10th Young Investigators' Meeting 2018

TAKING THE PULSE OF BIOLOGY IN INDIA

IndiaBioscience
ENGAGING COMMUNITIES. ENABLING CHANGE

RGCB
Leading Discovery & Innovation

The Young Investigators'

BUILDING A COMMUNITY OF YOUNG INDIAN BIOLOGISTS

The YIM series aims to build a community of well-networked biologists by allowing young Indian scientists from different regions and institutions to establish friendships, initiate collaborations, and learn from peer-to-peer mentoring.

Perhaps, the greatest accomplishment of the YIM series is building a future community of well-networked biologists, allowing young Indian scientists from different regions and in-stitutions to establish friendships, initiate collaborations, and learn from peer-to- peer mentoring.

YIM 2018 is the tenth in a series that began in 2009, and has grown in popularity, size and content since then. This year's YIM is special as hopes bring together attendees from all the previous YIMs under one roof to deliberate on some of the most urgent issues in biology research in India.

Meeting Series

Every year the YIM is organised by a different committee, comprised of young faculty members from institutions across the country. IndiaBioscience plays an administrative and advisory role in each year's YIM.

Young Investigators' Meeting

2015

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Organizers

Debashree Datta, *Rajiv Gandhi Centre for Biotechnology*

Debasree did her M.Tech and PhD from Jadavpur University, Kolkata. In 2007, immediately after her PhD, she joined University of Kansas Medical Centre,USA, to pursue her postdoctoral studies in cell and developmental biology. She was awarded the prestigious American Heart Association fellowship and an international patent on stem cells. She joined RGCB, Trivandrum in 2012. Debasree has received six extramural grants from different funding agencies, published in esteemed peer-reviewed journals and was awarded the DST fast track fellowship. Her lab focusses on studies related to stem cell biology, disease modelling and cancer biolo-gy.

Piyali Mukherjee, *Presidency University*

Piyali Mukherjee is an Assistant Professor at the Dept. of Life Sciences, Presidency University, Kolkata. After her PhD at Bose Institute Kolkata in 2006, she joined Dr Mark Alexandrow at Moffitt Cancer Center, Tampa, Florida for her postdoctoral fellowship where she studied the assembly and function of pre-replication complex proteins. In 2010, she joined the Rocky Mountain Laboratories, NIH, USA as staff research fellow in Dr Karin Peterson's Laboratory to work on neurotropic viruses. Her laboratory is currently studying the molecular mechanisms underlying age-related neurodegeneration, how ageing correlates with susceptibility to environmental stress and the role of the neurodegenerative molecule Sarm1 in the process.

Sharmistha Banerjee, *Hyderabad Central University*

Sharmistha's laboratory is engaged in deciphering the coalition between two human pathogens: Mycobacterium tuberculosis [TB-causing bacteria] and Human Immunodeficiency Virus (HIV), the synergistic pandemic of which is a major health concern in India and worldwide. In the last five years, her laboratory has added important baseline information on molecular mechanisms behind pathogenesis of HIV and mycobacteria, during both mono and co-infection, identifying potential targets and biomarkers.

Smita Jain, *IndiaBioscience*

Smita has a PhD from the Indian Institute of Science, Bangalore in the field of Cancer Biology. After exploring industry for a couple of years, she moved into the field of scientific management. With her keen interest in management, ability to communicate, she played a key role in establishing the business and processes at C-CAMP, Bangalore. She also has experience of working as a research analyst with a digital content organization. She is deeply motivated to take the activities of IndiaBioscience to all possible corners of the country and make a strong knit network of Indian Biologists. Her interests are being with nature, travelling and interacting with a wide range of people on different topics.

IndiaBioscience
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IndiaBioscience, a non-profit program, fills a unique niche in the ecosystem of the life sciences in India, being a catalyst to promote changes that affect the culture and practice of the field, through engagement with academia, government and industry at various levels. IndiaBioscience aims to increase the visibility of science in society, by being a hub for policy discussions, science communication, and as an aggregator of information.


Manjula Harikrishna


Manoj Rangan


Manupriya


Navodita Jain

Supporting Institutions & Sponsors

Department of Biotechnology

This Department, set up in 1986, gave a new impetus to the development of the field of modern biology and biotechnology in India. In more than a decade of its existence, the department has promoted and accelerated the pace of development of biotechnology in the country. DBT is the largest supporter of both YIM and India-Bioscience.

Wellcome Trust-Dbt India Alliance

The Wellcome Trust/DBT India Alliance is an initiative funded equally by The Wellcome Trust, UK and Department of Biotechnology, India. The broad aim of the India Alliance is to build excellence in the Indian biomedical scientific community by supporting future leaders in the field.

Rajiv Gandhi Centre For Biotechnology

The Rajiv Gandhi Centre for Biotechnology in Thiruvananthapuram, began in 1990 amongst humble surroundings as a small charitable society called the Centre for Development of Education, Science and Technology (C-DEST). In 1991, recognizing its potential, the C-DEST was made a “Grant-in-Aid” institute of the Government of Kerala and renamed as Rajiv Gandhi Centre for Development of Education, Science and Technology (RGC-DEST). In 2007 the Union Cabinet of the Government of India took the landmark decision to make RGCB a national research centre.

Schedule

DAY 01

Monday, 05 March 2018

15:00–17:00	Registration and social
17:00–17:20	Introduction to the meeting: Opening remarks by *Satyajit Mayor*
17:20–17:30	Welcome note by organizing committee member: *Sharmistha Banerjee*
17:30–18:15	Keynote: The role of young biologists in India: past, present and future by *Ron Vale,* HHMI and UCSF
18:15–19:00	Keynote by *K VijayRaghavan*
19:00 onwards	Dinner

DAY 02

Tuesday, 06 March 2018

07:30 onwards	Breakfast
09:00–09:15	Science Outreach: Why and How? by *LS Shashidhara,* IISER Pune
09:15–09:35	Engaging communities, enabling change: *Smita Jain,* IndiaBioscience
09:35–9:45	Talk by organising committee member: *Piyali Mukherjee,* Presidency University
09:45–10:30	YI talks: 1. Formation of Transport Carriers at the Endocytic Recycling Compartment by *Thomas Pucadyil*, IISER Pune 2. My Journey with Salmonella and SUMO in India: an ongoing quest to leave a trail by *Srikant Chittur,* RCB, Faridabad 3. Dynamics of Molecular Motors and other out of Equilibrium Systems by *Debjani Bagchi,* MSU, Baroda
10:30–11:00	Tea/Coffee Break
11:00–11:30	Setting up the breakout sessions

11:30–13:00	Breakout session for Theme 1: Best practices for recruitment and mentoring of YIs in India
13:00–14:00	Lunch
14:00–14:45	Special talk 1:*Shinjini Bhatnagar and Satyajit Rath*
14:45–15:30	YI talks: 1. Social organisation and behaviour: elephants and academia by *TNC Vidya*, JNCASR, Bangalore 2. Young and Responsible: The Beginning of a Journey by *Anindita Bhadra*, IISER, Kolkata 3. Talk on i-wonder science magazine by *Chitra Ravi,* APU
15:30–16:00	Tea/Coffee Break
16:00–17:30	Breakout session for Theme 2 : Sharing of resources and collaborations for better science
17:30–19:00	Poster Session 1
19:30 onwards	Dinner

DAY 03

Wednesday, 07 March 2018

07:30 onwards	Breakfast
09:00–09:10	Talk by organising committee member – *Debasree Dutta*
09:10–10:10	Reports on Breakout session 1 and 2 followed by discussion
10.10–10:55	YI talks: 1. Biomaterials for clinical translational research: Prophylactic technologies to prevent pesticide induced toxicity by *Praveen Vemula*, inStem, Bangalore 2. Tumor Viruses: A Tool to Understand Cancer Biology by *Abhik Saha*, Presidency University, Kolkatta 3. Genetic and epigenetic regulation of cell death by *Richa Arya,* ACBR, University of Delhi
10:55–11:25	Tea/Coffee break
11:25–13:00	Breakout session for Theme 3: PhD and Post-Doctoral training in India

13:00–14:00	Lunch
14:00–14:15	International collaboration opportunity for researchers by *Arabinda Mitra,* DST
14:15–15:15	Panel discussion 1: Funding: challenges before and after (*Suman Govil* & *Meenakshi Munshi,* DBT; *Shahid Jameel,* IndiaAlliance; *MR Pillai,* RGCB; *Shekhar Mande,* NCCS; *Vandana Gambhir,* IISER Pune)
15:15–15:35	HFSP: Funding International Research Collaborations in the Life Sciences by *Barbara Pauly,* Director of Fellowships, HFSP
15:35–15:45	*Savita Ayyar,* Research Management Consultant, Jaquaranda Tree
15:45-15:55	Funding Session: Q & A
15:55-16:20	Tea/coffee break
16:20-17:00	Biological Research in India: A Historical Perspective and Future Possibilities by *S C Lakhotia,* BHU, Varanasi
17:00-17:30	YI talks 1. Plant nutrients and invading pathogens: how plant defense use SWEETs to stop fuel to the fire by *Senthil-Kumar Muthappa,* NIPGR, New Delhi 2. The secrets for long shelf life of Penjar Tomatoes-Do we know them yet? by *Sreelakshmi Y*, UoH, Hyderabad
17.30–19:00	Poster Session 2
19:00–20:00	Cultural Event
20:00 onwards	Dinner

DAY 04

Thursday, 08 March 2018

07:30 onwards	Breakfast
09:00–10:00	Panel discussion 2: Science Communication (*Apurva Sarin,* inSTEM; *Dinakar Salunke,* ICGEB; *Dhrubajyoti Chattopadhyay,* Amity University; *Jyotsna Dhawan,* CCMB; *Rakesh Mishra,* CCMB; *Shubha Tole,* TIFR; *Uday Kumar Ranga,* JNCASR)

10:00–10:45	YI talks: 1. Physics on a Phagosome by *Roop Mallik,* TIFR, Mumbai 2. A beautiful journey with the tiny-regulator: a tale of life and death of microRNA by *Suvendra N Bhattacharyya,* IICB, Kolkata 3. Building Ecosystem for Life Science Innovations: A C-CAMP Perspective by *Taslimarif Saiyed,* C-CAMP, Bangalore
10:45–11:15	Tea/Coffee Break
11:15–13:00	Breakout session for Theme 4: Future of Indian Biological Science
13:00–14:00	Lunch
14:00–15:00	Reports on Breakout session 3 and 4 followed by discussion
15:00–16:00	Open discussion: The future of YIM and the role of IndiaBioscience after year 10
16:00–16:30	Tea/Coffee break
16:30–18.00	Poster Session 3, with tea/coffee break
18.00–19:00	Concluding remarks and open comments on collaborations that emerged from the meeting
19.30 onwards	Dinner

DAY 05

Friday, 09 March 2018

07:30 onwards	Breakfast and Departure

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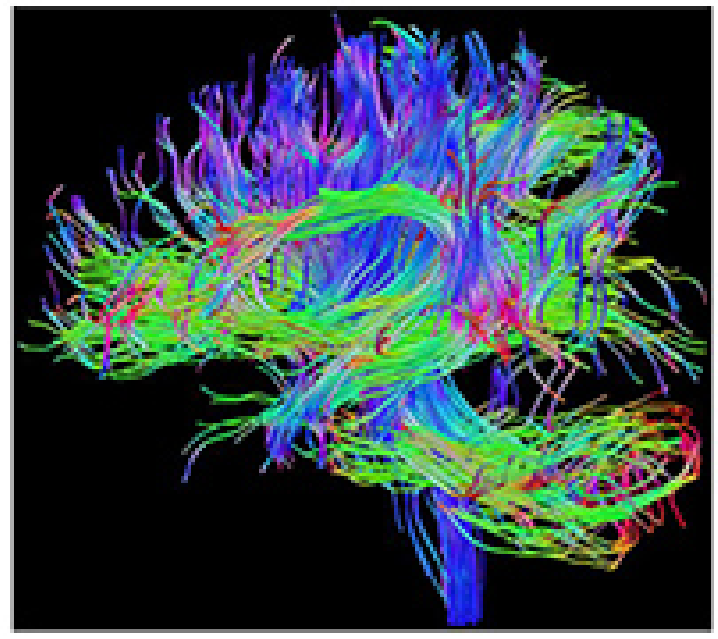
Enabling biomedical research in India through funding and engagement



The Wellcome Trust/DBT India Alliance is a visionary partnership funded equally by the Wellcome Trust, UK, and the Indian government's Department of Biotechnology. It aims to build excellence in the Indian biomedical research community by identifying and supporting future leaders in basic, clinical and public health research for improving human and animal health.

Fellowships for biomedical research in India

Since its inception in 2009, the fellowship programme has awarded 280 fellowships at 82 different institutions in 29 Indian cities. About a third of the Fellows are women and about a quarter do clinical and public health research. The focus is on funding the best people early in their careers and set them on a leadership track.

Besides supporting exceptional biomedical research scientists at Indian institutions through fellowships and a continuous system of engagement and mentoring, India Alliance aims to build a strong research ecosystem in India that can drive innovations to tackle health challenges, and inspire the next generation of researchers. More information on the India Alliance Fellowship schemes can be found on our website. Find out more about our Fellows here.

Training workshops for biomedical scientists and clinicians

Science Communication Workshops

To train Indian scientists in communication, the India Alliance conducts one-day SciComm101 and two-day SciComm workshops. Since 2011, more than 2,000 PhD students, postdoctoral scientists and clinicians from around 100 institutions have received communication training through these workshops. In 2016, India Alliance formed a partnership with Nature India and Nature Jobs (India) for Science Communication and Career workshops, held in tandem with major scientific meetings. In 2017, India Alliance and Nature India held a two-day workshop Visualising Science that armed scientists and those in allied fields with visual tools and methods to convey their research more effectively. Find out more about our Science Communication initiatives here.

Research Leadership workshops

Leadership and management skills are critical for a successful science career. India Alliance organizes leadership workshops for its Fellows and other young Indian researchers to help them recognize and develop their leadership style, and gain critical lab management and communication skills. More information on these workshops can be found on our website

Developing Indian Physician Scientists (DIPS) workshops

India Alliance launched Developing Indian Physician Scientists (DIPS) workshops in 2017 to ignite the research interests of young doctors, while promoting an understanding of the frontiers of medicine and related sciences. The workshops, presented by eminent physician scientists, provide training in quantitative methods and research methodology, and an opportunity to discuss biomedical research and career options. More information on the DIPS workshops can be found here.

Supporting interdisciplinary scientific meetings in India

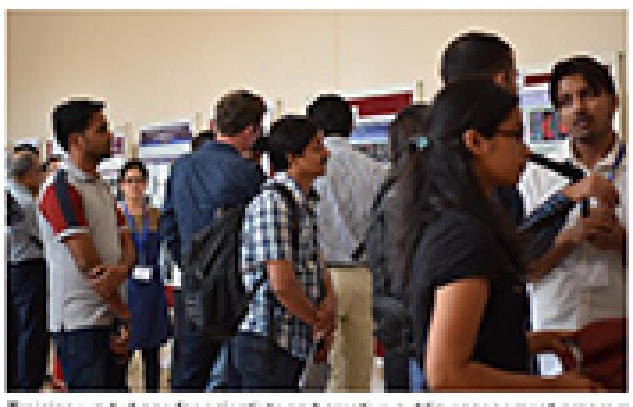
India Alliance has financially supported many major scientific events including the Young Investigator Meetings, which provide an excellent platform for young investigators to meet senior scientists from across the country to discuss existing opportunities which would help them to establish their research careers in India.

India I EMBO Symposia

The India Alliance and European Molecular Biology Organization (EMBO) entered into a partnership in 2017 to co-fund up to three meetings per year in India. These meetings are expected to address discovery and innovation through an interdisciplinary approach, with the speakers and participants discussing important global challenges in the context of the life sciences. To find out more about this funding opportunity, visit India Alliance website.

Public Engagement Connecting science to society

The India Alliance also aims to increase the public understanding of science and health issues through its Public Engagement activities. Through this it brings the scientific community and the public together to share, debate and deliberate on important matters of science, especially human health, which have implications for the society at large. To fulfil this vision, India Alliance regularly organizes public events in different Indian cities and supports its Fellows, other individuals and organizations that undertake public engagement activities. Find out more about these Public Engagement initiatives on our website.



Training workshops for scientists and creative public engagement programs are central to India Alliance's vision of building a robust biomedical research ecosystem in India. Top image represents a whole brain's anatomical connections as measured with diffusion MRI followed by tractography. Image credit: Dr. Dr Sridharan Devarajan, IISc Bangalore.

For more information on India Alliance programs visit **www.wellcomedbt.org**

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YIM 2018 Keynote Lecture

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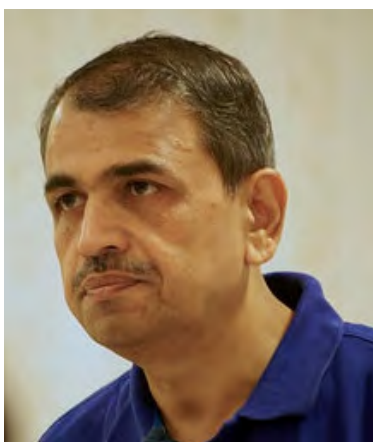

L S Shashidhara

Science Outreach: Why and How?

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Ron Vale

YIM 2018 Keynote Lecture

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Satyajit Mayor

Introduction to the meeting – Opening remarks

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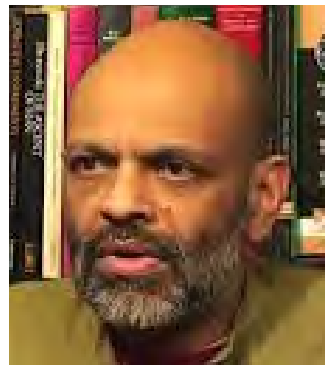

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YIM 2018 Themes

THEME 1:

Best practices for recruitment and mentoring of YIs in India

Under this theme, the YIs will share first hand experiences about recruitment and mentoring leading to shortlisting of the practices that young investigators think should be in place for more transparent and effective processes. For ease of discussions, the session will be divided into following sub-themes:

» Best practices of recruitment
» Creating visibility of job opportunities in India (through national forums)
» Peer review
» Leadership–YIs as mentors and their evolution as leaders of the future
» Outreach and its importance

THEME 2:

Sharing of resources and collaborations for better science

Under this theme we will deliberate on changing the culture and mindset of research community towards sharing resources and infrastructure, on policies that would facilitate access to high-end facilities across nation, and on overcoming challenges to maintain high-end facilities etc . The session will be divided into following sub-themes:

» Cultivation of open environment for scientific exchange
» Building a Collaborative Culture (domestic and international collaborations/interdisciplinary collaborations)
» Easy accessibility of resources across nation
» Towards developing new technologies—interdisciplinary approaches
» Challenges with maintaining high end facilities

YIM 2018 Themes

THEME 3:

PhD and Post-Doctoral training in India

This theme revolves around discussing the role of YIs as mentors. YIs can share their experiences towards building successful careers of their PDFs, ways of encouraging positivity in the lab, limitations of the present policies for the future of postdoctoral training in India. The session will be divided into following sub-themes:

» Empowering PhDs and PDFs
» Work culture
» Job opportunities in science
» Challenges in mentoring PhDs and Postdocs
» Professional development/ Skill building

THEME 4:

Future of Indian Biological Science

This theme will explore what factors should drive selection of research areas by YIs, if research should be driven by the need of society, the funding possibilities, translational opportunities, inter-disciplinary, sheer excitement of doing science with no consequence etc. The pros and cons of doing biomedical science as business may also be discussed.

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001

EPSTEIN-BARR VIRUS ONCOPROTEIN EBNA3C PROMOTES B-CELL SURVIVAL BY UPREGULATING AUTOPHAGY

Keywords Tumor virology, Protein degradation, Unfolded Protein Response (UPR), Autophagy, Epigenetic mechanisms

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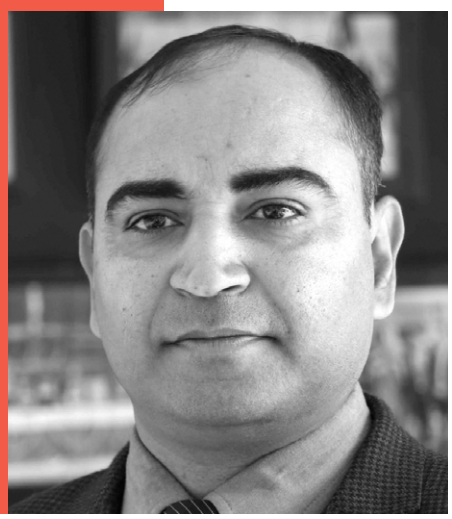
Epstein-Barr virus (EBV) oncoprotein EBNA3C is indispensable for primary B-cell transformation and maintenance of lymphoblastoid cells outgrowth. EBNA3C usurps two putative cellular pathways – cell-cycle and apoptosis, essentially through modulating ubiquitin-mediated protein-degradation or gene transcription. In cancer cells these two pathways are interconnected with autophagy. Tumor viruses including EBV can manipulate autophagy as a survival strategy. Here, we demonstrate that EBNA3C elevates autophagy, which serves as prerequisite for apoptotic inhibition and maintaining cell-growth in both normal and growth limiting conditions. EBNA3C recruits several histone-activation epigenetic marks (H3K4me1, H3K4me3, H3K9ac and H3K27ac) for transcriptional upregulation of several autophagy genes, notably ATG3, ATG5 and ATG7 which are responsible for autophagosome formation and EIF2AK3 in the unfolded protein response (UPR) pathway under growth limiting conditions. Knockdown of ATG5 and EIF2AK3 sensitized EBNA3C positive B-cells for rapid cell-death in the presence of autophagy-inhibitor and UPR-inducer, respectively. This study provides a new insight for the role of EBNA3C in regulating autophagy-UPR network and offers novel-targets for potential therapeutic expansion against EBV induced B-cell lymphomas.

002



DIMERIC STATE OF HUMAN PEROXREDOXINS: AN *IN VIVO* MARKER FOR REDOX HEALTH OF CELLS

Keywords Yeast genetics, Gene regulation, Protein synthesis
Oxidative stress, Forest microbes

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Peroxiredoxins (Prxs), scavenge cellular peroxides by acquiring dimeric state using conserved Cys residues. However, under oxidative stress, active-site Cys residue of Prx is hyperoxidized resulting in loss of peroxidase activity. *Saccharomyces cerevisiae* deficient in human Prx (hPrx) orthologue TSA1 can be complemented with hPRXI but not by hPRXII suggesting their phylogenetic conservation. But still it is not clear how the dimerization and hyperoxidation states of the hPrx vary in oxidative stress *in vivo*. Herein, we used tsa1tsa2Δ yeast strain, which is sensitive to redox stress to express hPRX to understand the relation between the peroxidase active state of hPrx and its *in vivo* relevance. We found that hPrxI in yeast exists both as dimer and monomer but attains hyperoxidative monomeric form upon significant elevated oxidative stress. In contrast, hPrxII has lower threshold and exist as non-hyperoxidative monomeric form even at milder oxidative stress. Interestingly, we found that plant extracts containing antioxidants, as analyzed by ABTS assay, rescued the redox stress as well as hyperoxidation induced growth defects of the tsa1tsa2Δ strain in hPrx dependent manner. Plant extracts shift the equilibrium towards peroxidase active dimeric form of hPrx. Same phenomenon was analyzed in mammalian cells and we found that hyperoxidation of hPrx in HeLa cells caused by oxidative stress can also be strongly mitigated by the extracts as shown by reduction in the levels of Cys-SO2/3 using immuno-blotting. Thus, dimeric form is an indicator of redox health of cells.

003

IS 'TROUBLED TRANSLATION' A CONVERGENT FEATURE OF AUTISM: WHAT TRACKING CELL-TYPE SPECIFIC TRANSLATION IN BRAIN CIRCUITS OF MULTIPLE RAT AUTISM MODELS TELLS US.

Keywords Neuroscience, Autism, Protein Synthesis, mTORC1- S6 Kinase 1

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Spatially and temporally-restricted translation has been shown to be the cornerstone of learning and memory. Dysregulated translation also has been shown to be a strong contributor to the etiology of specific developmental and degenerative conditions of the brain. But is it a convergent phenomenon for a multi-genetic, heterogenous condition like Autism Spectrum Disorder (ASD).
We looked at cell-type specific translation of three rat models of ASD with genetic mutations unlinked to translation control. We found microcosms of consistent translational imbalance across specific neurons and glia. We then tracked how the mutation alters downstream signaling and association to adapter proteins in synapse. Our work uncovers a heretofore unaccounted convergent signature for ASD, which may provide a common platform of intervention strategies in this condition.

004

TLR9 LIGATION MODULATES B-CELL RESPONSES BY RAPID REORGANIZATION OF CYTOSKELETON

Keywords Immunology, B cell biology, B cell receptor signaling, Toll like receptor signaling

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B cells recognize and respond to foreign antigens through antigen-specific B cell receptors (BCRs) driving the cells to secrete antigen-specific antibodies. In addition to the BCRs, B cells also express Toll-like receptor 9 (TLR9) that recognize highly conserved unmethylated CpG sequences in microbial DNA. B cells respond differently to antigens and CpG-DNA by undergoing antigen-specific and polyclonal activation respectively. Many of these differences are only evident after several hours following receptor engagements, however, early responses that occur within several seconds of stimulation are unknown. Early responses to the activating ligands are often manifested in morphological changes in cells. We show that treatment of B cells with an antigen to trigger the BCR versus CpG-DNA to engage TLR9 results in striking differences in the morphology and surface topography of the B cells as early as 15 seconds after stimulation. Treatment of B cells with antigen results in uniform expansion of cell membrane followed by an actin cytoskeleton dependent contraction. On the contrary, TLR9 signaling induces two distinct waves of morphological changes in B cells. The first wave initiates as early as 30-45 seconds after TLR9 ligation and results in the formation of membrane blebs in a Src kinase- and Calcium-dependent manner. Live cell imaging showed that blebs are continuously initiated, expanded and contracted rapidly. In contrast, the second wave of morphological changes occurs only after at least 45-60 minutes and induces the formation of multiple tunneling nanotubes (TNTs). Intriguingly, within a few minutes of their formation, TNTs exhibits bead on a string appearance and ultimately beads release as vesicles. Interestingly, prior engagement of the BCR abrogates the TLR9-mediated morphological changes. These observations indicate that B cells utilize multiple distinct and unique mechanisms to discriminate antigens from danger signals such as TLR9 ligands.

005

IMMUNE CHARACTERIZATION OF EXCRETORY/ SECRETORY (ES) PROTEINS FROM IN-VITRO CULTURED TAENIA SOLIUM CYST

Keywords Inflammation, Neurocysticercosis Antigen presentation, Lupus nephritis, Herbal medicine

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OBJECTIVE

Larvae of *Taenia solium* causes Neurocysticercosis (NCC), which is the most widespread cause of acquired epilepsy. Excretory/secretory (ES) proteins released by larvae of *T. solium* are crucial for parasite survival and represent potential targets for novel intervention strategies. The current study was carried out to immune characterise ES proteins of *T. solium*.

METHOD

Cysts were isolated from infected pork muscles and cultured in RPMI-1640 media for 24 hours. ES proteins were characterized by silver staining, 1D-NMR spectroscopy and EITB. Human macrophages isolated from buffy coat were stimulated with the ES proteins to look for their immune cell stimulating capabilities.

RESULTS

NMR spectra showed a number of metabolites being excreted by the cyst. We identified several bands of <50kDa on EITB. QPCR and ELISA had shown significantly high IL6, IL1β and diminished IL4 cytokines expression.

CONCLUSION

The ES proteins of *T. solium* suppress the Th1 immune response and help in parasite survival in host.

