochemical, and biophysical investigations. The main motive to carry this work is to first; maintain the structural integrity of recombinant human insulin (rHI) to be feasible carrier vials for diabetic patients; secondly, a worrisome solution for insulin injection amyloidosis.

Key words: Recombinant human insulin; Protein aggregation; Trehalose; THT; Md Simulations

Helicobacter Pylori Secretory Proteins Downregulate NLRP3 Inflammasome by Producing Oxidative Stress

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Helicobacter pylori is a leading cause of gastric ulcers and related cancer. *H. pylori* not only survives the killing by infiltrated immune cells produced reactive oxygen and nitrogen species (ROS and RNS) but also modulates their functions. Uncontrolled immune responses triggered excess ROS and RNS further lead to mucosal damage. Persistent

oxidative stress related to mucosal damage is a major reason for stomach cancer. *H. pylori* regulates oxidative stress by controlling host nicotinamide adenine dinucleotide phosphate (NADPH) oxidases (NOXs), nitric oxide synthase 2 (NOS2), and polyamines through lesser-known mechanisms. ROS and RNS produced by these pathways are also responsible for the differentiation of macrophages and T cells. Pathogens-associated molecular patterns (PAMPs) induced ROS and RNS targets NOD, LRR and pyrin domain-containing protein 3 (NLRP3) inflammasome and regulates pro-inflammatory immune responses. Current study evaluates the role of *H. pylori* secreted concentrated proteins (HPSCP) in oxidative stress, NLRP3 inflammasome activation and macrophage differentiation. HPSCP-induced oxidative stress was evaluated in THP-1 and AGS cell lines and the expression of $gp91^{phox}$ (NOX2), NOS2, NLRP3, CD86 and CD163 was analyzed by confocal microscopy. THP-1 macrophages growth declined, whereas gastric epithelial AGS cells proliferated in response to HPSCP. ROS and myeloperoxidase (MPO) increased in THP-1, whereas nitric oxide (NO) and lipid peroxidation decreased in AGS cells. Expression of $gp91^{phox}$ was unchanged, whereas HPSCP downregulated NOS2 and NLRP3 expressions. HPSCP-induced NLRP3 expression increased after inhibition of NO, ROS and MPO. HPSCP upregulated the expression of M1 and M2 macrophage markers, CD86 and CD163 respectively, whereas it decreased after the inhibition of ROS. In conclusion, HPSCP-induced oxidative stress was found to regulate the NLRP3 inflammasome activation and macrophage polarization. Regulation of NLRP3 by *H. pylori*-induced ROS and RNS could be a possible mechanism for macrophage polarization and modification of immune responses.

Key words: Helicobacter Pylori, Oxidative Stress, Reactive Oxygen Species, Reactive Nitrogen Species, Nod, LRR, Pyrin Domain-Containing 3 (NLRP3) Inflammasome

BCH-356 POSTER

Anticancer Efficacy of Garcinia Indica and its Phytoconstituents Against Breast Cancer using Molecular Docking Algorithms

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Background: Currently, one in four cancer cases in women are diagnosed with breast cancer, making it the most common malignancy in this group. Natural products have drawn more attention due to their potential as cutting-edge cancer therapeutic and/or preventive agents and have no any negative effects on healthy cells. *Garcinia* species are abundant and priceless sources of bioactive chemicals with important medicinal qualities, including antioxidant and anticancer properties. Nowadays, *in silico* approaches for drug discovery are booming over the decades because of their affordability and less time-consuming features. **Aim and Objectives**: The aim of the present study was to examine the anticancer potential of the bioactive phytoconstituents of *Garcinia indica* against breast cancer target proteins *viz.* survivin, estrogen receptor α (ERα) and progesterone receptor (PR) using *in silico* methods. **Materials and methods**: In the present study, five phytoconstituents *viz.* Garcinol, HCA, Anthocyanin, Isoxanthochymol and Xanthochymol from *Garcinia indica*, were screened for their interaction and binding affinity with three selected breast cancer proteins *viz.* ERα (PDB ID: 1R5K), PR (PDB ID: 3HQ5) and Survivin (PDB ID: 1E31) using molecular docking. Bioactivity score and Prediction of Activity Spectra for Substances (PASS) analysis were performed using chemoinformatic softwares Molinspiration and Osiris Data Explorer, respectively to assess the feasibility of selected phytoconstituents as potential drug candidates. **Result**: PASS analysis of the selected phytoconstituents revealed no violations of Lipinski's parameters. Additionally, good absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties were predicted for *Garcinia* phytoconstituents. The docking analyses revealed that isoxanthochymol displayed the greatest binding affinity with Survivin (BE= -7.26, K_d = 4.79uM) and ERα (BE= -7.12, K_d= 6.06uM) proteins. However, anthocyanin displayed a potent binding affinity with PR (BE= 6.42, K_d= 19.65uM) protein. **Conclusion:** The present *in silico* study reports would serve as a significant foundation for the lead identification and drug development against breast cancer using *in vitro* and *in vivo* investigations, if studied further.

Key words: Breast cancer, Garcinia indica, Molecular docking, Anticancer

Discovery of Gamma Globin Inducers as Therapeutics for Sickle Cell Anaemia

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Sickle cell disease (SCD) is the most common hemoglobinopathy affects about 4.5 million people worldwide. Patients with severe sickle cell disease exhibit defects in the development of the adult globin chain (single mutation (GAG to GTG), resulting in the substitution of glutamic acid (Glu6) for valine (Val6) at the 6th position in the -globin chain) and produce mutant sickle haemoglobin HbS(α2/ βs2), which polymerizes in low oxygen environments and bends red blood cells into the distinctive sickle shape when the switch of hemoglobin from fetal HbF (α2 γ2) to adult HbA (α2 β2) is completed . Increases in HbF have a clear positive impact in these latter settings because they prevent polymerization, and reduce molecular interaction and polymerization in sickle cell anaemia.The benefits of increased HbF in people with β-hemoglobinopathies have been thoroughly documented and recognised by scientists, pharmacologic activation of HbF expression has been proposed as a viable method for controlling anaemia and associated symptoms. Pharmacological induction of the fetal γ globin gene in adult erythroid cells is a feasible therapeutic strategy for sickle cell disease (SCD). Hydroxyurea (HU) is the only FDA approved drug which is in clinical use for the treatment of sickle cell anaemia but serious side effects such as leucopenia, thrombocytopenia, and myelosuppression limit its clinical use. Moreover, 30 to 50% of Sickle cell anaemia patients are resistant to HU treatment. So, various pharmacological companies around the world are looking for new drugs for the treatment of sickle cell disease. In this regard our research group discovered compound IIIM-001 and IIIM-019 as novel and potent inducers of γ globin expression in MEL cells by using novel fluorescent-based cellular reporter assay system with two reporter genes, DsRed and EGFP under the control of γ-globin promoter and β-globin promoter, respectivelyand the molecular mechanisms involved in human K562 erythroleukemic cells. compound IIIM-001 and compound IIIM-019 showed more potent activity than known gamma globin inducer sodium butyrate. We further confirmed our result by flow cytometery and western blot analysis. The role of signalling pathways, p38 mitogen-activated protein kinase (MAPK), was also investigated.

Key words: Sickle Cell Anaemia, Hemoglobinopathy, Fetal Hemoglobin (HBF), Hydroxyurea (HU), Mel (Mouse Erythroleukemic), K562 (Human Erythroleukemic) Cells

BCH-358 POSTER

Therapeutic Strategies Targetting 'Cellular Senescence' and 'Chronic Ailments'

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The accumulation of certain molecular and cellular damages over time results in ageing. Ageing predisposes humans to chronic diseases, geriatric syndrome (old age diseases) and death. About 35% of the variations in human longevity are due to genetic factors. Our grasp of the biological basis of ageing is far from complete; research suggests that addressing the ageing process could improve several age-related diseases. Senescence is a cellular response marked by sustained growth arrest and other phenotypic modifications, including the production of proinflammatory secretions. In this regard, the current hypothesis demonstrates that senescent cells' genetic or pharmacological elimination extends life duration and enhances health span. Here we examine the cellular and molecular connections between cellular senescence and ageing and the unique treatment possibilities that this connection offers up.

Key words: Ageing, Senescence, Genetics

Role of Micro-RNAs in Coronary Artery Disease

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Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and include coronary artery disease, cerebrovascular disease, rheumatic heart disease and other conditions. CVDs are the leading cause of death globally (17.9 million deaths every year).
Coronary artery disease (CAD) is a condition which affects the arteries that supply the heart with blood. It is usually caused by atherosclerosis which is a buildup of plaque inside the artery walls.This buildup causes the lumen of the arteries to become narrower and slows down the flow of blood. CAD is often diagnosed at very late stages. A rapid and effective test for early prediction or detection of stable coronary disease and, more importantly, pre-atherosclerotic disease or condition is still lacking. Moreover, most of the current diagnostic methods are invasive in nature. Micro-RNAs are a class of small noncoding RNAs which are an emerging source of candidate diagnostic/prognostic biomarkers. Several micro-RNAs have been shown to be expressed in cardiac tissues and have a known distinct role in heart development and fuction. They are also key regulators of several cardiovascular disorders such as myocardial infarction, ischaemia, hypertrophy etc. Micro-RNAs such as mir-128 and mir-195 have been shown to regulate the expression of several genes related to inflammation, autophagy and cholesterol metabolism. These processes play an important role in development and disease progression of coronary artery disease (CAD). Mir-128 & mir-195 are also differentially expressed in serum samples of diseased as well as control samples of CAD. Therefore, these micro-RNAs might be a potential source of biomarker for CAD.

Key words: Coronary Artery Disease, Atherosclerosis, Micro-RNA, Biomarker

BCH-360 POSTER

Binding Studies of Tepotinib to Hemoglobin using Multispectroscopic and Molecular Docking Techniques

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Tepotinib (TPT) is an anticancer agent that suppresses receptor tyrosine kinase activity. It has been primarily characterised as a strong anti-tumor agent, particularly for the treatment of patients with non-small cell lung cancer (NSCLC) whose tumours contain an aberrant mesenchymal epithelial transition (MET) gene. The objective of this study is to analyse the interaction of TPT and haemoglobin (Hb). The results of the study may aid in the knowledge of the transport of tyrosine kinase inhibitors and the pharmacokinetics of tinib-type drugs. The absorption spectroscopy measurements confirmed the development of the ground state complex between Hb-TPT. The absorption and fluorescence spectroscopic analysis was used to identify the occurrence of static quenching during the interaction of Hb with TPT, as well as changes in the microenvironment surrounding hydrophobic domains, particularly tyrosine residues. The binding affinity of TPT with Hb was examined using multiple spectroscopic techniques. The Stern Volmer constant (K_{SV}) and the binding constant (K_b) were found to be 4.25 x 10^3 M^{-1} and 3.54 x 10^6 M^{-1}, respectively. The interaction of TPT with Hb leads to change in α-helical content of Hb and was reduced from 33.98% to 31.13%, as revealed from circular dichroism studies. Molecular docking was also carried out to see the binding pattern of TPT with Hb and it was found that TPT binds to β-subunit of the Hb. The results obtained shows that the interaction between TPT and Hb caused conformational and structural changes in Hb.

Key words: Tepotinib, Anticancer, Hemoglobin, Spectroscopy, Circular Dichroism, Molecular Docking.

BCH-361 POSTER

T Follicular Helper Cell Response is Defective in Severe Covid-19 Patients

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Coronavirus disease (COVID-19) shows various clinical manifestations such as viral pneumonia ultimately progressing to acute respiratory distress syndrome (ARDS), extensive alveolar damage and even multi-organ failure in severe cases. Host immune response plays a significant role in the pathogenesis of disease, thereby impacting the clinical outcome. In fact, dysfunctional T cell mediated responses have been reported in severe COVID-19 patients. However there is lack of data determining the perturbation of CD4+ T helper cell subsets in the spectrum of SARS-CoV2 infection. Overall goal of this study was to determine association of the circulating CD4+ T cell sub-populations that include Th1, Th2, Tregs, Tfh cells as well as the key systemic cytokines with the severity of COVID-19 disease. For this, 15 patients from each of the three disease states; i.e., severe, mild and asymptomatic were recruited after obtaining the ethical approval from the Institutional Human Ethics Committee. Age-matched healthy individuals were included as control. Gene expression profiles of transcription factors and cytokines associated with their respective subsets was done using real time RT-PCR and/or ELISA. No significant difference in the expression of T-bet and GATA-3 was observed among all the groups. Interestingly, we observed significant down regulation of FOXP-3 in severe patients indicating the failure of T regulatory cell response which potentially leads to hyper inflammation and severity in COVID-19 disease. While no difference was observed in the expression of Bcl-6 responsible for the differentiation of T follicular helper cells, a significant increase in its effector cytokine IL-21 was observed in severe group with respect to control. Furthermore, the cytokine milieu of severe patients had significantly higher levels of the pro-inflammatory cytokines, IL-6, IL-1β and MCP-1 suggesting that the factors leading to inflammatory environment enhance the severity in COVID-19.

Key words: Covid-19, T Follicular Helper Cells, Interleukin-21

BCH-362 POSTER

The Difference in the Architecture and Branching Morphogenesis of Tracheal Terminal Cells of Drosophila Melanogaster in Normoxia and Hypoxia

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Tubular organs are essential for the transportation of gaseous and nutrients. The tracheogenesis of Drosophila is structurally and functionally conserved with the angiogenesis of vertebrates. The developmental cues for branching are well integrated into the genome, and a lot of research is going on to decipher them. But little is known about how they react to different environmental conditions. Our goal is to study how tubular organs respond to a different environment. Hypoxia is sensed immediately by the organism and induces many hypoxia-related genes to survive. The tracheal terminal cells (TTC) of Drosophila melanogaster undergo subcellular tubulogenesis and change rapidly in response to hypoxia. Here, we investigate the changes in the architectures and branching pattern of TTC in hypoxia. We performed standardization experiments to check the mortality, developmental delay, and stress behavior of Drosophila larvae in different hypoxia doses. We then, examined the architecture and branching morphogenesis TTC by microscopy and image analysis in a standardized hypoxic dose. The architecture was distinctive where branching frequency was proliferated in hypoxia. We characterized the branches from the major Primary branch (PB), Secondary branch (SB), and Tertiary Branch (TB) to the finer Quaternary branch (QB). It is observed that although the hypoxic signal is the same in the whole tracheal system, there is a response gradient where frequency increased in hypoxia by QB is 780%, TB by 141.25%, SB by 66.4%, and PB Frequency remained the same. We then investigated the post-hypoxia pruning of excessive branching after hypoxic treatment. The branch frequency of post-hypoxia larvae was less compared to hypoxic ones suggesting pruning events took place. Our finding indicates that a predominant response is observed where the finest branches (QB) are relatively more amplified as compared to the major branches (PB). We

propose a model suggesting that either there is a gradient in breathless receptors or branching resources. Post-hypoxia pruning effect is also observed which indicates that the recycling of branching resources is ongoing, and in the future, it can be a model to study neuronal pruning.