006

NEXT-GENERATION SPATIOTEMPORAL DATA ANALYSIS AND VISUALIZATION

Keywords Bioinformatics, Mass Spectrometry, Proteomics, Posttranslational Modifications, Systems Biology

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Mass Spectrometry-based proteomics has infiltrated molecular biological labs and system-wide analysis of proteomes is rapidly becoming commonplace. Instead of qualitative protein profiling, cutting-edge technologies now enable quantitative proteomics measuring the spatio-temporal dynamics of biological systems in high-throughput manner at unparalleled scale. We have developed several tools to enable the quantitative analysis of such complex and voluminous data. We have developed QuantWizIQ tool that enables large scale isobaric quantitation from iTRAQ (upto 8-plex) or TMT (upto 10plex) data and supporting tool HyperQuant that can integrate identification and quantification results from hyperplexing experiment (18plex). Large datasets are cumbersome to analyse in static charts or spreadsheets and development of interactive visualization facilitates facile analysis using modern web technologies and JavaScript based applications. Standardized file format interoperability and support for most HUPO-PSI standard formats makes these apps compatible with most proteomics analysis workflows and our rich biological data can really “come to life” wherein specific biological questions of interest can be quickly answered and newer hypotheses posed easily

007

COMPUTATIONAL STUDIES ON BROAD SUBSTRATE SPECIFICITY OF LACCASE

Keywords Microbiome, Microbiota, Gut, Microbial, Metabolite

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Laccase (E.C. 1.10.3.2) is a well known enzyme for its broad specificity for variety of substrates and potential industrial application. In order to study the broad substrate specificity we used X-ray crystal structures of laccase enzymes with PDB IDs 1gyc (*Trametes versicolor*) and 1uvw (*Bacillus subtilis*) and performed virtual screening against compounds selected from the EPA's (U.S. Environmental Protection Agency). Protein-ligand docking was performed using GOLD tool. Around 30 and 17% of the selected datasets showed good average GOLD fitness score for fungal and bacterial laccase enzyme respectively, hinting at being subtrates for laccase enzyme. We also carried out experiments to validate computationally predicted substrates. The oxidation of predicted substrate by laccase (*Trametes versicolor*)was measured by change in absorbance at specific λ max of each predicted substrate. Sinapic acid and tyrosine were used as positive and negative controls, respectively. Oxidation was observed in m-chlorophenol, 2,4 di-chlorophenol, 2,4,6 tri-chlorophenol, captan, atrazine and thiodicarb, except malathion, which showed no activity.

008

OPTOFLUIDIC PLATFORMS FOR CELL INTERROGATION AND MONITORING CELL COLONY GROWTH

Keywords Lasers, Optofluidics, Biophotonics, Quantum Optics, Rehabilitation Engineering

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We have developed a lab prototype of a microfluidic flow analyzer, which is capable of quick and efficient analysis of biological samples. Low cost and portability makes it suitable for point of care diagnostics in rural area of developing countries. Size reduction was achieved by choosing a microfluidic flow and pumping system, micro-electronic components, integrated circuits boards, and fibre optics. A two dimensional microfluidic chip fabricated with nanolithography technique integrates the fluidics and optics into a single platform. Forward scatters (FSC), side scatter (SSC) and fluorescence (FL) are measured from polystyrene beads as well as from different live cells. The efficacy of the platform has been enhanced using nanosecond gated avalanche photo-detection, while the cost of the platform has been reduced by working with inexpensive visible and IR lasers.

In an allied effort, we also developed an optofluidic device, attached to a smartphone camera, to monitor cell colonies. We are able to study the effect of nutrient concentration and use image processing algorithms to automatically count the number of cells in each colony. In doing so, we reduced the incidence of human error introduced by researchers manually counting cells in a colony, and also standardize the nutrient concentrations used in the study.

009

GROWING UP IN THE HUMAN JUNGLE – THE PUP PERSPECTIVE

Keywords Animal Behaviour, Ecology, Evolution, Cognition, Dogs

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Free-ranging dogs are a ubiquitous presence in human habitations across India. They are scavengers, primarily dependent on human generated resources for sustenance, and have adapted to living among humans for centuries. They live in small social groups that display interesting cooperation-conflict dynamics. Pups receive extensive care from their mothers during early development, and also from other related adult group members. There is evidence for sib-sib competition over parental care, and even between non-siblings within a group, as the pups exploit lactating female relatives through milk-theft. However, there is also ample evidence for care towards pups by related females and some males within the group. Pups compete over resources, but also indulge in extensive play, which enhances social bonding. Pups begin to forage as early as the 7th week of age. Weaning occurs by the 13th week, when the pups enter the juvenile phase and have to rely on foraging for food. The weaning period marks a highly active period of learning for the pups. They encounter humans throughout their development, and show an innate tendency to follow human pointing gestures. However, as they grow older, they show reduced trust in humans, probably due to negative experiences. Only 19% of the pups born in the population reach the stage of sexual maturity, and humans are responsible for 62% of the mortality. I will discuss work done in the Dog Lab over the last eight years, which has led to some understanding of the social interactions that a dog experiences during early development, both with their conspecifics and humans, and the implications of these interactions in the life of the dogs.

010

AN ACTIVATOR/INHIBITOR MODULE REGULATES TUBER DEVELOPMENT IN POTATO- THE THIRD MOST IMPORTANT FOOD CROP IN THE PLANET

Keywords RNA transport and long distance signaling, Plant Growth and Development, Sex expression and modification, microRNAs and plant defense

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Potato development (tuberization) is a highly dynamic and complex mechanism that involves interaction between different environmental, biochemical, and genetic factors. Under inductive conditions, a specialized underground modified stem (stolon) passes through several stages of developmental transitions to form a mature tuber (potato). The stolon acts as a focal point that coordinates several mobile signals, transcription factors (TFs) and plant hormones to stimulate tuberization process. Among the many molecular players that were identified as tuberization regulators, StBEL5 mRNA, StSP6A protein and a DOF family finger protein StCDF1 function as the most important signals. Thirteen BEL1-like TFs have been identified in potato and they work in tandem with KNOTTED1- TFs to regulate the expression of numerous target genes. The first identified BEL1-like gene in potato (StBEL5) has been shown to function as a long-distance mobile RNA signal that is transcribed in leaves and moves into stolons. Over-expression of StBEL5 enhanced tuber numbers and RNAi lines reduced the tuber yield suggesting its role as a positive regulator for tuberization. The two close homologs of StBEL5, StBEL11 and -29 though share about 90% similarity in amino-acid sequences, however, function as repressors of tuberization. These three BELs together make up more than 70% all StBEL transcripts. Using heterografting experiments, we have recently showed that mRNAs of both StBEL11 and -29 are also phloem mobile. All three StBELs target same set of genes to regulate tuber formation. Thus it appears that a system of activation and repression of growth is consistent with the development of a new tuber from the stolon tip, and this tripartite BEL module could readily contribute to cell fate determination in the stolon apex during the transition process from stolon to tubers. I will summarize our results as we investigate this fascinating biological process

011

MOLECULAR DISSECTION IN GLAUCOMA PATHOGENEIS

Keywords Cell Signaling, Glaucoma, Metabolic disorders, Runx, miRNA

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Glaucoma is the second leading cause of irreversible blindness throughout the world. Several studies have reported that, intraocular pressure (IOP) is the critical causative risk factor for glaucoma. At present, the only effective approach available to treat glaucoma is to reduce IOP. Which is controlled by the balance between aqueous humor secretion from the ciliary body (CB) and its drainage through the trabecular meshwork (TM). Though there are several causative factors involved in glaucoma pathogenesis, large number of genes associated with glaucoma has been reported, but the mechanisms are still in speculation. In order to explore the mechanisms involved in pathogenesis, we have identified a novel miRNAs (not disclosed) targeting the known glaucoma candidate genes and it's modulation in gene regulation and alteration of extra cellular matrix proteins (ECM) that mimics in glaucoma pathogenesis. And our In-vitro experimental studies have shown downregulation of identified miRNAs in glaucoma models. Overexpression of these miRNAs in the human trabecular meshwork cells lead to the decreased levels of F-actin and focal adhesions by modulating the Rho-Rock signaling pathway. Our findings not only provide molecular insights to the pathogenesis of glucocorticoid induced glaucoma but also suggest that understanding the signaling pathway that modulates the cytoskeletal structural proteins that will be helpful for developing new modalities in glaucoma therapy.

012

THROWING "LIGHT" TO ACHIEVE "DARKNESS" IN CANCER!

Keywords Nanomedicine, Cancer Nanotechnology, Photothermal Therapy, Nanotoxicology, Theranostics

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Light has always been associated with life and sustainability. But, it could also be used to bring in death (darkness) of diseased cells when combined with suitable nanosystems. Polymeric/ liposomal nanoparticles (NPs) were made to entrap bioactive plant extracts (eg A. Cadamba). Further these NPs were engineered to make them photo thermally active by using gold or near infra-red (NIR) dyes. NIR light showered on such NPs, generate heat to cause irreversible damage to the cellular constituents leading to cancer cell death. The inherent fluorescence property of the plant molecules was deployed to understand the cellular uptake and drug release profile. Polymer nanoparticles were observed to be uniformly distributed everywhere within the cytoplasm, while the lipid based nano carriers seemed to get attached with the cell wall and localize the drug release. We have used a combinational approach in which anti-cancer agent and PTT are used together, so as to maximize therapeutic efficiency. The photothermally active nanoformulations were found to be biocompatible with normal cells. We have also evaluated the photothermal mediated cytotoxicity in cancer cell lines and found a synergistic effect compared to individual treatments. The combinational therapy resulted in 80% of cancer cell death with minimum concentrations of anti-cancer agent. We have also tested the nanoformulation in animal model (B16 – Xenograft), wherein, the combination of photothermal with biomolecular fraction showed increased tumor regression when compared with controls, denoting their translational potential in cancer therapeutics.

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013

“METABOLIC HYGIENE HYPOTHESIS”- FILARIASIS MEDIATED IMMUNOMODULATION AND DIABETES

Keywords Diabetes, Inflammation, Immunity, Tuberculosis, Filariasis

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BACKGROUND
Previously, we have shown reduced prevalence of filariasis among diabetic patients (both Type-1 and Type-2) which was associated with downmodulation of chronic. In the present study we looked at the effect of diabetes on anti-filarial immunity

AIM
To study the various effector functions of T cells including cytokine secretion, apoptosis, cellular activation and antigen presentation in filarial antigen positive subjects with and without diabetes.

METHODOLOGY
Longitudinal; Case –controlled; Observational study. Lymphatic filariasis serum antigen positive (LF+) subjects were followed up after 10 yrs and their innate and adaptive immune functions were evaluated. Whole blood cultures were stimulated with TLR ligands and antigens and in vitro cytokine secretion was evaluated by ELISA. The expression of FoxP3, Cox-2, HO-1, p47Phox, iNOS and Arg-1 were determined by real time PCR. Cellular activation was studied by flowcytometry.

RESULTS
TLR induced secretion of pro-inflammatory cytokines (TNF-α, IL-6 and IL-1β) were not significantly different between the groups. However, TLR induced IL-10 secretion was significantly augmented in presence of diabetes which was associated with the upregulation of Cox-2 and HO-1 mRNA. Basal level secretion of IL-9 and PPD induced secretion of IL-33 were significantly agumented under diabetic condition

CONCLUSIONS
Diabetes was found to affect both innate and adaptive arms of anti-filarial immunity

014

OCT4 AND SMAD3 DIFFERENTIALLY REGULATE EMT-ASSOCIATED FACTORS IN BREAST CANCER PROGRESSION

Keywords Immunology-Tumor and Malarial Immunology

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The multifunctional cytokine TGF-β crucially participates in breast cancer (BCa) metastasis and works differently in the disease stages, thus contributing in BCa progression. We address connections between TGF-β and the stem cell-related transcription factor (TF) Oct4 in BCa. In 147 BCa patients with infiltrating duct carcinoma, we identified a significantly higher number of cases with both moderate/high Oct4 expression and high TGF-β in late stages compared to early stages of the disease. In vitro studies showed that TGF-β elevated Oct4 expression, which in turn, regulated Epithelial-to-Mesenchymal transition (EMT)-regulatory gene (Snail and Slug) expression, migratory ability, chemotactic invasiveness and extracellular matrix (ECM) degradation potential of BCa cells. Putative binding sites for Oct4 on the snail, slug and cxcl13 promoters and for Smad3 on the snail and slug promoters were identified. Promoter activities of snail and slug were greater in dual-treated cells than only TGF-β-treated or Oct4-overexpressing cells. CXCL13 mRNA fold changes, however, were low in cells induced with TGF-β, compared to dual-treated or Oct4-overexpressing cells. Our co-IP studies confirmed that Oct4 and Smad3 form heterodimers that recognize specific promoter sequences to promote Slug and Snail expression, but which in turn, indirectly inhibits Smad3-mediated repression of CXCL13 expression, allowing Oct4 to act as a positive TF for CXCL13. Taken together, these data suggest that TGF-β signaling and Oct4 cooperate to induce expression of EMT-related genes Slug, Snail and CXCL13, which accelerates disease progression, particularly in the late stages, and may indicate a poor prognosis for BCa patients.

015

SEXUAL DIMORPHISM AND THE HUMAN PLACENTA: IMPLICATIONS FOR PLACENTAL ADAPTATION IN FETAL GROWTH RESTRICTION

Keywords Molecular physiology, Developmental biology, Human placenta, Epigenetic regulation

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Despite rapid economic growth, India still faces the intractable problem of high incidence of low birth weight. Apart from the immediate health, social and economic consequences, the 'fetal origins' hypothesis postulates suboptimal fetal growth as the foundation for higher risk of adult-onset non-communicable diseases. Therefore, understanding the underlying molecular pathway perturbations that modulate fetal adaptation to suboptimal intrauterine exposures is key to improving maternal and child health. Sex of the fetus is a well-known determinant of fetal growth and fetal as well as neonatal morbidity and mortality. Sex-specific differences in placental adaptation to intrauterine stressors such as maternal malnutrition, is a likely pivotal mechanistic explanation.

We are routinely preserving placentae from the St. John's birth cohort to address this tenet in the context of fetal growth restriction. Utilizing placental samples from these deeply phenotyped births, we have reported sex-differences in association with placental transcript abundances of an imprinted gene, growth receptor binding protein 10 (GRB10) and that of DNMT1, the maintenance DNA methyltransferase coding gene, with human fetoplacental growth1,2.

Based on the above findings, our group is currently engaged in deeper mechanistic explorations of the role of sexual dimorphism of the human placenta in manifestations of fetal growth restriction, with the eventual goal of informing sensible preventive strategies to tackle the burden of low birth weight in India.

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016

UNIQUE EPIGENETIC PLAYERS OF HUMAN MALARIAL PARASITE *PLASMODIUM FALCIPARUM*

Keywords Plasmodium, Nucleic Acid Methylation, Chromatin modifications, Epigenetic Reader, Antigenic variation

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In eukaryotes, methylation at DNA and histone tails regulates diverse biological processes such as gene expression, development and maintenance of genomic integrity. However, nucleic acid methylation and lysine methylation at histone proteins and its functions in pathogenic apicomplexan protozoans remains enigmatic. To address this, we investigated the presence of cytosine methylation in the nucleic acids of the protozoan *Plasmodium falciparum*. Interestingly, *P. falciparum* has TRDMT1, a conserved homologue of DNA methyltransferase DNMT2. However, we found that TRDMT1 did not methylate DNA, *in vitro*. We demonstrate that TRDMT1 methylates cytosine in the endogenous aspartic acid tRNA of *P. falciparum*. Through RNA bisulfite sequencing, we mapped the position of 5-methyl cytosine in aspartic acid tRNA and found methylation only at C38 position. *P. falciparum* proteome has significantly higher aspartic acid content and a higher proportion of proteins with poly aspartic acid repeats than other apicomplexan pathogenic protozoans. Proteins with such repeats are functionally important in host-pathogen interactions. In addition, we identified various novel methylation marks on the histone tails of *P. falciparum* and modification specific epigenetic reader proteins in the parasite. This suggests that parasite evolved with unique epigenetic players which may involve in regulation of unknown mechanisms of antigenic variation of *P. falciparum*.

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017

PINA, A HOMOLOG OF SCESS1, IS IMPORTANT FOR CELL PROLIFERATION AND CELL PATTERNING IN *Dictyostelium discoideum*

Keywords bZIP, PinA, PPIase, Wee Kinase, Dictyostelium

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D. discoideum cells exist as unicellular haploid amoeba in moist soil under temperate conditions. Upon starvation, cells secrete cAMP and undergo a developmental program in which unicellular undifferentiated amoeba come together to forma multicellular structure, a fruiting body consisting of two terminally differentiated cell-types, spore cells and stalk cells. These homogenous cells respond to different signaling molecules, such as cAMP, DIF-1 etc. and differentiate into presumptive spore (prespore)/presumptive stalk (prestalk) cells. Towards our goal of understanding the mechanism underlying cell differentiation, we initiated to characterise PinA, a novel parvulin-type PPIase having FHA and PPIase domains. Parvulins are highly conserved enzymes belonging to peptidyl prolyl cis/trans isomerases (PPIases) that catalyze reversible cis/trans isomerization of the peptide bond preceding proline and regulate activity, stability and localisation of target proteins. These enzymes thus control eukaryotic cell proliferation, cell cycle progression and gene regulation. PinA shares 51% identical amino acid sequence with ScEss1 in PPIase domain and can complement the growth defect associated with S. cerevisiae ess1H164R mutant at high temperature. Expression profiling showed that pinA is temporally and spatially regulated during *D. discoideum* growth and development. Localisation of PinA is both nuclear as well as cytoplasmic in growing cell. PinA is not required for survival however loss of PinA affects cell proliferation and developmental process. Loss of PinA affects the cell patterning in slugs. Our findings suggested that PinA is required for normal cell proliferation and morphogenesis in D. discoideum. Further studies include generation of pinA mutants by random PCR and their characterisation to understand the important residues in PinA. Results from genetic and molecular analyses will be presented.

018

CHROMATIN REMODELLING FACTORS: ADDING NEW DIMENSIONS TO OUR UNDERSTANDING OF THEIR FUNCTION AND IMPLICATION IN HEALTH AND DISEASE

Keywords Chromatin remodelling factors, TIP60, PXR, *Plasmodium falciparum*, RUVBL

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TIP60, an essential histone acetyl transferase protein is known to regulate steroid receptor function. Recently, we have identified that TIP60 interacts with a xenobiotic receptor, PXR in a ligand-independent manner and together this novel complex promotes cell migratory & adhesion properties. TIP60 NR Box is involved in its interaction with PXR LBD region and TIP60 acetylates PXR at lysine 170 to induce its intranuclear reorganization. Also, RXR (an obligatory heterodimeric partner of PXR) is not required for TIP60-PXR complex formation and this complex does not induce ligand-dependent PXR target gene transactivation. Interestingly, we also observed that the catalytic activity of TIP60 for histones is augmented in presence of PXR. This is the first report demonstrating the exclusive interaction of TIP60 with PXR and uncovers a potential role for the TIP60-PXR complex in wound healing. Currently we are working to explore the gene(s) & the downstream signalling pathways targeted by this complex.

Despite tremendous efforts to control & eliminate malaria, it still causes 6 lakh deaths annually. Understanding the basic biology of malaria parasite in-depth is a requisite for identifying novel molecular targets for anti-malarial therapy. Knowing the relative paucity of defined transcription factors in *Plasmodium,* epigenetics and chromatin remodelling factors serve as major contributors in bringing epigenetic changes in the genome to regulate 'on demand' gene expression in the parasite. We have functionally characterized RUVBL proteins of malaria parasite. Complementation studies in yeast verified PfRUVBLs to be the true homologs of yeast counterparts. Most importantly, we have identified new DNA modifying functions of PfRUVBL proteins that can be inhibited in presence of some tested anti-malarial drugs used in this study. Our future plans include dissecting the implications of PfRUVBL proteins in regulating various metabolic pathways of malaria parasite.

019

FMN2: A NEW REGULATOR OF ACTIN, MICROTUBULE AND ADHESION DYNAMICS IN NEURONAL GROWTH CONES

Keywords Neuroscience, Cell Biology

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Directional translocation of neuronal growth cones to their synaptic targets is necessary for the development of neural circuits. Coordinated remodelling of the actin and microtubule cytoskeletons regulate growth cone motility at multiple levels, including the generation of protrusive structures, dynamics of adhesion sites, generation of traction forces and directionality.

We have recently identified Formin-2 (Fmn2) as a key regulator of axonal pathfinding in spinal commissural neurons. We show that Fmn2 organises actin bundles in filopodia necessary for optimal mechanotransduction and, in turn, regulate filopodial lifetimes by stabilising filopodial tip adhesions. Filopodial contractility and translocation rates of growth cones are compromised upon Fmn2 depletion as is directional motility in response to guidance cues. Depletion of Fmn2 increases the F-actin retrograde flow rates, implicating compromised engagement of the actomyosin contractile machinery to the adhesion sites. Further, Fmn2 cross-links growing microtubules to actin bundles in filopodia and increase the frequency of microtubule capture and is critical for directional motility.

This work not only identifies Fmn2 as a key regulator of growth cone motility but also uncovers new mechanisms coordinating actin, microtubule and adhesion dynamics.

020

CRISPR-CAS ADAPTIVE IMMUNITY: MOLECULES, MACHINES AND MECHANISMS

Keywords SRNA Biology, CRISPR-Cas Adaptive Immune System, Ribosome Assembly, Riboswitches, RNA mediated Gene Regulation

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CRISPR-Cas system represents an adaptable and heritable immune system that defends the bacteria and archaea against the invasion of mobile genetic elements such as phages and plasmids. Exploitation of this immune system fanned out into a versatile genome editing technology referred to as CRISPR/Cas9. Though this prokaryote specific immune system is functionally analogous to the RNA interference (RNAi) in the higher organisms, it is mechanistically distinct. The defence mechanism proceeds via three distinct stages: acquisition of immunological memory from the invading genetic elements, maturation of CRISPR RNA and RNA guided target recognition and cleavage. Using a combination of biophysical, biochemical and molecular genetics approaches, we have embarked to decipher the underlying mechanism by which this RNA guided targeting occurs. Here, we will present a brief account of our recent past and ongoing investigations on CRISPR immunity that revealed new insights on the specificity of molecular recognition between CRISPR machinery and the target genetic element.

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021

TOXIC TOPOISOMERASE1-DNA CLEAVAGE COMPLEXES IN THE MITOCHONDRIA ACCUMULATES MITOCHONDRIAL DYSFUNCTION AND ACTIVATES MITOPHAGY

Keywords DNA repair and Genome instability, Mitochondrial DNA metabolism and mitophagy, Cancer, DNA topoisomerases

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AIM

Mitochondrial DNA (mtDNA) are unprotective due to lack of histones, and accumulation of mtDNA damage causes several neurological disorders. Tyrosyl DNA phosphodiesterase 1 (TDP1), a key enzyme that hydrolyze Topoisomerase 1-induced DNA lesions (Top1cc), are also attributed for the maintenance of mtDNA. Active site mutation of TDP1 (H493R) leads to severe neurodegenerative disorder called spinocerebellar ataxia with axonal neuropathy (SCAN1). Here we investigate the mechanism of TDP1H493R associated with mitochondrial dysfunction.

RESULT

We show that TDP1 knock out murine embryonic fibroblasts (TDP1 /-) or patient derived human SCAN1 lymphoblastoid cells exhibit dysfunctional respiration, which leads to decreased ATP production and increased accumulation of reactive oxygen species (ROS). These cells were markedly deficient in repairing mitochondrial Top1-DNA cleavage complexes (Top1mtcc) and were also hypersensitive to oxidative DNA damages and mitochondrial chain uncouplers. ROS inhibitors protect TDP1-deficient cells from oxidative stress. We further show that TDP1 functional deficiency severely imbalance mitochondrial transcription and up regulates mitochondrial biogenesis by activation of several nuclear genes involved in the maintenance of mitochondrial topology for promoting mitochondrial biogenesis. Using targeted delivery of Irriotecan (SN-38) to the mitochondria, we established that Top1mtcc impair the mitochondrial framework, transcription, dynamics and subsequently triggers mitophagy in TDP1 mutated cells.

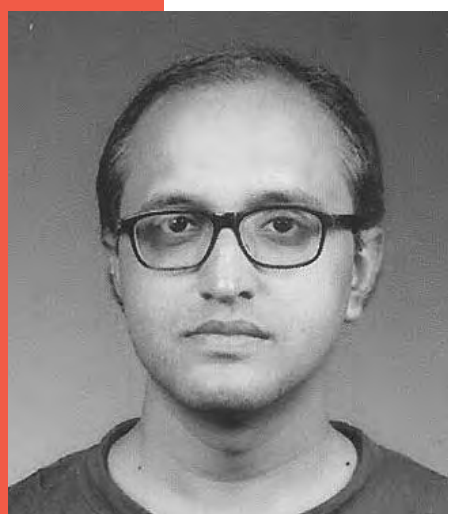
CONCLUSION

SCAN1 cells utilize a neuroprotective mechanism where mitochondria harbouring TDP1 H493R inculcate mitophagy to foster the loss of postmitotic neurons.

SIGNIFICANCE

Our study unravelled the new role of TDP1 in regulation of the mitochondrial gene transcription, integrity and conferring cellular protection against Top1mtcc and ROS-induced mitochondrial DNA damage

022



IN VITRO AND *IN VIVO* STUDIES ON THE EFFECT OF ZINC TOXICITY ON THE NERVOUS SYSTEM

Keywords Neurobiology, Toxicity, Cell Line, Behavioral Assay, *Caenorhabditis elegans*

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Zinc (Zn) is an essential micronutrient in human body and is believed to play a major role in neuromodulation of several important receptors including AMPA, NMDA, and GABA receptors and participates in synaptic plasticity. Previous studied have indicated that at a higher Zn concentration neurotoxicity sets in, as evident from clinical and preclinical studies of traumatic brain injury, stroke, epilepsy, Alzheimer's disease, and other neurodegenerative disorders. We studied Zn toxicity using both *in vivo* (involving *Caenorhabditis elegans* as a model system) and *in vitro* system (comprising of C6 glioma cells). Our results suggest that Zn has toxic effects on the nervous system beyond a certain threshold concentration. Interestingly, the threshold level is different for different sensory systems. The outcome of neural dysfunction could be seen through various behavioral assays. Moreover, our *in vitro* study on glial cells suggests that Zn affects glial cell survival and functioning beyond 150μM concentration.

023

ENGINEERING PLANTS FOR ADVANCED BIOFUELS

Keywords Metabolic engineering, genetic profiling, biofules, metabolomics, plant tissue culture

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Dwindling fossil reserves and global warming has catalyzed a worldwide trend to utilize plant biomass for the production of biofuels and other biomaterials. Plant biomass is the most abundant renewable resource on the earth. However there are currently various limitations to use this biomass for biofuels. Towards this end our research team focuses on the engineering of plants for biofuel production. We are trying to tailor a biofuel feedstock that would be easily converted to bioethanol and for this our current approach is to express some thermophilic enzymes directly in plants.

024

COLON CANCER STEM CELLS EXHIBIT OPPOSING BEHAVIOR OF PROLIFERATION VERSUS CELL KILLING UPON LOW VERSUS HIGH DOSES RESPECTIVELY OF VITAMIN C AND NIACIN TREATMENT

Keywords CD34+/45- regenerative stem cells, Colon and breast cancer stem cells, Eye stem cells, Vitamin C, Nicotinamide, Liver mesenchymal stem cells

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Cancer stem cells (CSCs), the rogue sub-population responsible for relapse of cancer are possibly generated as chemo-radioresistant cancer cells. Hence, targeting CSCs is the most sought-after cancer therapie. As colorectal cancer is one of the leading causes of global deaths and has presence of cancer stem cells upon relapse, in this study, we studied the possible effects of common dietary vitamins such as Vitamin C and Niacin on colorectal CSCs. Standard water-soluble vitamins have no recommended guidelines for possible prevention of colorectal cancers. Also, high doses of vitamin C reportedly kill colon cancer cells harbouring BRAF and KRAS mutations via induction of oxidative stress. However, in this study we show for the first time, an interesting observation of opposing effects of low and high doses of these water-soluble vitamins on colon cancer stem cells isolated from two cell lines, HT-29 (harbouring BRAF) mutation and HCT-15 (harbouring KRAS) mutation. Low doses (5-25μM) of both these water-soluble vitamins exerted a proliferative effect on the colon CSCs. However, high doses (100-10,000 μM) were able to induce cell killings as high as 60% in CSCs from HT-29 cell line and only ~30% in CSCs from HCT-15 cell line. On the contrary, non-stem cancer cells and mixed parent populations (WT) did not exhibit enhanced proliferation at low doses of both the vitamins. Also, upon treatment with high doses of each of the vitamins, the non-CSCs and WT failed to exhibit any trend in substantial cell killings. From the translational viewpoint, this work has future scope for studying the therapeutic doses of Vitamin C and Niacin.

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025

ATYPICAL G PROTEIN B5 PROMOTES CARDIAC OXIDATIVE STRESS, APOPTOSIS, AND FIBROTIC REMODELING IN RESPONSE TO MULTIPLE CANCER CHEMOTHERAPEUTICS

Keywords Cardiotoxicity, Chemotherapy, Gβ5, Fibrosis, Hypertrophy

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The clinical use of multiple classes of cancer chemotherapeutics is limited by irreversible, dose-dependent, and sometimes life-threatening cardiotoxicity. Though distinct in their mechanisms of action, doxorubicin, paclitaxel, and 5-FU all induce rapid and robust upregulation of atypical G protein Gβ5 in the myocardium correlating with oxidative stress, myocyte apoptosis, and the accumulation of pro-inflammatory and pro-fibrotic cytokines. In ventricular cardiac myocytes (VCM) Gβ5 deficiency provided substantial protection against the cytotoxic actions of chemotherapeutics including reductions in oxidative stress and simultaneous attenuation of ROS-dependent activation of the ATM and CaMKII pro-apoptotic signaling cascades. In addition, Gβ5 loss allowed for maintenance of Δψm, basal MCU and mitochondrial Ca2+ levels, effects likely to preserve functional myocyte excitation-contraction coupling. The deleterious effects of Gβ5 are not restricted to VCM, however, as Gβ5 knockdown also reduces chemotherapy-induced release of pro-inflammatory cytokines (e.g. TNFα), hypertrophic factors (e.g. ANP) and pro-fibrotic factors (e.g. TGFβ1) from both VCM and VCF with the most dramatic reduction occurring in co-cultured cells. Our experiments suggest that Gβ5 facilitates the myofibroblast transition, the persistence of which contributes to pathological remodeling and heart failure. The convergence of Gβ5-mediated, ROS-dependent signaling pathways in both cell types represents a critical etiological factor in the pathogenesis of chemotherapy-induced cardiotoxicity. Indeed, intracardiac injection of Gβ5-targeted shRNA allowed for heart specific protection against the damaging impact of chronic chemotherapy. Together, our results suggest that inhibition of Gβ5 might represent a novel means to circumvent cardiotoxicity in cancer patients whose treatment regimens include anthracyclines, taxanes or fluoropyrimidines.

026

MOLECULAR STAKEHOLDERS IN THE ART OF SURVIVAL BY CANCER CELLS UNDER METABOLIC STRESS

Keywords Cancer Biology, Tumor metastasis, Cancer Cell Survival Tumor Microenvironment, Cell migration

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Tumor cells display more plasticity to ensure survival in different fitness landscapes including hypoxia. Unlike a normal cell, a transformed cell acquires survival ability even under stressful conditions like hypoxia by exploring minor modifications of regulatory signaling circuits inside the cells. Therefore, understanding the mechanism of action and the role of upstream regulators of these pathways is important because it provides a therapeutic option for cancer treatment. PBXIP1/HPIP, an estrogen receptor interacting protein, has been reported to act as an upstream regulator of PI3K/AKT/mTOR signaling in cancer cells. Here we report that HPIP expression is induced under hypoxia in breast cancer cells. Silencing of HPIP by lentiviral-mediated HPIP shRNA rendered MDA-MB231 cells to lose the cancerous properties under hypoxia. HPIP promoted cancer cell survival, invasion and metastasis under hypoxia by modulating the secretory pathway in MBA-MD231 cells. Clinical studies indicated that HPIP and HIF1alpha expressions correlate in triple negative breast cancer (TNBC) specimens. Together these results suggest the involvement of a novel signaling pathway in the development of triple negative breast cancer (TNBC) and influence of hypoxic microenvironment. This pathway could be a potential therapeutic target to treat TNBCs.

027

PREFERENTIAL SELECTION OF ARGININE AT THE LIPID-WATER-INTERFACE OF TRPV1 DURING VERTEBRATE EVOLUTION CORRELATES WITH ITS SNORKELING BEHAVIOUR AND CHOLESTEROL INTERACTION

Keywords Pain receptors, Ion channels, Cytoskeleton, Mitochondria, Vesicular recycling

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TRPV1 is a thermo-sensitive ion channel involved in neurosensory and other physiological functions. The trans-membrane helices of TRPV1 undergo quick and complex conformational changes governed by thermodynamic parameters and membrane components leading to channel opening. However, the molecular mechanisms underlying such events are poorly understood. Here we analysed the molecular evolution of TRPV1 at the lipid-water-interface region (LWI), typically defined as a layer of 6Å thickness on each side of the membrane with less availability of free water. Amino acids demarcating the end of the trans-membrane helices are highly conserved. Residues present in the inner leaflet are more conserved and have been preferentially selected over others. Amino acids with snorkeling properties (Arginine and Tyrosine) undergo specific selection during the vertebrate evolution in a cholesterol-dependent and/or body temperature manner. Results suggest that H-bond formation between the OH- group of cholesterol and side chain of Arg557 or Arg575 at the inner leaflet is a critical parameter that can regulate channel functions. Different LWI mutants of TRPV1 have altered membrane localization and deficient colocalization with lipid raft markers. These findings may help to understand the lipid-protein interactions, and molecular basis of different neuronal functions. Such findings may have broad importance in the context of differential sensory responses, pathophysiologies, and application of pharmacological drugs such as anaesthetics acting on TRPVs.

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028

SALMONELLA ORCHESTRATES A SUMOYLATION DEPENDENT SUB-PROGRAMMING OF HOST GENE EXPRESSION DURING INFECTION

Keywords Microbiology, Inflammation, Gut Infections, *Salmonella,* SUMOylation, PTMs, Autoimmunity

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Pathogens have evolved sophisticated strategies to subvert host defence mechanisms to manifest successful infection. Understandably, post-translational modification (PTM) pathways of the host are desirable targets that enable the pathogen to achieve instantaneous control over host function. Our findings reveal, for the first time, modulation by intestinal pathogen *Salmonella enterica* serovar Typhimurium (here after referred as *Salmonella*) of host SUMOylation, a PTM pathway central to all fundamental processes of a cell. We observed, both in cell culture and murine model, a dynamic alteration of the SUMO-proteome triggered by *Salmonella* infection. A comparative mass-sepectrometric analysis of SUMOylated proteins revealed alteration of crucial regulators of host-endocytic pathway, including Rab7a and Lamp2. Intracellular survival of *Salmonella* was dependent on host SUMO status as revealed by reduced infection and Salmonella induced filaments (SIFs) in experimentally SUMO-upregulated cells. Salmonella dependent SUMO modulation was seen as a result of depletion of crucial SUMO-pathway enzymes Ubc-9 and PIAS1, both at the protein and transcript levels. To modulate the SUMO-pathway, *Salmonella* harnessed the cellular microRNA machinery, namely miR30e and miR30c, which we demonstrate to be necessary and sufficient for successful ST infection. Thus, our data reveal a novel mechanism of bacteria-mediated perturbation of host SUMOylation, an integral mechanism underlying pathogenicity.

029

HIGH THROUGHPUT SINGLE MOLECULE ASSAYS USING MAGNETIC TWEEZERS FOR REAL-TIME STUDY OF PROTEIN-NUCLEIC ACID INTERACTIONS

Keywords Dynamics, Single molecule micro-manipulation, Single molecule fluorescence, Protein-nucleic acid interactions, Protein-protein interactions

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Magnetic tweezers have simplified the way by which tens of single molecules can be parallely micro-manipulated, and yield a huge statistics of enzymatic, binding, or interaction kinetics(1,2,3). The experimental setup consists of magnetic beads, each attached to a nucleic acid (DNA/RNA), held in the tweezers by a pair of magnets that produce a vertical force, typically ranging from 0.01-20 pN. The force is calibrated by the Brownian fluctuations of the tethered bead. A 100X 1.2 N.A. microscope objective images the bead onto a CCD camera for real-time position 3D tracking at 30Hz. The image of the bead displays diffraction rings that are used to estimate its 3D position. The accuracy of the z tracking is 3 nm from one frame to the next and the tracking can be performed simultaneously on 40-50 beads. Using this, we have obtained real-time dynamics of helicase binding to an RNA/DNA substrate and its enzymatic activity. I would be discussing the case of some helicases we have studied, most notably, RecQ(4), which is involved in DNA damage repair in bacteria as well as humans, its diffusive dynamics on a single stranded DNA, the mechanism by which it unzips double stranded DNA, and real time interactions with other proteins during DNA damage repair.

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030

CLATHRIN MEDIATED ENDOCYTOSIS IS REQUIRED FOR THE TRAFFICKING OF E-CADHERIN TO MAINTAIN THE PLURIPOTENCY OF EMBRYONIC STEM CELLS

Keywords Embryonic stem cells, Endocytosis, Pluripotency, Clathrin, E-cadherin

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Cell fate determination in the early embryo is regulated by a number of mechanisms. Recently, vesicular trafficking has been shown to play an important role in cell fate choice, although the exact identity of pathways and molecules remains poorly understood. Using a combination of high-throughput screening approaches and data mining, we identify a role for clathrin-mediated endocytosis in the maintenance of embryonic stem cell pluripotency. We demonstrate that the endocytosis and recycling of E-cadherin by CME is essential for the pluripotency of mouse embryonic stem cells. Additionally, we also uncover novel mechanisms for the suppression of specific endocytic pathways in stem cells. Our results establish that a fine balance exists between trafficking pathways that play a role in the regulation of cell fate choices.

031

YEAST SSA HSP70 REDUCES A-SYNUCLEIN TOXICITY BY PROMOTING ITS DEGRADATION THROUGH AUTOPHAGY

Keywords Chaperones, Neurodegeneration, Amyloid, Hsp70 Hsp90, prions

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The Hsp70 chaperones are known to protect cells from toxicity associated with accumulation of toxic protein inclusions such as those formed of α-synuclein or PolyQ. Though the underlying mechanism is still unclear, the chaperoning action of Hsp70 is generally believed to counteract the cellular toxicity. In the current study, we examined both chaperoning and non-chaperoning roles of yeast cytosolic Ssa Hsp70 isoforms on α-synuclein mediated cellular toxicity. The study shows that yeast cells expressing stress inducible Ssa3 or Ssa4 as the sole Ssa Hsp70 isoform, reduce α-synuclein toxicity better than those expressing constitutive counterpart. The protective effect of stress inducible Ssa Hsp70s is not α-synuclein specific but more general to other inclusion forming proteins such as polyQ. Unexpectedly, we found that Ssa3 promotes cellular survival not through classical chaperoning function but by promoting α-synuclein degradation through autophagy. The present study reveals that effect of Hsp70s on protein inclusion mediated toxicity is Hsp70 isoform dependent, and their role in protein degradation is more effective than anti-aggregation activity to protect cells from deleterious effects of toxic protein inclusions.

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032

GEOMETRY OF LIPID DROPLETS AND 3D GEL LIKE CELLULAR MICROENVIRONMENT DURING DEVELOPMENT AND DIFFERENTIATION.

Keywords Biophysics, Microscopy, Fluorescence, Lipid-Droplet, Cell mechanics

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I will discuss two different projects on my poster

1. Lipid droplets (LDs), reservoirs of cholesterols and fats, are organelles that hydrolyse lipids in the cell. Until 4 day post fertilization, the biochemical energy needed for the development of zebrafish embryos are sustained mainly by the maternally supplied embryonic nutrients. Since lipids are important precursors for biochemical energy the functioning of embryonic LDs are vital for its development. We explore the metabolism of LDs during early development of the zebrafish embryos to demonstrate that until 3 hpf in zebrafish embryos, the LDs undergo extensive lipolysis that generates free fatty acids (FFAs) which are involved in the homeostasis of embryonic ATPs and oocyte-to-embryo transition. We have identified two distinct states of LDs, an inactive and an active state caused by periodic regulation of lipase activity. In this poster I will also discuss the regulation of LDs geometry, number and intra-embryonic distribution during development.

2. During tissue inflammation, blood resident monocytes migrate to the site of injury and subsequently get differentiated into macrophages. The process of differentiation involves concomitant changes in the chemical and the physical microenvironment of the cell. The literature suggests that specific chemical microenvironments such as exposure to cytokines, PMA or LPS primarily drive the monocyte differentiation. In this poster, I will discuss the effect of physical microenvironment on the process of differentiation. Our studies with chemical stimulation of monocyte differentiation in adhesion incompatible conditions suggest that adhesion is necessary for differentiation. We hypothesize that the cytokines or other chemical inducers primarily promote adhesion which then activates other crucial signaling pathways necessary for differentiation.

033

UNDERSTANDING STRUCTURE-FUNCTION-DYNAMICS OF SIGNALING PHOTORECEPTORS

Keywords LOV, Cry photoreceptors, Structural Optogenetics Structure-based designs, Molecular spectroscopy, Photocycle kinetics

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Light is essential for the survival of life. Signaling photoreceptors effectively control light-dependent behavioral patterns in living organisms that includes circadian rhythm in mammals, jet lag in humans, phototaxis in bacteria, phototropism in plants etc. This is achieved when the chromophore in sensor domain of a photoreceptor absorbs photons of visible light and undergoes a structural or dynamic transition to generate a signal. This local structural change is then transmitted through the chromophore containing sensor (or input) domain to an effector (or output) domain, in which biochemical function(s) such as kinase catalytic activity or DNA binding activity becomes light-regulated. Optogenetics that confers light sensitivity to genetically encoded molecules, has enabled scientists to directly tweak an intricate signaling network and subsequently observe the physiological manifestation with great spatio-temporal precision, simply using light. We discuss the importance of understanding the basic photoreceptor structure-function-dynamics in enriching this new generation technique. We discuss how subtle changes in residue interaction network of photoreceptor's 3D structure at different light conditions could contribute towards designing temporal optogenetic variants. Finally we discuss our most recent investigations on complexities in optogenetic designs from an interdisciplinary perspective with interdependent analytical methodologies. Besides technological advancements, the ability to detect even small changes in light intensity to decipher proper behavioral and developmental responses is important. A very fundamental question of how a protein's structural dynamics is translated into signal is not only important to address optogenetic designs but also to understand photo-adaptation and basic photoreceptor mechanism in general.

034

PEACOCK'S TALE: VICINITY TO HUMANS MAY CHANGE THE FEEDING ECOLOGY OF INDIAN PEAFOWL

Keywords Human-animal interactions, Animal behavior, Ecology

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Natural habitats for animals are shrinking at an increasing rate all across the world and particularly in India due to high human population density, changing land usage, and decline in the forested areas. Wild animals are increasingly finding themselves near human habitation. Human-animal interactions and conflicts have risen as a result. The impact of local human population on animal populations living close to or within rural, semi-urban, and urban areas has rarely been studied. Vicinity to human population can change natural behavior and life history of animals in multiple ways: e.g. feeding by humans, availability or scarcity of food in the form of crops might change feeding habits, inter-individual competition and demographics of a species.

We studied diet composition as well as feeding and related behaviors of Indian Peafowl in three areas (2 in Maharashtra, 1 in Rajasthan) which differed in the extent of human- peafowl interactions. Diet composition varied according to the quantity of food provided by humans in the study areas. Sites where humans provided plenty of food (Morachi Chincholi), contribution of cereals to the peafowl diet was maximum while they were seen eating minimum amount of non-grain food items. In contrast, site where food is offered by humans in relatively less amount or infrequently, majority of peafowl diet consists of non-grain food items and minimum amount of cereals. Feeding ecology (no. of pecks/ bout and group size) of Indian Peafowl, thus, may differ at these field sites, also with respect to breeding or non-breeding season. Data collected through questionnaire based surveys indicate local traditions and beliefs may influence how people interact with wild life around them. Thus, "taming of wild peafowl" due to active feeding by humans as well as attitude of locals towards the peafowl may change feeding ecology of Indian Peafowl in areas where they regularly come in contact with human population.

035

AKT KINASE ISOFORMS DISPLAY DIFFERENTIAL ROLE IN INVASIVE BREAST CANCERS AND TREATMENT RESPONSE

Keywords Cancer Stem Cell, Dormancy, Metastasis, Autophagy, Drug Discovery

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The serine/threonine protein kinase B (PKB) also known as AKT plays a vital role in various malignancies and is considered as one of the attractive targets for cancer drug discovery. It exists in three individual isoforms (AKT1,AKT2, AKT3) encoded by three distinct genes. Contrary to the conventional opinion of AKT as tumor promoter, emerging evidences suggest that AKT isoforms are functionally non-redundant and may not work in parallel. It is demonstrated that AKT isoforms play conflicting roles in the cancer, so discovering isoform specific inhibitors can be more relevant and useful than those of pan-AKT inhibitors. We tried to unravel the role of AKT isoforms in the regulation of breast cancer stem cells (CSCs) and their response to the treatment of chemotherapeutic agent. We generated stable cell clones with si-lenced (sh) as well as constitutively expressing (AKTO) individual AKT isoforms of non-maliganant MCF10A and aggressive triple negative BT549 breast lines. Our results demonstrated that AKT isoforms differentially regulate the invasive and proliferative properties of cells. We found knockdown of AKT1 (shAKT1) increased, while that of shAKT2 reduced the cell proliferation in both in MCF10A and BT549, however no considerable change was observed in shAKT3 cells. To demonstrate the effect of each iso-form on invasive cellular program of epithelial mesenchymal transition (EMT), it was observed that shAKT1 decreased the expression of mesenchymal markers with attendant increase in epithelial markers. However, in case of shAKT2 and shAKT3 cells, increase expression of mesenchymal markers was observed indicating induction of EMT. Similarly, among AKTO cell clones of MCF10A, AKT1O triggered transition towards EMT. Further AKT isoform specific IHC staining of metastatic TN breast cancer clinical samples revealed relatively dominant expression of AKT1. Additionally, AKT isoforms deferentially responded to the treatment of chemothereapeutic agent Cisplatin.

036

JOURNEY FROM GAMETES TO EMBRYOS

Keywords Reproduction, Sperm, Egg, Fertility, Development

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Mammalian fertilization involves a complex series of interactions between the egg and the sperm which culminate in embryo formation. The initial interaction of gametes occurs between the egg's extracellular zona pellucida matrix and sperm membrane proteins. In mice, the zona pellucida (ZP) is composed of three glycoproteins ZP1, ZP2 and ZP3 that form a matrix to which sperm bind. Following fertilization, sperm do not bind, which ensures the critically important block to polyspermy.

The most recent and accepted model which tries to explain how this process takes place is the 'ZP2 cleavage' model. A central premise of this model is that the cleavage status of ZP2 determines the 3-D structure of the zona matrix, rendering it permissive (uncleaved ZP2) or non-permissive (cleaved ZP2) for sperm binding. Thus, capacitated sperm would be able bind to an unfertilized but not a fertilized embryo. However, it is now being suggested that O-glycosylation of a conserved Threonine residue present on ZP3, along with the cleavage status of ZP2, together determine if the sperm-egg binding will take place or not. In order to test this hypothesis, our lab is expressing the mZP1, mZP2 and mZP3 proteins in the baculovirus system. This will enable us to understand the role of carbohydrates in sperm-egg interaction, specifically the role of O-glycosylated Threonine present on ZP3 along with the cleavage status of ZP2. For this, the recombinant proteins are being expressed with a His tag for purification and GFP tag for ease of detection during in vitro studies/ binding assays.

037

HOW PHOSPHORYLATION-DEPHOSPHORYLATION REGULATE K+ DEPRIVATION STRESS SIGNALLING IN PLANTS?

Keywords Stress signalling, Calcium sensors, Kinases, Phosphatases, Transcription factors

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Potassium (K+) is a major macronutrient required for plant growth. In response to low K+ condition, an adaptive mechanism entails activation of the Ca2+ signaling network that consists of calcineurin B-like proteins (CBLs) and their interacting kinases (CIPKs) in plants. The CBL-interacting protein kinase 9 (CIPK9) has been previously implicated in low-K+ responses in Arabidopsis thaliana. Here, we report identification of an Arabidopsis protein phosphatase 2C, AP2C1, as a novel interactor of CIPK9 by yeast two-hybrid and protein pull-down assays. In-vivo co-localization and bimolecular fluorescence complementation (BiFC) analysis revealed that CIPK9 and AP2C1 interact in the cytoplasm. In-vitro en-zyme activity assays showed that AP2C1 dephosphorylated the auto-phosphorylated form of CIPK9, presenting one possible mechanism for CIPK9 regulation by AP2C1. Furthermore, genetic analysis revealed that ap2c1 null mutants (ap2c1-1 and ap2c1-2) were more resistant to low-K+ conditions than the wild type plants. In contrast, transgenic plants overexpressing AP2C1, like the cipk9 null mutants (cipk9-1 and cipk9-2), were more sensitive to low-K+ conditions as compared to the wild type. These findings support the hypothesis that AP2C1 and CIPK9 interact genetically and functionally, to regulate K+-deficiency responses in Arabidopsis. While CIPK9 functions as positive regulator, AP2C1 acts as a negative regulator of Arabidopsis root growth and seedling development under low-K+ conditions.

038

EXPLORING CARBON CONCENTRATING MECHANISMS IN THE UNICELLULAR ALGA CHLAMYDOMONAS

Keywords Phytochemistry, Photosynthesis, Computational Biology

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Inorganic Carbon is fixed into sugars by RuBisCo, the most abundant protein on our planet, through a reaction that is famously known as the bridge between the living (organic) and non-living worlds. Despite its importance, RuBisCo is also one of the laziest and most inefficient enzymes known to biology, a trait that has been ascribed to its large size and a preference for Oxygen as substrate instead of Carbon Dioxide. Despite decades of research towards improving photosynthetic efficiency, several fundamental systems-level questions in the area remain unanswered, particularly about the evolution of carbon con-centrating mechanisms (CCMs) in the plant kingdom. The unicellular green alga Chlamydomonas rein-hardtii (""Chlamy"") is a powerful model photosynthetic organism with a highly conserved green plant photosynthetic apparatus.

In this work, we describe our ongoing investigation of the circadian transcriptome of Chlamy at varying intervals in the Light/Dark stages and Hi/Lo Carbondioxide, in order to identify genes that may regulate CCM induction. Molecular signatures related to RuBisCo packaging within the pyrenoid were assessed through construction of Co-expression networks based on RNA-seq analysis of Chlamy transcriptomes at each interval. This data was topologically superimposed with GRNs developed using cis-element signa-tures of the corresponding genes in the network. We present insights gained as well as new genes and Transcription factors that were found to be clustered with genes previously known to be involved in CCM. Further investigations in the short term will pave the way for incorporating Chalmy photosynthetic strategies into higher plants, and we hope in the long term to translate our work towards enhancing food security and biomass crop productivity in the developing world.

039

POTENTIAL ROLES OF BACTERIA AND VIRUS IN GASTRIC CANCER AND MULTIPLE SCLEROSIS

Keywords Gastric Cancer; Multiple Sclerosis; Epstein Barr Virus; *Helicobacter Pylori;* infection; early detection.

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Various reports suggest the association of EBV and *H. pylori* in gastric cancer (GC) worldwide4. GC pa-tients are diagnosed in an advanced stage of the disease. Hence, there is an urgent need for early detection of biomarkers in GC. Moreover, to find etiology in co-infection with EBV and *H. pylori* for GC progression is important. Worldwide, more than 2.5 million people are affected by MS annually. Interestingly, EBV DNA is found in CSF samples of MS patients. How EBV cross blood brain barrier and what are the consequences in disease pathogenesis is still unknown.

This study will evaluate the mechanistic progression of GC and MS pathogenesis through viral and bacterial pathogens. Also, what are the conditions in a human which makes them more susceptible is crucial to explore. In neuronal part, ganglia, motor or sensory neuron, axons, desmosomes are responsible for infection needed to explore.

We will utilize Optical methods, FTIR and RAMAN spectroscopy to investigate cell/tissue morphology and for non-invasive diagnosis of GC and MS. CRISPR knockout/ shRNA knockdown will be utilized for the validation of biomarkers in MS and GC. Our study shall include cell lines (gastric epithelial, neuronal cells, astrocytes, and microglia), primary gastric/primary neurons and *in vivo* mice models to facilitate the disease pathogenesis in stage specific manner. Overall, this study will demonstrate the important and potential host targets of these infectious agents. Analysis of cell compositions and ratios of lipid, protein, DNA, and RNA indicative of pathogen infection or burden and normal to disease stage conversion will be established in this study. Further, changes in these tissue images along with cellular composition can be used as a prognostic marker.

040

THE MACROPHAGES: POTENTIAL TARGET FOR THE TRANSLATIONAL MEDICINE

Keywords Macrophages Immunobiology; Host Pathogen Interaction; Tumor Immunology ; Cell based Cancer Im-mune therapies; Radiation Biology / Oncology; Signal Transduction

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I have been exploring macrophages as my research model for more than a decade in various discease models like hemopoietic and respiratory Syndrome, ALRTI and pancreatic cancers. Macrophages are unique, ubiquitous and integrated part of both innate and adaptive immunity as well as components of tissue homeostatic apparatus. Both peripheral and tissue macrophages together constitute the Reticulo-endothelium system which play major role in sensing pathogens and tumor antigens for their effective eradication. Out of several immune cells, the macrophages display a range of plasticity in their phenotype in different pathological conditions which qualify them as one of potential target cells of body for the management of various human diseases clinically. Due to their plastic nature, these cells are literally involved in most of immunological and physiological process. In view of above, my vision lies mainly in the management of M1/ M2 imbalance to minimize the risk of having cancer by chronic and persistent lung infection with intracellular pathogens like Chlamydia or Mycobacteria. This may be achieved by targeting major signaling pathways which drive M2 phenotype and are involved in cancer development e.g. Sphingolipids, Th2/Th17 responses. In the frame of above, our second major goal is to scan molecular events which are important for the initialization of polarization of M1 phenotype of macrophages to M2 during cancer development and to explore how selective activation of M1 macrophages could improve existing anti-tumor immune therapies in both mouse and human model of tumor with special emphasis on pancreatic, colorectal, lung cancers and various gastric inflammatory discease like IBD which are responsible for global mortality.

041

EXPERIMENTAL EVOLUTION OF INSECT IMMUNE MEMORY VS. PATHOGEN RESISTANCE

Keywords Ecology and Evolution, Immune response, Immunopathology, Immune memory, Social immunity

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Under strong pathogen pressure, insects often evolve resistance to infection. Many insects are also protected via immune memory ('immune priming'), whereby sub-lethal exposure to a pathogen enhances survival after secondary infection [1]. Theory predicts that immune memory should evolve when the pathogen is highly virulent, or when pathogen exposure is relatively rare [2]. However, there are no empirical tests of these hypotheses, and the adaptive benefits of immune memory relative to direct resistance against a pathogen are poorly understood. To determine the selective pressures and ecological conditions that shape immune evolution, we imposed strong pathogen selection on flour beetle *(Tri-bolium castaneum*) populations, infecting them with *Bacillus thuringiensis* (Bt) for 11 generations. Populations injected first with heat-killed and then live Bt each generation evolved high basal resistance against multiple Bt strains. In contrast, populations injected only with a high dose of live Bt evolved a less effective but strain-specific priming response. Control populations injected with heat-killed Bt did not evolve priming; and in the ancestor, priming was effective only against a low Bt dose. Intriguingly, one replicate population first evolved priming and subsequently evolved basal resistance, suggesting the potential for dynamic evolution of different immune strategies. Our work is the first report showing that pathogens can select for rapid modulation of insect priming ability, allowing hosts to evolve divergent immune strategies (generalized resistance vs. specific immune memory) with potentially distinct mechanisms.

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042

A NEWER THERAPEUTIC APPROACH TO TARGET CANCER CELL PROGRESSION BY INHIBITING HUMAN PROTEIN KINASES USING NATURAL PRODUCTS

Keywords Structural Biology, Structure based Drug Design and Discovery, Kinase Inhibitors, Life style diseases, Protein Folding and Dynamics

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Protein phosphorylation regulates most aspects of cell life, whereas abnormal phosphorylation is a cause or consequence of disease. Kinases of AMPK-like family have recently become an important drug target against neurodegenerative, cancer and other related metabolic disorders. In this study, we have evaluated different natural dietary polyphenolics including rutin, quercetin, ferulic acid, hesperidin, gallic acid and vanillin potential inhibitors of CAMK4, MARK4 and FASTK. To study the binding, initial screening of all these compounds was done using molecular docking in the active site cavity of kinases. *In silico* observations were further complemented by fluorescence binding studies and ITC measurements. Binding results shows that out of all studied compounds only rutin and vanillin showed significant binding with MARK4. While b-carotene is showing strong binding to the CAMK4. To signify the extent of en-zyme inhibition ATPase assay was performed. Cell proliferation, ROS quantification and Annexin-V staining elucidated the apoptotic potential of these compounds. Results suggest that selected compounds may be potential inhibitor for MARK4 and other kinases which can be further studied as a pharmacophore and implicated for therapeutic purposes. To see the role of these compounds on cell proliferation and apoptosis, cancerous cells (HeLa, HuH7and MCF-7) and normal (HEK-293-T) cell lines were used. An admirable anticancer activity was observed. We further performed propidium iodide and DAPI (4',6-diamidino-2-phenylindole) assays to understand the mechanism of anticancer activity at molecular level. Our findings provide a newer insight into the use of these natural products in cancer prevention and protection via inhibition of APM kinases by regulating the signaling pathways.

043

IS TREELINE EXPANSION CONSTRAINED BY SOIL BIOTA?