Key words: Hypoxia, Drosophila Melanogaster, Tracheal System, Tracheal Terminal Cells, Branching, Subcellular Tubulogenesis

BCH-363 POSTER

Identification of the Interacting Partners of *Plasmodium falciparum* GCN5 Histone Acetyltransferase

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The pathogenesis of human malarial parasite *Plasmodium falciparum* is interlinked with its timely control of gene expression during its complex life cycle. In this organism, gene expression is partially controlled through epigenetic mechanisms, the regulation of which is of utmost importance for the parasite. The *P. falciparum* GCN5 (PfGCN5) histone acetyltransferase (HAT), is an essential enzyme, acetylates histone 3 and regulates global gene expression in the parasite. Therefore, it is crucial to study PfGCN5 function in *P. falciparum* throughout the parasite's asexual stages that can serve as potential drug target in the backdrop of emerging drug resistance. Here we report the generation of 3' GFP tagged GCN5 endogenous parasite line that has served as useful tool for the above purposes. GFP-PfGCN5 protein like endogenous protein is constitutively expressed throughout the three intraerythrocytic developmental stages namely, ring, trophozoites and schizonts in parasite. Live cell microscopy also demonstrates that PfGCN5 is predominantly localized in the nucleus of the parasite. GFP-PfGCN5 protein was successfully immunoprecipitated from the transgenic parasites using GFP-TRAP beads. Further, interacting partners of PfGCN5 were identified through LC-MS/MS after immunoprecipitation that revealed the presence of Food Vacuolar proteins including proteases. These results shed light on the processing and trafficking of PfGCN5 protein in the parasite. Further, PfGCN5 interacting proteins also represent different class of nuclear proteins including an AP2 transcription factor, which signifies a new paradigm for targeting the co-activator complex to regulate general and parasite-specific cellular processes in this low-branching parasitic protist.

Key Words: Malaria, *Plasmodium falciparum*, GCN5, Histone acetyltransferase (HAT), Histone acetylation, Immunoprecipitation, Mass Spectroscopy, Food Vacuole, Interacting Partner

BCH-364 POSTER

Assessment of Anti-Glycating activity of Phytoestrogen Biochanin A, an Isoflavone Phytoestrogen

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Biochanin A (BCA), is an O-methylated isoflavone (5,7-dihydroxy-4'-methoxyisoflavone). It is found mainly in leguminous plants of the family fabaceae like clovers, chick peas, etc. Various recent studies have attributed many health benefits to BCA. This study was carried out to assess its anti-glycating potential. **Methodology:** In the current investigation, anti-glycating potential of BCA was assessed by glycating Human Serum Albumin (HSA) by Methylglyoxal (MGO) in presence of various increasing concentrations of BCA followed by examination of various biochemical and biophysical analysis. The analytical tools used were UV-visible absorption studies, Analysis of fluorescent AGEs, structural analysis by circular dichroism (CD), scanning electron microscopy (SEM), transmission electron microscopy (TEM) and sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE). The investigation showed a positive correlation on the inhibition of glycation of HSA by MGO with the increase in the concentration of BCA. Conclusions: The present study found that BCA has significant anti-glycating property.

Key words: Biochanin A, Anti-Glycation, Human Serum Albumin, Methylglyoxal

BCH-365 POSTER

Hypertension Scenario in Jammu Region

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Hypertension or high blood pressure is also known as the condition when there is abnormally high blood pressure than the normal blood pressure. Hypertension in patients remains ignored because it does not show any symptoms; for this reason it is also known as a silent killer. Untreated hypertension can lead to many secondary complications like stroke, heart disease and kidney diseases. Considering the rising current scenario of hypertension in J&K. The study was conducted on 100 cases and 100 controls by taking different parameters into consideration. Blood pressure of the individuals was measured and was categorized under hypertensive and normotensive group. The mean age was found to be 58.24 years old among the hypertensive population. The onset of the hypertension was found to be around the age of 21 years old among the individuals who were having their parents and grandparents suffering from hypertension and diabetes was found to be common co-morbidity among hypertensive individuals.

Key words: Hypertension, co-morbidity, Diabetes

BCH-366 POSTER

The Expression and Purification of Main Protease of SARS- CoV-2

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The evolution of SARS- CoV-2 and the eventual outbreak of COVID-19 has put the burden on medical fraternity and scientific community to identify the means of containment of this lethal biological entity. This can only be achieved by achieved by extensive in-vitro, in-vivo as well as in-silico efforts backed up by advances in molecular and structural virology. Thus, the discovery of anti-viral drugs and the development of other clinical therapies are critical in the battle against COVID-19 and the spread of SARS-CoV-2. The main protease, Mpro of SARS-CoV-2 which governs the proteolytic cleavage of viral polyprotein to yield functional proteins is seen as one of the important enzymes in the processing of new virus particles. As a consequence, Mpro is a promising target for the development of anti-COVID-19 treatments. In the presented study , we have successfully expressed and purified Mpro from the prokaryotic system harbouring the recombinant gene. The molecular biology protocols reported in this study are simple yet efficient in yielding recombinant proteins.The central dogma of gene to protein is exploited *in-vitro* to optimise the expression and purification conditions to obtain protein in its native-like conformation with highest purity.The purified protein is the pre-requisite for biophysical and biochemical experiments to gain deeep insight of structural characterization, structure- based drug discovery and their mode of inhibition against Mpro.

Key words: COVID-19, SARS-COV-2, Main protease, Recombinant protein, Chromatography, Transformation

BCH-367 POSTER

Role of Regulatory Elements in Increasing the SiRNA Based Inhibitory Effects on Hbv Replication in Cell Lines of Hepatic Origin

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Hepatitis B virus (HBV) is a small DNA virus which is highly species and tissue-specific in nature, affecting human hepatocyte, is a major cause for severe end stage liver disease such as liver cirrhosis and hepatocellular carcinoma (HCC). Despite the availability of Hepatitis B vaccine, around 296 million people worldwide remains HBV infected due to its poor coverage in endemic regions, with an average increase of 1.5 million newly infected patients every year. Although the current licensed antivirals effectively control the viral replication, it still remains a challenge to completely

eradicate the viral load in chronically infected patients. A novel therapeutic drug is a need of the hour which could either work by targeting the replicative cycle of HBV or by modulating host immune system. RNA interference (RNAi), a biological mechanism in which double-stranded RNA (dsRNA) is targeted to complementary mRNA, results in inducing gene silencing at post transcriptional level, followed by mRNA degradation, is a breakthrough innovation in novel therapeutic treatment of incurable diseases. Small interfering RNA (siRNA), an RNAi modality, is a promising therapeutic approach which supports functional cure of HBV. The RNA molecules of HBV encoding viral proteins are immensely essential for its replication. Thus, inactivating these RNAs would drastically reduce the viral load in HBV infected patients. Irrespective of the potential approach of RNAi technology, multiple obstacles lie in practically delivering the siRNA to the target organ. Only a highly liver specific siRNA could effectively suppress the target gene. siRNA works under extensive control of regulatory elements such as promoters and enhancers. Strong regulatory elements could help in achieving enhanced expression. If the regulatory elements are liver specific in nature, the expression of siRNA would be restricted to hepatocytes. Selection of target genes and designing of siRNA constructs including combinations of specific regulatory elements, targeting multiple sites in HBV genome would prove to be a promising novel therapeutic approach in the field of HBV.

Key words: HBV, RNA Interfernce, Small Interfering RNA, Regulatory Elements

BCH-368 POSTER

Modulation of metabotropic Glutamate Receptor 1 Internalization and Synaptic AMPA receptor Endocytosis by PICK1

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Group I metabotropic glutamate receptors (mGluRs) have been implicated in various neuropsychiatric disorders like autism, fragile X syndrome and they are also believed to be in various synaptic plasticity including learning and memory formation. Trafficking of these receptors plays the critical role in regulating the spatio-temporal localization of the receptor in the neuron. Improper positioning of the receptors can affect receptor signaling and such alterations can lead to severe pathological consequences. The aim of this study is to unravel the role for protein interacting with C kinase 1 (PICK1) in regulating the agonist-induced internalization of mGluR1 using elegant techniques like "live cell dual antibody feeding assay", "molecular replacement" etc. Our data shows that PICK1 specifically regulates the internalization of mGluR1 but it does not have any role in regulating the internalization of the other member of group I mGluR family, i.e., mGluR5. We have studied the role of various regions of PICK1 viz., the N-terminal acidic motif, PDZ domain and BAR domain in the agonist-mediated internalization of mGluR1. Finally, we demonstrate that PICK1-mediated internalization of mGluR1 is critical for the resensitization of the receptor. Upon knockdown of endogenous PICK1, mGluR1s could not get resensitized and stayed at the cell membrane as inactive receptors. These inactive mGluR1s were unable to upregulate the MAP-kinase signaling. They also could not induce the AMPAR endocytosis, a cellular correlate for mGluR dependent synaptic plasticity. Thus, this study unravels a novel role for PICK1 in the agonistmediated internalization of mGluR1 and mGluR1-mediated AMPAR endocytosis that might have clinical importance to the function of mGluR1 in neuropsychiatric disorders.

Key words: mGluR1. mGluR5, Endocytosis, Desensitization, Receptor Trafficking, AMPA Receptors, Map-Kinase, Long Term Depression

BCH-369 POSTER

Role of Chromatin Remodellers in Maintaining Higher Order Chromatin Structure

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Genome is organized in a hierarchical manner scaling from nucleosomes, topologically associating domains (TADS), to chromosome territories. ATP-dependent chromatin remodellers play an important role in modulating the chromatin structure. ISWI and CHD1 ATP-dependent remodellers have been shown to be involved in maintaining the proper

nucleosome spacing by sliding them along the DNA. But their role in regulating global chromatin accessibility and higher order chromatin structure in not known. We used triple deletion strain in which genes encoding Isw1, Isw2 and Chd1 were deleted and its corresponding wildtype for comparison to address this problem. MNase-Seq analysis showed that in absence of these ATP-dependent chromatin remodellers there is change in nucleosome occupancy and spacing. We found changes in accessibility of chromatin in triple deletion strain when compared with wildtype. To find the role of remodellers in three-dimensional chromatin organization we used chromosome conformation capture based methods, Hi-C and Micro-C. We found that deletion of these remodellers leads to the change in 3D chromosomal interactions. Our findings suggests that ATP-dependent chromatin remodelers have a role in regular nucleosome spacing at primary level and this spacing is possibly linked to chromatin accessibility, gene expression and proper three-dimensional chromatin organization.

Key words: Chromatin Remodellers, Tads, Hi-C, Micro-C, MNase-Seq

BCH-370 POSTER

Analyzing Structural Differences between Insulin Receptor (IR) And IGF1R or Designing small Molecule Allosteric Inhibitors of IGF1R as Novel Anti-Cancer Agents

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IR and insulin-like growth factor-1 receptor (IGF1R) share high degree of sequence and structural similarity that hinders the development of anticancer drugs targeting IGF1R, which is dysregulated in many cancers. Although IR and IGF1R mediate their activities through similar signalling pathways, yet they show different physiological effects. The exact molecular mechanism(s) how IR and IGF1R exert their distinct functions remain largely unknown. In this study we performed *in silico* analysis of IR in seven different species and generated IR-GFP and K1079R mutant analyze their subcellular localization, and downstream signaling in comparison to IGF1R and its K1055R mutant. K1079R mutation does not significantly decrease autophosphorylation activity of IR when compared with its homolog residue K1055R in IGF1R. Furthermore, K1079R mutation does not affect the subcellular localization and nuclear activities of IR. Moreover, K1079 residue in IR is seen to be sitting in a pocket which is different than the allosteric inhibitor binding pocket present in its homologue (IGF1R). This is for the first time such a study has been conducted to identify structural differences between these receptors that could be exploited for designing small molecule allosteric inhibitor(s) of IGF1R as novel anti-cancer drugs

Key words: Allosteric Inhibitor, Subcellular Localization, IGF1R, IR

BCH-371 POSTER

***Celastrus Paniculatus (Cp)* Seeds Extract Modulates Paraquat-Induced Oxidative Stress and Cell Death in a Cellular Model of Parkinson's Disease (SH-SY5Y Cells)**

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Parkinson's disease (PD), a common neurodegenerative disease is characterized by the progressive loss of dopaminergic neurons in the substantia nigra. The cause of PD onset remains unknown for a long time. However, recent reports suggest oxidative stress and mitochondrial dysfunction play key roles in the pathogenesis of PD. The drugs used for the treatment of PD show suboptimal results, and those that have shown some kind of neuroprotection in the animal models have failed to show any significant efficacy in clinical trials. Several plants'extracts and bioactive

components that exhibit therapeutic properties in PD and do not show any side effects even in extended use. *Celastrus paniculatus* (CP) seeds extract also has been reported to show neuroprotection against PD-related pathology. However, studies on its neuroprotective role and the underlying mechanisms are scarce, therefore the present study will explore the potential neuroprotective role of *Celastrus paniculatus* (CP) seeds extract in paraquat (PQ)-induced parkinsonism in SH-SY5Y cells. The present study determined the effect of *Celastrus paniculatus* (CP) seeds extract on PQ-induced cellular toxicity by measuring cell viability, oxidative stress and apoptosis in SH-SY5Y cells. Our results show that *Celastrus paniculatus* (CP) seeds extract treatment in SH-SY5Y cells resulted in increased cell viability, decreased oxidative stress, reduced the PQ-induced cell death. In conclusion, *Celastrus paniculatus* (CP) seeds extract exhibits neuroprotection against PQ-induced neurotoxicity in SH-SY5Y cells indicating its therapeutic potential against PD. The development and identification of selective inhibitors based on these parameters will provide approaches for treating PD progression.

Key words: Paraquat, Parkinson's disease, Celastrus Paniculatus, Cell viability, Oxidative stress

BCH-372 POSTER

Clinically Relevant Mutants of Hepatitis B Virus Small Surface Protein (HBsAg) Contribute to the Differential Level of HBsAg Secretion in HepG2 Cells

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Hepatitis B Virus small surface protein, referred to as HBsAg is synthesized by the small surface gen of the S-ORF. HBsAg which is also known as small or major surface protein plays significant role in viral life cycle, more particularly at the stage of viral morphogenesis. Second important role of the HBsAg is its involvement in interaction with host immune proteins, the event assumed to be one of the key players in viral clearance and persistence. HBV small surface gene (HBsAg) mutants in comparison to wild type makes hepatocytes more susceptible to liver injury which ultimately causes chronicity and liver failure. HBsAg mutants significantly causes changes in immunoproteins secretion which overpower antiviral response leading to persistent viral infection and subsequent immune pathologic outcomes associated with disease progression towards fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Hepatocellular injury is primarily attributed to host immune response and not only to the viral replication. So, it becomes necessary to understand the host immune response elicited especially by HBsAg mutants. In the present study we created A128V, G145R, W196S and M204I mutants of HBV by site directed mutagenesis. These mutants have known clinical significance. Then we performed ELISA of HBsAg in HepG2 cell line. The difference in secretion of HBsAg mutants was clearly observed. HBsAg mutants like A128V showed the least amount of secretion of HBsAg. This differential secretion of HBsAg in host cells may lead to varying degree of secretion of host immune proteins which may lead to varying nature of pathogenesis. Varying levels of HBsAg may also be attributed to alterations in the process of morphogenesis. The result of present study demonstrates that different mutants of HBsAg produce the differential level of its secretion. However, the molecular basis to understand this newly observed finding needs to be unravelled by doing the HBsAg ELISA in cellular extract also to know if the level of HBsAg retention also varies from mutant to mutant. Secondly immune proteins expressed under the influence of mutant HBsAg needs to be studied.

Key words: Hepatitis B Virus, Small Surface Protein, Immunoproteins, Immune Response, Pathogenesis

Small Molecule Oral Agonist of the Glucagon-Like-Peptide-1 Receptor

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An absolute or relative deficiency of pancreatic β-cells mass and functionality is a crucial pathological feature common to type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Glucagon-like-peptide-1 receptor (GLP1R) agonists have been the focus of considerable research attention for their ability to protect β-cell mass and augment insulin secretion with no risk of hypoglycaemia. Presently commercially available GLP1R agonists are peptides that limit their use due to cost, stability, and mode of administration. To address this drawback, strategically designed distinct sets of small molecules were docked on GLP1R ectodomain and compared with previously known small molecules GLP1R agonist. One of the small molecule PK2 (6-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl) methyl)-6H-indolo[2,3-b] quinoxaline) displays stable binding with GLP1R, induces GLP1R internalization and increasing cAMP levels. PK2 also increases insulin secretion in the INS-1 cells. The oral administration of PK2 protects against diabetes-induced by multiple low-dose streptozotocin (STZ) administration by lowering high blood glucose levels. Like GLP1R peptide agonists, treatment of PK2 induces β-cell replication and attenuate β-cell apoptosis in STZ treated mice. Mechanistically, this protection was associated with decreased thioredoxin-interacting protein (TXNIP) expression, a potent inducer of diabetic β-cell apoptosis and dysfunction. Together, this report describes a small molecule, PK2, as an orally active non-peptide GLP1R agonist that has efficacy to preserve or restore functional β-cell mass.

Key words: Diabetes, PK2, Insulin Resistance, GLP-1R

BCH-374 POSTER

Lipin-1 is Regulated by Plk1 and Pp2a and has a Role in Mitosis in Mammalian Cells

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Lipins are a family of proteins, which in mammals consists of three members: lipin-1, lipin-2 and lipin-3. They are phosphatidic acid phosphatases that catalyze dephosphorylation of phosphatidic acid to produce diacylglycerol. Among these homologs, lipin-1 is the most studied member. Lipin-1 has been shown to play versatile roles in different cellular processes like lipid metabolism, metabolic homeostasis, peripheral nerve function and nuclear envelope cytology. The most studied aspect of lipin-1 is its role in lipid metabolism. In this study we demonstrated the novel role of lipin-1 in mitosis. Using mass spectrometry, bioinformatic analysis and biochemical approaches, we demonstrate that lipin-1 is phosphorylated and regulated by the mitotic kinase PLK1. In addition, we used murine polyomavirus small T antigen as a tool, and showed that lipin-1 is regulated by PP2A, an important cellular phosphatase which has a critical role in the regulation of mitosis. Our results also show that during mitosis, lipin-1 undergoes peculiar phosphorylation changes and is localized to centrosomes. Our study further shows that the silencing of lipin-1 gene as well as its pharmacological inhibition causes mitotic defects. In summary, our study uncovers that apart from its other important functions lipin-1 has an important role in mitosis.

Key words: Lipin-1, Mitosis, PLK1, PP2A, Centrosome

BCH-376 POSTER

Antitumor effect of Colchicine Derivative on Glioblastoma

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Cancer is one of the leading causes of death worldwide, accounting for roughly ten million deaths in 2020. Glioblastoma (GBM) is the most prevalent malignant primary CNS tumor, accounting for more than half of all gliomas epidemiologically. Glioblastoma is nearly untreatable due to intra-tumor heterogeneity, as well as being less differentiated and more invasive. Although one of the highly lethal and difficult cancer, with disproportionally high morbidity and mortality, because of its localization in the brain, its infiltrating behavior, and extremely poor response to treatment. The current standard treatment for GBM involves surgical resection, radiotherapy, and chemotherapy. Due to the very invasive nature of GBMs, surgical resections are difficult and complete resections are almost impossible. Despite the identification of well-defined molecular markers, therapeutic targeting and disease prognosis in GBM is poor. Colchicine, an anti-microtubule, and the anti-mitotic drug is a common therapeutically agent for gout, which is thought to have potential anti-tumor effects. Owing to the concerns of colchicines poisoning, the development of derivatives with low dose efficacy and fewer side effects is of obvious interest. In this regard, our research group discovered the compound IIIM-001 as a potent inhibitor of glioblastoma by cell proliferation assay. Compound IIIM-001 shows more potent inhibitory activity than colchicine. Then we further confirmed our results by DAPI, colony formation assay, and western blotting.

Key words: GBM, Anti-Microtubule, Anti-Mitotic drug, DAPI, Colchicine

BCH-377 POSTER

Assessment of Heavy Metal Pollution Load in River Yamuna using Heavy Metal Pollution Index (HPI)

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Yamuna river is one of the most important rivers of India and is highly polluted. The present study was conducted to evaluate the concentrations of heavy metals in Yamuna river water using the heavy HPI approach. The stretch of Yamuna River from Yamunotri, Uttarakhand (origin point) to Prayagraj, UP (ending point) was chosen for determining the concentration of heavy metals like Fe, Cu, Co, Zn, Pb, Ni, Cd, Mn, As, and Cr by using ICP-MS. The arithmetic weightage-based heavy metal pollution index (HPI) was also computed considering all the metals together to evaluate the pollution status of the Yamuna river. Results of water quality analysis indicate that the level of iron was considerably higher than its permissible limit in all the sites and the maximum heavy metal content was found at Wazirabad (Delhi). HPI of Yamunotri and Paonta sahib water was found to be within limits i.e., free from heavy metal pollution.

Key words: Heavy Metal, HPI, ICP-MS, Maximum Permissible Limit

Characterization of Antimicrobial Potential of Indigenous Probiotic Lactobacillus isolates against Skin Pathogen *Staphylococcus aureus* and *Propionibacterium acne*

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The skin microbiota, which is made up of millions of bacteria, fungi, and viruses, lives on our skin. The skin, the body's biggest organ, is home to a variety of helpful bacteria and acts as a barrier against diseases. Dysbiosis in the skin microbiome is linked to a changed immune response, which supports a number of illnesses, including skin cancer. Due to a more health-conscious culture and a shift in consumer perception, food is now seen by consumers not just as a source of sustenance but also as a powerful tool for managing their health and well-being. Probiotics are live microorganisms that, when administered in the proper dosage, have positive effects on one's health. The most well-known microbiota for its medicinal properties is *Lactobacillus*. In this investigation, we attempted to evaluate the bacterial isolates obtained from fecal samples in terms of their probiotic qualities and possible antibacterial activity against the skin pathogen *S. aureus and P. acne*. For the experiment, 40 Lactobacillus spp. strains from 10 different species were gathered. Tolerance tests were performed to determine their viabilities in the presence of lysozyme (81-99%), bile salts (81-92%), acid, auto-aggregation (39--50%), and hydrophobicity (6-53%) assay. By using the test pathogen *S. aureus and P. acne*, the agar well diffusion experiment was used to evaluate their antibacterial properties. Inhibition zones were measured after a 24-hour incubation period at 37C. Few probiotic isolates in our investigation showed strong antibacterial ability with zones of inhibition (24 mm and 26 mm) against the test pathogens *S. aureus and P. acne*. These probiotic isolates might serve as an alternate treatment for skin-related diseases.

Key words: Keywords: Dysbiosis, Probiotics, Auto-Aggregation, Antimicrobials

BCH-379 POSTER

β-Catenin Inhibitor i.e. XAV939 impairs Aerobic Glycolysis in Triple-Negative Breast Cancer (TNBCS)

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Recently, we and others demonstrated that TNBC cells are highly glycolytic, and one of the oncoproteins that might be associated with increased aerobic glycolysis is β-catenin. In the present study, we investigated the role of β-catenin, PFKP (Phosphofructokinase-Platelet), and MCT1 (Monocarboxylate Transporter 1) in TNBC patients and cell lines. Immunohistochemistry for β-catenin, PFKP, and MCT1 were performed on 64 TNBC patients and its association with clinicopathological parameters wasfurther evaluated. For *in vitro* analysis, MDA-MB-231 and MDA-MB-468 cell models were used, where we assessed the expression pattern of β-catenin, PFKP, LDHA and MCT1. The therapeutic relevance of β-catenin was further evaluated using a XAV939, a tankyrase inhibitor. Of the 64 TNBC cases analyzed, 37 (58%) showed cytoplasmic or nuclear staining of β-cateninin tumor cells. Cytoplasmic accumulation of PFKP was observed in 36 (56%) TNBCs examined, while elevated membranous expression of MCT1 was observed in 47/64 (73%) cases. Statistical analysis revealed positive associations between β-catenin expression with cytoplasmic PFKP ($p = 0.0001$) and membranous MCT1 ($p = 0.028$), suggestingβ-catenin mediated positive regulation of PFKP and MCT1 proteins in TNBCs.Additionally, both the TNBC cells lines exhibited elevated expression levels of β-catenin, PFKP, and MCT1 proteins, and inhibition by XAV939 significantly inhibited the expression of PFKP and MCT1 thereby validating ours*in vivo* results. We further show that XAV939 significantly reduced lactate production in TNBC cells. Our study showed that increased β-catenin levels regulate the expression of key glycolytic markers i.e., PFKP and MCT1 in TNBCs. Furthermore, the ability of XAV939 to inhibit β-catenin-PFKP-LDHA-MCT1axis as well as lactate production advocates possibility of XAV939 to be used in the therapy and management of aggressive TNBCs.

Key words: Triple Negative Breast Cancer, Aerobic Glycolysis, β-Catenin, PFKP (Phosphofructokinase-Platelet), MCT1 (Monocarboxylate Transporter 1)

BCH-380 POSTER

Spectroscopic and Biophysical Studies on LDL Modified with Crotonaldehyde

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Crotonaldehyde, a highly toxic α, β- unsaturated aldehyde, is a major compound of cigarette smoke (CS) and a ubiquitous environmental pollutant. Exposure to crotonaldehyde-rich pollutants such as CS is associated with development of different types of cancers in humans. Toxicity of crotonaldehyde is caused by its strongly reactive electrophilic carbonyl group. It directly or enzymatically conjugates with glutathione (GSH), thereby reducing the GSH levels. Crotonaldehyde can modulate biological reactions through various downstream signaling pathways, and cause cellular oxidative stress. It elicits interleukin-8 release in pulmonary cells through the MAPK (mitogen activated protein kinase) pathway. The unstable crotonaldehyde strongly reacts with protein amino groups to form the stable protein-bound molecule represented by Ne-(2,5-dimethyl-3-formyl-3,4-dehydropiperidino)lysine (DMFDPL) adducts. This study has been designed to explore the details of structural alterations in LDL modified by crotonaldehyde, and identify the sites of modification and their potential for therapeutic targeting. The structural alterations in LDL were analyzed by UV-Vis, Fluorescence, Circular dichroism spectroscopy, FTIR and Thioflavin-T assay. Enhanced Thioflavin T fluorescence suggested the presence of fibrillar structures. This was further confirmed by electron microscopy (scanning and transmission electron microscopy) which pointed the formation of characteristic amorphous and amyloid like aggregates. We also measured free thiol groups, ketoamine, carbonyl and HMF content. Liquid chromatography mass spectrometry (LC–MS) spectral results showing the formation and decomposition of carboxymethyllysine (CML), and similar base peaks of m/z value for standard CML and that of Crotonaldehyde-modified LDL explain the decline in the lysine content. Formation of CML in the LDL confirms oxidation of the protein. Formation of carcinogenic aldehydes like crotonaldehyde during lipid peroxidation is believed to be involved in the pathophysiological effects associated with oxidative stress that can lead to cancer.

Key words: LDL (Low Density Lipoprotein), Crotonaldehyde, Oxidative Stress, Lipid Peroxidation

BCH-381 POSTER

Dynein Motor Protein in Regulation of Cellular Endocytic Pathways, Cellular Migration and Invasion

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Multiple endocytic pathways operate in cells in tandem for uptake of multiple cargo, metabolites, signaling molecules, etc. Most well studied pathways involve the well-defined coat proteins such as clathrin. Endogenous lectin, galectin-3 (Gal3), uses membrane receptors along with glycosphingolipids (GSLs) to drive membrane bending, leading to the formation of a morphologically distinct class of uptake structures, termed clathrin-independent carriers (CLICs). This finding has allowed us to address how cargo proteins are recruited to endocytic pits in pathways of clathrin-independent endocytosis. What components from cytoskeletal machinery are involved in the biogenesis and cellular dynamics of CLICs yet remains to be explored. We propose that Dynein motor protein, a retrograde motor is recruited at the sites of tubules generated by Gal3 and provides the pulling force to the membrane invaginations leading to formation of CLICs. Inhibition of Dynein shows the uptake of Gal3 and its cargoes (CD98 and CD147) are significantly dependent on Dynein activity whereas transferrin (a marker for clathrin mediated endocytosis) uptake remains unaffected of dynein inhibition. Using ATP depletion assays, we show that dynein provides the pulling force for the membrane tubules generated by Gal3. Dynein inhibition also affects cell migration and wound healing process in 2D and 3D model systems, which gives us an insight on the diverse functions of this motor on the processes like individual and collective cell migration in 2D as well as in 3D. We are currently exploring the mechanistic details about how dynein machinery is recruited on membrane tubules and how it generates the force for the biogenesis of CLICs. Our studies bring out the new functionalities of motor proteins involved in specific cellular endocytic pathways as well as cellular migratory processes. This study may also lead to the discovery of new therapeutic strategies for the clinical management of diseases associated with this motor protein, such as dyneinopathies.