Keywords Biodiversity, Plant invasion, Climate change, Mycorrhizae, Insect-plant interaction

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Treelines are temperature sensitive transition zones that are expected to respond to climate warming by advancing beyond their current position. However, observed responses at treelines are quite inconsistent and sometimes contradictory, straddling the entire gradient from static treelines with rather trivial responses to dynamic treelines substantially migrating upslope (Harsch et al., 2009). To explain the gradient from complete treeline inertia to rapid upslope migration, the local-scale complexity of abiotic and biotic site factors have to be considered that result in nonlinear responses to climate. Soil biota, including symbionts such as mycorrhizal fungi and nitrogen-fixing bacteria, as well as fungal and bacterial pathogens, are considered important biotic factors affecting terrestrial plant diversity and growth patterns (Teste et al., 2017). To understand the role of soil biota in shifting treelines across mountainous regions, we collected soil from treeline ecotones and the adjoining areas. This soil was used as an inoculum with the autoclaved background soil, to see the effect of soil biota on the seedling performance of the treeline species, under greenhouse conditions. The experiment is underway and the results are ex-pected to help in better understanding of the differential regional treeline dynamics in the mountainous regions of the world.

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044

PLEOTROPIC HES-1 MAINTAINS NSCs AND ITS TRANSITION TO NEURAL PROGENITORS DURING NEOCORTICAL DEVELOPMENT: DOES CANCER STEM CELLS FOLLOW THE SAME?

Keywords Notch signaling, Neural stem cells, Retinal Ganglion cell differentiation, Axonal guidance, Neural differentiation

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Notch signaling is involved in the maintenance and differentiation of neural progenitors in the mammalian central nervous system during development. Hes-1 and Hes-5 are the downstream targets of canonical Notch signaling that act as repressors of pro-neural genes. Our lab has previously shown in ES cell derived neural progenitors that Hes-1 expression can be regulated by alternate signaling pathways such as FGF-ATF2 pathway that is independent of canonical Notch/CBF1 interaction. We have also demonstrated that in developing neocortex Notch independent Hes-1 (NIHes-1) expression maintains neural stem cells (NSCs) that later attain Notch dependency (NDHes-1) while progressing to a progenitor and then to a differentiated state[1]. Recapitulating our finding as the fundamental mechanism behind maintenance and transition of cancer stem cells (CSCs) to cancer cells in neuroblastoma, we have found that consistent expression of NIHes-1 maintains CSCs and a shift in mode of Hes-1 expression (NDHes-1) transforms the CSCs to cancer cells. We were able to efficiently FACS sort and separate the neuroblastoma cells into two distinct populations such as NIHes-1 and NDHes-1 expressing cells based on the mode of Hes-1 expression using a novel reporter system. Further characterization of the two populations showed that the NIHes-1 expressing cells are CSCs that transit into cancer cells by acquiring notch dependency (NDHes-1). Overall our finding show that the CSCs with NIHes-1 expression transits into cells with NDHes-1 expressing cancer cells recapitulating the developmental process and thereby progressing into neuroblastoma.

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045

THE ROLE OF NITRIC OXIDE AND ETHYLENE IN THE DEVELOPMENT OF AERENCHYMA IN WHEAT ROOTS UNDER LOW OXYGEN STRESS

Keywords Nitric Oxide, Hypoxia, Aerenchyma, Nitrite, Nitrate Reducatse

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Oxygen is essential for making energy as it acts as terminal electron acceptor in mitochondrial electron transport chain. But during flooding/water logging plants experience energy crisis due to lack of oxygen. To cope up with this plants have developed several strategies. One of the strategies is the formation of lysigenous aerenchyma which helps in delivery of oxygen to roots. Ethylene, plays a major role in the formation of aerenchyma, however other signals those play role in aerenchyma is not known. Under hypoxic conditions plant generate significant amount of nitric oxide (NO). In this study, we investigated whether hypoxia induced NO is able to stimulate ethylene mediated aerenchyma formation in wheat roots under hypoxic stress. We found that under hypoxic condition scavenging of NO leads to reduced levels of aerenchyma. We also found that NO can induce ethylene biosynthetic genes encoding ACC synthase and ACC oxidase under hypoxia. These findings provided a link between NO and ethylene in aerenchyma formation under hypoxia. Increased levels of NO modulated ROS lipid peroxidation and protein tyrosine nitration and activation of RBOH/NOX (NADPH oxidase) gene under hypoxia leading to lysegenous cell death . Hypoxic NO induced expression of signal transduction genes such as phospho-lipase C, G protein alpha subunit, calcium-dependent protein kinase family genes CDPK, CDPK2, CDPK 4, Ca-CamK, inositol 1,4,5-trisphosphate 5-phosphatase 1 and protein kinase. These results clearly demonstrate that hypoxically-induced NO is essential for the development of ethylene-induced aerenchyma.

046

ARABIDOPSIS–ALTERNARIA BRASSICAE PATHOSYSTEM UNRAVELS THE COMPLEX GENETIC ARCHITECTURE OF THE RE-SISTANCE RESPONSE AGAINST THE PATHOGEN.

Keywords *Arabidopsis thaliana,* Brassicas, *Alternaria brassicae,* disease resistance Necrotroph, fungal pathogen

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Alternaria brassicae, a necrotrophic fungal pathogen, causes Alternaria blight, one of the most important diseases of oleiferous Brassica crops. No source of complete resistance against A. brassicae is available in the cultivated Brassica species. The main focus of our laboratory is to decipher the genetic architec-ture of defense against *A. brassicae* using Arabidopsis as a model host. Significant phenotypic variation that was largely genetically determined was observed among Arabidopsis accessions in response to pathogen challenge. Linkage analysis of three biparental mapping populations developed from three resistant accessions viz. CIBC-5, Ei-2, and Cvi-0 and two susceptible accessions - Gre-0 and Zdr-1 (commonly crossed to CIBC-5 and Ei-2) revealed very interesting insights. A total of six QTLs governing resistance to *A. brassicae* were identified, five of which were population-specific while one QTL was common to all the three mapping populations. Two of the QTLs had moderate-to- large effects, one of which explained nearly 50% of the variation. Our findings demonstrate that while the defense response against *A. brassicae* involves multiple loci, which are additive in nature, there are large effect QTLs where further study can help in finding genes that could play a significant role in conferring resistance even in the heterologous hosts.

047

LIGNOCELLULOSIC BIOMASS DIRECTED DEVELOPMENT OF NANOARCHITECTURES FOR APPLICATIONS IN NANOBIOTECHNOLOGY

Keywords Biomass Derived Nanoparticles, Biomass Valorization, Nanophotosensitizers

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Lignocellulosic biomass is the main source of aromatic renewable material in the world. Reduction of agro-waste through the development of nanomaterials can be an advantage to the environment. Lignin, which is present in the agricultural biomass, is an important source of polyphenols and can serve as a biodegradable source of nanomaterials. Due to their biocompatibility as well as antioxidant properties, lignin nanoparticles can be employed in various nanobiotechnology applications. Lignin nanoparticles (LNPs) were developed by green technology. Also, metallo-lignin nanoparticles (MLNPs) were developed for use in anti-microbial applications.
The LNPs to their surface functionalization characteristics has the potential to incorporate therapeutic, diagnostic and targeting moieties through conjugation as well as by adsorption. Thus, theranostic LNPs can be developed as multifunctional biomedical nanoscaffolds. Overall, biomass derived biodegradable and biocompatible LNPs will employ dual benefit by lowering environmental pollution and simultaneously by being applicable in nanobiotechnology.

048

REGULATORS OF MITOCHONDRIAL RIBOSOME ASSEMBLY/ACTIVITY IN RESPONSE TO CELLULAR ENERGY REQUIREMENTS

Keywords Mitochondria, Translation, Ribosome Biogenesis,Quality control, GTPases

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Mitochondrial genome encodes components of OXPHOS complex. Their translation and subsequent assembly are tightly coupled to cellular energy requirements. Biogenesis and activity of mitochondrial ribosome (mitoribosome) is critical as numerous human diseases are caused due to defects in mitochondrial translation. Mitoribosomes have a reduced rRNA size, compensated by an increase in the mitochondrial ribosomal protein numbers. Mitoribosomal proteins, assembly factors and regulators are either species specific or universally conserved. MTG3 belongs to circularly permuted class of GTPase that is conserved from yeast to humans containing a central GTPases pocket flanked by N and C terminal domain and is essential for cellular respiration. We have shown that MTG3 associates with both small and large subunit of mitochondrial ribosome and is involved at a late step in their biogenesis. Our studies also indicate that MTG3 associates with the ribosome via the C-terminus independent of the bound nucleotide, although, MTG3 requires guanine nucleotide binding as well as hydrolysis to carry out its *in vivo* function at the late step of mitoribosome biogenesis. MRX8, a YihA class of GTPase, predicted to func-tion in translation, has orthologues in bacteria, yeast and vertebrates including humans but none in in-vertebrates. We have shown Δmrx8 cells have compromised cellular respiration. Consistent with a role in translation regulation, we have shown Mrx8p is localized to the mitochondrial matrix and associates with the 74S monosome. Mutations in MRX8 that abolished nucleotide binding were not able to support cellular respiration whereas, contrary to expectation, mutants wherein the protein is predicted to be locked in a GDP-bound form weren't compromised. Thus *in vivo* function of Mrx8p might involve communication of NTP/NDP cellular pools to mitochondrial ribosomes. Consistent with conservation in function, human orthologue of Mrx8p restored cellular respiration in Δmrx8 cells.

049

MATCHED FREQUENCIES OF ACOUSTIC CALL PRODUCTION AND RECEPTION SYSTEMS IN A PALEOTROPICAL BUSHCRICKET

Keywords Behaviour, Neuroscience, Evolution, Ecology, Cognition

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Crickets and bushcrickets (Order: Orthoptera, Suborder: Ensifera) rely heavily on acoustic communication to find their mates. We are interested in the question of the match between sound production and sound reception systems, in order to enable successful communication. Pseudophylline bushcrickets predominantly call at high, often ultrasonic broadband frequencies. We investigated the behavioural and mechanical frequency tuning of one bushcricket species, *Onomarchus uninotatus*, that produces a narrow bandwidth call at an unusually low carrier frequency of 3.2 kHz. We found that unlike the high-pass filter characteristic of other bushcricket tympana, the anterior tympanal membrane of this species acts as a low-pass filter, precisely attenuating sounds at frequencies above 3.5 kHz, i.e: above that of the male call and below most acoustically competing Orthopterans in the same rainforest. Responses to higher frequencies are partitioned to the posterior tympanal membrane - a novel feature. The use of such low-frequency, long-wavelength sounds poses directional challenges for small animals, but we find that both membranes show some directional sensitivity. Behaviourally, we find that the female shows band pass selectivity around the frequency of the male call, measured using the rate at which she tremulates to the male call. If we assess her directional ability based on phonotaxis, which is a lower likelihood event than tremulation, we find an error rate. We investigate this error rate as well as the choice between tremulation and phonotaxis with respect to parameters of the male call. At the neurophysiological level, the most frequently recorded neuron in the ascending nerve is a T-cell that shows strong responses in the high ultrasound range, with no discernable response in the range of the conspecific call. We contextualize these results with respect to predator pressure.

050

UNDERSTANDING ANTI-POTENTIATION AT THE *C. ELEGANS* NEUROMUSCULAR JUNCTION

Keywords *C. elegans*, Neuromuscular Junction (NMJ), Claudin, Wnt, Acetycholine Receptors (AChR/ACR-16)

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Normal synaptic transmission is required for normal functioning of animals. Post-synaptic receptor maintenance is important for normal synaptic transmission to take place. The *C. elegans* Neuromuscular junction (NMJ) contains cholinergic and GABAergic motor neurons that synapse onto body-wall muscles. Cholinergic neurotransmission occurs through Acetylcholine receptors (AChR/ACR-16). We are interested in understanding the molecules and mechanisms required for maintaining normal levels of these post-synaptic receptors at the NMJ. Work till date has implicated The Wnt signaling pathway in maintain-ing normal AChR/ACR-16 levels at the *C. elegans* NMJ (Babu et al., 2011; Jensen et al., 2012; Pandey et al., 2017).

I will discuss our recent findings on a Claudin-like gene in *C. elegans* and it's role in maintaining normal levels of AChR/ACR-16 at the NMJ. Our work goes on to elaborate on the mechanism of how this Claudin functions at the NMJ. Briefly, the Claudin functions by regulating Wnt secretion from motor neurons, which in turn affects the delivery of AChR/ACR-16 at the NMJ. We are in the process of dissecting out the interacting partner/s of this molecule and my presentation will elaborate on the binding partner for the Claudin and how they function together to maintain Wnt secretion.

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051

CONFORMATIONAL ANALYSIS OF VENOMOUS PEPTIDE TOXIN

Keywords Peptide toxins, Conformation, Peptide chemistry, Natural peptides, Cysteine rich peptides

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Peptide toxins are natural venom peptides derived from snake, scorpion, spider, cone snails, other venomous species. Characteristic features of peptide toxins are the presence of intramolecular disulfides which generally varies from 1-5 in the sequence. These peptide toxins have innumerable applications as tools in neuroscience and lead compounds of therapeutics. They have also attracted considerable interest as scaffolds for the design of functional miniature proteins. In the presentation, we will be addressing the two questions on structural features of peptide toxins: (1) Structural space of venomous peptide toxins, and (2) conformations of cysteine disulfides in peptide toxins. The result will be of interest for the growing field of structural venomics.

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052

LAMIN B2 MODULATES NUCLEOLAR MORPHOLOGY, DYNAMICS AND FUNCTION

Keywords Nucleus, Lamins, Chromosomes, Nucleolus, Nucleoporins Cancer

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The nucleolus is required for ribosomal RNA (rRNA) and protein synthesis. Here we show that nuclear Lamin B2 surprisingly localizes also at the border of the nucleolus in addition to its conserved location at the nuclear periphery. Furthermore, Lamin B2 associates with bonafide nucleolar proteins such as Nucleolin and Nucleophosmin. Interestingly, Lamin B2 knockdown severely disrupts and aggregates the nucleolus, which was rescued to intact and discrete nucleoli upon Lamin B2 overexpression. We also identified two mutually exclusive Lamin B2 mutants - ΔHead and ΔSLS, which rescue defects in nuclear and nucleolar morphology respectively, induced in Lamin B2 depleted cells. This highlights independent roles of Lamin B2 at the nucleolus and nuclear envelope. Lamin B2 knockdown enhanced aggregation of Nucleolin in the nucleoplasm, implicating Lamin B2 in stabilizing Nucleolin within the nucleolus. Remarkably, Lamin B2 knockdown upregulates nucleolar specific transcripts - 45S rRNA and IGS (Intergenic transcripts). Interestingly, we detected the colocalization of IGS transcripts with Nucleolin aggregates that were sustained in the nucleoplasm upon Lamin B2 depletion, monitored using immuno-RNA-fluorescence *in situ* hybridization (Immuno-RNA FISH) and live cell imaging. Taken together, these studies uncover a novel role for Lamin B2 in modulating the morphology, dynamics and function of the nu-cleolus.

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053

ESSENTIAL FUNCTIONS OF UBIQUITIN LIGASES IN MAINTAINING GENOME STABILITY

Keywords DNA Damage Response, Genomic Instability, Replication and Recombination, Ubiquitylation, SUMOylation

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In response to DNA damage, cells activate series of surveillance mechanisms to coordinate replication with repair and cell cycle transitions, known as DNA Damage Response (DDR). Recently, cross talk between various post-translational modifications such as phosphorylation, SUMOylation and Ubiquitylation were suggested in fine-tuning the DNA Damage Response[1]. These modifications occur on multiple factors at the damage site and intercept to regulate the choice and outcome of the DNA repair. The SUMO-targeted ubiquitin ligase (STUbL), Slx5-Slx8 (RNF4) complex plays important role in genome stability by controlling the turnover of SUMOylated factors via proteasome-dependent pathway in response to DNA damage. We have identified the anti-recombinase, Srs2 helicase, as one of the targets of Slx5/Slx8[2]. Mms22 (Mms22L) is part of multi-subunit Cullin family of ubiquitin ligase (CRLs) implicated in regulating Rad51-mediated recombination repair. Mms22L is identified as an oncogene, which is overexpressed in most of the clinical lung and esophageal cancers. The proposed functions of cullins are highly diverse and appear to be involved in myriad cellular processes. We found that Mms22 cooperates with replisome components and the structure-specific endonuclease Mus81-Mms4 at the damaged fork (Manuscript under preparation). In conclusion, we provide mechanistic insights into how two ubiquitin E3 ligases exert their essential functions during replication.

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POST-TRANSCRIPTIONAL GENE SILENCING MEDIATED BY RNA-BINDING PROTEINS

Keywords Strucutral Biology, Biomolecular NMR, RNA Biology, Noncoding RNA, RNA binding proteins

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How do RNA-binding proteins effect post-transcriptional gene regulation? Our group explores the role of regulatory proteins which bind to a variety of RNA molecules and effect post-transcriptional gene regulation.

In prokaryotes, the gene regulation is manifested by a set of long non-coding RNA which are globally regulated by Hfq and specifically controlled by Crc, RapZ etc. Our lab has derived the solution structure of Crc (~ 32 kDa) using solution NMR techniques. We find that Crc is divergently evolved from AP endo-nucleases and regulates lncRNA using a non-canonical RNA binding surface.

In higher eukaryotes, the RNA interference (RNAi) uses two key enzymes, Dicer and Argonaute, which are assisted by a variety of multiple dsRNA binding domains (dsRBDs) containing proteins (dsRBPs) to regulate RNA mediated gene silencing. A seemingly conserved pathway of RNAi exhibits significant heterogeneity across organisms. To understand the origin and necessity of the evolutionary divergence in RNAi, we have defined the functional roles of RDE-4 *C. elegans* as well as DRB4 and DRB2 *A. thaliana* using solution structures and complementary assays. Results elaborate on the divergence in seemingly conserved and highly homologous proteins implying a fine balance in which subtle changes can “make or break” the small RNA mediated gene silencing in plants. The results further exemplify that the process of RNAi initiation is unique for each organism and is heavily dependent on step-wise assembly of the Dicer, its partner proteins, and the trigger small RNA.

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055

NANOPARTICLES-BASED ANTITUBULIN DRUGS FOR CANCER CHEMOTHERAPY

Keywords Cancer metastasis, Microtubule biology, Drug resistance mechanisms, Novel design strategies of tubulin-targeted -anticancer agents, Nanomedicine

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Humans' fascination for gold started thousands of years ago for its ornamental value. Gold has also been known for its therapeutic uses. Gold powder (swarna bhasma), for example, has been used in several Ayurvedic formulations. With the advent of nanotechnology, this precious metal has been investigated extensively for its therapeutic value. We report a novel, tubulin-targeted antiproliferative mechanism of action of tryptone-stabilized gold nanoparticles (TsAuNPs). TsAuNPs, synthesized using HAuCl4.3H2O and tryptone and characterized by a variety of spectroscopic methods and transmission electron microscopy, were found to be inhibitory to the viability of human pancreatic, cervical, and breast cancer cell lines. TsAuNPs-mediated inhibition of cell viability involved an unusual mode of cell cycle arrest (arrest at both G0-G1 phase and S-phase) followed by apoptosis. In vitro, TsAuNPs bound purified tubulin and suppressed tubulin assembly. In cells, tubulin-TsAuNPs interactions were manifested as a disrupted microtubule network, defective reassembly of cold-disassembled microtubules, and induction of tubulin acetylation. Our data indicate that TsAuNPs inhibit cell viability by inducing differential cell cycle arrest, possibly through disrupted dynamicity of cellular microtubules.

056

UNDERSTANDING PLANT INVASIONS THROUGH MOLECULAR ECOLOGICAL APPROACHES AT A BIOGEOGRAPHICAL SCALE

Keywords Plant Invasions, Molecular Ecology, Mycorrhizas, Kashmir Himalaya

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Understanding plant invasions across native and non-native regions is facilitated a great deal through common distributed experiments (CDE). We used field studies to understand variations in the impact of of some invasive plant species across ranges and through molecular ecological approaches worked out their population genetic variations. The data suggests that the target species have stronger impacts in terms of affecting co-occuring species diversity in non-native ranges far more than in their native ranges. These species vary significantly in functional traits across ranges besides exhibiting significant variation in the genetic structure of their populations. Some useful insights into the nativity of such species can be drawn from these data. We discuss the management implications of these studies.

057

DNA-DEPENDENT PROTEIN KINASE PLAYS A CENTRAL ROLE IN TRANSFORMATION OF BREAST EPITHELIAL CELLS FOLLOWING ALKYLATION DAMAGE

Keywords DNA Damage, Cell Cycle Checkpoints, 3-Dimensional Breast Spheroid Model, Emt, Cellular Transformation

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DNA alkylating agents form the first line of cancer chemotherapy. They not only kill cells but also behave as potential carcinogens. N-methyl N-nitrosourea (MNU), a DNA methylating agent, is well known to induce mammary tumours in rodents. However, the mechanism of tumorigenesis is not well understood. Our study reports a novel role played by DNA dependent protein kinase (DNA-PK) in methylation damage-induced transformation using three-dimensional breast acinar cultures. We report that exposure of breast epithelial cells to MNU inhibited polarisation at the basolateral domain, increased dispersal of the Golgi at the apical domain and induced an epithelial-to-mesenchymal transition (EMT)-like phenotype as well as invasion in the acinar cultures. The altered Golgi phenotype correlated with impaired intracellular trafficking. Inhibition of DNA-PK resulted in almost complete reversal of Golgi dispersal and partial rescue of the polarity defect as well as EMT-like phenotype. Our results confirm that methylation damage-induced activation of DNA-PK is a major mechanism in mediating cellular transformation.

058

DYNEINS AND DEVELOPMENT: ROLE OF DYNEIN LIGHT INTERMEDIATE CHAINS IN EMBRYONIC DIVISIONS AND VERTEBRATE EMBRYOGENESIS.

Keywords Developmental Biology, Cell Biology, Evolutionary Developmental Biology, Developmental Genetics, Embryology

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The regulation of somatic cell division (mitosis) forms the basis for key morphogenetic processes during early embryogenesis. We are studying the mitotic functions of the multifunctional molecular motor cytoplasmic dynein in embryonic development. Dyneins have been shown to perform a variety of roles during mitosis. The Light Intermediate Chain subunits of dynein, LIC1 and LIC2define two mutually exclusive dynein complexes that asymmetrically distribute several mitotic functions and are hypothesized to be cargo-binding adaptors that enable the diversity of dynein functions. The aim of this study is to determine the functions and mechanistic roles of the dynein LIC subunits during vertebrate embryonic development. We hypothesize that zebrafish LICs are required for these functions and that loss of or defects in these subunits impair proper spindle formation and orientation, leading to developmental defects. We used a gene knockdown approach to understand the functional role of the LICs in the developing zebrafish embryo. The LIC1/2 depleted embryos show distinct mitotic defects such as increased spindle length, spindle pole focusing defects and chromosome congression defects. Our results also show discernibly distinct spindle pole formation defects in LIC1 and LIC2 morphants, which are conceivably due to discrete mechanisms of action. LIC2 morphants also show gross developmental defects, suggesting that these subunits mediate key mitotic functions to regulate normal embryonic development. Further studies are focused on the molecular mechanisms regulating the function of these important members of the dynein motor.

059

NANOENGINEERING FOR DISCOVERY AND DISEASE MECHANISM RELATED TO CYTOSKELETON

Keywords Structural Biology, Cytoskeleton, Molecular motors, Biophysics, Cell biology

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Eukaryotic biological motions across scales and orders of magnitude involve cytoskeleton elements. Because of their importance in cell division, motility and muscle contraction, mutations in cytoskeleton are frequently associated with human pathology. Our lab is focused on understanding how cytoskeleton assemblies coordinate during physiological and their deregulation during disease conditions. Our lab utilizes the power of nanoengineering, biophysics and cell biology to uncover new findings in cytoskeleton biology, and how we can bridge the knowledge gap between clinical findings and molecular

060

GENOME EDITING OF BCL11A ERYTHROID SPECIFIC ENHANCER IN PATIENT DERIVED HEMATOPOIETIC STEM FOR THE TREATMENT OF β-HEMOGLOBINOPATHIES

Keywords Genome Editing for Gene and Cell Therapy, Cancer Stem Cells, Tumor modeling using the CRISPR/CAS9 system, Cancer Immunotherapy, Cancer Genomics

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The switch from fetal to adult hemoglobin is a very important developmental event that occurs in erythroid cells during the months following birth. Reversing the fetal to adult hemoglobin switch is substantial therapeutic interest for sickle cell disease, since persistence high levels of HbF ameliorates clinical symptoms of SCD[1]. Genome wide association studies identified transcriptional repressor BCL11A as a major regulator of the hemoglobin expression. Inactivation of BCL11A in mice carrying a human β-globin cluster transgene leads to profound delay in globin switching and impaired HbF silencing. Knock-out of Bcl11a alone is sufficient to rescue phenotype of mouse model of sickle cell disease[2]. BCL11A is dispensable in non erythroid functions such as for normal lymphoid and neural development. Genomic analysis identified the enhancer that is specific in erythroid but not B-lymphoid cells for BCL11A expression. Functional mapping of the Bcl11A enhancer identified the minimal critical sequence that is necessary for its function[3]. The effects of deletions of these specific regions of enhancer have the same effect as altering the whole enhancer. In this study, we plan to utilize targeted genome engineering platform based on CRISPR/CAS9 system to edit BCL11A erythroid specific enhancer in patient HSC for the treatment of β-hemoglobinopathies.

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061

REGULATION OF CORAZONIN AND SNPF BY INTRACELLULAR $Ca2^+$ SIGNALLING: IMPLICATIONS FOR DEVELOPMENT UNDER NUTRITIONAL

Keywords Nutrition, Behaviour, Hormone, Development, *Drosophila*

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Neuropeptides are a class of hormones secreted by neurons which can modulate neural circuits to critically regulate organismal behaviour. Elevation of cytosolic $Ca2^+$ is primary mechanism by which external signals are converted to neuronal activity. In addition to depolarisation, cytosolic $Ca2^+$ can be elevated by the release of $Ca2^+$ from ER stores and the subsequent activation of store-operated $Ca2^+$ entry (SOCE). We are particularly interested in how inositol 1,4,5 trisphosphate receptor (IP3R), an ER $Ca2^+$ channel and STromal Interacting Molecule (STIM), a regulator of SOCE, contributes to neuropeptide action in neurons. In particular, we sought to identify neuropeptides that required IP3R and STIM in order to coordinate larval to pupal metamorphosis under nutritional stress. Typically, *Drosophila* larvae starved post critical-weight are able to pupariate and the majority eclose as adult, albeit of smaller size. We observed that an IP3R mutant, known to exhibit reduced SOCE, was unable to pupariate under these conditions. Further, a role for IP3R and STIM in neuropeptide-producing neurons was observed to contribute to pupariation under nutritional stress, suggesting that ER-store $Ca2^+$ and SOCE may regulate neuropeptide function. We therefore undertook a mass spectrometric and genetic approach to uncover what these neuropeptides might be. Two neuropeptides, sNPF and Corazonin, have been identi-fied. Neuronal populations that produce these neuropeptides have been located. Preliminary data suggest that intracellular $Ca2^+$ signalling does not regulate them at the level of transcription, but at the level of translation and release.

062

MOLECULAR SIGNATURES ASSOCIATED WITH SEED DEVELOPMENT AND SEED SIZE DETERMINATION IN CROP PLANTS

Keywords Plant Genomics, Epigenomics, Genome Informatics, Abiotic Stress, Seed Development

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Seeds besides being the progenitor of next generation, provide human and animal nutrition worldwide. Seed development is a complex trait controlled by multiple biological processes/ pathways. Seed size is an important trait of crop plants determined by several factors during seed development. Several studies in model/ crop plants have described pathways and networks along with their interactions, and epigenetic mechanisms/imprinting that regulate seed development and seed size. We used RNA-seq technology to analyze the transcriptomes of seeds of two chickpea cultivars (differing significantly in their seed size) at different stages of development. We revealed transcriptome dynamics and transcriptional regulatory network associated with seed development and identified key differences that determine seed size/weight in chickpea. The transcripts and/or modules of co-expressed genes expressed predominantly/specifically at different stages of seed development and/or cultivars, were identified. The overlap of known quantitative trait loci (QTLs) with differential gene expression and discovery of single nucleotide polymorphisms (SNPs) identified candidate genes that might determine seed size/weight. In addition, we explored the epigenetic regulation of seed development and seed size via analyses of DNA methylation and studying its effect on gene expression. This study provides new insights into the molecular mechanisms underlying seed development and the factors determining seed size/ weight in chickpea.

063

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IN-SILICO ANALYSIS PREDICTED RLM1P AS NOVEL TRANSCRIPTIONAL REGULATOR OF F-BOX ENCODING GENE SAF1 OF *S. CEREVISIAE* DURING STRESS

Keywords Genome stability regulation, Genome editing technologies, Biotechnological applications & Drug discovery, DNA Replication & Protein-Protein interactions mechanisms for novel drug targets, Susceptibility to Infectious diseases, agents and mechanism

F-box motif containing proteins have been associated with many cellular functions such as signal transduction and regulation of cell cycle. The Fbox encoding, SCF associated factor gene, SAF1 of *S. cerevisiae* has been shown to involve in the degradation of, adenine deaminase factor Aah1p in SCF dependent ubiquitination manner during entry of cells into quiescence stage. The regulation of the crucial nucleotide metabolism enzyme, Aah1p by Saf1p suggests its role in nucleotide metabolism and cell cycle progression. The known substrates of the Saf1p protein has been reported as Aah1p and Prb1, where former act as adenine deaminase and later as protease. Here we wish to study the transcriptional regulation of SAF1 during stress to understand the mechanism of cell cycle transition and genome maintenance. There are four transcriptional regulators such as BUR6, MED6, SPT10 and SUA7 genes listed into the SGD for SAF1 gene. We studied the expression profiling database (GEO) of *S.cerevisiae* cells for expression status of the SAF1, AAH1 and their correlation with the global transcription factors using yeastract (http://www.yeastract.com/) web tool. Our analysis of GEO dataset and yeastract web tool predicted Rlm1p as a novel transcriptional regulator of both the genes AAH1 and SAF1 during stress.

064

SPHINGOLIPIDS: ITS IMPACT ON DRUG SUSCEPTIBILITY AND VIRULENCE OF *CANDIDA GLABRATA*

Keywords Human fungal pathogenesis, Biofuels, Yeast metabolic engineering, Recombinant protein production, Metagenomics

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Although lipid metabolic pathways are fairly well established in yeast, our knowledge of lipid compositional profile, particularly in pathogenic species, is rather limited. Fungal lipids are important on two accounts; firstly, they possess sphingolipids which are unique to Candida species and are absent in mammalian host hence are novel drug targets. Secondly, the functionality of MDR export proteins is depend-ent upon optimal lipid environment implying their role in clinical drug resistance. The comprehensive high-throughput lipidomics combined with genetic approaches is being applied to human pathogenic haploid *Candida glabrata* to assess strategies aimed at disrupting Candida lipids and particularly functional interactions between lipids, virulence, and MDR determinants.

Phylogenetically, *C. glabrata* is closer to *S. cerevisiae.* Despite it, some of the genes of sphingolipid pathway are essential in case of S. cerevisiae but are non-essential in *C. glabrata.* In our study, we have made knockout mutants of some sphingolipid pathway genes cgIPC1 (catalyzes the transfer of phosphoinositol from phosphatidylinositol to ceramide to form IPC), cgDPL1(Dihydrosphingosine phosphate lyase, degrades phosphorylated long chain bases,), cgISC1(Inositol phosphosphingolipid phospholipase C, catalyze the degradation of complex phospho-sphingolipids) and cgIPT1 by using fusion PCR based method, Gene deletion cassette was constructed by fusing dominant marker NAT1 with the flanking UTR regions of the gene. Cassettes are then transformed and allowed for homologous recombination, which replaces the gene with NAT1. The knockout was selected on a nourseothricin plate and confirmed by gene specific PCR. Drug susceptibility the case of IPT1 K/O, (the terminal step of the MIP2C synthesis) increased towards azoles and cell wall damaging agents. The other K/O such as cgIPC1 and cgISC1 show increased susceptibility to H2O2, acetic acid, caffeine, and SDS.

065

LAYING HEN, A SPONTANEOUS MODEL OF HUMAN OVARIAN CANCER IN PREVENTION AND TREATMENT THROUGH DIETARY INTERVENTION OF NATURAL PRODUCTS

Keywords Preventive Oncology, Ovarian Cancer Biology, Nutrigenomics, Cancer Biomarkers

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Since it is impossible to conduct research in human, researchers take advantage of animal model to study the role of genes, molecular pathways and networks, and environmental factors that relate to carcinogenesis. These studies are also designed to qualify the animal model as an eventual source of pre-clinical evidence that will justify the introduction of promising cancer prevention agents into clinical trials. One such model, the white leghorn hen (a strain of *Gallus domesticus* bred for high egg production), has received several decades of attention for its unique attributes and scientific promise for exploring the etiology and prevention of epithelial ovarian cancer. Early reports about ovarian tumor incidence in the white leghorn chicken showed that laying hens are subject to the spontaneous development of ovarian and oviductal adenocarcinomas. By the time a hen has completed two years of egg laying, she has ovulated about as many times as a woman approaching menopause, when ovarian cancer manifests. Ovulation is an inflammatory event and ovarian cancer is driven by inflammation. Each time woman ovulates, the surface of the ovary is ruptured, which is followed by a healing response. This observation is consistent with the hypothesis that incessant ovulation contributes to ovarian cancer risk in the laying hen model, just as it is thought to increase the risk of ovarian cancer in humans. Because ovarian cancer in the laying hen is a spontaneous event, studies utilizing this model are able to examine the early events to gain insight into the etiology of the disease. The laying hen provides an ideal model to test prevention and therapy strategies using natural products, and is well suited for large-scale dietary intervention studies.

066

INTEGRATION OF PALLIATION IN PRIMARY CARE : ESSENTIAL YET NEGLECTED

Keywords Non Communicable Diseases, Primary Care , Community Hospice, Primary Care Physicians, Chronic Dis-Eases Epidemiology

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Palliative care especially at end stage focusses primarily on maintaining comfort and quality of life[1]. Existing evidence emphasizes upon establishing home based palliative care as patients preferred set-ting for receiving end of life care and as cost effective option[2]. Providing quality care at home and especially responding to disease associated symptoms and complications may pose an array of challenge as no formal institutional mechanism exists to respond to patient and care giver's wishes. NPCDCS program has introduced need of home based palliative care team comprising of nurse and counsellor trained in identifying symptoms, pain management, communication, psychosocial and emotional care.

Our work explores the dimensions of providing appropriate palliative care , existing challenges and effective measures in addressing those challenges to provide home based palliative care. The main aspects of home based palliative care focused upon providing supportive care, enabling patient and care givers to make their decisions regarding choice of treatment, location of care and establishing empathetic physician patient communication. Further, we explored the role of primary care physicians in bridging the gaps between demand and supply regarding institutionalising home based palliative care.

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067

BIOCHEMICALLY DEFINING DIFFERENTIAL IMMUNE RESPONSE IN RETINAL GLIA TO CLADE SPECIFIC HIV 1 TAT VARIANTS

Keywords Neuroimmunology, Retina, Immunity, HIV, Endocannabinoid

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Individuals with HIV-1 often suffer from visual impairment and opportunistic retinitis. In the retina, Müller glia is a dominant player of immune response. HIV infected cells produce HIV-1 transactivator viral protein (Tat), early in infection. HIV-1 Tat induce production of several neurotoxic cytokines in retinal cells. In this study, we investigate differences in innate immune response and ability to attract monocytes on exposure to clade B and clade C HIV-1 Tat in retinal Müller glia. Further, we show that the endocannabinoid anandamide (AEA), functions as an effective immune modulator but through different pathways for clade B and C. The study shows that HIV-1 clade Tat B and C act differentially on Müller glia, which reflects in cell viability, cell death pathway components, anti- and pro-inflammatory cytokine production. The more aggressive immune-mediated pathology of Tat B as opposed to the milder effects of Tat C was mediated at several signal transduction pathways, notably, STAT, MAPK, the NFκB signalosome, and RNA-binding protein Tristetraprolin. In activated cells, AEA acting as an immune-modulator, sup-presses Tat B effect through MKP-1, but Tat C action by means of MEK-1. AEA reduces nuclear NF-κB for both variants, while elevating the negative regulator of the transcription machinery, IRAK1BP1 in ac-tivated Müller glia. Müller glia exposed to Tat shows enhanced PBMC attachment. AEA decreases Tat-induced leukocyte adhesion to Müller cells. Leukocyte attachment to Müller glia for clade B and C are through different regulatory components. This work demonstrates that immune-mediated pathology and neuro-virulence in HIV Tat can be driven at multiple signalling components. Further, the neuroprotective effect of AEA occurs at various stages in cytokine generation and is clade-dependant.

068

TRANSLATIONAL AND POST-TRANSLATIONAL CONTROL OF POLYAMINE HOMEOSTASIS

Keywords ODC antizyme, Polyamines, Protein degradation, Translational control, +1 ribosomal frameshifting

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Polyamines are essential, aliphatic, polycations having roles in various cellular processes. Polyamine levels are deregulated in cell death as well as diseases such as cancer. Ornithine Decarboxylase (ODC) is the rate-limiting enzyme of polyamine biosysthesis. In a highly conserved, and complex homeostatic feedback loop, polyamines regulate their biosynthesis by controlling ODC levels. The identification of long missing ODC Antizyme (an negative regulator of ODC) in *Saccharomyces cerevisiae* lead to the exploration and understanding of the molecular mechanisms controlling polyamine biosynthesis in eukaryotes. Our findings revealed that, nascent ODC Antizyme (OAZ1) protein functions as the sensor of polyamine levels by direct binding of polyamines. As a consequence, polyamine binding to nascent OAZ1 results in completion of OAZ1 translation and release from the ribosome as well as induction of +1 ribosomal frameshifiting (RFS) event at the internal stop codon of OAZ1 mRNA. As a result, induction of the OAZ1 mRNA decoding leads to in higher OAZ1 levels. When present OAZ1 binds to ODC and, targets it for ubiquitin-independent degradation by the 26S proteasome. In addition, OAZ1 is subject to ubiquitin-dependent protein degradation by the proteasome. Interestingly, polyamines regulate OAZ1 levels both translationally and post-translationally by inhibiting its ubiquitin-dependent degradation. By applying various genetic and biochemical approaches, our research focused at understanding the co-translational sensing of polyamines by OAZ1 in eukaryotes. Further we are interested to identify and, understand similar auto regulatory mechanisms controlling the expression of novel cellular genes in eukaryotes. Additionally our study is also focused on the regulation and deregulation of the polyamine homeostasis in various disease conditions such as cancer and cellular senescence.

069

NOTCH IN PEDIATRIC B –CELL ACUTE LYMPHOBLASTIC LEUKEMIAS

Keywords Maternal and Child health, preterm birth, placenta, cancer, exosomes

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Our group is interested in elucidating the possible role of Notch and its synergies in pediatric B-ALLs. Childhood acute lymphoblastic leukemia (ALL) is an aggressive type of hematologic malignancy that results from malignant transformation of normal developing B cells. The Notch signaling pathway plays crucial roles in proliferation, differentiation, survival and apoptosis in many developmental processes. While Notch 3 and Notch 4 have been shown to be linked to acute B- ALL, but Notch 1 has not been explored. Gene expression analysis using quantitative Real-time PCR (qPCR) has been carried out on Pediatric B-ALL patients (n= 77) for Notch1 and its synergistic partners and comparing them to age matched healthy controls. Our data reveal a significant association of Notch 1 expression alteration in the B-ALL patients. The pattern of expression revealed presence of two distinct categories, a very low and a moderately altered group. Interestingly the extent of alteration appeared to be correlated with disease severity index as well as known markers of B- ALL such as Hes 1. Ongoing experiments are focused to probe similar patterns of expression for all the synergistic partners of Notch. To get better understanding of the underlying mechanism we will be using a B-ALL cell culture model which is amenable to genetic and molecular biology manipulations. We anticipate that our study would connect Notch 1 and its allies to B-ALL and would also shed light into molecular mechanism of the involved phenomenon. This would be a small step towards diagnosis and possible therapeutic interventions.

070

IDENTIFICATION OF PEDF-ATGL-COP1 AXIS IN FATTY LIVER DISEASE

Keywords Metabolism, Metabolic Disorders, Type 2 Diabetes, Fatty Liver Disease, Cancer Metabolism

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Optimal control of hepatic lipid metabolism is critical for organismal metabolic fitness. In liver, adipose triglyceride lipase (ATGL) serves as a major triacylglycerol (TAG) lipase and controls bulk of intracellular lipid turnover. We show that E3 ubiquitin ligase COP1 binds to the consensus VP-motif of ATGL and targets it for proteasomal degradation by K-48 linked polyubiquitination, predominantly at lysine 100 res-idue. COP1 thus serves as a critical regulator of hepatocyte TAG content, fatty acid mobilization and oxidation. *In vivo*, adenovirus-mediated depletion of COP1 ameliorates high fat diet induced steatosis in mouse liver and improves liver function. Moreover, we have identified pigment epithelium-derived factor (PEDF), a secreted multifunctional glycoprotein as the physiological inducer for ATGL degradation in the hepatocyte nucleus. We further show that inflammasome activation in liver resident Kupffer cells robustly induces PEDF expression in hepatocytes through interleukin (IL)-1b. Conversely augmented TNFα expression is associated with progressive reduction of PEDF expression during methionine and choline deficient (MCD) diet induced murine non-alcoholic steatohepatitis. Adenovirus-mediated depletion of PEDF in livers of MCD diet fed mice induced lipid accumulation, inflammatory and fibrotic gene expressions and promoted hepatocellular death through extrinsic apoptosis pathway which was further accentuated following TNFα challenge in these mice. Our study thus provides new insights into the regulation of hepatic lipid metabolism by linking imflammasome activation, ubiquitin-proteasome system (UPS) and lipolysis through PEDF-ATGL-COP1 pathway and suggests novel therapeutic targets for non-alcoholic fatty liver disease.

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071

WHEN LIKE CHARGES ATTRACT EACH OTHER: MODEL SYSTEM AND PROTEIN-PROTEIN INTERACTION

Keywords Theoretical Biophysics, Computer Simulation, Protein & Nucleic Acid, Electrostatics, Free energy Calculation

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In gas phase in the absence of any other particle, two particles having same sign of charges repel each other as is known from Coulomb's law. However, in condensed phase in the presence of counterion and/or salt two like charges may attract each other [1]. This is the main reason for two like charged colloids and proteins to attract each other [2]. Although like charge interaction has been observed and studied extensively, the fundamental microscopic mechanism behind it is still controversial. With a combination of integral equation theory and computer simulation techniques, we have investigated model systems and proteins of globulin family to understand the microscopic mechanism of their interaction. This may be useful in more general problem of protein aggregation and phase separation.

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072

BIOMATERIALS AND BIOENGINEERING CONCEPTS FOR CLINICAL APPLICATIONS

Keywords Translational Research, Biomaterials, Drug Delivery, Gene Delivery, Inflammatory Diseases

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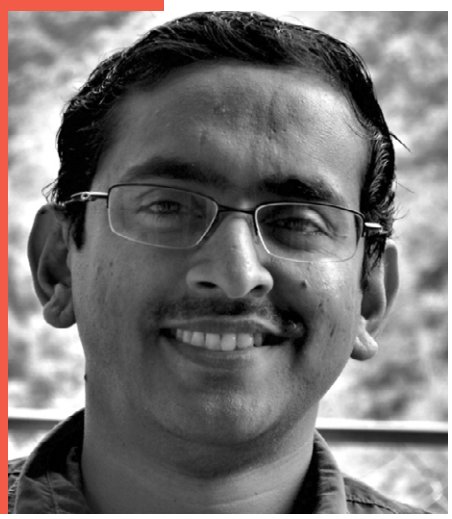
Our lab is focusing on developing biomaterials and bioengineering concepts for solving unmet clinical needs. Primarily focused on clinical pull approach, where novel biomaterials are being developed for multiple medical applications, including implantable biomaterials to protect transplanted organs without rejections, inflammation-targeting materials for the efficient treatment of inflammatory bowel diseases, and novel materials to protect agriculture farming workers from pesticide exposure.

073



RENAL CLEARABLE NEW NIR PROBE: PRECISE QUANTIFICATION OF ALBUMIN IN BIOFLUIDS AND FATTY LIVER DISEASE STATE IDENTIFICATION THROUGH TISSUE SPECIFIC HIGH CONTRAST IMAGING *IN VIVO*

Keywords Type 2 Diabetes, Beta-Cell Biology and Insulin Secretion Obesity, Non Alcoholic Fatty Liver disease, Bioconjugate Therapeutics

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Non-Alcoholic Fatty Liver Disease is the leading cause of chronic liver disease worldwide. An epidemic of liver diseases prompted us to design and synthesize a small molecule which can be used for high resolution noninvasive liver imaging as well as to identify patients at risk of liver disease progression. As liver is the only organ which produces albumin, we hypothesized that the dye with strong binding affinity toward albumin can be used for specific imaging of liver. Development of a highly photostable, renal clearable and nontoxic new NIR probe (CyG) for precise quantification of albumin in different biofluids and liver targeted *in vivo* albumin visualization is demonstrated. CyG's inherent property to interact selectively with albumin among different biomolecules in intracellular environment with high degree of sensitivity helps CyG in targeted liver imaging. In addition to its long excitation/emission wavelengths (λex = 740 nm, λem = 804 nm) which are much above the biological tissue opaque window (400 – 700 nm) ensuring better photon penetration, diminished tissue auto fluorescence and high contrasts, its molecular mass and size are far below the renal cut-off and hence, CyG qualifies as imaging material for clinical studies. We anticipate that CyG will provide new strategies to overcome the pitfall of present day albumin detection methods as well as accelerate the detection process at relatively lower costs without compromising the accuracy of detection. Moreover, the renal excretion kinetic and intra-hepatic albumin binding affinity of CyG can further be used to differentiate between fatty liver from healthy liver in an experimentally arrived mouse model using non-invasive technique.

074

TISSUE FACTOR FVIIA COMPLEX IN COAGULATION TO CANCER

Keywords Blood Coagulation, Cancer Signaling, Tissue Factor-FVIIa, Microvesicles, Differentiation

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Tissue factor (TF)- FVIIa is a multifunctional protein complex having role in blood coagulation to cancer. We are intrinsically involved in elucidating different aspects of the both. It is well established that upon binding, TF allosterically modifies FVIIa structure and thus enhanced its proteolytic activity but the detail information regarding what structural modulations, TF impart on FVIIa have not been evaluated due to lack of crystal structure. Through Molecular Dynamic (MD) study we have identified two unique interactions those play a vital role in allosteric modification. Further through MD we have identified the differential behavior of soluble TF vs full length TF towards its ligand FVIIa. With the help of MD study we have evaluated the role of the allosteric disulfide bond of TF in the context of TF-FVIIa interaction. Phospholipds, specifically phosphatidyl serine (PS) enhances TF-FVIIa activity but at the molecular level mechanism remains unidentified. We tried to evaluate the role of different functional group of PS in FXa generation by TF-FVIIa complex by adopting functional group replacement method in combination with in vitro FXa generation. Briefly we have synthesized large number of PS derivatives with modified functional group. Along with wild type PS we have prepared relipidated TF with these modified PS and measure comparative FXa generation and mapped the contribution of each functional group of PS. We have also tried to identify the mechanistic details related with TF-FVIIa mediated cancer progression and propagation. We found TF-FVIIa mediated cellular signaling through PAR2 activation leads to accumulation of beta catenine, upregulation of MMP2 expression to enhance cancer progression. We also found that TF-FVIIa mediated PAR2 activation enhanced microvesicle (MVs) release from the breast cancer cells by modulating cellular actomyocine dynamics and these MVs have the high potential to infuse with non-metastatic cells to transduce metastasis.

075

GLOBAL GENE EXPRESSION PROFILING OF EPIGENETIC FACTORS IN DIFFERENT STAGES OF HUMAN MYELOPOIESIS

Keywords Chromatin, Epigenetics, Myeloid Lineage, Chromatin Remodeling Complexes

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Hematopoiesis or blood cell development starts with Hematopoietic Stem Cells (HSCs) in bone marrow and through progressive stages of lineage commitment and differentiation gives rise to different mature blood cell types. Epigenetic factors, a distinct class of gene regulators are the key players in modulating chromatin landscape, essential for regulating gene expression during normal hematopoietic differentiation. Mutations or aberrant gene expression has been linked to various hematopoietic disorders and leukemia. We are interested in understanding how the gene expression of different epigenetic factors is modulated during the course of normal hematopoiesis, which dictates myeloid lineage choice.

We have categorized more than 500 epigenetic factors into different groups such as DNA/histone modifiers, chromatin remodelling complexes, polycomb complex and chaperones. Their expression profiles was curated from available high-throughput transcriptome data from HSC, CMP (common myeloid progenitors), GMP (granulocyte macrophage progenitor), monocytes and granulocytes. The analysis revealed both unique and differential gene expression patterns of epigenetic factors in myeloid develop-mental stages.

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076

INSIGHTS INTO MYCOBACTERIAL TRANSMISSION AND PATHOGENESIS USING COMPARATIVE GENOMIC AND TRANSCRIPTOMIC STUDIES IN LEPROSY

Keywords Leprosy, Comparative transcriptomics and genomics of mycobacterial diseases, Next Generations Sequencing, Biomarkers, Molecular Epidemiology

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Mycobacterial diseases Tuberculosis and Leprosy are important health issues. Leprosy is a chronic disease caused by uncultivable pathogen *Mycobacterium leprae* and *M. lepromatosis*. Over 220,000 new leprosy cases are recorded worldwide annually, nearly 2/3 of which are in India. The dynamics of *M. leprae* transmission and pathogenesis mechanisms largely unknown.
Our previous studies in Prof Stwart Cole's lab at EPFL, Lausanne, Switzerland used whole-genome se-quencing approach, which led to SNP-genotyping scheme with excellent association with geographic origins of *M. leprae*[1]. These studies provided molecular evidence for zoonotic link between armadillos and human leprosy in southern US [2]. Further studies contributed in tracing the origin of this zoonotic strain to the medieval leprosy skeletons from Europe[3].

Subsequently, we developed innovative and inexpensive methods for DNA-enrichment and sequenced the first-ever genome of *M. lepromatosis* associated with a severe form of leprosy called "diffuse lep-romatous leprosy. Its comparative analysis with *M. leprae* reveals that both species have undergone reductive evolution together and diverged around 13.9 million years ago[4].

In addition to the Pathogen Genomics, our ongoing projects aim to investigate the host Gene Expression signatures of active leprosy in blood samples in humans and armadillos using RNA-Sequencing to identify transcriptional signatures characteristics of active leprosy. This can be useful for detecting leprosy at an early stage and for a better understanding of peripheral neuropathies, which affect millions of diabetic patients also.

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077

STRUCTURAL BASIS FOR Nup93 MEDIATED ANCHORING OF THE CENTRAL TRANSPORT CHANNEL

Keywords Nuclear pore complex, nucleocytoplasmic transport Nucleoporins, Structural biology, Biochemistry

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Nuclear pore complexes (NPCs) are the largest macromolecular assemblies embedded in the nuclear envelope and form the selectivity barrier for nucleo-cytoplasmic transport. They are composed of ~30 proteins called Nups. These Nups can be classified into various sub-complexes comprising of central transport channel (CTC; Nup62, Nup58, Nup54) that imparts permeability barrier and an adapter ring (composed of Nup93, Nup205, Nup188, Nup155, Nup35), which holds up the central channel at the core of NPCs via extensive interactions among these Nups of the adapter ring and membrane proteins. Despite of advances in this area of research, interactions among these vertebrate Nups remain poorly understood and thus limit generating accurate architecture of NPCs. It was shown earlier that Nic96, a homolog of Nup93 anchors the central channel (Nsp1•Nup49•Nup57 complex) in yeast. Also a complex of three Nups (Nup62•Nup54•Nup58) is critical to interact with Nup93. We fine mapped the CTC interact-ing regions on human Nup93 and established that Nup93 N-terminus 150 amino acid region is sufficient to interact with Nup62•Nup54•Nup58 complex. The quaternary complex of Nup93 with minimally interacting CTC complex was biochemically assembled and characterized. It was further analyzed using electron microscopy for 3D reconstruction. Our model indicates that Nup93 is arranged in parallel to three-helix bundle of the CTC complex to form ‘U shape architecture’. The N-terminus helices (1-150) are intertwined with C terminus short three-helix bundle to form the junction. We also docked our model’s density into the available human NPC tomography structures and showed the possible arrangement of these 4 Nups (Nup62, Nup54, Nup58 and Nup93) in entire human NPC. In summary we show first structure of the Nup93•Nup62•Nup54•Nup58 quaternary complex that demonstrate how short helices at the N-terminus of Nup93 are crucial for anchoring the CTC in the symmetric core of the NPC.

078

“PARTLY LEARNED, PARTLY INNATE VOCALIZATIONS HELP THE ZEBRA FINCH BRAIN GET “”READY”” TO SING”

Keywords Songbirds, Movement Initiation, Movement Sequences, Motor Learning, Neural Control Of Behavior

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Throughout our lives, we learn to perform a number of different complex movement sequences like executing a tennis serve or playing a musical instrument. With extensive practice, we become very good at performing these movement sequences accurately and hardly notice initiating them. The importance of movement initiation is clear only when movement initiation becomes difficult in diseases like Parkinson’s disease. However, how the brain initiates movement sequences is an age-old unanswered question in neuroscience. Here we address this question using the zebra finch, a songbird, as our model system.

The song of the adult male zebra finch is a stereotyped sequence of sounds interleaved with silent periods that is learned by young birds in a process similar to human speech learning[1]. Zebra finches begin their song bouts with a variable number of repetitions of a short sound called an introductory note (IN). We have previously suggested that INs represent some kind of warm-up (like ball-bouncing before a tennis serve) that helps the bird brain get “ready” to sing[2]. My lab is focused on understanding how INs are produced and what role they may play in song initiation. We find that in individual birds, mean IN number shows very little variation with age and is mostly independent of real-time sensory feedback. Surprisingly, mean IN number of individual birds is correlated with mean IN number of their father. This correlation remains even when birds are isolated at an early age and reared without social exposure to their father. These data suggest that INs are a reflection of an innate, sensory feedback independent process by which the zebra finch brain gets “ready” to sing.

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079

SLT2 DEPENDENT FLOCCULATION OF YEAST, INDUCED BY GENETIC CHANGES IN SEN1 IS ESSENTIAL FOR SURVIVAL IN RESPONSE TO OXIDATIVE AND CELL WALL DAMAGE

Keywords Genomic Integrity, Epigenetics, Yeast Flocculation, Cancer, Anti-cancer molecules

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Yeast cells can grow on many surfaces including medical devices, cells and tissues. Pathogenic yeasts adhere in the form of flocks to form drug-resistant biofilms. In contrast, adherence or flocculation property of yeast is useful in biotechnological applications. Adhesion/flocculation of yeast occurs due to expression of a special class of cell wall proteins, called adhesins/flocculins. Furthermore flocculation property of yeast cells allows them to survive in stressful environmental conditions.

The signalling mechanism that regulates the expression of flocculins is not very well understood. Normally FLO genes that encode flocculins are repressed by the binding of global repressor complex, Cyc8-Tup1 which in association with histone deacetylases, maintains positioning of de-acetylated nucleosomes[1]. Under stress conditions, Swi2/Snf2 and histone acetylase complexes occupy the promoters to activate the expression of FLO genes. We have identified the role of Yeast Sen1, a RNA/DNA hel-icase in regulation of FLO genes[2] and redox homeostasis[3]. Our studies suggest that cooperation among Sen1, Tup1, histone modifications and Swi2 is essential for the expression of FLO genes

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080

MOLECULAR BIOLOGY OF VIRUS MEDIATED CANCERS: ROLE OF VIRUS CODED PROTEINS IN CANCER METASTASIS

Keywords Tumor virology, Cancer Metastasis, EMT, Epstein Barr Virus, Hepatitis C Virus

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Metastasis is the single most important cause of cancer-related deaths. The development of strategies aimed to contain the cancer by preventing it from metastasizing is an important step in containing cancer. We investigated role of EBV and HCV coded viral proteins in cancer metastasis. Cancer cells ex-pressing EBV latent viral antigens EBNA3C and/ or EBNA1 show higher motility and migration potential and have a propensity for increased metastases. Our data shows that both EBNA3C and EBNA1 can modulate cellular pathways critical for epithelial to mesenchymal transition (EMT) of cancer cells. The primary tumors as well as metastasized lesions derived from EBV antigen-expressing cancer cells in nude mice display EMT markers expression pattern suggesting their greater propensity to mesenchymal transition. A distinct feature of HCV associated hepatocellular carcinoma (HCC) is the substantially increased incidence of metastasis. Nm23-H1 is the first reported human metastasis suppressor down-regulated in many human metastatic cancers. Our study shows that HCV E1 protein expression as well as HCV infection induces pro-metastatic effect on cancer cells coincident to Nm23-H1 transcriptional down-regulation and Nm23-H1 protein degradation. Nm23-H1 intracellular localization is significantly altered in cells expressing HCV E1 protein. Importantly, overexpression of Nm23-H1 can rescue the cancer cells from pro-metastatic effects of HCV E1 and HCV infection. Our study provides evidence for role for Nm23-H1 in HCV mediated cancer metastasis.