Key words: Dynein, Clathrin Independent Carriers, Endocytosis, Cell Migration and Invasion

BCH-382 POSTER

Physical, Chemical and Biological Analysis of Different Soil Ecotypes from Delhi, India

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Soil is a natural body of mineral and organic material differentiated into horizons, which differ among themselves as well as from underlying materials in their morphology, physical make-up and chemical composition. Biological components of the soil can vary from one site to another site depending upon the inorganic and organic make up of the soil. Soil microbes are an integral part of the soil community. In the present study, the physical, chemical properties and microbe diversity was investigated from 2 different sites, namely Acharya Narendra Dev College (ANDC) and Okhla Landfill (OL), Delhi. Physical and chemical analysis of soil samples were conducted which included pH, soil texture, water holding capacity, moisture content, inorganic salts, electrical conductivity, cation exchange capacity, nitrogen content, organic carbon, calcium carbonate, phosphorous, calcium and magnesium content estimation using standard procedures. Biological analysis included study of ciliate and bacterial diversity. An understanding of soil microbe diversity, physical and chemical parameters may help us to drive decisions about the best practices to apply for improving soil quality and conservation practices in future. Community structure of ciliates & bacteria appeared to be of major importance for soil formation and they could serve as sensitive soil indicator in future.

Key words: Ciliates, Soil Indicator, Physical, Chemical, Landfill

BCH-383 POSTER

Control of Organ Size and Shape During Differential Development of Wing and Haltere in Drosophila

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How genes and mechanical properties of individual cells combine and determine an organ's shape and size remains a mystery. Drosophila wing-a flat structure and the globular haltere are two homologous flight appendages emerging from a similar group of progenitor cells. The differential development of wing and haltere, which differ in cell size, number, and morphology, is dependent on the function of Hox gene Ultrabithorax (Ubx), which is only expressed in developing halteres and not the wings. Ubx modulates multiple growth regulatory and patterning gene pathways to fine-tune the specification of haltere shape. However, for determining the final shape of an organ, the various signalling networks and cues from the external environment have to converge at the level of altering the individual cell behaviours such as cell shape, size and its mechanical properties- thus dictating the overall tissue geometry. Our studies on differential development of wing and haltere shapes suggest that the localization and abundance of actomyosin complexes, apical contractility, properties of extracellular matrix, cell size and shape, which is a resultant of various cell intrinsic and extrinsic forces, can influence the flat vs globular geometry of these two organs. Some of the mutants of major growth regulatory pathways showing partial homeotic haltere to wing transformation exhibit respective cellular level transformation. This links growth regulatory pathways and cellular biophysical properties in determining tissue and organ morphology.

Key words: Organ shape, Organ size, Cell shape, Cell size, Ubx, Haltere, Wing, Actomyosin Cytoskeleton, ECM, Contractility, Cell Junctional Tension

Novel ABA-NMDAR Signaling Nexus Provides a Unique Opportunity for Antimalarial Drug Discovery

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The presence of a plant like hormone abscisic acid, ABA, in human serum has been correlated with several human diseases including malaria. Here, we demonstrate an orchestration of ABA-NMDAR signalling nexus in *Plasmodium falciparum* infected host Red Blood Cells (RBC) that regulates the invasion and egress of the parasites. Once taken up by infected RBCs, ABA binds to its intracellular cognate receptor LANCL2 and triggers the downstream ABA signalling cascade. Binding of ABA to host LANCL2 increases the intraerythrocytic levels of cAMP which in turn activates protein kinase A (PKA). PKA phosphorylates and activates the NMDAR1 for the channelling of extracellular calcium inside the cell. Overall, this signalling nexus defines the mechanism by which plasma abscisic acid can enhance the surge of calcium inside the RBCs. Blocking the ABA signalling by targeting the LANCL2 with Pioglitazone results in imbalance of calcium homeostasis and blocks invasion and egress of malaria parasites from host RBCs. Encouraged by the antimalarial activity of pioglitazone, we further tested its effect in combination with artemisinin, a known antimalarial drug, both in vivo and in vitro. We found that pioglitazone serves as a good partner drug with artemisinin by synergistically decreasing the parasite load. Collectively this study indicates a new opportunity to exploit the host signalling pathways for repurposing an over the counter drug pioglitazone for malaria intervention.

Key words: Abscisic Acid, Plasmodium, Malaria, Calcium, cAMP, NMDAR, LANCL2, Pioglitazone, Red Blood Cells.

BCH-385 POSTER

Heterologous Boost Vaccination: Best of Both Worlds

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During the second SARS-CoV-2 wave, the northern Indian state of Uttar Pradesh was witness to a 'mix and match' incident of two different vaccines (Covaxin and Covishield) administered to 18 individuals inadvertently, under the national immunization program. This provided the spark for exploration of this unconventional mode of vaccination based on different mechanisms of action, apparently yielding 'supra-additive' results. Initial studies on this heterologous mode of vaccination demonstrated significantly higher immunogenic parameters compared to the homologous modes. Reactogenicity of the former mode was sufficiently tolerated as well. The ideal heterologous regimen was a viral vector-based vaccine combined with either an inactivated vaccine or an mRNA vaccine. This resulted in the elicitation of immunity via different arms of the immune system providing for a much more comprehensive coverage against SARS-CoV-2 variants. Many studies showed significantly higher elicitation of Neutralizing and binding antibodies, stimulation of polyclonal antibodies and strong T-cell responses using different combinations of the vaccines. Additionally, logistical concerns and reduced risk of adverse events makes the heterologous mode of vaccination a much for viable and effective option, especially in developing countries with limited resource settings. This may allow the healthcare setup to stay one step ahead of the ever-mutating virus. In this oral presentation, we attempt to explore the existing evidence on heterologous boost vaccination especially against variants of SARS-CoV-2.

Key words: Heterologous Vaccine, Covaxin, Covishield, Viral-Vector Vaccine, Inactivated Vaccine.

BCH-386 POSTER

Structural and Conformational Characterization of Methyl Methanesulfonate (MMS) Modified Calf Thymus DNA: Possible Role in Carcinogenesis

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Objectives: 1) To analyze and quantify the effects of methyl methanesulfonate (MMS) on the DNA molecule. 2) To probe the role of MMS-modified DNA in carcinogenic induction. 3) To identify the presence of cancer antibodies against MMS-modified epitopes in different groups of cancers. **Methodology:** The changes in the gross structure of calf thymus DNA (ct-DNA) induced by MMS were studied using biophysical techniques like S1 nuclease assays, FT-IR spectroscopy, ITC. Molecular interactions between DNA and MMS were assessed using molecular docking and MD simulations. ELISA's were used to probe the epitope recognition by antibodies isolated from cancer patients. **Results**: MMS causes a dose dependent damage to the structure of DNA. Spectroscopy and S1 assay revealed the presence of strand breaks. Findings of FT-IR showed a specific mode of interaction with guanine and the backbone of DNA. The binding was found to be spontaneous with low affinity. Molecular docking and molecular dynamic simulations confirmed that MMS could interact with DNA at two levels, one at the nitrogenous bases and another at the DNA backbone. Lung cancer IgG was found to recognize epitopes significantly on ct-DNA as a result of modification by MMS. **Conclusion**: MMS could induce structural and conformational changes in the DNA molecule. Accumulation of these modified products could cause cancers, specifically lung cancer. The presence of antibodies identifying such epitopes could be used for the early detection of lung cancers.

Keyword:ct-DNA, MMS, methylation, mutations, anti-MMS-DNA.

BCH-387 POSTER

Understanding the Role of Glucose-6-Phosphate Dehydrogenase (G6PD) Metabolism in Covid-19 Induced Neuroinflammation In-Vitro

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Human COVID-19 has affected more than 506 million people worldwide. It has caused over 6.2 million deaths and especially perpetrated high casualties among the elder and people with co-morbid illnesses. COVID-19 triggers a pro-oxidant response, leading to the production of reactive oxygen species (ROS) as a common innate defense mechanism. Excessive ROS generation during COVID-19 infection can be regulated by cellular redox regulators, which will further support recovery from infection. However, ROS are regulated by a key enzyme called G6PD via the production of reduced nicotinamide adenine dinucleotide phosphate (NADPH), which controls the generation and removal of ROS in a tissue-specific manner. Therefore, deficiency of G6PD can lead to the dysregulation of ROS leading to severe inflammatory response in COVID-19 patients. This study aims to understand the importance of functional dichotomy of G6PD in COVID-19 induced neuroinflammation and severity. Based on epidemiology status of G6PD deficiency, we have cloned the G6PD mutants into retroviral cassettes to generate viral particles. We then stably overexpressed the G6PD variants in human microglia for studying their effects on ROS regulation during COVID-19 infection. Towards this, we have used self-replicating SARS-CoV-2 RNA for inducing inflammatory condition in microglia. Our preliminary findings demonstrated aggravated inflammatory responses by microglia, as evident with high level of nitric oxide (NO) production following SARS-CoV-2 RNA transfection. Interestingly, an increased number of lysosomal bodies were detected in healthy microglial cells in comparison to other G6PD deficient cell types. Additionally, G6PD over expressing microglial cells transfected with the SARS-CoV-2 RNA showed nitric oxide toxicity suggesting a definitive pro-oxidant function by G6PD enzyme. Further studies are going on to understand both pro- and anti-oxidative function of G6PD in

COVID-19-induced neuroinflammation and severity. The findings from this study may aid in designing of novel interventional preventive measures for the same.

Key words: SARS-CoV-2 RNA; G6PD; NADPH; Microglia

BCH-388 POSTER

To Evaluate the Promoter Methylation Status and Expression Profile of DcR-1 Gene in the Progression of Breast Cancer

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Breast cancer is one of the most common neoplasms worldwide. According to the *GLOBOCON 2020,* female breast cancer has surpassed the lung cancer and became the most commonly diagnosed cancer with an estimated rate of 2.3 million new cases. Apoptosis contributes to a balance between cell proliferation and cell death in normal cells and any disturbance in this pathway leads to many human diseases including cancers. Cancers cells develop numerous strategies of resistance to cell death such as DNA mutations in genes coding for pro-apoptotic proteins, increased expression of anti-apoptotic proteins, or pro-apoptic gene silencing mediated by DNA hypermethylation.DcR-1 (Decoy Receptor 1) plays an inhibitory role in apoptosis and this study will determine the methylation and expression profile of this DcR1 gene in Breast Cancer. Out of 50 samples, 47 tissue specimens (both normal and tumor) were obtained from the Breast cancer patients from the Department of General Surgery, Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Srinagar. The DNA samples were extracted from all the 47 normal and tumor tissues and were processed for CT- Conversion followed by Methylation Specific PCR (MSP) technique. Methylation-specific PCR was carried out to investigate the promoter methylation status of DcR1 gene. Proteins were also isolated from all the 47 normal and tumor tissues followed by western blotting technique. As per the MS-PCR studies of DcR1 gene, 18/47(38.3%) of tumor samples were Methylated and 29/47(61.7%) were Non-methylated. Whereas, in normal samples, 37/47(78.7%) were methylated and 10/47(21.3%) were Non-methylated. Also, as per the western blotting results, it was found that 36/47(76.6%) of tumor samples showed a high expression and only 11/47(23.4%) showed a low expression of DcR1 protein whereas, as only 6/47(12.8%) of normal samples showed a high expression and 41/47(87.2%) showed a low expression. In conclusion, tumor tissues were found to have low methylation and high gene expression of DcR1 protein as compared to the normal tissues. All these results may vary once all the samples will be processed and after proper statistical analysis.

Key words: DcR-1(Decoy Receptor 1), MS-PCR

BCH-389 POSTER

Aptasensing Platform for Multiple Biomarker based Detection of Tuberculosis

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Tuberculosis infected patients release certain immunodominant antigens into the blood, cerebrospinal fluid, urine and saliva. Early diagnosis of people with a high probability of having active TB is crucial for breaking the chain of transmission. One group of these secretory antigens consisting of the 6-kDa early secretory antigenic target (ESAT-6), ESAT-6 like protein EsxB (also known as culture filtrate protein CFP10), diacylglycerolmycolyltransferase antigen (Ag85B) & immunogenic protein MPT64 are important clinical biomarkers. Designing aptamers (which are artificial oligonucleotides selected in vitro that bind cognate ligands with high affinity and specificity functioning as recognition

elements) against these biomarkers and developing them into biosensors is a viable and alternative approach to conventional diagnostic procedures which are costly, cumbersome, and often misleading due to false negative outcomes. The proposed technology adheres to the ASSURED (i.e. affordable, specific, sensitive, user-friendly, rapid, equipment free and deliverable to end users) criteria for point-of-care (POC) healthcare diagnostics. Thus, harnessing the capability of aptamers to capture the biomarkers from blood forms the underlying rationale of this study. Towards this end, cloning, expression and purification of the four *Mycobacterium tuberculosis* genes were done followed by western blot analysis of purified proteins to confirm their biological activities. Further, a random 69-mer single stranded DNA library pool consisting of 10^{14} to 10^{15} sequences was designed followed by symmetric and asymmetric PCR optimizations that could generate substantial amount of DNA before each round of SELEX. Results show that the PCR program was optimized at 30 cycles, with 1µM primers, 500ng template and 0.25mMdNTPs at 60-70°C annealing temperature. Atomic force microscopy confirmed the immobilization of proteins and DNA on the PVDF membrane for SELEX. Further, BSA-gold nanoclusters as aptamer labels were synthesized and characterized through spectrophotometric, spectrofluorimetric, FETEM and FESEM-EDX elemental analyses to confirm the desired shape, size and composition of the nanomaterial.In conclusion, the current approach highlights multiple biomarker-based confirmatory diagnosis of tuberculosis. Further, this aptasensing technique can be modified to generate a common POC screening platform for different types of respiratory infections like COVID for patients presenting similar symptoms in future.