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081

UNDERSTANDING THE PATHO-BIOLOGY OF FUNGAL PATHOGENS

Keywords Chemical Biology, Host-Pathogen Interaction, Fungal Patho-Biology, Molecular Mimicry, Microbiology & Plant Biotechnology

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Oxylipins, the oxygenated lipids derived from polyunsaturated fatty acids, play a crucial role at the plant-fungus interface. While plant oxylipins such as jasmonic acid are involved in development and disease resistance, those of fungal origin are known to play roles in pathogenesis strategies and synthesis of toxins. We previously showed that the rice-blast fungus *Magnaporthe oryzae* produces jasmonic acid (JA), and converts it into 12-hydroxyjasmonic acid (12OH-JA), using the Abm monooxygenase, to suppress the plant immunity at the time of host invasion1. However, other than a critical role in evading host immunity, it was hitherto unclear why *M. oryzae* produces a so-called plant hormone. We found that *M. oryzae* fails to form a normal appressorium (infection structure) with a normal length of germ tube, when endogenous JA biosynthesis is blocked upon loss of the Opr3 (oxophytodienoate reductase) function. Importantly, exogenously added JA not only rescues the opr3Δ mutant phenotype but also induces appressorial development on a non-inductive surface. This suggests that fungal JA is most likely involved in appressorial development in *M. oryzae.* Our further studies suggest that JA likely acts in concert with cAMP signaling, and directly activates the downstream MAP kinase cascade necessary for appressorium formation. We propose that *Magnaporthe oxylipin* JA plays a dual role during both the pre- and post host penetration phases.

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URINARY BIOMARKERS IN LUPUS NEPHRITIS

Keywords Systemic Lupus Erythematosus (SLE), Lupus Nephritis Biomarker discovery, Vasculitis, T cell biology

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Lupus Nephritis (LN) is an autoimmune disease affecting almost 70% of SLE patients with considerable morbidity and mortality. It is believed that circulating immune complex deposition in glomeruli initiates the nephritis and involves innate as well as adaptive immunity in pathogenesis. *In vivo* renal immunological events may be reflected in urine which may serve as a better source for biomarker discovery. Earlier studies have shown that in spite of being an immune complex mediated disease, urinary B cells do not reflect disease activity.[1] Moreover, we noticed high urinary levels of sCD25 and MCP-1 in LN and hy-pothesized that urinary T cells and macrophages may have pathogenic role and reflect renal disease activity. SLE patients are divided into 3 groups based upon their disease activity (active disease with/without nephritis and inactive disease). Urine is centrifuged (supernatant stored for soluble cytokine analysis by ELISA) and sediment is taken for analyzing relative frequency of T cells and macrophages by multicolor flowcytometry. Similarly, T cells and macrophages are analyzed in blood for all 3 groups and control patients (vasculitis with renal involvement). The relative frequency of these cells is also seen in renal biopsy by immunohistochemistry to prove their pathogenic role.[2] To see if the signature cytokines of these cells can be used as biomarkers, urinary levels are tested by ELISA and correlated with renal disease activity.[3]

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083

TOWARDS THE UNDERSTANDING THE ROLE OF CARDIAC GLYCOSIDES IN TUMOR IMMUNOLOGICAL SIGNALING PATHWAYS

Keywords Cancer Genomics, Human Infectious Diseases, Microbial Genomics, Antibiotic Drug Resistance Genes Based Metagenomics

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Cardiac glycosides (CGs) are naturally derived organic compounds from plants secondary metabolites that contain sugar and steroid moiety. CGs increase cardiac contractility by inhibiting the sodium-potassium-adenosine triphosphatase (Na+/K+ ATPase) of plasma membrane and are widely used in the treatment of chronic heart failure. However, inhibition of Na+/K+ ATPase by CGs induces anti-proliferative downstream effects which are related to cell growth and apoptosis such as inhibiting the general protein synthesis, angiogenesis, anoikis sensitizers and tumor growth. The recent studies sug-gest that different types of cancer cells showed various sensitivities to different CGs, possibly due to different cellular content. Apart from the membrane transporter function , Na+/K+ pump also involved in various signal transductions and cellular processes relating to cell death and survival, etc.

In the current study we focused to identify the role of Peruvoside, Strophanthidin and Lanatoside- C in antitumor immunological activity by CD47-SIRP α (alpha) pathways as novel molecular targets by naturally derived CG's in various cancers like breast, lung and liver. We find out the mechanism of action of this CGs by time dependent inhibition of proliferation in gene level and protein level expressions in adherent cells. Moreover, our group focuses the activity of these CG's in MAP kinase, NF-Kβ, Autophagy signaling interaction, Pi3/AKT signaling, JA/STAT signaling pathways.

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PROTEIN PYROPHOSPHORYLATION: TEN YEARS AND COUNTING

Keywords Cell signalling, Inositol polyphosphates, Protein pyrophosphorylation

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Inositol pyrophosphates are a class of water soluble inositol phosphates which contain pyrophosphate and monophosphate moieties. The most abundant inositol pyrophosphate in mammalian cells is 5-diphosphoinositol pentakisphosphate (5PP-IP5 or 5-IP7). 5-IP7 is synthesised from inositol hexakisphosphate (IP6) by IP6 kinases (IP6Ks), and participates in a variety of cellular functions. Inositol pyrophosphates can modulate protein function by specific binding or by transferring their β-phosphate to a phosphoserine residue to bring about protein pyrophosphorylation. Our laboratory uses different model systems to examine the diverse functions of inositol pyrophosphates in eukaryotic cell physiology. We are particularly interested in examining how pyrophosphorylation of specific proteins regulates their function, and in turn modulates cellular homeostasis. We have demonstrated that 5-IP7-mediated pyrophosphorylation of RNA polymerase I regulates ribosome synthesis in budding yeast, and shown that pyrophosphorylation of the motor protein dynein is essential for vesicle trafficking in mammalian cells. While protein pyrophosphorylation was discovered a decade ago, the impact of this novel modification on diverse cellular pathways is only now being appreciated. We are developing tools to aid the detection of pyrophosphorylated proteins *in vivo*, with the hope that these will lead to an exponential advance in our appreciation of the functions of inositol pyrophosphates and protein pyrophosphorylation.

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REGULATION OF AUTOPHAGY FLUX BY CHEMICAL BIOLOGY AND GENETIC APPROACHES

Keywords Megakaryocyte, miRNA, Thrombocytopenia, Platelets, Hematopoietic stem cell

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MicroRNAs (miRNAs) have been shown to play a crucial role in the regulation of stem-cell differentiation in normal as well as malignant haematopoiesis, but their role in the regulation of biological differences between adult and neonatal megakaryopoiesis is unknown.

Out of 88 miRNAs involved in stem cell development, let-7b was the only miRNA down regulated (~10-fold) in neonates compared to adult megakaryocyte (MK), and the levels of let-7b was differentially expressed in all stages of MK development (progenitors to maturation). Our results showed the inhibitory effect of let-7b on wnt signaling pathway by regulating Frizzled-4 (Fzd4) and thereby regulating proliferation as well as differentiation. Let-7b down regulation induced mitochondrial biogenesis and its markers PGC-1α and NRF1. Suppression of wnt signalling using let-7b mimetics was associated with decrease in downstream targets such as Fzd4, pGSK-3, LEF-1, HMGA2 and CCND1, and down regulation of mitochondrial specific proteins (VDAC & COX IV) and megakaryocyte proliferation signals (pERK and pAKT). We observed that let-7b expression was inversely correlated with mitochondrial biogenesis.

Our study provided the role of let-7b in human megakaryocytopoiesis, and for the first time identified let-7b as a molecular regulator of organelle biogenesis through wnt signaling in megakaryocyte develop-ment[1]. Further, our data suggest the role of mitochondria in megakaryocyte development. These studies will help in defining the mitochondria mediated effects such as proliferation and differentiation pathways that control the fate of megakaryocytes.

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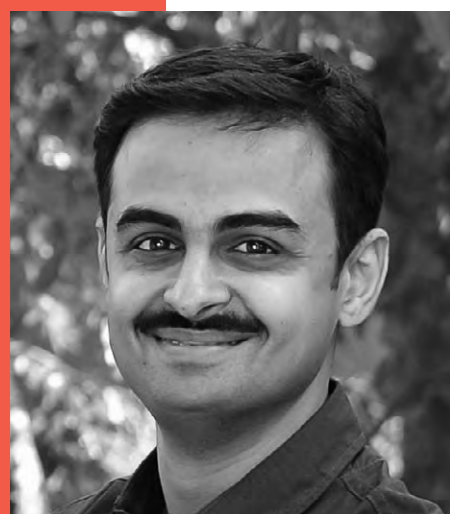

TRANSLATIONAL AND POST-TRANSLATIONAL CONTROL OF POLYAMINE HOMEOSTASIS

Keywords Cell Biology, Molecular Biology, Biochemistry, Chemical Biology, Autophagy

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My laboratory utilizes genetic and chemical biology approaches to study macroautophagy (herein autophagy) flux. Autophagy is an evolutionarily conserved intracellular eukaryotic process that is required for cellular garbage removal and recycling. It involves the formation of *de novo* double membrane vesicles, autophagosomes, that capture cellular cargo and deliver them to the lysosomes for degradation and recycling. This process critically impacts cellular homeostasis and also impinges on several physiological and pathophysiological processes including development and differentiation, aging, intracellular infections, neurodegeneration and cancer. Cells have potential to modulate autophagy flux to effectively bring about cellular homeostasis and in many diseases with dysfunctional autophagy, restoring it has been shown to be a promising therapeutic approach. Chemical biology approaches to identify small molecule modulators of autophagy have dual benefits: these can be used to provide insights into mechanisms of autophagy flux especially where genetics strategies have failed to make inroads, and two, they can be of therapeutic value. Identifying specific and potent autophagy modulators using HTS has been beset with limitations primarily due to unavailability of specific cargoes with high turnover rates. We have identified specific and potent autophagy modulators that not only work across three different kingdoms of life but also show therapeutic potential in neurodegenerative intracellular infectious diseases.

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REGULATION OF THE CELL DEATH FATE OF NEURAL STEM CELLS IN *DROSOPHILA*

Keywords Developmental Biology, Stem Cells, Epigenetics, *Drosophila*

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Stem cells are multipotent, and can give rise to diverse differentiated progeny upon receiving the correct signals. Despite the potential therapeutic usefulness of stem cells, our understanding of the regulation of stem cell behavior is fairly limited. Transcriptional changes, epigenetic regulators and chromatin re-modelers together fine-tune timely gene expression to decide stem cell fate and identity. By using an *in vivo* system, we are studying how temporal and spatial signals control stem cell behavior. The neural stem cells in the *Drosophila* embryo are an ideal model to analyze genetic and epigenetic fate determi-nants.

In an *in vivo* RNAi screen for stem cell fate regulators, we have identified 50 transcription factors and epigenetic modifiers that regulate the timely death of neural stem cells. Interestingly, most of these identified factors have human homolog and some have been recently implicated in various types of cancers. Here we focus on cut, one of the transcription factors identified in the RNAi screen, and show its role in regulating neural stem cell death. Cut is a homolog of the mammalian cux1 and cux2 genes. These genes are reported to act as both oncogenes and tumor suppressors in various cancers. However, it is largely unclear how these genes regulate tumorogenesis. Here we show that cut modifies the chromatin landscape for timely activation of key cell death genes.

088

TEASING OUT BACTERIAL INTERACTIONS FOR NEW ANTIMICROBIALS

Keywords Bacterial Morphogenesis, Bacterial Cell wall, Cell division, Biofilms, Environmental Microbiology

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Soil represent a favorable habitat for microorganisms and is inhabited by a wide range of bacteria. As microbial numbers are high in soil there is intense competition for food and resources. Due to this, bacteria develop antagonistic relationships such as antibiosis, where the antibiotics or metabolites produced by one bacterium inhibits growth of another bacteria. Thus, bacteria residing in soil communities are potentially good sources for new antimicrobials. During our study of soil microbial ecology of Dadri Wetland in Uttar Pradesh, India, we obtained a purple/blue pigmented bacteria which was identified to be *Janthinobacterium lividum* by 16S sequencing and blast analysis. *Janthinobacterium lividum* is a gram-negative, aerobic, soil-dwelling bacterium with dark violet colonies due to the production of a pigment violacein. Violacein is an indole derivative and is proposed to have antibacterial activities but its mode of action is largely unknown. Our preliminary results show that violacein has antimicrobial properties against Gram-positive bacteria. Violacein was able to inhibit growth of Staphylococcus aureus, Streptococcus mutans and Bacillus cereus. S. aureus cells grown in sub-inhibitory concentration of violacein displayed morphological defects including increase in cell volume and formation of cell clusters. Similarly, B. cereus in presence of violacein grew as cells attached in chains, indicating defects in cell division. SEM and TEM imaging of S. aureus treated with violacein displayed severe deformities in cell wall, cell membrane and presence of unseparated cells, confirming defects in cell division. Fluorimetric assays showed that violacein was able to disturb membrane potential similar to the ionophore carbonyl cyanide m-chlorophenylhydrazone (CCCP). Taken together our data suggest that violacein inhibits growth of gram-positive bacteria by disrupting membrane potential and cell division.

089

ANALYSIS OF MITOCHONDRIAL DISTRIBUTION, DYNAMICS AND FUNCTION IN STEM CELL DIFFERENTIATION.

Keywords Embryogenesis, Morphogenesis, Differentiation, Polarity, Mitochondria

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Epithelial cells differentiation is triggered by signaling cascades activated during tissue patterning. The epithelial plasma membrane and organelle architecture caters to their function. Our studies have found that mitochondria distribution is essential for follicle cell patterning in *Drosophila* oogenesis. Mitochondria are present in a polarized manner along the apico-basal axis in follicle epithelial cells and early epithelial-like cells in embryos in *Drosophila*. Follicle cells undergo differentiation in early stages to form polarized epithelial cells. Notch signaling at stage 6 causes further differentiation into anterior, main body and posterior follicle cells. Mitochondria are dispersed in posterior follicle cells and aggregated in main body follicle cells. EGFR signaling regulates dispersed mitochondria and mitochondrial membrane potential in posterior follicle cells. Mitochondrial fusion in posterior follicle cells by inhibition of mitochondrial fission protein Drp1 results in loss of Notch mediated follicle cell differentiation. Hyperfused mitochondria in drp1 mutant posterior cells have increased mitochondrial membrane potential and retention of cytoplasmic activated ERK downstream of EGFR. I will discuss how these interactions between EGFR-ERK and mitochondrial membrane potential in fragmented mitochondria are essential for Notch mediated differentiation of posterior follicle cells.

090

CLIMATE AND TOPOGRAPHY IMPACT BIRDS ON SHOLA SKY ISLANDS OF WESTERN GHATS

Keywords Ecology, Evolution, Sky Island, Bird Song, Biogeography

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Many tropical montane understorey insectivorous birds are known to respond strongly, and negatively, to climate change over longer time periods, and to forest edge at shorter time periods. My research has focussed on examining the demographic and evolutionary impacts of such species' response to isolation in the Western Ghat Shola Sky Islands. Isolation at a small scale (tens of kilometers) could lead to disruption of genetic connectivity and changes in birdsong. Effects of isolation over long time scales (thousands to millions of years) and large geographic distances (hundreds of kilometers) can accumulate changes that lead to evolution or extinction.

We examined how an entire montane bird community of the Western Ghats responds to topographic valleys that host different habitats. Our results reveal a nested phylogeographic effect of valleys, with several species (10 of 23) demonstrating the oldest divergences associated with the widest and deepest valley in the mountain range, the Palghat Gap. Further, a subset of these ten species revealed younger divergences across shallower, narrower valleys. We recovered discordant divergence times for all spe-cies, highlighting the role of climatic fluctuations in driving species evolution.

We also found contemporary gene flow was lower relative to historic differentiation in anthropogenic fragments, despite the species' ability to historically traverse shallow valleys. Simulations confirm recent isolation in Western Ghats anthropogenic fragments, making these fragments akin to islands within natu-ral islands of montane habitat.

My recent research includes biogeography research in the Andaman & Nicobar islands and a collaborative project with human speech engineers to detect birds from automated bird song recorders placed in various forests, to detect the movement of birds.

091

LIPID-MOTOR INTERACTIONS: SOAP OPERA OR SYMPHONY?

Keywords Molecular Motor, Cytoskeleton, Lipoprotein Secretion, Lipid Membranes, Optical Trapping

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Motor proteins are ATPases that convert chemical energy into mechanical energy to drive many cellular functions including intracellular transport of vesicles. Vesicular transport entails cargo recognition by the respective motor, transport and possible cargo-motor dissociation at destination. Recognition of a cargo by motor(s) can be mediated by heterogeneities in protein and lipid composition of the cargo. Each sub-cellular organelle has a characteristic set of membrane lipids that encloses its inner contents within a bilayer membrane. This membrane is the substrate on which motors must attach (directly or indirectly) before they can effect transport. Lipid composition and local membrane heterogeneity are therefore important for recruiting motors, and perhaps also in deciding the micro-organization of motors on the cargo surface. However, the role of lipids is less appreciated in the literature that discusses regulation of motors on a cargo. Given the vast variety of cellular vesicles, their lipids and their motors, reliable mechanisms must ensure cargo-motor recognition. This requires a set of diverse protein domains to be matched to another set of even more diverse lipids on the membrane. Is this matching just like a television soap opera where characters meet each other transiently to develop random intimacy/ hatred, or is it like a well-orchestrated symphony where precise rules dictate matchmaking in a spatio-temporally controlled manner?

092

AN ERROR-PRONE DNA POLYMERASE PREVENTS ERRORS

Keywords Replication-transcription Conflicts, Mechanisms of Mutations, DNA repair, Antibiotic Resistance, Cancer Mutagenesis

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Chromosomes are accurately duplicated by high-fidelity polymerases. Genome duplication is occasionally impeded by transcription due to collisions between replication and transcription machineries. Such replication-transcription collisions increase mutagenesis and cause two distinct types of mutations. Several transcription factors, accessory helicases and DNA damage response factors have been implicated in resolving collisions.

Here, we are investigating the role of error-prone DNA polymerase in modulating the mutation landscape of replication-transcription collisions. Cells require low-fidelity polymerases for specialized functions at times of DNA damage. Although, low-fidelity polymerases have the exceptional ability to replicate dam-aged DNA, they can be error prone on undamaged DNA. One such polymerase is PolIV (DinB) in bacteria belonging to Y-family, which is universally conserved. DinB is implicated in bypassing bulky DNA lesions, adaptive mutagenesis and replication-restart.

We are hypothesizing PolIV plays a role in resolving replication-transcription collisions and may reduce mutagenesis. To examine the role of PolIV in collision-induced mutations, we used a deletion mutant of *B. subtilis* homolog of dinB (yqjH) and measured the mutation rates of a reporter gene. Surprisingly, we found that mutation rate is marginally increased in the deletion mutant compared to wild-type. We further sequenced the reporter gene and found that indels are increased in the deletion mutant, implicating Pol4 in minimizing generation of indels.

This intriguing observation leads us to propose a novel and unexpected role for PolIV being anti-mutagenic contrary to its well-established mutagenic function.

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093

TUG-OF-WAR BETWEEN CDK1 AND PP2A DURING MITOSIS REGULATES PROPER SPINDLE ORIENTATION

Keywords Cell Division, Spindle Positioning, Dynein, Kinases , Phosphatases

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Proper orientation of the mitotic spindle is critical for error-free mitosis. It further controls the proper distributions of the cell fate determinants during development and in stem cells. In metazoan spindle orientation is regulated by an evolutionarily conserved cortically anchored ternary complex (Gαi1-3/LGN/NuMA in human). It is well established that a component of the ternary complex 'NuMA' interacts with minus-end motor protein complex dynein and enrich it at the cell cortex. It is the activity of this cortical dynein on the astral microtubules toward the spindle pole that generates the pulling forces that orient the mitotic spindle at a particular axis. We have previously shown that CDK1 activity negatively regulates cortical NuMA and thus dyein localization by phosphorylating it at Threonine 2055. Interestingly, NuMA that is non-phosphorylated at T2055 localizes at the cell cortex. To understand how non-phosphorylated NuMA species is generated in metaphase, we have conducted an RNAi-based screen to discover the PP2A holoenzyme that interacts and de-phosphorylates NuMA at T2055. RNAi-mediated loss of PP2A complex causes loss of cortical NuMA/dynein and impact spindle orientation. Additionally, we have uncovered molecular mechanisms by which PP2A complex recognize NuMA and de-phosphorylates it at T2055. In summary, our study enlightens a novel pathway by which CDK1 and PP2A-phosphatase complex or-chestrate cortical dynein levels in a spatiotemporal manner for accurate mitosis.

094

LOCAL NANOPARTICLE-BASED APPROACHES TO TARGET PERIPHERAL AXONS FOR MANAGEMENT OF CHRONIC PAIN CONDITIONS

Keywords Non-spherical drug deliverable nanoparticles, Cancer induced bone pain, Intra-neural drug delivery, Local, prolonged drug delivery, Peripheral Nerve regeneration

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Chronic cancer induced bone cancer pain (CIBP) is a debilitating condition observed in 1/3rd of all patients with bone metastasis. The current standard of care includes the use of systemic opioids, but inadequate pain control and severe toxicity are some well-known drawbacks. In our laboratory, we are attempting to develop alternative approaches to manage CIBP using micro- and nano-particulate drug delivery systems that are locally administrable and can attenuate pain for prolonged periods of time.

One such strategy is to develop nanoparticles that can bind to peripheral axons located in the tumor-nerve interface and modulate pain signals. In this presentation, we discuss a segment of a larger study that focuses on the binding of lectin conjugated nanoparticles to peripheral neurons upon local applica-tion on the skin. We have synthesized gold nanoparticles (AuNp's) of varying sizes to test transdermal penetration and neural binding. AuNp size and content was determined using DLS, TEM, and ICP-AES. Tissue distribution of AuNP's and dermal response was assessed using dark-field microscopy and histological studies respectively. We further conjugated AuNp's with pain-neuron specific-isolectin B4, and tested for neuronal specificity and uptake in primary sensory neurons harvested in a microfluidic device that allowed spatial separation between peripheral axon and cell soma of DRG neurons. Our results demonstrate that nanoparticle based drug delivery systems may hold much promise in targeting peripheral neurons, especially in chronic pain conditions.

095

DECIPHERING THE ROLE OF HUMAN PROTEIN DEGRADATION MACHINERY IN METABOLIC SYNDROME

Keywords Ubiquitin proteasome machinery, E3 ligases

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Ubiquitination is a post-translational modification mechanism used to control protein levels through proteasome mediated proteolysis. Regulatory functions of the ubiquitin proteasome system (UPS) are exercised by ubiquitin ligases (E3s) and deubiquitinating enzymes (DUBs). Degradation of proteins by UPS is central to maintenance of cell health, and dysregulation of this process underlies several metabolic disorders. Therefore, it is the view that interrogating protein turnover in cells can offer strategy for delineating disease-causing mechanistic perturbations, and facilitate identification of drug targets. Here we are targeting TRIM72 E3 ligase and Ate1 protein from the N-end mediated protein degradation machinery. In both the studies we are interested in deciphering their molecular mechanisms of action, their interaction and active residues. Briefly, TRIM72 is identified as a novel E3 ligase targeting the ubiquitin-mediated destruction of insulin receptor and IRS1 and we aim to understand the role of TRIM72 in IRS1 degradation. While Ate1 gene involves in arginylation, adds arginine at the N-terminus of protein and dictates the half-life of protein. Recent studies show that arginylation regulates important cell processes such as heart development, angiogenesis and tissue morphogenesis. We have recently initiated to explore the role of arginylation (Ate1 gene) in the cardiomyocytes. With the preliminary data generated we are interested to establish Ate1 mechanism of action and further establish the regulatory role of its in the cardiac hypertrophy.

096

STUDIES ON SIRTUINS: UNIVERSAL MOLECULAR REGULATOR

Keywords Macromolecular interactions, Epigenetic regulation Infectious diseases, Host pathogen interaction, Drug designing

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Sirtuin family of proteins are quite ubiquitous in nature. In eukaryotes, they play a very important role in regulating various cellular processes ranging from metabolism to genome stability. They achieve this by mainly deacetylating the acetyl-lysine residues of the histone and non-histone targets, requiring NAD+ in the process. In humans, sirtuin family has seven members (HsSIRT1- 7) in different cellular locations. HsSIRT6 and 7 are class IV members. Recent reports have unraveled the biological role of HsSIRT7 in tumorigenesis via deacetylation of H3K18Ac. But the molecular mechanism behind it is not clear. Interestingly, HsSIRT6 has anticancerous effect. We are using both biochemical and structural biology approach to understand this mechanism in the maintenance of tumor phenotype. Three dimensional structures of HsSIRT7 with ligands will provide answers to its catalytic mechanism, substrate binding and overall structure. This will also help us in understanding the diversity of enzyme reactions within sirtuin family. HsSIRT7 is very specific for H3K18Ac and requires other protein partners like ELK4 for this deacetylation activity, biochemical studies are being carried out to understand these protein-protein in-teractions, which can be a potential inhibitor target. Mapping of the HsSIRT7 active site will also facilitate the structure based inhibitor studies with sirtuins.

RNAi analysis suggests down-regulation of OsSRT1 gene in rice resulting in DNA damage and cell death under oxidative stress conditions. Overexpression of this gene in Arabidopsis have shown in-creased tolerance against this stress. We are enzymatically characterizing rice sirtuins (OsSRT1 and OsSRT2) and their interacting partners leading to understand their physiological roles in plants. Using biochemical and biophysical techniques we will figure out sirtuins' regulatory mechanisms and answer the question whether it acts as a linker between the stress signals and DNA repair system in plants.

097

ONCOGENIC SPLICING SWITCH AND GLUCOSE METABOLISM IN BREAST CANCER

Keywords Epigenetics, Alternative splicing, Cancer, DNA methylation, Hypoxia

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The cancer cells thrive on glucose by converting it to lactate at the end of glycolysis. The phenomenon is known as aerobic glycolysis or Warburg effect and promotes the growth of the cancer cells. The alternative spliced isoform Pyruvate kinase M2 (PKM2) contributes to the Warburg effect by promoting aerobic glycolysis whereas PKM1 isoform promotes oxidative phosphorylation. The PKM gene contains two mutually exclusive exons, exon 9 and 10 which are alternatively included in the final transcript to give rise to PKM1 and PKM2 isoform respectively. In this study, we report that the intragenic DNA methylation-mediated binding of BORIS (Brother of regulator of imprinted sites) at the alternative exon of Pyruvate Kinase (PKM) is associated with cancer-specific splicing that promotes Warburg effect and breast cancer progression. Interestingly, inhibition of DNA methylation or BORIS depletion or CRISPR/Cas9-mediated deletion of BORIS binding site leads to splicing switch from cancer-specific PKM2 to normal PKM1 isoform. This results in the reversal of Warburg effect and inhibition of breast cancer cell growth, which may serve as a useful approach to inhibit the growth of breast cancer cells. Importantly, our results show that in addition to PKM splicing, BORIS also regulates alternative splicing of several genes in a DNA methylation-dependent manner. Our findings highlight the role of intragenic DNA methylation and DNA binding protein, BORIS in cancer-specific splicing and its role in tumorigenesis.

098

UNDERSTANDING MULTIDRUG RESISTANCE IN MYCOBACTERIA AND STRATEGIES TO COUNTER IT

Keywords Systems and Computational Biology, Genomics, Antibiotic Resistance, Production of Biologics in Mammalian systems

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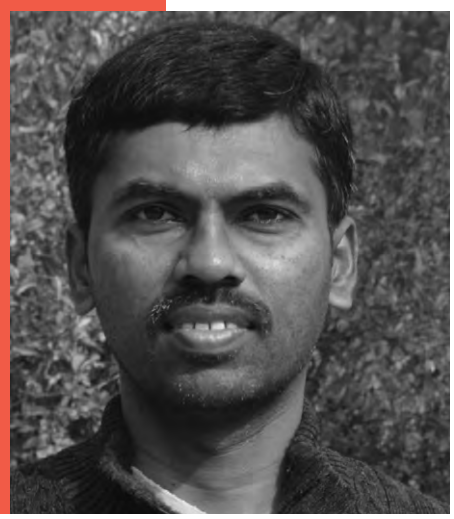
Emergence of antimicrobial resistance has emerged as a major public-health crisis, especially in developing countries as more and more clinically relevant pathogens are developing resistance. With the emergence of multi drug-resistant (MDR) and extreme drug-resistant (XDR) strains, there is a need to understanding the multiple ways in which bacteria develop resistance, especially to multiple drugs, to devise effective solutions and to develop novel antimicrobials.

Using *Mycobacterium smegmatis* as a model system, we are studying how bacteria respond, adapt and evolve under stress such as that from antibiotics. We use a combination of gene sequencing, expression analysis, biochemical studies and microscopy to understand the varied survival mechanisms that makes these bacteria tolerant to various antimicrobial drugs.

A detailed characterization of laboratory derived resistant mutants will also be presented to illustrate how resistance was found to be interplay of multiple mechanisms. Through measurement of transport kinetics of drugs into and out of cells, using fluorescent tracers, alteration in efflux of drugs in cells was found to be primarily responsible for multiple drug resistance. We are also working at ways to counter both intrinsic and acquired resistance using a variety of approaches such as drug repurposing and adjuvant therapy using nanoparticles and PNA. I will present some of the recent work in each of these areas.

099



ATSWEET12 SUGAR TRANSPORTER PLAYS ROLE IN NON-HOST RESISTANCE OF PLANTS

Keywords Nonhost Resistance, Sugar Transport, Plant Immunity

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Sugars are predominantly synthesized in the mesophyll cells and then transported into the phloem for long-distance translocation throughout the plant. The sugar transporters located on the plasma membrane are involved in the sugar efflux at the site of phloem loading. A new class of SWEET (Sugar Will Eventually be Exported Out) sugar efflux transporters have been identified in Arabidopsis with 17 members and few were shown to be involved in plant development and pathogenesis. For example, *Psuedomonas syringae* pv. tomato DC3000 infection in Arabidopsis highly induces the expression of few SWEET genes including AtSWEET11, AtSWEET12 and AtSWEET15. Further, under normal condition AtSWEET11 and AtSWEET12 are involved in phloem loading and efflux the sucrose from phloem parenchyma into the apoplast. We have identified the role of AtSWEET11 and AtSWEET12 transporters in the plant defense against nonhost pathogens namely, *P. syringae* pv. *phaseolicola* and *P. syringae* pv. tabaci and host-pathogen namely, *P. syringae* pv. tomato DC3000 by performing reverse genetic screening and transcript profiling. Our study, based on double and triple mutant analysis and apoplast sugar profiles, suggest a role for AtSWEET12 in regulating the sugar availability in response to non-host and host-pathogen and restricting the pathogen multiplication. Further, in-vitro quantification of bacterial pathogens in the apoplast extracts from single and double mutants indicate suggest that AtSWEET12 could regulate AtSWEET11 transporter to regulate sugar efflux mechanism during plant defense against bacterial pathogens.

THE EVOLUTION OF A TRANSPOSASE: WHY DO SOME GENES JUMP?

Keywords Mobile genetic elements, Transposable elements, Nucleic acid-protein interactions, Domesticated genes, GTP binding, hydrolysis & regulation

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The human genome contains ~ 50 genes that were derived from transposable elements and many are now integral components of cellular gene expression programs. Our research focuses on the newly discovered vertebrate homologs (THAP9) of the Drosophila P element transposase (TNP). The TNP protein is involved in the cleavage and subsequent integration of mobile P-element DNA transposon. P-elements are a family of DNA-based transposons in *Drosophila melanogaster* that move about the fruit fly genome, cause hybrid dysgenesis and have been used extensively as tools for *Drosophila* genetics and genomics. We have made the surprising discovery that human THAP9 is an active DNA transposase that, although domesticated, still retains the catalytic activity to mobilize transposons. This is the first report, beyond the V(D)J recombination system, of an active DNA transposase in the human genome.

The exact cellular function and physiological role of THAP9 is, however, still unknown although THAP proteins have been broadly implicated in various cellular processes like cell proliferation, apoptosis, pluripotency and transcription as well as human disease. Interestingly, THAP9 shares significant amino acid sequence homology with the amino-terminal THAP domain (involved in zinc-dependent DNA-binding), leucine-zipper coiled-coil dimerization domain, GTP-binding domain and catalytic domain of the *Drosophila* TNP.

Our current investigations include (1) Global analysis of *Drosophila* P element transposon-related genes as well as other transposon-derived genes in vertebrate genomes, (2) Mechanisms, regulation and functions of the vertebrate transposase THAP9 and its role in DNA binding and cleavage, possible nucleotide binding and oligomerization.

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CELL ORGANIZATION OUT OF EQUILIBRIUM

Keywords Collective behaviour in living systems, Synthetic ecology, Active matter, Soft condensed matter physics, Dynamical systems

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Cell theory, the concept of the cell as the basic unit of life, is a cornerstone of biology. But despite close to two centuries of probing them, cells and their functioning remain enigmatic. To a physicist, a cell is a bag of macromolecules, maintained out of equilibrium by appropriate chemical means, from which complex behaviors emerge. But how did the configuration of such a bag come about in the first place? After providing a brief overview of efforts so far to address this issue, I will present our experimental proposal in this direction. Continuing from there, I will present our efforts in understanding the organization of a cell that is driven far from its homeostatic equilibrium and discuss the mechanisms a cell employs to survive extreme perturbations.

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REGULATION OF CILIOGENESIS BY CYTOSKELETAL REARRANGEMENT IN MAMMALIAN CELLS

Keywords Ciliogenesis, Cell cycle, Cytoskeleton, Signaling, Tumorigenesis

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Centrioles either form the core of a centrosome or transform into basal bodies that assemble cilia in a cell cycle dependent manner. Centrosomes serve as the poles of the mitotic spindle that ensures accurate genome segregation. Cilia are membrane-ensheathed microtubule-based projections from cell surface. Non-motile primary cilia (PCs) are found in most mammalian cells, generally during interphase or cellular quiescence (G0-phase), and are resorbed once cells re-enter S-phase. PCs perform sensory functions or mediate critical signaling pathways such as Hedgehog signaling. Numerous human disorders are associated with ciliary dysfunction. Also, PCs may both promote and prevent tumorigenesis through regulating aberrant signaling. I have previously found that VDAC1 and VDAC3, two of Voltage Dependant Anion Channel proteins, best known as mitochondrial porins, suppress cilia assembly in growing cells. VDAC3 also regulates the centrosomal targeting of Mps1 kinase, a spindle assembly checkpoint protein and a regulator of centriole assembly. Based on these data and other studies, I hypothesize that VDAC1 and VDAC3 perform non-overlapping functions to control ciliogenesis and that actin cytoskeletal dynamics at the vicinity of apical membrane regulate ciliogenesis. I will address the following aims to test my hypotheses:

AIM-1
How does cytoskeleton rearrangement regulate ciliogenesis?

AIM-2
How do the VDACs regulate centriole assembly and ciliogenesis?

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INFLAMMATION AND DIABETES: CHARACTERIZATION AND TREATING DIABETIC ULCERS

Keywords Drug delivery, Biomaterials, Immune cell longevity, Immuno-engineering, Innate immunity

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Inflammation is an integral part of diabetes, however, the link between the two remains poorly characterized. Previous studies on Caucasian populations has shown that obesity causes inflammation leading to diabetes[1], but such a link has not been confirmed in the Indian population. To specifically address this gap in knowledge, we are studying the independent effects of obesity and hyperglycemia on innate immune cell activation. We have initiated a pilot study to characterize innate immune cell numbers and phenotype in obese and non-obese diabetics. This study is currently at the stage of subject recruitment.

Simultaneously, we are developing a sequential drug release system that could treat the problem of both inflammation and tissue regrowth in diabetic ulcers. Current treatment strategies for diabetic ulcers focus on either wound management through debridement and bandaging, or trying to heal the wounds using biologics[2]. However, a vast majority of ulcers still do not heal completely. Recent studies suggest that the presence of a chronic inflammatory environment at ulcer sites might contribute to the absence of complete healing seen with current treatment options[3]. To address this issue, we are developing drug delivery systems that sequentially release an immunomodulatory factor and tissue healing growth factors. These systems will eventually be tested in animal models for their potential to heal diabetic ulcers.

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DIFFERENTIAL ACTOMYOSIN CONTRACTILITY IN MIGRATION OF TUMOR CELL

Keywords Cell Migration, Tumorigenecity, Neuritogenesis, Nonmuscle Myosin Ii, Alternative Splicing, Actomyosin Complex

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Bleb formation has been correlated with nonmuscle myosin II (NM-II) activity. Whether three isoforms of NM-II (NM-IIA, -IIB and -IIC) have the same or differential roles in bleb formation is not well understood. Here we report that ectopically expressed, GFP-tagged NM-II isoforms exhibit different types of membrane protrusions, such as NM-IIA induces multiple bleb protrusion and NM-IIC1 induces lamellipodia, whereas multiple blebs or lamellipodia formation was not affected by over expression of NM–IIB in tumor MCF-7 cells. Of interest, NM-IIB has an almost 50% lower rate of dissociation from actin filament than NM-IIA and –IIC1 as determined by FRET analysis both at cell and bleb cortices. Interestingly, when cor-tex was ablated in metastasis tumor MDA MB 231 cells, we find majority of cells (88%) show multiple blebs formation whereas majority of normal MCF-10A cells (57%) show only single bleb formation at the site of cortex ablation, suggesting the presence of differential actomyosin contractility in the different degree of tumor cells. We correlate that differential actomyosin contractility is dependent on the type of NM II isoform present in the actomyosin complex. This study also suggests tumorigenecity can be evolved by changing the actomyosin contractility.

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VIRTUAL SCREENING AND BIOLOGICAL EVALUATION OF NOVEL AGONISTS TARGETING BETA-2 ADRENERGIC RECEPTOR TO INHIBIT BRONCHIAL ASTHMA

Keywords Rational drug designing, Asthma, Diabetes, Cancer, Structural Biology

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Asthma is a multifactorial complex disorder caused mainly by environmental risk factors along with hereditary, which currently affects about 340 million people across the globe and incurs a significant healthcare cost. Studies in the asthma-related research proven that Beta-2-adrenergic receptor, encoded by the ADRB2 gene (GPCR family) plays a vital role in bronchodilation. Unfortunately, current therapy lacks satisfactory success due to several reasons few among them is limited understanding of poly-morphs (SNP) role, SNP's impact on binding affinity of present existing agonist in refractoriness of asth-ma. Unfortunately, few subset of patients may not reach an optimal medication owing to the difference in genetic pattern with resistance to bronchodilator therapy. Considering virtual screening was carried out to identify new analogues of highly potent novel efficacious beta-2 agonists from nature, chemical databases, organic labs by logical pharmaceutical developments for better management of asthma to overcome the drawbacks of traditional beta-2 agonists. Further molecular level studies will pave the way for structure-based drug designing with more specificity and sensitivity.

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PHYSICS IN BIOLOGY AND MEDICINE: FROM IMAGE PROCESSING AND NONINVASIVE DIAGNOSTICS TO PHAGE-BACTERIA INTERACTIONS

Keywords Systems Biology (Theory and experiments), Network Science, Complex Systems,Physics in Biology and Medicine, Mathematics, algorithms, and, Computation

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Networks have provided new insight into a variety of biological systems[1-3]. Herein, we use networks to present a fresh and general approach in the classic problem of feature extraction from dynamic, multidimensional images. In collaboration with clinicians of Calcutta Medical College, we test our methods on patients with dry eye disease[4]. We show how our process can be used to construct smart and portable non-invasive diagnostic devices[5].

We employ an iterative cycle of modeling and experimentation to study the dynamics of Mycobacteriophage-Mycobacterial host interactions[6]. Combining experiments with delay differential equations and Monte Carlo simulations, we observe that phage infection leads to increased production of ROS which appears to be a new mechanism for host lethality in addition to lysis.

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SIZING AND SHAPING EMBRYONIC DEVELOPMENT, ONE PLOIDY AT A TIME

Keywords Zebrafish, Early embryogenesis, Altered ploidy, Zygotic genome activation, Cell Biology

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Deviation of ploidy from an endogenous state is incompatible with normal development of all animal species. However, experimentally generated zebrafish haploids and tetraploids execute an early developmental program but die by 6-7 days post fertilization. Such altered ploidy lethality has been attributed to molecular changes in embryos due to change in genome content. However, molecular changes can occur only when the zygotic genome becomes transcriptionally active, which occurs a few hours after fertilization. Much earlier than this, fertilization of an egg triggers embryonic development of the one-cell zygote by executing iterative rounds of reductive divisions to form a multicellular embryo. Co-ordinated inter-cellular interactions after zygotic genome activation trigger epiboly and gastrulation movements, which reorganize the mass of blastoderm cells into layers of tissue, which eventually form organs in the embryo.

We find that altered ploidy also changes fundamental attributes like cell shapes and sizes in the zebrafish blastoderm. During the key developmental phases of epiboly and gastrulation, altered cell shapes and sizes trigger suboptimal cell migration movements, which places tissues in spatially different contexts at the end of gastrulation in haploids and tetraploids. I will discuss our attempts to understand the molecular mechanisms that could determine cell shapes and sizes in rapidly dividing embryos and the consequence of altering such mechanisms in haploids and tetraploids. Our work reveals that early cell biological defects in addition to dosage compensation errors (perhaps due to faulty zygotic genome activation) may exacerbate a faulty developmental program that culminates in eventual lethality of non-diploid embryos. Fundamentally, our work also sheds light on the ability of DNA content to dictate sizes of cells and intracellular organelles in a dynamically evolving system such as a developing vertebrate embryo.

METABOLIC CHARACTERIZATION OF PENJAR ACCESSIONS DURING RIPENING AND POSTHARVEST STORAGE

Keywords Tomato fruit ripening, Functional genomics, Proteomics and metabolomics, Fruit quality, Fruit shelf life

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Many of the Penjar accessions of tomato that are widely grown in the Mediterranean region are known to exhibit a prolonged shelf life. The molecular basis for the long shelf life of many of these accessions was shown to be the alcobaca mutation, which leads to a substitution of valine to aspartic acid at 106th position of NAC-NOR protein. In the present study, we examined 4 different Penjar accessions in greater detail to uncover the metabolic basis underlying the prolonged shelf life. Out of four Penjar accessions, three had alc mutation as expected, whereas, one turned out to be a novel allele for nor, with only 6 amino acids in the encoded protein. Consistent with the nature of the mutations, all these accessions exhibited delayed ripening, and prolonged shelf life, both on-vine and off-vine compared to AC (Ailsa Craig, reference cultivar). Interestingly, these accessions displayed differences in the fruit phenotype, and the fruit colour varied from orange to red. Apparently, mutations in nor also attenuated carotenoid levels in Penjar accessions by suppressing the gene expression of phytoene synthase 1, a key rate limiting enzyme for carotenoid biosynthesis. Though the pattern of ethylene burst is similar in AC and Penjar fruits, consistent with delayed ripening and lower carotenoid content, the ethylene emission from Penjar fruits was significantly lower than AC. In addition, a concerted down regulation of a number of cell wall modifying genes was observed in Penjar fruits compared to AC, contributing to their prolonged shelf life. Metabolite profiling using GC-MS during ripening and postharvest storage revealed the differential accumulation of Krebs cycle intermediates and other primary metabolites in Penjar fruits which may contribute towards long shelf life and the data would be presented.

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DYNAMIC RECIPROCAL CONDENSATION OF ALTERNATE LAMINA AND INTER LAMINA ASSOCIATION DOMAINS ACCOMPANIES EMBRYONIC STEM CELL DIFFERENTIATION

Keywords Nuclear Organization, Genome Architecture, Cellular Differentiation, Epigenomics, Chromatin Dynamics

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Based on electron and fluorescence imaging of interphase cell nucleus and biochemical fractionation and characterization of nuclease digested nuclear chromatin, it has been demonstrated that chromatin is segregated into decondensed, gene rich, often centrally located euchromatin and condensed, gene poor, often peripherally located heterochromatin. However, formal depiction of high resolution condensation states of chromatin on genome-scale is lacking. Using a novel chromatin compaction capture methodology, we have generated genome-wide chromatin condensation maps of undifferentiated embryonic stem cells and compared it with other differentiated cell-types such as neural progenitors, astrocytes and foetal, adult liver cells. Our analysis not only suggest cell-type specific nature of chromatin condensation but also uncovers that regions of chromatin condensation and decondensation alternate with each other across all chromosomes and is a unifying property of interphase chromosome organization both in undifferentiated as well as differentiated cell-types. We further characterized alternate domains of compaction and decompaction as cell-type specific Lamina and inter Lamina Associated Domains respectively. By deriving, integrating and comparing differential compaction maps, genome-wide chromosome conformation capture (Hi-C) derived long-range chromatin interactions and gene expression profiles of multiple cell-types with ESCs, we postulate that reciprocal compaction of alternate lamina and inter lamina associated domains might facilitate cell-type specific long-range chromatin interactions to execute cell-type specific gene expression patterns in the genome.

MACROSCOPY TO MICROSCOPY: A BIOMEDICAL IMAGING PERSPECTIVE – INTRODUCING NON-INVASIVE PHOTOACOUSTIC IMAGING

Keywords Photoacoustic Imaging

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Tissue characterization in a non-invasive manner has always been a very important problem to be tackled. In this context, photoacoustic imaging is a laser-based ultrasound technique that has shown very high sensitivity in tissue characterization particularly in the diagnosis of cancer and other related diseases. Photoacoustic imaging can be called a pump-probe technique. The excitation of the sample is performed using a pulsed nano-second laser while the signals originated from the sample, due to excitation, is acquired using an ultrasound sensor. After excitation of the biological sample (e.g., biological tissues, blood etc.) by a pulsed laser, the sample absorbs the light and converts into heat. The sample, after absorption, experiences non-radiative relaxation through the form of acoustic waves. Acquiring these acoustic waves through ultrasound sensors can provide tissue imaging abilities better than the existing techniques. The advantage with this technique is that the excitation happens optically and the acquisition is through ultrasound waves, thereby reducing scattering by one order in tissues.

While the above-mentioned conventional photoacoustic system is being built in the lab, this project would focus on continuous wave (CW) laser-based photoacoustic technique. The advantage of CW based technique is the compact system which can be easily translated to hospitals and biomedical research centers for clinical trials. In addition, the cost of the system would go down to a large extent, thereby having the ability to realize the potential of photoacoustic imaging in developing countries like India.

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MICROGLIAL INTERNALIZATION AND POST-TRANSLATIONAL MODIFICATIONS OF TAU

Keywords Pathological conformations of Tau in neuronal system, Signaling cascades of Tau (CDK5, GSK3 beta and their inhibitors, Nuclear transport of Tau (Ran GAPs and Ran GTPases), Extracellular Amyloid βeta (Aβ) mediated Tau (axonal protein) Glycation, Chaperone mediated Tau (axonal protein) Glycation/ Phosphorylation

Alzheimer's disease (AD) is a neurodegenerative disorder caused by protein misfolding, aggregation and accumulation in the brain. Tau tangles and amyloid-β plaques are the key players in the pathogenesis of AD. Tau is a microtubule-associated protein present in the axons of the neurons, which help in assembly and stabilization of microtubules. In AD, the hyperphosphoryated Tau is found in abnormal fibers, which are one of the histopathological hallmarks in AD brain. Furthermore, Tau is primarily an intra-cellular protein normally bound to microtubules and critical for promoting the assembly and disassembly, more recent evidences suggests that presence of substantial soluble extracellular Tau in brain interestial fluid as wells the release of Tau from neurons following their depolarization. Microglia have been shown to co-localize with both amyloid plaques and neurofibrillary tangles (NFTs) although their exact role in plaque and or tangle formation is unclear. Whether or not microglia play a role in Tau clearance in the aspect of posttranslational modification and spread in brain has to our knowledge never been studied. The role microglial cells in the development and the progression of Alzheimer's disease has not been elucidated yet. However, it is not known whether microglia play a similar role in the clearance of intracel-lular Tau, the major component of neurofibrillary tangles (NFTs).

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ER STRESS - A LINK TO ORGANELLE BIOGENESIS AND SKIN HOMEOSTASIS

Keywords Protein Trafficking, Organelle Biogenesis, Skin Pigmentation, Lysosome-Related Organelles

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Human epidermis is composed of basal and suprabasal layers consist of proliferative and differentiated keratinocytes respectively. The cells of suprabasal layer terminally differentiated further into corneocytes and form stratum corneum, the outermost layer of epidermis. Thus, the epidermal integrity of skin is maintained through a tight regulation between keratinocytes proliferation, differentiation and death processes. To understand the homeostasis mechanisms, we have studied the processes of autophagy and lysosome biogenesis during the differentiation of neonatal primary human epidermal keratinocytes (NHEK). Our study provides first evidence that mTOR-independent, ER (endoplasmic reticulum) stress-dependent Golgi-associated lysosome biogenesis is essential for keratinocyte differentiation, which is critical towards the understanding of skin health and hygiene.

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HIWI2 PLAYS AN IMPORTANT ROLE IN RETINAL PATHOLOGIES BY REGULATING TGFB AND VEGF SIGNALING PATHWAYS

Keywords SNARE, PIWI/piRNA, Retina, Neurodegeneration, Vesicular Trafficking

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BACKGROUND

PIWI-like proteins, which were initially thought to be germline specific, have been recently reported to have importance in somatic cells as well. HIWI2 is needed to maintain the integrity of retinal pigment epithelium by influencing the tight junction proteins. In this report, we studied the effect of HIWI2 in relation with diabetic retinopathy, where loss of tight junctions is a crucial step.

METHODS

Real time PCR was done to analyse the expression of EMT markers in dsi-RNA treated HIWI2 cells. Zymography was carried out to examine the expression of matrix metalloproteases.Western blot was performed to observe the expression of TGFβ. Real time PCR and ELISA was carried out to analyse the expression of VEGF. HIWI2 blot was performed in the vitreous humour of patients with proliferative diabetic retinopathy (PDR).

RESULTS

Silencing of HIWI2 in retinal pigment epithelial (RPE) cells reduces the expression of TGFβ. Ac-cordingly, the expression of alpha smooth muscle actin and MMP9 transcripts were downregulated whereas E-cadherin was increased in Si-HIWI2 cells. In addition, protein expression of MMP9 was also downregulated upon HIWI2 silencing. VEGF, which is known to be induced by TGFβ, is also downregulated both at mRNA and protein levels in Si-HIWI2 cells. Further, expression of HIWI2 is elevated in the vitreous of patients with PDR.

CONCLUSION

HIWI2 influences VEGF and TGFβ pathways in RPE, thus might regulate the epithelial to mesenchymal changes. Collectively, our data suggests that HIWI2 may control fibrosis formation during retinal pathology.

FORMATION AND STABILITY OF PREBIOTIC AMPHIPHILIC SYSTEMS: IMPLICATIONS FOR THE ORIGINS OF CELLULAR LIFE

Keywords Origins Of Life, Astrobiology, Prebiotic Processes, Informational Polymers, Molecular Evolution

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How life chemically originated is an intriguing mystery. Though the sequence of events remains elusive, processes crucial for the transition from chemistry to biology have been delineated. One of these is abiogenic origin of polymers on the early Earth, a fundamental step in the transition from non-life to life as most functions in biology are driven by polymers. Many pertinent theories have been put forward[1], with a general hypothesis that these reactions would have been chemically driven in environments sub-jected to dehydration and rehydration (DH-RH) cycles[2]. One proposed niche is that of terrestrial geo-thermal fields that support energetically uphill oligomerization reactions[3]. Importantly, lipids[4] catalyze the formation of informational molecules [5]; a prebiotically pertinent process as encapsulation of functional polymers in membranes would have been crucial for the evolution of cellular life[6]. Although modern membranes are formed from complex lipids, primitive membranes are thought to form from simpler amphiphiles like fatty acids (FAs) and their derivatives[7]; their formation occurring under specific conditions of pH and temperature[8]. However, the repertoire of FAs that can form vesicles and their overall stability has not been systematically studied. I will detail FAs that result in vesicles under laboratory-simulated & realistic conditions, and their stability in DH-RH regimes. Our results suggest that mixtures of FAs and derivatives form stable vesicles robustly and that the origin of cellular life would have been both, niche & geochemical context dependent.

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SOPHISTICATED SYNAPSES - A QUANTITATIVE INSIGHT INTO CRUCIAL COMPONENTS OF HIGHER FUNCTION

Keywords Neuroscience, Synaptic Plasticity, Alzheimer's Disease, Calcium signalling, Computational

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Synapses, highly specialised components of neuronal networks comprise a plethora of molecular mechanisms that operate over multiple timescales in distinct morphologies across brain areas. The patterns of activity that arise determine information transmission and storage. Small changes in this high-dimensional system can have far reaching consequences that transcend levels of organisation in the nervous system and can also be causally linked to pathological conditions.

Our approach is to devise physiologically realistic computational models of these sophisticated neural components that allow for 'In-Silico' experiments. A detailed modelling paradigm can lead to new insights, especially since direct measurements within the confines of a typical synapse are difficult.

The poster will show distinct roles played by different sources of calcium in orchestrating the precise spatiotemporal calcium signal underlying plasticity and its implications in Alzheimer's Disease.

Given the degeneracy in the molecular machinery that can potentially arrive at the same down-stream effects, we constrain our investigation to a CA3-CA1 synapse, and ask the relevance of some these degrees of freedom available to the synapses. Our ultimate goal is to understand the contribution of each of these pathways to higher level function.

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INTRODUCTION OF BULKY SIDE CHAINS AFFECT THE FUNCTIONAL ACTIVITY OF *VIBRIO CHOLERAE* DIGUANYLATE CYCLASE

Keywords Structural Biology, Cholera Biology, Natural Therapeutics Phage Proteins, Micrornas in Cancer

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Vibrio cholerae, the cause of seven noted pandemics leads a dual lifecycle – one in the human host in its virulent form, and the other as a sessile bacteria in aquatic bodies, residing as non-virulent forms in surface biofilms. Surface biofilms are almost always, associated with a GGD(/E)EF protein, responsible for diguanylate cyclase activity. The Sebox3 protein, a diguanylate cyclase from *V. cholerae* has been shown to be an important component of the biofilm formation process in the bacteria[1]. The crystal structure of Sebox3 too has revealed typical GGEEF architecture in its active site.

Site-directed mutants of Sebox3 at the central residues of the GGEEF domain in the wild type protein, have distinct reduction in their ability to form surface biofilms, as well as in the synthesis of cyclic-di-GMP from GTP (diguanylate cyclase activity)[2]. This inability has been traced to the structure of two of the mutants of Sebox3, further named as Sebox5 and Sebox 6. In Sebox5, the second glycine has been replaced by an arginine, and in Sebox 6, the the first glutamate was replaced by a lysine. The wild type Sebox3 has an eminent GTP-binding pocket, where the glutamate forms extensive contacts with an in-coming GTP. In the mutants, the shape of the pocket is altered due to the arginine or the lysine side chain which interferes with the entry of the GTP, and thereby leads to a loss of activity. The understanding of the activity of the diguanylate cyclase and the mechanism of steric inhibition in the mutants can go a long way in the design of functional mutants in *V.cholerae*.

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MOLECULAR CHARACTERIZATION OF THE NATIVE AND ENGINEERED OPTOGENETIC TOOLS FOR STUDYING CAMP SIGNALING

Keywords Optogenetics, Ciliopathies, Channelopathies, Photoreceptor, Ciliary GPCR

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The application of rhodopsins to remotely control neural activity has sparked interest to search and develop other genetically encoded photoswitch(s) for controlling signaling and protein-protein interaction events in target cellular system. Light sensitive proteins (rhodopsins, BLUF-coupled cyclase and phyto-chromes etc) have been used to control intracellular ion fluxes (action potential), cAMP and protein-protein interaction events in the cells simply by illumination. Initially, photoactivated adenylate cyclase (PAC) identified in *Euglena* as blue light receptor, which was responsible for photophobic response. *Euglena* PAC (ePAC) was utilized as optogenetic tools for controlling cAMP level in cells and in whole animals (*Drosophila* and Nematodes). A smaller bacterial PAC (bPAC) was characterized for the blue light activated cyclase activity and bPAC was used as optogenetic tool for manipulating cAMP *in vivo* condition. Recently, we have shown modulation of cyclic nucleotide-mediated cellular signaling and gene expression using photoactivated adenylyl cyclase (bPAC) as an optogenetic tool(Scientific Reports 7, 12048, 2017). Optogenetic modulation of the cyclic nucleotides (cAMP and cGMP) mediated signaling will be presented in detail.

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INTEGRATIVE GENOMICS IDENTIFIES NCoR1 AS A MASTER REPRESSOR OF TOLEROGENIC PROGRAM IN DENDRITIC CELLS

Keywords Immunogenomics, Functional genomics, Immunology, Dendritic Cell Biology, Systems Biology

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Dendritic cells (DCs) fine-tune the balance between immunity and tolerance. Therefore, the therapeutic potential of tolerogenic DCs for autoimmune and graft versus host diseases has been widely proposed. Here, we show that nuclear receptor co-repressor 1 (NCoR1) repressed DCs become tolerogenic upon activation regardless of the stimulus. A wide variety of tolerogenic molecules are upregulated in these DCs upon activation and as a consequence, they induce Treg differentiation *in vitro* and *in vivo*. Interestingly, we identified NCoR1 as a switch repressing DC tolerogenicity by masking the effects of transcription factors such as NFkB (RELA) after activation. Furthermore, bacterial and parasite infection in NCoR1DC-/- animals enhance Tregs in draining lymph nodes with a concomitant increase in disease burden. We thereby found that adoptive transfer of CpG pulsed NCoR1 knockdown DCs in helminth-infected mice increased both Treg and intestinal worm load. Collectively, our results identify NCoR1 as a promising target to generate tolerogenic DCs.