Key words: Tuberculosis, Biomarker, Point-of-Care, Aptamer, SELEX, Diagnostics

BCH-390 **POSTER**

Role of Plasmodium PhiL-1 Interacting Protein (PhiP) in Malaria Transmission

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Malaria is a mosquito-borne infectious disease that kills nearly half a million people each year. Blocking the disease transmission could be one of the major initiatives in preventing spread of malaria. *Plasmodium* are unicellular parasites, that are delimited by a plasma membrane and an underlying inner membrane complex (IMC). The IMC contains several proteins that aid in mechanical stability and motility. An unexplored aspect of transmission is to understand the importance of IMC proteins during sexual commitment. We showed for the first time that PhiL-1 Interacting Protein (PhIP) is a constituent of IMC and its depletion affected gametocyte formation. In particular we noted the mutant lacking exflagellation capacity and also lack formation of female gametes. This results in failure to complete sexual reproduction as evident by absolute lack of oocyst formation. Concomitant with this finding, *Pb*PhIP mutant manifested dramatic changes in gene expression with downregulation of flagellar and dynein related proteins, male gamete fusion factor, secreted ookinete proteins and plasmepsin. These studies reiterate an important role of PhIP in commitment to sexual reproduction.

Key words: Plasmodium, Gametocytes, Gametes, Sexual developement, Malaria

BCH-391 POSTER

Functional Genomics of Susceptibility Genes involved in CD and their Role in Nervous System

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Background: Confirmatory diagnosis criteria of celiac disease (CD) include histological evaluation of duodenal tissue biopsy and titer of serum antibody against tissue trans-glutaminase (anti-tTG). Identification of tissue specific histological marker is warranted to improve the diagnosis. Recent genetic study in CD identified association of 'A', which is a known protein that connects membrane bound 'B' with 'C' in epithelial cells of the duodenal tissue. **Aims:** We attempted to investigate the expression differences of 'A' along with associated proteins namely 'B' and 'C' in duodenal biopsy tissue of CD subjects compared to non-CD controls. **Methods:** Duodenal (D2 biopsy) tissue was collected from a total of 83 study participants, of which 50 were CD and 33 were non-CD controls. Whole RNA was isolated from available tissues from 32 CD and 23 non-CD controls and differential mRNA expression of 'A', 'B' and 'C' were compared using real-time PCR. Tissue sections from 18 cases and 10 controls were subjected to immunostaining using specific monoclonal antibodies against 'A', 'B' and 'C'. Tissue immunohistochemistry were evaluated for differential expression and pattern of expression of proteins. **Results:** RT-PCR revealed significant reduced expression of 'A' (FC=0.63; p=0.005) and 'B' (FC=0.50; p=0.01) among CD subjects compared to non-CD controls. Tissue immunohistochemistry confirmed the reduced expression of 'A' and 'B' in CD. Differential expression is grossly limited within outer columnar epithelial cell layer. **Conclusion:** Reduced expression of two key cytoskeletal proteins ('A' and 'B') was observed in CD. Reduced expression of 'A' was previously reported in neurological diseases, whereas 'B' play critical role in neurological developments. Pathogenic role of these two proteins in CD suggests shared pathological determinants of CD and neurological disorders/conditions. Functional studies may unravel the contribution of 'A' and 'B' complex in CD pathophysiology.

Key words: Celiac Disease, Duodenum biopsy, Immunohistochemistry, mRNA Expression

BCH-392 POSTER

Ciliates as Model System for Ecotoxicological Studies

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Ciliates have been used extensively as model systems for ecotoxicological studies as they have very short generation time, easy to handle (majority being non-pathogenic), easy to culture and maintain under laboratory conditions and also easily available from aquatic/terrestrial ecosystems. Above all, they do not have cell wall due to which they are more sensitive to environmental stress which is important for any kind of toxicological studies. In the present study, toxicity assays for heavy metals (Cd and Cu) were carried out in the two ciliate species, *T. saprai* n. sp. and *E. aediculatus* to determine the tolerance degree limits. Heavy metals induce oxidative stress (directly or indirectly) leading to induction of antioxidant enzymes like Superoxide dismutase (SOD), Catalase (CAT) and Glutathione peroxidase (GPx). The activities of all the three antioxidant enzymes, viz. SOD, CAT and GPx increased in concentration dependent manner in the presence of heavy metals (Cd and Cu). The expression of stress responsive genes in the freshwater ciliates, *T. saprai* n. sp. and *E. aediculatus,* in response to heavy metals (Cd and Cu) exposure, was also studied. Stress responsive genes involved in antioxidant defense system, viz., Manganese superoxide dismutase (*Mn-sod),* catalase (*cat)* and heat shock protein genes (cytosolic *hsp70*) were selected for the present study. The activities of these enzymes were found to be regulated at the level of transcription in both the ciliate species. For the first time, in this study, stress responsive

genes; viz., *Mn-sod, cat*, cytosolic *hsp70* of *T. saprai* n. sp. and *cat*, cytosolic *hsp70* of *E. aediculatus* were also sequenced and characterized. The stress responsive genes like *Mn-sod, cat, gpx* and cytosolic *hsp70* may act as good biomarkers to study cell mediated stress in aquatic environment. In conclusion, the freshwater ciliates in future may act as an effective cellular and molecular tool for ecotoxicological studies.

Key words: Superoxide dismutase, Catalase, Antioxidant, Ciliates, Glutathione peroxidase

Elucidation of the promotor methylation status of an apoptotic pathway gene, TRAIL-2 and expression profile of caspase 3 gene in breast cancer patients

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Breast cancer is the most frequent cancer in women and the second most common cause of cancer related death. It has been estimated that approximately 1.5 million women worldwide are diagnosed with breast cancer each year. Epigenetic silencing of the apoptotic pathway genes and evasion of apoptosis has been demonstrated in breast cancer as a result of promotor methylation. Thus, the aim of this study is to elucidate the promotor methylation status of TRAIL-2 gene and expression of caspase-3 gene of apoptosis in breast cancer. Tissue specimen (both normal and tumour) of 50 newly diagnosed breast cancer patients from Department of General Surgery, Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Srinagar will be included in this study. Out of 50 samples, 34 samples have been collected till now and the DNA has been extracted by phenol/chloroform method and treated with sodium bisulfite using the EZ DNA methylation kit and also 27 samples were processed for protein extraction to perform the western blot. Methylation analysis was performed by Methylation Specific PCR (MSP) technique. As per MSPCR results of trail 2 gene,32/34(94.1%) of the normal samples were unmethylated while as only 2/34(5.8%) were found to be methylated. Also, in case of tumour samples,22/34(64.7%) were methylated and 12/34(35.29%) were non-methylated. Tumour tissue samples were found to be highly methylated as compared to normal tissue samples. As per the western blot results of caspase 3, it was found that out of 27 samples,17/27(62.9%) of normal sample showed high expression of caspase 3 protein and 10/27(37.03%) of normal samples showed a low expression of caspase-3 protein. Whereas, only 8/27(29.62%) of tumour samples showed high expression of caspase 3 protein and 19/27(70.03%) of normal samples showed low expression of caspase- 3 protein. In conclusion, tumour tissues were found to have high methylation status as compared to normal and proteins expression was high in normal samples as compared to tumour tissues. All these results may vary once all the samples will be processed and after proper statistical analysis.

Key words: Breast Cancer, Epigenetics, Methylation, Apoptosis.

BCH-395 POSTER

IN00604 Induces Autophagy and Inhibits NLRP3 Inflammasome; A Novel Approach against Neurodegenerative Diseases

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Neurodegenerative diseases (NDD) are a group of disorders characterized by progressive degeneration of nervous system. Amongst them, Alzheimer's disease (AD) and Parkinson's disease (PD) are the most common NDDs. The similarity in pathogenesis of AD & PD; accumulation of misfolded proteins like amyloid-beta, phosphorylated tau and alpha-synuclein, disruption of autophagy-lysosomal pathway, mitochondrial dysfunction and neuroinflammation, lead

us to search for a compound that could be a potential drug candidate for both the diseases. Autophagy is a lysosomal dependent cellular homeostatic pathway which clears the cellular waste and recycles them. NLRP3 inflammasome is the component of innate immunity and is a multi protein complex activated by wide range of microbial motifs. NLRP3 inflammsome comprises of three proteins; the receptor NLRP3 protein, the adaptor ASC and the effector pro-caspase-1. The activation of NLRP3 inflammasome leads to the release of proinflammatory cytokines; IL-1beta and IL-18. Our study focuses on targeting autophagy and NLRP3 inflammasome together through single molecule and to study the crosslink between these two cellular pathways.
Through our screening we have found IN00604 as a hit molecule. It is a natural compound which is safe upto 100 µM concentration. It can induce autophagy by upregulating AMPK pathway. It clears the accumulation of amyloid-beta in the primary astrocytes through induction of autophagy. It enhances the LAMP-1 and LC3 colocalization. IN00604 can also inhibit NLRP3 inflammasome, activated in response to accumulated proteins in AD and PD and is a major contributor to the neuroinflammation. IN00604 treatment inhibits ASC oligomerization in primary astrocytes. The inhibition of NLRP3 inflammasome by IN00604 is AMPK dependent which signifies that the mechanism behind inhibition of NLRP3 inflammasome is regulated by autophagy. Also, the mitochondrial dysfunction can be targeted through IN00604 as it has been seen that it positively regulates the mitochondrial health observed through up regulation of certain mitochondrial proteins. Considering the efficacy of IN00604, we present it as a potential drug candidate for AD and PD. The future studies involve studying the effect of IN00604 in transgenic mice model of AD and PD.

Key words: Neurodegenerative diseases, Alzheimer's disease, Parkinson's disease, Autophagy, NLRP3 Inflammasome, AMPK

BCH-396 POSTER

IN00615 Impedes Cellular Senescence by Upregulating AMPK Mediated Autophagy in age Related Neurodegenerative Diseases

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The process of physiological aging is associated with decline in the efficiency of autophagic degradation. As age progresses defects in Autophagy are known to promote the cellular senescence and this has well knitted association with neurodegeneration. Autophagy is a lysosomal degradative process which is used to recycle obsolete cellular constituents and eliminate damaged organelles and protein aggregates. Completion of process involves dynamic interactions among compartments of the autophagy and lysosome pathways.As the brain ages, neurons and astrocytes are particularly more vulnerable to these disruptions. Dysfunctional Autophagy causes neurodegenerative diseases across the age spectrum with exceptional frequency. This mainly depends on fusion of autophagosome with lysosome where lysosomes introduce necessary degradative machinery, including a proton pump vATPases and other hydrolytic enzymes. Ageing and cellular senescence is also classically associated with neuroinflammation which augments the progression of neurodegeneration. The defection of Autophagy is also known to increase the incidents of NLRP3 inflammasome activation which is the major cause of neuroinflammation in many age related neurodegenerative diseases. The focus of our study is to target defective Autophagy and thus correct the machinery in neurodegenerative disorders associated with age mainly Alzheimer's and Parkinsons's disease. Through our screening of natural compounds we have found a hit molecule IN00615 which can induce autophagy by upregulating AMPK pathway. We have checked its safety profile through MTT assay and it is safe upto 100µM concentration. It also promotes the colocalisation of LAMP1-LC3 which is reduced during ageing as autophagosome doesn't fuse with lysosome. The compound is also restoring the pH of lysosomes needed for its hydrolytic activity as indicated by our results through immunofluorescence assay.The β-galactosidase activity which enhances with senescence and ageing. The compound IN00615 is shown to reduce the β-galactosidase activity in aged primary astrocytes. P16, a marker protein for

senescence is also downregulated in presence of IN00615. Il-1beta, a pro–inflammatory cytokine released by the activation of NLRP3 inflammasome is inhibited by the treatment of IN00615. Our data conclusively indicates that IN00615 can correct the Autophagy and ameliorate cellular senescence and neuroinflammation. Thus it can be a potent candidate for neurodegenerative diseases which progress with defective Autophagy.

Key words: AMPK, Autophagy, Senescence, Ageing, Astrocytes, Neuroinflammation

BCH-397 POSTER

Protease anchored Biodegradable Nanocarriers for Improved Delivery of Anticancer Drugs

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The therapeutic efficacy of the drugs depends on the access of the target to the drug moiety. Repeated failure of cancer therapies could be attributed to the abnormal physiological features of the tumor tissues. The concept of nanomedicine brought a new hope in the cancer treatment. By relying on the enhanced permeability and retention (EPR) effect nanomedicine reaches the tumor tissues but their delivery to the target cells is hindered by the transport barriers created by the unique tumor physiology. The homogenous distribution of the nanomedicine throughout the tumor tissues is limited at various stages such as during vascular, transvascular and interstitial transport. The tumor microenvironment (TME) normalization could help in improving the drug delivery and efficacy of nanomedicine and other anticancer drugs. There are several approaches for TME normalization and the degradation of tumor extracellular matrix components is also one of such approaches. In the present study, we have investigated the potential of collagenase in improving the delivery of Gemcitabine-loaded human serum albumin NPs (GEM NPs). For carrying out the present study, we have prepared collagenase coated and uncoated GEM NPs by desolvation and crosslinking of HSA. The prepared NPs were characterized for size, drug loading, morphology, hemo compatibility and drug release. The collagenase coated over the NPs surface was quantified using collagenase assay. The cytotoxic potential and intracellular uptake of the prepared NPs was investigated *in vitro*. The role of collagenase in improving the drug delivery was investigated in the 3D tumor spheroids embedded in a mixture of collagen and matrigel matrix. The collagenase coated GEM NPs has shown improved uptake into the tumor spheroids that could be attributed to the degradation of collagen present in the matrix. Thus, the study has shown the role of collagenase in improving the drug delivery and anticancer potential of the nanomedicine via the ECM degradation.

Key words: Nanoparticle, Extracellular Matrix, Drug Delivery

BCH-398 POSTER

Selective & Sensitive Sensing of Ceftriaxone via Chemically Functionalized Nanodeposits

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Highly selective and sensitive electrochemical sensing of ceftriaxone (CRO- a widely used cephalosporin antibiotic) over glutathione functionalized gold nanoparticles supported over sulphur doped grapheme (GSHfAuNPs@S-Gr) is presented. GSHfAuNPs@S-Gr we show offers exceptionally high selectivity and sensitivity toward electrochemical sensing of CRO with negligible interference from biological electroactive compounds, and exhibits satisfactory recovery values in real sample analysis. We demonstrate that with GSHfAuNPs@S-Gr as electrode CRO can be sensed selectively with a limit of detection (LOD) as low as 3μM.

Key words: Ceftriaxone, Glutathione, Functionalized Gold Nanoparticles , Supported Over Sulphur Doped Graphene (Gshfaunps@s-Gr), Electrochemical Sensing

BCH-399 POSTER

Pharmacological Intervention for Alzheimer's Disease via Targeting Autophagy and NLRP3 Inflammasome

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Autophagy is a vital, ubiquitous and homeostatic process by which it recycles the cellular waste and damaged organelles. The inflammasome is a multi-protein oligomer complex that is formed to mediate host immune responses against cellular damage and microbial infection. Activated inflammasome promotes the maturation and secretion of caspases-1. Caspase-1 cleaves the inactive pro-IL-1β into active IL-1β, which will be secreted from cells and mediate tissue inflammation. Autophagy and inflammasome complex formation are physiological processes, controls immunity, homeostasis, inflammation. Excessive activation and impairment of both processes are associated with inflammatory and autoimmune diseases such as Alzheimer's disease, sepsis, and cancer. Alzheimer's disease (AD) Sis the most common cause of dementia and it is a neurocognitive disorder, its account for 60-80% of dementia in an older people. Two hallmarks of Alzheimer's disease are extracellular beta-amyloid deposition and intracellular neurofibrillary tangles are known to activate NLRP3 inflammasome and cause Neuroinflammation in AD. For the treatment of Alzheimer's disease many clinical candidates (drugs) are available but effective in suppressing dementia only for limited period and cannot revert or halt the disease progression. In the last decade many research projects have failed which were targeting either inflammasome or autophagy in Alzheimer's disease. In the present study, we are investigating the effect of targeting both the pathways simultaneously in Alzheimer's disease. In the experimental setup, we have screened a library of the test drugs (TD) (which are known autophagy inducers) against ATP induced NLRP3 inflammasome activation in primary astrocytes. Levels of pro-inflammatory cytokine IL-1β were assessed by using mIL-1β ELISA kit. Out of the drugs screened, TD-4 was found to be a potent inhibitor of IL-1β. Further mechanistic studies were also done for TD-4 and it shows significant inhibition of caspase-1, IL-1β and NLRP3 inflammasome, validated by western blotting. In addition to inflammasome inhibition, autophagy induction was also rechecked by evaluating the expression of LC3-II. LC3-II is the hallmark of autophagosome formation. Interestingly, TD-4 was found to increase the expression of LC3-II. The present study shows the potential of simultaneous targeting of autophagy and inflammasomes in treatment of Alzheimer's disease.

Key words: Alzheimer's disease, NLRP3 Inflammasome, Autophagy

BCH-400 POSTER

All epigenetic changes lead to promotion of neovascularization in esophageal squamous cell carcinoma (ESCC)

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Esophageal squamous cell carcinoma (ESCC) has very high mortality due to its certain peculiar features including aggressive new blood vessel formation in growing tumors. Understanding the causes of the aggressive neovascularization in ESCC is undoubtedly of great therapeutic value. The change in epigenetic landscape, can switch on pro-cancer genes and silence down the anticancer gene expression that favor ESCC blood vessel formation respectively. Our whole transcriptome microarray data of ESCC, showed a significant upregulation of EZH2 and HDACs (*HDAC3* and *HDAC8)*, along with a down-regulation of anti-angiogenic genes (AAGs) (*CD36, ANGPTL1* and *TIMP4*) and acetyl transferases (*KAT2A, KAT8, KAT6A, BRD4, BRF2*). Based on the data we hypothesize the possible epigenetic role of upregulated histone methyl-transferases (EZH2), histone de-acetyltransferases (HDAC3, HDAC8) and down-regulating acetyl-transferases in the down regulation of AAGs. We found that the mRNA levels of EZH2, HDAC3 and HDAC8 were significantly higher than ANGPTL1, CD36, and TIMP4 in clinical samples as well as in cancer cell lines, which validated our microarray analysis data. Next, we found that activities of EZH2 and HDACs lead to gain of H3K27me3 and loss of H3K9ac, H4K16 markers on the histones (H3, H4) of AAG gene promoters. Interestingly, in addition to harboring

the H3K27me3 enrichment, the promoter DNA of ANGPTL1 and CD36 was found methylated. Use of the drugs that stop the EZH2 or HDAC 3/8, role of modifications specific to these epigenetic modifiers in down regulation of AAGs was confirmed. Using Ebastine, the EZH2 inhibitor, expression of ANGPTL1, and CD36 in a dose dependent manner. Similarly, we found the treatment with SAHA (Vorinostat) inhibits the enzyme activity of HDAC3/HDAC8 and resulted in retention of the acetylation at H3K9ac and H4K16ac and end up with upregulation of AAGs.

Key words: Esophageal Squamous Cell Carcinoma (ESCC), histone methyl-transferases (EZH2), Histone deacetylases (HDACs), acetyl transferases, anti-angiogenic genes (AAG)

BCH-401 POSTER

Characterization of Acharya Narendra Dev College (ANDC) Campus Soil: A Pilot Project To Access The Soil Quality

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There is a need for continuous assessment of soil quality as soil is a complex and dynamic constituent of Earth's biosphere that is continuously changing by natural and anthropogenic disturbances. The overall health of the soil is maintained by the soil enzymes. Enzymes catalyze reactions that are required for critical soil microbial functions, soil structure stabilization, organic waste degradation, and nutrient cycling. In the present study, physical, chemical and enzymatic activity of Acharya Narendra Dev College (ANDC) campus soil was determined. The average values of each studied parameter were as follows: temperature at the time of collection was 37.24°C, pH 7.45, electrical conductivity (EC) from 4.773 µS/cm, water holding capacity 87.48%, Organic carbon 0.0528%, CaCO3 0.0925%, Ca^{2+} + Mg^{2+} ions 0.56mcq and CEC 8.42/100g soil. Another parameter to study biochemical status of soil is to study the activity of the various enzymes. In the present study, we have studied the activity of urease. Urease is an enzyme that acts on cn non peptide bonds in linear amides to break down urea into carbon dioxide and ammonium ions. Urease activity in soils has been reported to be correlated with soil parameters such as organic matter, soil moisture texture, ph and cation exchange capacity (CEC) and it is known to boost by mixing organic wastes with soils. our finding suggest to conclude that more field-based, long term study is required to determine unknown elements in the ecosystem that influence the efficiency of urease.

Key words: Urease, Cation Exchange Capacity, Electrical Conductivity, Ecosystem

BCH-402 POSTER

Anti-Tuberculotic Thionamide Antibiotics show Antioxidative and Neuronal Cytoprotective Nature by Inhibiting Amyloid Formation in Human Insulin and Amyloid β- 42

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Oxidative stress, amyloid formation, impaired proteasomal degradation are hallmarks of neurodegenerative diseases like Alzheimer's (AD) and are targets for developing therapeutics against such diseases. Thionamide antibiotics are second-line anti-TB drugs. We studied the inhibitory action of two thionamide drugs, prothionamide and ethionamide, against amyloid formation using various biophysical techniques. We also studied the ability of these drugs to act as antioxidants. Here,we showthat both drugs are potent inhibitors of in-vitro amyloid formation of human insulin and Aβ42 and protect cultured neuroblastoma cells against the toxic effects of amyloids. Various biophysical techniques like thioflavin-T binding assays, dynamic light-scattering (DLS), circular dichroism (CD), and transmission electron microscopy studies confirm that these drugs prevent amyloid fibril formation. CD and DLS measurements reveal that

these drugs exert their anti-amyloid potency by stabilizing the proteins in their native state. Their cytoprotective behaviour could be attributed to their antioxidant properties and their ability to inhibit in vitro lipid peroxidation, as confirmed by various antioxidant assays. This study reports for the first time a newfacet of thionamide antibiotics as potential amyloid and oxidation inhibitors, with implications in reducing oxidative stress-related manifestations of AD, thereby opening avenues to be used as a therapeutic in AD.

Key words: Amyloid beta-human Insulin, antioxidant, lipid Peroxidation, thionamide, Alzheimer's disease

BCH-403 POSTER

Conserved Saga Complex Mediates Stress Response and Filamentation in *Candida Albicans*

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SAGA (Spt-Ada-Gcn5-acetyltransferase) is an evolutionarily conserved multi-functional transcriptional regulatory complex bearing histone acetylation (HAT), histone deubiquitylation (DUB), TBP interaction and activator interaction functions. The genome of the opportunistic fungal pathogen *C. albicans* encodes orthologous sequences of all subunits of the yeast SAGA complex. To gain insights into the subunit requirement of CaSAGA complex, we constructed null mutants of ten non-essential subunits. Deletion of all SAGA subunits tested, barring *ubp8,* led to severe impact on growth in rich medium. We also tested the growth of the mutant strains for phenotypes under varied stress conditions. While each of the HAT module mutants showed impaired growth under all stress conditions tested, the SPT subunit mutants showed severe growth defect under oxidative stress and iron deprivation conditions. However, the DUB module subunit mutants showed varied growth defects under stress conditions. Whereas the *sgf73* conferred susceptibility to all stress conditions, the *sus1* mutant showed a defect only under specific stress conditions. Surprisingly, the *ubp8* mutant showed wild-type growth under all conditions tested. We cloned each of the wild-type genes, and showed complementation of the mutant phenotypes. We also uncovered the requirement of CaSAGA in filamentation. While *spt7, spt20, taf12l, gcn5, ada2* and *sgf73* mutations led to pseudohyphal morphology, *spt8* and *spt* mutations led to hyperfilamentation. In contrast, *sus1* deletion led to impaired filamentation. We also tested bulk H3K9 acetylation levels and found that while the *gcn5* and *ada2* HAT module mutations led to substantial loss of global H3K9 acetylation, the other SAGA mutants tested did not. Together our functional genetic analysis revealed a module-specific involvement of the SAGA complex in *C. albicans* stress response and filamentation.

Key words: *Candida Albicans*, Saga Complex, Stress, Filamentation

BCH-404 POSTER

A Rapid, Conditional Strategy to Study Gene Function in the Human Fungal Pathogen *Candida albicans*

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Molecular genetic studies thus far have identified ~1658 essential genes in *C. albicans* out of a total ~6198 haploid set of ORFs. Gene deletion by null mutation of non-essential genes in the diploid *C. albicans* has also problematic due to haploinsufficiency and aneuploidy in the mutant strains. Moreover, promoter-based inactivation are also of limited utility due to leaky expression under promoter-shut off conditions. Therefore, we are adapting the anchor-away technology in *C. albicans*, originally developed in the budding yeast, which allowed studying the function of candidate proteins in a rapid manner. In this method, rapamycin mediates interaction between the humanFK506-binding protein (FKBP12) and FKBP12-rapamycin-binding (FRB) domain containing proteins to relocalize nuclear proteins of interest onto ribosomes in the cytoplasm. We first, created a *C. albicans* strain resistant to rapamycin by targeted mutagenesis. Next, we tagged the ribosomal 60S subunit protein L13A (RPL13A) with codon-optimized 2xFKBP12

domain in the genomic locus to create *C. albicans* base strain bearing homozygous RPL13A::2xFKBP12 as anchor protein. Furthermore, we constructed a plasmid system bearing the mammalian FRB domain sequence and was codon-optimized for epitope-tagging of target proteins with the FRB domain. As a proof of principle for the *C. albicans* Anchor Away technology, we chose two nuclear proteins- the general transcription factor TATA-Binding Protein (TBP), and SuPpressor of Ty (Spt8), a subunit the SAGA histone modifying complex. Our results showed that *TBP1::AA* was inviable (lethal phenotype), and the *SPT8::AA* strain showed a filamentous phenotype in rapamycin-containing medium but not in control. The filamentation phenotype of the *SPT8::AA* was highly comparable to the *spt8DD* null mutant demonstrating that the anchor-away strategy is well suited for functional genomics studies in *C. albicans* to induce the same phenotype as null mutants. We shall further present studies on the kinetics of depletion of these proteins and the impact on cellular phenotype and gene expression. This toolbox can be invaluable to evaluate the antifungal activity of different drugs on diverse targets and help in studies on their mechanism of action in *C. albicans.*

Key words: Candida Albicans, Anchor Away Technology, Tata- Binding Protein, Rapamycin

BCH-405 POSTER

TGF-β producing B regulatory cells alters anti-tumor immune response in cervical cancer

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The interplay between immune effector cell subsets and regulatory cell subsets plays a significant role in cancer development. T regulatory cells (Tregs) are widely recognized as a major player in tumor progression, however recently a new subset of B cells that is B regulatory cells (Bregs) are also thought to play a role in tumor development and is been explored. Bregs through the secretion of anti-inflammatory mediators, such as IL-10 and TGF-β, can lead to inhibition of T cells, thus attenuating anti-tumor immune responses. Though the role of IL-10 producing Bregs has been reported in cervical cancer but there is lack of data in spectrum of TGF-β producing Bregs. Therefore the objective of this study was to determine role of these cell subsets in the progression of cervical cancer. For this subject were categorized into three groups', cases with cervical cancer, cases with cervical intraepithelial neoplasia (CIN) and control. Percentage frequency of CD19+IL10+ Bregs, CD19+TGF-β+ Bregs and CD8+ T cells in the PBMCs isolated from peripheral blood was determined using flow cytometry. Interestingly we observed decreased CD19+IL10+ Bregs cell subset frequency in both the groups with respect to control. However increasing trend in the percentage frequency of CD19+TGF-β+ cell subset was observed suggesting its role in the cervical cancer progression and subsequently declining trend is seen in the percentage frequency of CD8+ T cell subset among both the groups with respect to control. This suggests that Bregs through the production of TGF-β inhibit the cytotoxic effector CD8+ T cell proliferation thus altering the anti-tumor response in cervical cancer.

Key words: Cancer, cervical intraepithelial neoplasia, Flow cytometry, T regulatory cells (Tregs), B regulatory cells (Bregs)

BCH-406 POSTER

Molecular mechanism of Vitamin C on Immune System

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Vitamin C (L-Ascorbic acid) is a water soluble essential nutrient for the optimal function of the immune system. It is found in citrus fruits, berries, potatoes, tomatoes, peppers etc. Vitamin C has a number of activities that could conceivably contribute to its immune-regulating effects. It play important role in both innate and adaptive immune system and has profound effect on cellular and humoral immune response. It maintains the balance between Th1 and Th2 effector functions. Potential regulatory mechanisms of Vitamin C are correlated by influencing $CD4^+$, $CD8^+$ IFN-Y,

NK- cell activity, and DCs cell. It also inhibits pro-inflammatory cytokines such as TNF-α, IL-6, NF-kB and IL1β. Vitamin C enhances the macrophages, monocytes and phagocytic cell which are the pivotal components of the immune system.These cell act as first line of defense against invading pathogens. Vitamin C regulate B cell proliferation and function by increasing serum IgA and IgM concentration. Moreover, it is a highly effective antioxidant, due to its ability to readily donate electrons, thus protecting important biomolecules (proteins, lipids, carbohydrates, and nucleic acids) from damage by oxidants generated during normal cell metabolism Vitamin C divulge antioxidant scavenging free radicals and enzymatic co-factor for physiological reactions such as hormone production, collagen synthesis and immune potentiation. In addition it inhibits excessive activation of the immune system to prevent tissue damage.

Keywords: Antioxidant activity, adaptive, innate immunity, Th1cell, Th2 cells.

BCH-407 POSTER

Stigmasterol-A phytosterol for the treatment of Type 2 Diabetes Mellitus associated Alzheimers

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Introduction: Type 2 diabetes (T2DM) is a major risk factor for Alzheimer's disease (AD) which is a most common form of dementia. Therefore, this study determines the dual therapeutic effect of natural molecules using nanotechnology approach for targeting T2DM and AD simultaneously. **Aim and Objectives:** The study aims to develop dual therapeutic agents against T2DM associated AD initially via virtual screening of natural compounds. The screened compounds will further be validated for their efficacy against T2DM associated AD *in vitro*. **Material and Methods:** Database of anti-diabetic natural compounds was arranged on apache server. These natural compounds were screened through molecular docking, MD simulations and physicochemical parameters. Using enzyme kinetics analysis, Acetylcholinesterase (AChE) inhibition was identified as it a major cholinergic target for treating AD. **Results:** In a library of approximately 1400 anti-diabetic natural compounds, 750 compounds were screened through *in silico* approaches. We found that Stigmasterol showed best affinity towards enzymes AChE. AChE inhibitory effect was validat ed *in vitro* using enzyme kinetics studies where stigmasterol significantly inhibited AChE with an IC50 of 210µM and its nanoformulation S-GNPs with an IC50 of 0.340nM respectively. **Conclusion:** Stigmasterol can act as a potent dual inhibitor for T2DM associated Alzheimer's as depicted through our *in silico* and *in vitro* studies.

Keywords Type 2 Diabetes Mellitus, Alzheimers Disease, Acetylcholinesterase, Molecular Simulation, Enzyme kinetics

BCH-408 POSTER

Role of mechanical signaling molecules SRC and FAK kinases in endoderm formation in mouse embryos

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Embryonic stem cells have the potential to divide and differentiate into all the cell types of our body, except the extra-embryonic ectoderm. This remarkable process of development is dependent on the timely loss of the self-renewal capacity and expression of differentiation markers which pushes the ES cells into a lineage. Although the events associated with this process have been well described, the mechanisms underlying this process are still unknown.
In this study, we asked how primitive endoderm is defined as a single layer outside the epiblast during the development with a mechanical signaling perspective. We tried to understand which mechanical signaling components are involved in this process and how they regulate pluripotency, leading to PE formation. Integrin signaling was reported to affect PE formation in EBs. We selected two non-structural entities of Integrin signaling - SRC and FAK for the current study. From our studies, we found that SRC and FAK inhibition (SRCi and FAKi) increased the self-renewal of mouse ES cells. SRC inhibition in mESCs showed a significant increase in *Nanog* promoter activity while the effect of FAKi was minimal.

Our study for the first time shows that the mechanical signaling molecules SRC and FAK affect a core pluripotency factor NANOG in mouse ES cells. SRC negatively regulates *Nanog* at the post-translational level by downregulating STAT3 activity. FAK regulates NANOG at the post-translational level by phosphorylating at Y176 residue and destabilizing the protein. Our study also explains the long-standing question in the field that why the loss of NANOG and PE differentiation is spatially restricted to the outer cells facing the blastocoel in the embryos. We suggest that the basal-apical polarity of the outermost layer of cells in an ESC colony, embryoid body, or the ICM leads to actin polymerization and formation of cortical ACTIN. The cortical ACTIN activates the SRC signaling in these outer layer cells. SRC interacts and represses STAT3 in the outer cells, the repression of STAT3 prevents activation of *Nanog*. In the absence of *Nanog* expression, the Gata6 expression is activated to induce PE fate in the outer layer of cells.

BCH-409 POSTER

Furin-cleavage site is present in an antiparallel β-strand in SARS-CoV2 Spike protein

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) caused a local outbreak in Wuhan city in December 2019, which subsequently, at an alarming rate, gripped the other continents, pressing the World Health Organization to declare it a pandemic (1-3). SARS-CoV2 Spike (S) protein is composed of S1 and S2 subunit. Furin cleavage-site (FCS) present between the S1/S2 junction of S protein is critical to drive the fusion of SARS-CoV2 with the host cell. The available wild-type (Wt) SARS-CoV2 S protein with PDB ID: *6yvb* lacks a stretch of amino acid including FCS as well. Protein Homology/analogy Recognition Engine V 2.0 (*Phyre*^{2}) was used for modeling the Original wild-type SARS-CoV2 S protein with PDB ID: 6vyb. *PyMol* software was used for the analysis of protein.The available Wt. SARS-CoV2 S protein with PDB ID: 6yvb lacks a stretch of amino acid including FCS in between S1/S2 junction. All investigators till date have shown this stretch existing in the form of a loop. We are for the first time reporting that this stretch comprises of 14 amino acid residues (677QTNSPRRARSVASQ689) that forms an antiparallel β-sheet between the S1/S2 junction in SARS-CoV2 S protein rather than a loop. We anticipate that the anti-parallel β-sheet between S1/S2 junction is used as a scaffold by the host proteases to act on FCS in S protein to promote host cell virus fusion.

Key Words: SARS-CoV2, *Phyre*^{2}, Spike protein, Furin cleavage-site (FCS)

BCH-410 POSTER

Metabolic pathways in pluripotent stem cells

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Metabolic pathways are closely integrated with the developmental program. They fulfil energy requirements of the embryo and generate intermediate metabolites that act as cofactors for protein and epigenetic modifications. The metabolome-proteome cross-talk during acquisition, maintenance and progression of developmental stages is less studied. In this study, we explored the proteome changes that are associated with acetyl-CoA levels in mouse embryonic stem cells (mESCs). We found that increase in acetyl-CoA with supplementation of acetate or decrease in acetyl-CoA by inhibition of glycolysis affects lipid metabolism and DNA methylation in pluripotent stem cells. The loss of acetyl-CoA producing enzyme ATP citrate synthase (ACLY) in mESCs, shows de-regulation of epigenetic modifiers related to bivalent chromatin and DNA methylation. Our data gives an account of the plasticity of metabolic pathways that rewire to compensate the decrease in acetyl-CoA or loss of ACLY. In summary, we show that glycolysis derived acetyl-CoA links chromatin regulators and metabolic pathways in pluripotent stem cells.

BCH-411 POSTER

Role of m6A RNA methylation regulated miRNAs in oral squamous cell carcinoma (OSCC)

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OSCC is the most common malignant tumor of the oral cavity. A multitude of gene regulatory processes impact OSCC development and progression. One such process is reversible m6A RNA methylation, which influences a plethora of biological processes, by modulating various facets of cellular RNA metabolism like splicing, stability, translation efficiency, nuclear export and biogenesis of small regulatory RNAs i.e. miRNAs. The m6A regulators (the writer, eraser, and reader proteins of m6A) have been reported to be dysregulated in various cancer types. Mechanistically, METTL3, the primary m6A RNA methyl transferase, has been reported to modulate miRNA biogenesis by recruiting the microprocessor protein, Drosha/DGCR8 to the primary miRNA and facilitating its processing. Studies exploring the role of m6A regulated miRNAs in the context of oral cancer are lacking. We examined the expression of various m6A regulators in OSCC cell lines and found it to be significantly deregulated in most of the cell lines as compared with a normal epithelial cell line. Interestingly, the catalytic subunit of m6A writer complex METTL3 is significantly upregulated and the m6A erasers FTO and ALKBH5 were significantly downregulated in most of the OSCC cell lines. Furthermore, we find that siRNA mediated knockdown of METTL3 severely inhibits the proliferation and colony forming ability of these OSCC cells. In contrast, siRNA mediated knockdown of m6A erasers FTO & ALKBH5 promotes the proliferation and colony forming ability of OSCC cells. To specifically interrogate the role of m6A regulated miRNAs in OSCC, we carried out miRNA sequencing on OSCC cells depleted of METTL3. As compared to control cells, we find 85 differentially expressed miRNAs. Further validation and characterization of these candidate miRNAs are in progress and will provide novel insights into the functional and regulatory roles of m6A RNA methylation in OSCC.

Key words: m6A, miRNA, OSCC, RNA epitranscriptomics, METTL3

BCH-412 POSTER

Implication of active autophagic flux in chemoresistance and cancerstem cell differentiation

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Autophagy, a catabolic cellular pathway regulates the balance between survival or death of a cell in response to external and internal cues. Cancer cells often exploit autophagy to avoid drug induced lethality and thereby promote resistance. It is however, not clear whether active autophagy is required incessantly from initiation/early stage to completion/highly stabilized stage during the dynamic evolution of chemoresistance. Using several cellular models of acquired chemoresistance of Epithelial Ovarian Cancer, we demonstrated that completion of autophagic flux is an indispensable feature of early resistant (ER) cells when treated with drugs, but not for late resistant (LR) cells. Differential levels of hyperactivated ERK (in ER cells) and hyperactivated AKT (in LR cells) was found to be the key modulators of such stage specific autophagy induction. Utilizing a novel autophagy reporter and molecular imaging techniques, the kinetics of drug induced autophagy modulation was monitored in live mice.Next to inspect whether autophagy is truly a dispensable pathway for maintenance of resistance in LR cells, basal autophagic flux was examined in Cancer stem cell (CSC) and non-CSC population. Intriguingly, the CSC population was characterized with an active autophagy flux and further promotion of autophagy led to enhanced differentiation of these CSC into non-CSC population while blockade of autophagy had no effect. Through a detailed literature search, we identified Inhibitor of Differentiation (ID) proteins as probable molecular player/s in connecting autophagy and CSC differentiation. Indeed, pharmacological inhibition of these ID proteins (AGX51 treatment) enhanced CSC differentiation into their less resistant, non-CSC compartment. A bioinformatic analysis identified three E box transcription factors (TCF 3, 4 and 12) as probable interacting partners of ID proteins in autophagy modulation and stem cell differentiation. Detailed molecular

characterization of this TCF12-ID axis in cancer stem cell differentiation, chemoresistance and autophagy are under progress. Simultaneously, we investigated the autophagy flux in cancer associated spheroids (putative CSC population) isolated from malignant ascites of relapsed EOC patients. An intriguing association of active autophagy flux with a platinum influx transporter was observed in the relapsed patient's group who exhibit better response when re-challenged with platinum agents. Altogether our data divulge an intricate association between autophagy, cancer stem cell differentiation and chemoresistance from established cell lines to patient derived spheroid population.

BCH-413 **POSTER**

Insight into the hidden ciliate diversity of fresh water ecosystem of Delhi by metabarcoding approach

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Ciliates are present in the freshwater, marine and terrestrial ecosystems and play an important role in the microbial loop. Ciliate community structure and their distribution have been studied for a long time using traditional microscopic methods. In the present study, the hidden diversity of ciliates was determined using the metabarcoding, in which those ciliates that are not readily visible through microscopic approaches were deciphered. This was a pilot study to elucidate the hidden diversity was conducted using the metabarcoding involving extraction of the environmental DNA from the three sites. The three sites include OBS, SL and RJ in Delhi, India. The microscopic observations made during the study period, maximum number of species (species diversity) were observed from the OBS site (43 species), followed by SL (27 species), and RJ site (21 species). By next-generation sequencing (NGS), the maximum number of species was observed in the OBS site (101), followed by SL (100), and RJ (93). In microscopic observation, ciliates from eight classes, Spirotrichea, Oligohymenophorea, Prostomatea, Litostomatea, Phyllopharyngea, Karyorelictea, Heterotrichea, and Colpodea were observed. On the contrary, by NGS analyses, in addition to the above mentioned eight classes, ciliates from one more class (Nassophorea)was also observed, forming a total of nine classes..The genera that were observed in microscopic observation during the study period were *Aponotohymena, Gastrostyla, Laurentiella, Sterkiella, Stylonychia, Gonostomum, Halteria, Hemiamphisiella, Anteholosticha, Uroleptus, Pseudourostyla, Diaxonella, Urostyla, Aspidisca, Euplotes, Blepharisma, Spirostomum, Lacrymaria, Litonotus, Loxophyllum, Spathidium,* and *Frontonia.* The genera that were observed exclusively in the NGS analysis during the study period were *Hypotrichidium, Amphileptus, Protocyclidium, Levicoleps, Trithigmostoma, Tokophrya, Aceneria, Cryptocaryon, Prorodon,* and *Bromellothrix.* These genera may be contributing to the hidden diversity of the freshwater samples obtained during the study period.

BCH-414 **POSTER**

Morphological and molecular identification of unicellular ciliate, *Colpoda* n. sp. Isolated from sewage treatment plant (STP), Jasola, Delhi

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Colpoda belongs to the phylum ciliophora, class colpodea, order colpodida, family colpodidae. Few fspecies of *Colpoda*

has been reported as parasitic to humans. In the present study, morphology and phylogenetic position of free living *Colpoda* n. sp. isolated from digested sludge of sewage treatment plant (STP), Jasola, Delhi is described using classical and molecular methods. *Colpoda* n. sp. is characterised as follows: Size *in vivo* about 35-40 x 30-32 µm, after protargol staining 25-28 x 20-24 µm, broadly reniform, colorless, rigid, swimming in a spiral path. Extrusomes are present. One macronucleus of size 11.4 x 10.22 µm on average, micronucleus 1.93 x 1.33 µm on average. The shape of macronucleus is spherical or ellipsoid. The micronucleus is single and ellipsoid in shape, attached to macronucleus. The oral apparatus is located subapically, usually at the base of a distinct depression, making the shape reniform. There is single contractile vacuole pulsating once per 2-3 seconds. Frequent excystment, encystment and no conjugation is observed. The average number of somatic kineties is 28. The average dikineties in right lateral kineties are 25 in number. The mean length and width of left polykinetid are found to be 11.2 µm and 2.8 µm respectively. The mean length of right polykinetid was found to be 15.6 µm. The average distance from anterior end to distal edge of vestibulum is 14.2 µm and average distance from anterior end to proximal edge of vestibulum is 25.1 µm. The Indian isolate *Colpoda* n. sp. is found to be closest with the Korean population. The 18S or SSU rRNA gene has been sequenced. A comparison of *Colpoda* n. sp. with its congeners has also been done in the present study.

BCH-415 POSTER

Effect of High sugar Diet on Gut microbiota dysbiosis and Type 2 Diabetes

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Diabetes mellitus is a chronic metabolic disease which is spreading gradually in both developing and developed nations. The pathogenesis of diabetes is complex and unclear.Insulin resistance and pancreatic beta cell failure are the core pathological factors for this disease. Accumulated evidences has implicated genetic, immune disorder, obesity and diet are closely related to diabetes. Diet control, oral anti diabetic drugs, insulin injection are routinely used for the prevention and treatment of diabetes. However none of them can fundamentally prevent the development of diabetes and associated complication. During the last decade, the role of gut microbiome has drawn much attention across the world. Intestinal microbial dysbiosis caused by high frucrose and high Sucrose diet diet has devastating effect on diversity and the stability of intestinal microflora and it is characterised by decrease in beneficial microflora and increase in pathogenic microflora which induces metabolic endotoxemia,chronic low grade inflammation,metabolic disorder in intestine which may be due to increase in the gut permeability and lipopoysaccharide absorption with elevated levels of TLR2,TNF-α and IL 6 Pro-inflammatory expression in rats leading to occurrence of insulin resistance and type 2 diabetes(T2D).The Objective of the study is to understand the influence of the sugar rich diet on gut microbiota imbalance and its association with obesity and T2D in rat models. Inflammation can give rise to structural damage and dysfunction of islet β cells, promote apoptosis of β cells, and cause insufficient insulin secretion. Inflammation can also cause abnormalities in the structure and function of endothelial cells, bringing about insulin transport disorders in tissue cells,and cause insulin resistance.The intestinal hormone Glucagon like Peptidase-1(GLP-1) promotes insulin secretion from islet β cells, inhibits glucagon production by islet α cells, and exerts hypoglycemic effect, promotes islet cell proliferation and decreases the apoptotic rate of islet cells enhances insulin sensitivity through the "intestinal-islet axis", delays gastric emptying, suppresses appetite and reduces weight, protects islet cells from glycotoxicity and other inflammatory damage.The disorder of the flora can cause the decrease of GLP-1 secretion, leading to faster gastric emptying,increased appetite and body weight resulting in increased glycotoxicity and inflammatory damage in islet cells, then bringing about the increase of islet cell apoptosis, the diminishment of insulin secretion and sensitivity, which eventually leads to the occurrence of T2D. The study may provide the linkage of increased TLR 2, proinflammatory cytokines expression and GLP-1 expression and its association with insulin resistance, obesity and T2D. This study may provide new insights in diagnosis and the management of diabetes.

Key words: Gut Microbiome, Dysbiosis, T2D, Inflammation, Apoptosis, GLP-1

BCH-416 POSTER

Farnesol, a natural sesquiterpene inhibits cellular proliferation, migration and initiates apoptosis in human colorectal cancer *In-vitro*

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Background: Colorectal cancer (CRC) one of the most common and lethal malignancy emphasises the need for prevention and treatment. Herbal terpenoids have been proven as potential anti-cancer agents in colon cancer. Farnesol is a versatile sesquiterpene that has application in a variety of biological domains. With an advantage of mild adverse effects and cost effectiveness of Farnesol this study will be helpful to generate sufficient baseline data regarding its use in colon cancer. **Objective:** The present study was aimed to study the Farnesol induced anti-proliferative, anti-migratory and apoptosis effects in human CRC (HCT-116 cell line). **Materials and Methods:** Farnesol was obtained from Sigma-Aldrich (F203), HCT-116 Cells were cultured in RPMI medium, supplemented with FBS (10%) and 1% of antibiotics (penicillin/ streptomycin), and maintained in CO2 incubator at 37°C. MTT assay was used to assess cellular proliferation, AO/EB staining assay was used to assess apoptosis and wound healing assay was used to assess cellular migration. **Results:** Farnesol inhibited cellular proliferation in a dose dependent manner (IC_{50}: 64.37µM) and inhibited cellular migration which was evidenced by suppression of wounds of cultured human colorectal cancer cells compared with the untreated cells. Results showed that Farnesol induced apoptosis in HCT-116 cells. **Conclusion:** Our results suggest that Farnesol possess significant antiproliferative and anti- migration potential and initiates apoptosis in HCT-116 cells.

Keywords: Farnesol, Colorectal cancer, Apoptosis, Cytotoxic etc.

BCH-417 POSTER

Search for potent antibiotics with novel targets for drug resistant Tuberculosis

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Despite use of multi-drug regimens that are administered daily for a period of 6 to 9 months. Tuberculosis (TB) still claims 1.5 million human lives annually. Rapid emergence and global spread of drug resistant strains of *M. tb.* is still unstoppable and at present challenges researchers in dreadful forms those include multi-drug-resistant (MDR), extensively-drug-resistant (XDR), and total-drug-resistant (TDR). The current recommendation for the treatment duration of MDR-TB is at least two years as per WHO guidelines and one can judge the fate of MDR regimens when potent 6 month regimens are failing. Proceeding discussion clearly indicates the critical need of novel anti-TB drugs to curb TB before it will burst like pre-antibiotic era. The main reason of TB treatment failure is the requirement of long duration with multiple drugs. Thus the main aim for developing new anti-tubercular drugs is to shorten the duration of TB treatment. We propose high throughput end screening of the compounds that are in various stages of clinical development (especially those in Phase I, Phase II, and Phase III trials) with respect to sterilizing activity (activity to kill non-replicating TB bacilli; that are responsible for long duration of existing TB regimens). Emphasis should also be given to the development of new compound libraries with the structural scaffolds closely resembling these promising anti-tuberculosis agents or existing anti-TB drugs.

Elucidating the modification of Low Density Lipoprotein (LDL) with 4-Hydroxy-2-nonenal (HNE): a multi-technique approach

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Objective: To evaluate biophysical and biochemical changes in native LDL and HNE modified LDL. **Background:** Oxidation of human low-density lipoprotein (LDL) was found to be accompanied by the generation of several reactive aldehydes. 4-hydroxynonenal (HNE) is one such aldehyde which modifies LDL to a form which represents a good model of oxidized LDL (ox-LDL). HNE is able to react with the proteins thereby changing their conformation and altering the functions of LDL. **Materials and Methods:** LDL was incubated with increasing concentrations of HNE in PBS, pH 7.4 at 37°C for 24h. HNE-LDL was evaluated using various physicochemical techniques like UV-Vis spectroscopy, Fluorescence Studies, CD spectroscopy, FTIR, carbonyl content, (ANS) binding studies, LCMS DLS, Thermo-Stability Studies, molecular docking, MD simulations, SEM, TEM, PCA, FEL and XRD. **Results:** The HNE-LDL spectrum exhibited hyperchromicity with increasing concentrations of HNE. An increase in fluorescence intensity, synchronous fluorescence and decrease in ANS fluorescence point towards structural and conformational changes in HNE-LDL. Decrease in CD values and peak positions in FTIR spectroscopy demonstrated a change in the secondary structure of modified protein. Oxidation of protein resulted in an increase in carbonyl content which is a key marker of oxidative stress. LCMS studies confirmed the generation of N-acetyllysine in modified LDL by observing a peak in LCMS chromatogram. DLS was done to gain insights into the change in the size of the LDL after modification. TGA and DSC are employed to investigate the effect of HNE on the thermal stability of LDL. Molecular docking and MD simulation was done to explore the interaction between LDL and HNE. SEM and TEM confirmed HNE induced aggregation of LDL. PCA and FEL was shown to be a very useful approach to gain an overall view of the conformational landscape accessible to a protein. Xray crystallography showed the formation of complex structures in case of HNE-LDL. **Conclusions:** Incubation of LDL with HNE under *in vitro* conditions causes structural and conformational changes and induces oxidative stress, HNE-modified proteins can be used as biomarkers of oxidative stress due to their higher biological stability, compared to free HNE or even the oxidizing radicals itself. HNE-modified proteins have been detected in several diseases like systemic lupus erythematosus (SLE), RA and other diseases of auto-aggression.

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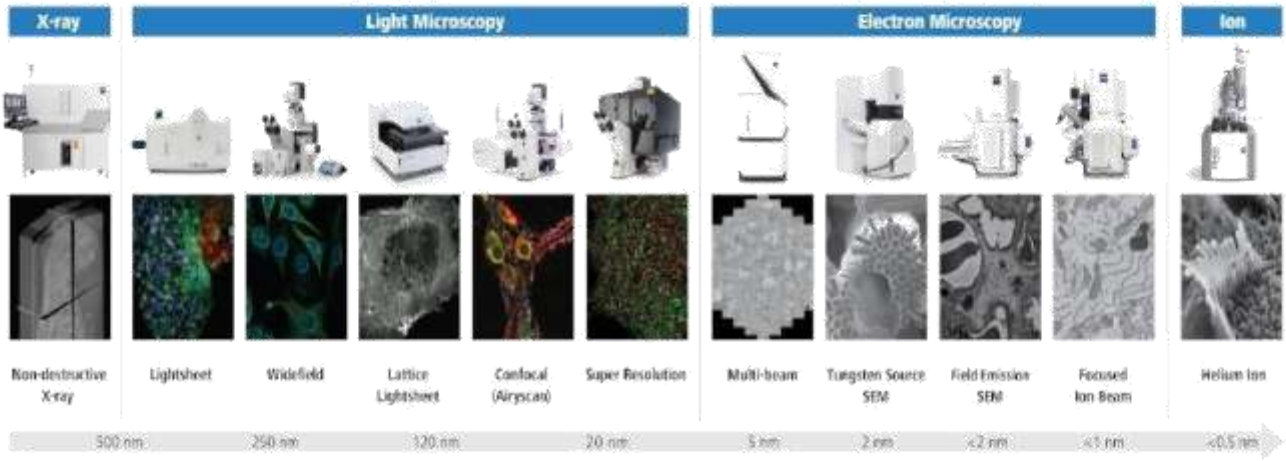

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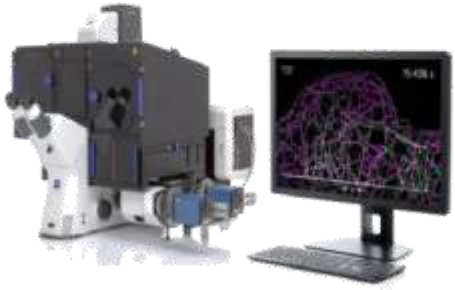

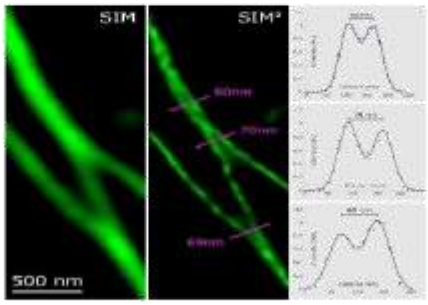

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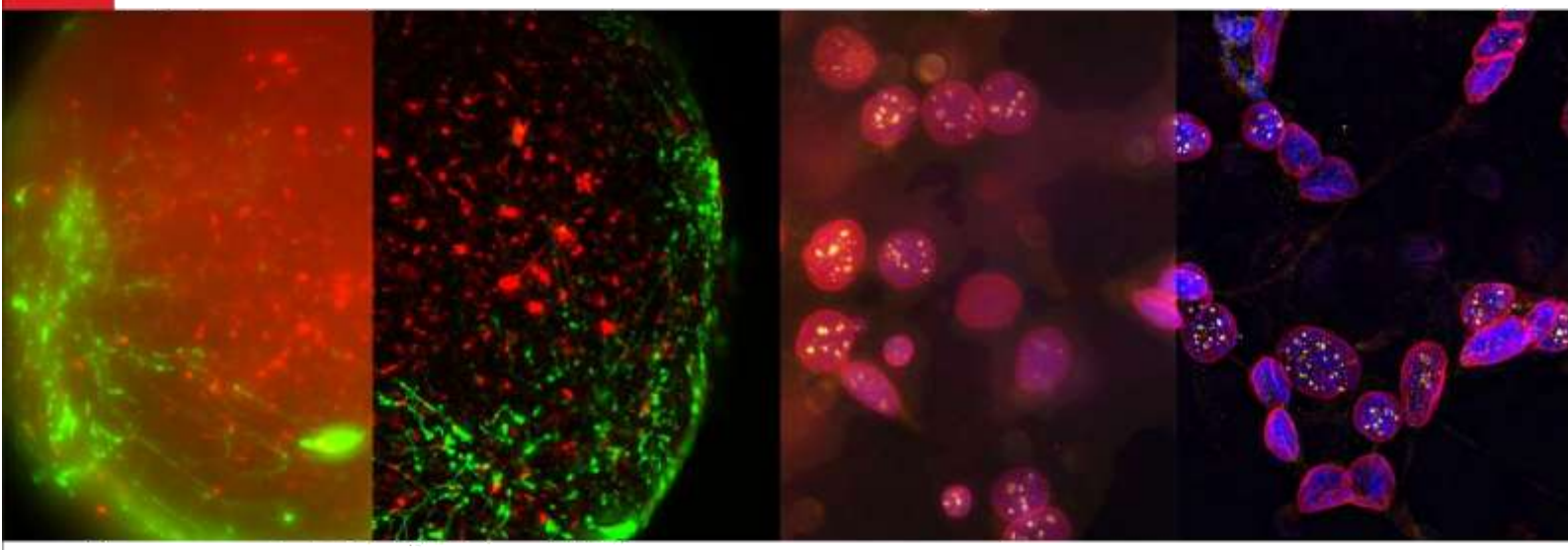

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Department of Biochemistry

University of Kashmir (NAAC Accredited A+)
biochemistry.uok.edu.in

About the Department

The Department of Biochemistry has a reputation of excellence in academics and research since its inception in the year 1983. The alumni from the Department have made valuable contributions in every field of biological research and development (R&D) across the globe, which bears testimony to the quality of our teaching, learning, research and extracurricular activities. The Department has highly trained, skilled and experienced faculty members who carry out high quality research in the areas of cancer biology, cancer epidemiology, signal transduction, epigenetics, medicinal plants, cell /molecular biology and reproductive health, as revealed by their high impact publications. We have obtained extramural grants worth crores from the reputed national and international funding agencies, which has enabled us to procure high-end instruments and hence substantially raise the infrastructure of the Department. The faculty members of the Department have also served on prestigious administrative positions including the ranks of vice-chancellors and registrars of different universities, directors of institutes, deans of schools, heads of departments/centres etc. Our overarching goal is to substantially raise the teaching and research horizons of our Department so as to get recognition at the national and international levels.

More Information

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