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NEUROFIBRILLARY TANGLES (NFTS) MEDIATED CONSERVED MECHANISM OF THE PATHOGENESIS OF NEURONAL TAUOPATHIES IN HUMAN AND *DROSOPHILA*

Keywords *Drosophila*, Neurodegeneration, Tauopathies, Polyglutamine (polyQ), Development

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Hyperphosphorylated tau mediated formation of toxic Neurofibrillary Tangles (NFTs) in brain tissues has been implicated as the hallmark of the pathogenesis of neuronal tauopathies such as Alzheimer's and Parkinson's diseases in human and mammalian models. However, *Drosophila* models of human tauopathies such as Alzheimer's and Parkinson's diseases were suggested to manifest the human-tau (h-tau) mediated neuronal loss and behavioural deficits without NFT formation. It was proposed that perhaps the soluble oligomers of phosphorylated h-tau lead to neurotoxicity and phenotypic manifestations in *Drosophila*. For the first time, we demonstrate discrete formation of typical neurofibrillary tangles in h-tau expressing neuronal cells in *Drosophila*, and this appears as the fundamental cause of disease pathogenesis. Intriguingly, our findings suggest a NFTs mediated conserved mechanism of the pathogenesis of neuronal tauopathies in human and *Drosophila* disease models. We further demonstrate that tissue specific downregulation of a *Drosophila* homolog of human c-myc proto-oncogene (dmyc) suppresses the manifestation of h-tau mediated neurodegenerative phenotypes by limiting abnormal tau hyper-phosphorylation and heterochromatin loss.

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FUNCTIONAL CHARACTERIZATION OF MALE REPRODUCTIVE TRACT PROTEINS

Keywords Antimicrobial Proteins, Male Contraception, Transgenesis, Sperm Function, Reproductive Toxicology

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The male reproductive tract secretes proteins belonging to different families. A vast majority of them remain uncharacterized. We identified and functionally characterized proteins belonging to the Sperm Associated Antigen 11 (SPAG11), Prostate and Testis Expressed (PATE) and Lysozyme-like (LYZL) families. Proteins of these families were found to possess potent antimicrobial activity. Further, they potentiated the efficacy of antibiotics when used in combination with antimicrobial proteins. Male reproductive tract antimicrobial gene and protein expression was epigenetically controlled. Epigenetic modulators boosted antimicrobial expression (innate immune responses). These observations gave a lead to develop them as alternatives for antibiotics to treat infections. On the other hand, proteins of the male reproductive tract were found to govern sperm function. Animal models to transiently or stably knock down testis specific genes were used to study their functional role. Under these conditions, the spermatozoa produced lacked the ability under capacitation and acrosome reaction, thus leading to severe loss of fertility. Our findings provided vital clues for the functional importance of testis specific proteins in sperm function and fertility.

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IDENTIFICATION OF NUCLEOTIDE-BINDING DOMAIN, LEUCINE-RICH REPEAT CONTAINING, PROTEINS IN GLIOMAS

Keywords Innate Immunity, Inflammasomes , Cell Death, Cancer, Glial Biology

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Malignant gliomas, arise from glial cells within the central nervous system, are among the most fatal human cancers[1]. Even after aggressive therapy most patients succumb to their disease within 2 years of diagnosis. There is an urgent need for development of therapies. Gliomas are heavily infiltrated by innate immune cells. Among these microglia and macrophages are prominent. These interact with tumor cells to promote tumor growth and migration. Our innate immune system consists of a sophisticated detection mechanism for pathogens, irritants and damage-associated molecular patterns. This detection mechanism consists of the several receptor families, including the recently discovered, Nucleotide-binding domain (NBD); leucine-rich repeat containing (LRR) proteins (NLRs)[2-4]. Genetic mutations in NLRs are known to cause autoinflammatory diseases in humans. Even though NLRs have been report-ed to play a role in inflammation in the brain there is no report of a link between NLRs and gliomas [5]. We aim to understand glioma molecular pathways in cells and human brains from the Indian subconti-nent to aid development of therapeutic interventions against gliomas.

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DYNAMICS OF SOIL ARSENIC AND MITIGATION THROUGH IRRIGATION MANAGEMENT IN BENGAL DELTA REGION: ASSESSMENT OF HUMAN HEALTH RISK

Keywords Biogeochemistry, Geomicrobiology, Biodegradation, Environmental Health Toxicology and Human Health Risk Assessment

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Arsenic is the greatest threat from the socio-environmental perspective, where contamination is getting outraged to every groundwater aquifers, forming a cyclic flow to the soil-plant system and reverted back to the water due to soil infiltration. A regular implementation of arsenic contaminated groundwater for rice cultivationraises diverse health issues for millions of peoples. West Bengal, to be particular, district Nadia is one of the most adversely affected zones where studies have been made in an attempt to mitigate arsenic to rice grains by changing redox condition. Primary identification of intensity of arsenic contamination to a particular area of that district helps to track the influential abiotic factors of soil likely pH, redox potential, organic content, with relative translocation pattern of arsenic from soil to rice grain. Earlier studies showed that the involvement of arsenic resistant soil microbiota in an association of some pteridophytes can participate as in prior mitigation approach of rice cultivation. Both monsoonal (Amon) and wintery (Boro) cultivation differ in their accumulation ad distributional pattern of arsenic in field soil due to a varied application of either rainwater or groundwater, respectively. This also depends on its subsequent wash out rate or percolation rate of arsenic in continuously water saturated or periodically water-saturated fields. Prior study of dry-wet water management in rice fields led to the introduction of intermittent cultivation process that involves the raised bed technique with a V-shaped furrow in between two beds filled with water compared to the conventional flooded cultivation. This practice proved to be effective in reducing a load of arsenic to the rice grain near around the safe limit with consecutive application reducing the bioavailability of arsenic making its applicability for the better rice production with less human health risk.

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IMPORTANCE OF CELLULAR ORGANELLES IN CONTROLLING THE MIRNA-MEDIATED GENE EXPRESSION IN MAMMALIAN CELLS

Keywords microRNA biogenesis and turnover in immune cells , Compartmentalization of Post-transcriptional events, Extracellular Vesicles and Cancer, microRNA export and metabolic processes, Neuro degeneration and microRNA

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miRNA-mediated repression controls expression of more than half of protein coding genes in metazoan animals. Translation repression is associated with target mRNA degradation initiated by decapping and deadenylation of the repressed mRNAs. Earlier evidence suggest Endoplasmic Reticulum (ER) as the site where miRNPs interact with their targets before the translation repression sets in but the subcellular location of subsequent degradation of miRNA-repressed messages was unidentified. We explore the subcellular distribution of essential components of degradation machineries of miRNA-target mRNAs. We have noted that interaction of target mRNAs with AGO2 protein on ER precedes the relocalization of repressed messages to Multivesicular Bodies (MVBs). The repressed messages subsequently get dead-enylated, lose their interaction with AGO2 and also become decapped. Blocking maturation of endosomes to late endosome and MVBs by targeting the endosomal protein HRS, uncouples miRNA-mediated translation repression from target RNA degradation. HRS is also targeted by the intracellular parasite Leishmania donovani (Ld) that curtails HRS level in infected cells to prevent uncoupling of mRNA-AGO2 interaction, prevent degradation of translationally repressed messages and thus stop recycling of miRNPs pre-engaged in repression. Importance of other players in this process will be discussed.

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LOSS OF SOLUBILITY AND FUNCTIONAL IMPAIRMENT OF RESPIRATORY CHAIN SUBUNITS MARKS THE ONSET OF PROTEOTOXICI-TY IN PROTEASOME-INHIBITED CELLS

Keywords Protein misfolding, Protein aggregation, Amyloids, Transcellular proteotoxicity, Respirasome

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All proteins tend to form aggregates at unfavourable conditions. Sometimes, slight perturbation of the environment may lead to misfolding and aggregation of a significant fraction of the cellular proteome. In many age-related diseases, presence of amyloids upsets the overall protein metabolism and reduced functionality of various nodes of the protein homeostasis network accelerates widespread protein aggregation. In this study, we blocked proteasome-mediated protein degradation in mammalian cells and performed quantitative mass spectrometry to investigate the proteome partitioning events from soluble to the insoluble fraction. We observed that a shorter exposure to proteasome inhibitor MG132 resulted in aggregation and dose-dependent loss-of-function of the proteostasis-sensor protein FlucDM-EGFP. Among the endogenous proteins, chromatin reorganization factors and respiratory chain subunits were found to be highly reorganized suggesting reprogramming of transcription and reduced respiratory function. Mitochondrial depolarization is a known outcome of long-term proteasome inhibition and our observations suggested that this may be seeded by slow but steady loss of functional components of respiratory chain complex I and IV with time. High resolution respirometry revealed significant decrease in com-plex IV activity by a shorter exposure to proteasome inhibitor while a longer treatment lead to decrease in both complex I and IV activities. Insolubility and aggregation of the EGFP-tagged respiratory chain subunits was confirmed by microscopy. Blue-Native PAGE followed by quantitative mass spectrometry experiments suggested destabilization of mitochondrial re.

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IDENTIFICATION OF A NOVEL PROKARYOTIC LIKE TOXIN-ANTITOXIN MACHINERY IN *LEISHMANIA DONOVANI:* A UNIQUE THERAPEUTIC TARGET

Keywords Molecular Parasitology, Leishmaniasis, Malaria, Host-Pathogen Interactions, Cell Signaling

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All prokaryotic genomes encode for toxin-antitoxin (TA) systems which have been linked to various cellular functions such as virulence, antibiotic resistance, programmed cell death, etc. Zeta toxin is a member of such TA family encoded "exclusively and throughout" the genome of pathogenic prokaryotes. We, for the first time identified and characterized such an interesting system in a deadly eukaryotic pathogen, *Leishmania donovani.* Zeta toxin is a small molecule kinase converting UDP-N-acetylgalactosamine (UNAG) to uridine diphosphate-N-acetylglucosamine-3'-phosphate (UNAG-3P). UNAG is conjugated to phosphoenolpyruvate by MurA enzyme eventually leading to the biosynthesis to peptidoglycan. UNAG-3P resembles MurA tetrahedral intermediate and could bind to MurA but does not get further processed or released leading to the termination of reaction. We identified a zeta toxin like protein (ZLP) encoded in the genome of *L. donovani* by homology search. *E. coli* cells expressing rZLP displayed massive cell death as compared to vector control. Further, cells expressing rZLP were PI positive, and were unable to undergo cytokinesis while karyokinesis was complete. We further found that rZLP displayed strong kinase activity in presence of UNAG, while in its absence it also, it exhibited weak kinase activity suggesting autophosphorylation of ZLP. Moreover, formation of UNAG-3P in the assay was identified by HPLC. IFA of promastigotes with anti-rZLP serum indicated strong expression of ZLP in the parasites which further was enhanced when parasites were shifted to lower pH at 37°C, the ambient conditions for amastigotes growth. The inhibition of ZLP, affects growth of the parasites. Take together, ZLP, an important component of TA system having kinase activity, is expressed in *L. donovani* parasites and blocking the activity affects the growth of parasites. Presence of zeta toxin in trypanosomatids and prokaryotes but not in higher eukaryotes makes it an excellent drug target.

SOCIAL ORGANISATION IN THE ASIAN ELEPHANT

Keywords Socioecology, Animal Behaviour, Phylogeography, Conservation Biology, Evolution

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We study social organisation in the Asian elephant and the relative roles of ecological factors and genetic relatedness in shaping it. Through long-term monitoring of elephants in Nagarahole and Bandipur National Parks (Kabini population), we have identified over 800 individuals. This is the first such study in India and one of the small numbers of studies worldwide monitoring such a large number of individuals of any mammalian species.

Based on elephant sightings and using social network analyses, we find female society to be structured into highly modular communities (clans). The society is intermediate between an individual-based and a flexibly-nested fission-fusion society, in which either individuals or small groups may merge together or split away temporarily. We also find that there are underlying similarities in social structure across populations, which may be obscured by differences in group sizes (set by ecological constraints). Unlike the function usually seen, of fission-fusion dynamics allowing for an increase or decrease in group size in response to (often seasonal) ecological factors, fission-fusion in this population seems to be a means of maintaining multiple associates under relatively constant, small group sizes. Close female associates are significantly related to one another based on genotyping females from dung-extracted DNA. However, unrelated females may also provide benefits during between-clan dominance interactions. We have been collecting data on food plant availability and distribution, and dominance interactions within and between clans to test predictions based on socioecological theory.

We also study male-male associations and find that associations are non-random, depending on the ages of the males and the presence or absence of females in the vicinity. We also use basic information from the Kabini population to assess census techniques such as sex ratio estimation or mark-recapture population estimation.

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TOWARDS STRUCTURAL UNDERSTANDING OF mRNPs INVOLVED IN TRANSLATIONAL CONTROL

Keywords Portein synthesis, Translational control, Molecular machines, Cryo-electron microscopy, Structural biology

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During translational initiation the start codon in mRNA is recognized and decoded at the P site of the small ribosomal subunit by a specialized methionyl-tRNA for initiation with the help of initiation factors. In eukaryotes, translation initiation is a complex process and involves many eukaryotic initiation factors (eIFs), some of which (eIF2, eIF3 and eIF4) are large multi-subunit complexes themselves. The eIF4 complex recruits the 43S ribosomal initiation complex onto the 5' end of the bound mRNA. Binding of eIF4G-binding proteins (eIF4G-BPs) to eIF4G, a component of eIF4 complex blocks the recruitment of mRNA carrying eIF4 complex to the 43S ribosomal initiation complex and thus represses translation. However, the structural details of eIF4 complex and the messenger ribonucleoprotein particles (mRNPs) formed by eIF4G-BPs is unknown. We aim to obtain mechanistic insights into eIF4G-BPs-mediated repression of translation initiation by providing the structural details of macromolecular complexes involved.

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DISCOVERY TO INNOVATION ACCELERATOR PROGRAMME AT C-CAMP

Keywords Early Translation, Innovation and Entrepreneurship

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In the field of lifescience, transformation of an invention/discovery into an application is a very important process. This process, a significant step, between lab research and final product – is commonly called early translation/pilot research. This requires an understanding of the invention, beyond its basic tenet, keeping its market/application in mind in addition to a combination of skills including further validation, development, engineering, product design, business, management among others. This programme DIA (Discovery to Innovation Accelerator) aims to nurture and further develop exciting academic discoveries, with market potential, through a combination of scientific and non-scientific expertise and infrastructure along with collaborators.

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NM23-H1 INDUCES APOPTOSIS VIA INHIBITION OF NF-KB SIGNALLING THROUGH INTERACTION WITH VFLIP K13

Keywords Epstein Barr Virus, Kaposi Sarcoma Herpes Virus, Primary Effusion Lymphoma, Nasopharyngeal Carcinoma, Nm23-H1

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Primary effusion lymphoma (PEL) is an aggressive form of non-Hodgkin lymphoma of B cells caused by Kaposi's Sarcoma-associated Herpes Virus (KSHV). KSHV encoded latent and lytic antigens promote oncogenic transformation and invade apoptosis through modulation of various host cellular signalling pathways. Nm23-H1 is a known metastatic suppressor whose expression inversely correlates with metastatic potential of different cancers. In view of its differential expression in various cancers, here we re-vealed down-regulation of Nm23-H1 expression in latently infected KSHV PEL cell lines and its overex-pression triggered mitochondrial mediated caspase-dependent apoptosis. Here we report Nm23-H1 interacts with KSHV latent antigen vFLIP K13 and disrupts vFLIP K13 induced active NF-κB signalling pathways with concurrent inhibition of autocrine and paracrine growth factors response required for the survival of KSHV infected cells. We also confirmed the efficacy of Nm23-H1 overexpression in PEL cell induced xenograft model accentuating therapeutic implication of Nm23-H1 for primary effusion lympho-ma.

FORMATION OF TRANSPORT CARRIERS AT THE ENDOCYTIC RECYCLING COMPARTMENT

Keywords Membrane Budding, Membrane Fission, Vesicular Transport, Organelle Dynamics

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The endocytic-recycling compartment (ERC) is an organelle that decides whether endocytosed membrane proteins are routed back to the plasma membrane or sent to the lysosome for degradation. This type of iterative sorting is managed by the production of transport vesicles from the ERC. The formation of such transport vesicles is commonly assumed to involve or require a dedicated apparatus to catalyze the energetically unfavorable step of membrane fission. The identity of such a catalyst at the ERC has remained obscure. Using an unbiased fluorescence microscopy-based screen on an assay system of supported membrane tubes (SMrT) and complemented by functional analysis in *C. elegans*, we have discovered a novel membrane fission catalyst that utilizes ATP hydrolysis to power membrane fission at the ERC. We discuss the mechanistic basis for membrane fission catalyzed by this ATPase and the functional implications of this process to protein trafficking.

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RELATIVE EXPRESSION LEVELS OF IL-22, MIF, NLRP1 AND FOXP3 GENES: A STEP TOWARDS SCREENING OF POTENTIAL BIOMARKERS IN GENERALIZED VITILIGO SUBJECTS

Keywords Clinical Biomarkers, Nano Drug Delivery, Carbon Nanotubes Scaffold, Unani System Of Medicine, Vitiligo

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Vitiligo, the most common hypopigmentary disorder, is viewed as a multifactorial process where different phenomena can lead to loss of functional melanocytes. Vitiligo affects 1% of the world population, but the prevalence has been reported as high as 3-4% of Indianpopulation[1]. Many independent studies with different approaches have revealed the association of many genes with different forms of vitiligo. Utmost consideration should be taken while studying this type of skin disease and for the same herein, we have taken only nonsegmental generalized vitiligo (NSV) type with progressive state of disease for evaluation.

OBJECTIVE

To elucidate involvement of IL22, MIF, NLRP1 and FOXP3 genes in the pathogenesis of active form NSV.

RESULTS

Expression of MIF mRNA levels after normalization with GAPDH expression as internal control gene shows significant ($P < 0.05$) change in expression levels in NSV subjects compared with healthy controls. Whereas, expression of IL22, NLRP1, FOXP3 and mRNA levels after normalization with GAPDH expression as internal control gene shows non-significant ($P > 0.05$) change in expression levels in NSV subjects compared with healthy controls. Conclusion: The present study suggests that only MIF among the studied genes participates in the pathogenesis of NSV; Further studies with larger sample size should be considered before establishing MIF as potential biomarker in our populations.

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MICROTUBULE DYNAMICS REGULATES MITOCHONDRIAL FISSION

Keywords Cell Biology, Biophysics, Cytoskeletal Biology, Microscopy Image Processing

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Mitochondria are organised as tubular networks in the cell and undergo fission and fusion. Equilibrium between the fission and fusion events is necessary to maintain normal mitochondrial function, with dysfunction of these dynamic processes correlated with disease states including neurodegeneration, cancer, and cardiomyopathy[1]. While several of the molecular players involved in mediating the dynamics of mitochondria have been identified, the precise cellular cues that initiate fission or fusion remain unknown. In fission yeast, as in mammalian cells, mitochondrial positioning and partitioning are microtubule-mediated[2]. In interphase, fission yeast mitochondria associate with microtubule bundles that are aligned along the long axis of the cell[3]. Here we show that perturbation of microtubule dynamics via kinesin-like proteins is sufficient to shift the balance between fission and fusion of mitochondria and consequently, change mitochondrial morphology. Our results additionally fit with a stochastic model for partitioning of mitochondria during closed mitosis in fission yeast, with the absence of cytoplasmic microtubules providing the basis for increased mitochondrial fission. Finally, we propose a model whereby association of mitochondria with microtubules inhibits proper assembly of the dynamin GTPase-related fission protein Dnm1 around mitochondria. Thus, we demonstrate a general mechanism by which mitochondrial dynamics may be dictated by the dynamics of the microtubule cytoskeleton.

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AUTOPHAGY-ENDOCYTOSIS NEXUS IN THE CONTROL OF INTRACELLULAR MYCOBACTERIA

Keywords Host-Pathogen Interaction, Tuberculosis, Endocytosis, Autophagy, Chemical Genetics

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Intracellular pathogens alter multiple pathways in the host cell for their survival, with manipulations of trafficking pathways being the most common. We are dissecting the pathways of autophagy and endocytosis to study their influence on intracellular mycobacterial survival. Endocytosis and autophagy interact with each other at multiple levels, they share common molecular mediators and have a similar fate i.e. they fuse with lysosomes and degrade their contents. While both the pathways are individually well studied in the context of bacterial infections, their inter-relationship and possible cross-regulation via the shared lysosome is not clear. We are developing high content analysis tools to understand this nexus. Using chemical perturbations and multiplexed high content assays, we have uncovered perturbations that alter the two trafficking pathways in distinct ways and have differential effect on intracellular mycobacterial survival, and vice versa. Our results validate known control mechanisms in intracellular mycobacterial survival, reveal potentially new ones and offer interesting insights into the broader connections between endocytosis and autophagy.

SIGNALING IN *MYCOBACTERIUM TUBERCULOSIS*

Keywords Tuberculosis, Protein Kinases, Phosphorylation, Signaling, Regulation

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Tuberculosis (TB) though curable, is the leading cause of death from bacterial diseases. In response to *Mycobacterium tuberculosis* infection, host mounts a robust immune response, which contains the bacterium in ~90% of the cases, leading to latent infection. During latency, bacilli becomes non-responsive to nearly all known anti-TB antibiotics, serving as the major reservoir of the pathogen. Sensing environmental cues is critical to the survival of *M. tuberculosis* as it encounters a variety of hostile factors within the host such as nutrient deprivation, ROS, RNS stress and hypoxia. The hallmark feature of any living cell rests in its ability to sense the microenvironment and adapt accordingly. The phosphorylation mediated signal transduction is one of the most studied mechanisms of response-stimulus coupling. In *M. tuberculosis,* phospho-dependent signaling is represented by 11 two-component signaling systems and 11 eukaryotic-like serine/threonine protein kinases. Two component systems have been shown to play important roles in mycobacterial pathogenesis, adaptation within the host, latency, and resuscitation. Several studies have suggested a role for serine/threonine protein kinases (STPKs) in the regulation of metabolic processes, transport of metabolites, cell division, cell wall synthesis and virulence. The fact that number of eukaryotic like STPKs is over-represented in *M. tuberculosis* as compared to other organisms of similar genome size highlights the important role played by these kinases in the biology of this bacterium. We present our recent efforts on elucidating the functional roles and the mechanism of signaling of an essential protein kinase, PknB and the only soluble protein kinase PknG.

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INTERLEUKIN-4 ANTAGONIST FOR POSSIBLE TREATMENT OF ASTHMA

Keywords DNA Mismatch Repair, DNA- Protein Interactions, Protein Chemistry

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Interleukin-4 is crucial for the pathogenesis and maintenance of asthma and allergy.

IL-4 and IL-13 uses the IL-4 receptor α chain (IL-4Rα) for signalling. Free thiol containing Cysteine muteins were essential for screening chemical libraries.

We have started with the problem - How to reduce only the recombinant cysteines selectively?

We were able to generate IL-4 mutants and enzymatically generate Free thiol containing Cysteine mu-tants as confirmed with mass spectroscopy and chemical modification.

BIACORE analysis of the interaction of IL-4 analogues with the γc and IL-13Rα1 was done to shortlist candidate Interleukin-4 mutants for further study. Agonist activity of IL-4 analogues and inhibition of IL-4 and IL-13 dependent activity was analysed in HEK-Blue cells.Dose-dependent inhibition of IL-4 activity by IL-4 mutein conjugates in Jurkat cells was calculated using inhibition of STAT 6 phosphorylation levels.

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BIOLOGY AND REGULATION OF AUTOTAXIN IN CANCER AND BEYOND

Keywords Vascular Immunology, Inflammation, Cancer, RAGE Skeletal muscle

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Our studies in broad fields of cellular differentiation and cancer on mouse models to normal and diseased humans have uncovered a significant role of Lysophosphatidic acid (LPA) in these settings. Studies on cellular differentiation focus on ligand and receptor signalling and molecular influences on the responses in the periphery. Muscle differentiation is a multifaceted and tightly controlled process required for the formation of skeletal muscle fibers. Satellite cells, a population of muscle stem cells are the direct cellular contributors to muscle repair in injuries or disorders. Our study has identified an essential master regulator in murine and human muscles identifying a promising extracellular ligand in muscle formation, regeneration and hypertrophy. In another study on monocytes we have found that LPA stimulated signaling is critical for LPA mediated macrophage development in mice. Additionally, transcriptome analysis revealed the key transcriptional regulator in the development of LPA induced macrophages. In humans, LPA mediates macrophage formation following similar pathways. These findings identify critical role for LPA in regulating innate immune system. Lastly, we have been engaged in a long-term efforts to develop and apply novel strategies to immunological problems, especially as concerns mechanisms of muscle repair, cancer and immune cells.

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LncRNAs IN DNA DAMAGE RESPONSE

Keywords LncRNAs in DNA Damage Response, lncRNA, DNA Damage, Cancer, Inflammation

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Long non-coding RNAs (lncRNAs) have been shown to contribute to DNA damage response (DDR) by regulating gene expression. However, very little is known about the role that lncRNAs play in regulating DNA repair. Using a genome-wide microarray screen we identified a novel ubiquitously expressed lncRNA, DDSR1 (DNA damage-sensitive RNA 1), which is induced upon DNA damage by several DNA double-strand break (DSB) agents. DDSR1 induction upon DNA damage is dependent on the ATM-NF-κB pathway. Loss of DDSR1 reduces DNA repair capacity by homologous recombination (HR). The HR defect upon DDSR1 knockdown is characterized by aberrant BRCA1 and RAP80 accumulation at DSB sites. Consistent with its role in regulating BRCA1 recruitment to DSB sites lncRNADDSR1 interacts with BRCA1. Interestingly, lncRNA DDSR1 also interacts with hnRNPUL1, an RNA-binding protein involved in modulating HR by regulating DNA end-resection. Similar to DDSR1 depletion loss of hnRNPUL1 also results in aberrant BRCA1 and RAP80 recruitment at DSB sites. Our results indicate that DDSR1/hnRNPUL1 depletion results in HR inhibition due to reduced end resection caused by aberrant accumulation of BRCA1 and RAP80 at DSBs. Our results establish a role for lncRNA DDSR1 in maintaining genome stability. Consistent with its role in maintaining genome stability DDSR1 is down-regulated in triple negative breast cancer samples. Our aim is to evaluate the use of DDSR1 expression as a tool for predicting breast cancer prognosis.

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LIMBAL STROMAL STEM CELL THERAPY FOR VISION RESTORATION

Keywords Stem Cell, Wound Healing, Cornea, Limbal Stem cells, Animal Models

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Human limbal derived stem cells have manifested and proven their efficacy through various, well established surgical interventions of SLET, CLET etc with a success rate of over 70%, in regenerating the ocular surface and restoring the corneal transparency, in patients with limbal stem cell deficiency (LSCD) ocular burns and other corneal related pathologies. In this investigator initiated-clinical trial, we used limbal biopsies obtained from donor/ cadaveric eyes. Limbal stromal stem cells were isolated ex-vivo using a previously standardized technique. Control groups received the standard medical therapy along with debridement and fibrin glue but without the stem cells. Compared to controls, eyes receiving LSSCs, irrespective of the source, showed: (i) faster epithelization ($p=0.002$); (ii) better corneal clarity, evaluated clinically ($P=0.012$) and on scheimpflug imaging ($P<0.0001$); (iii) greater improvement in best-corrected visual acuity ($P=0.003$); and lesser corneal vascularization ($p<0.0001$). None of the eyes receiving LSSCs required a second surgical intervention. Our findings also show that in SLET (Simple Limbal Epi-thelium transplantation) surgery a minimal amount of < 0.3 mm2 live tissue would be sufficient for ample limbal cell expansion in vitro. Comparatively, limbus from cadaveric tissues even though has similar potential as that of live tissues, demands larger amount of tissue for expansion (> 0.5mm2). . This technique of delivering autologous and allogenic hLSSCs was effective in enhancing corneal epithelization; improving vision and corneal clarity; and reducing corneal scarring and vasularization in superficial corneal pathologies like burns, ulcers and scars. Present study explores the various characteristics of the stromal cells before this can be made available to the millions.

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IN-SITU SINGLE PASS INTESTINAL PERMEABILITY AND PHARMACOKINETIC STUDY OF DEVELOPED LUMEFANTRINE LOADED SOLID LIPID NANOPARTICLES.

Keywords Pharmaceutics, Pharmacokinetics, Pharmacology, Drug Metabolism, Toxicology

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The present investigation aims to develop lumefantrine loaded binary solid lipid nanoparticles (LF-SLNs) to improve its poor and variable oral bioavailability. The oral bioavailability of LF is poor and variable due to its limited aqueous solubility and P-gp mediated efflux occurring in small intestine. LF-SLNs were prepared using binary lipid mixture of stearic acid and caprylic acid stabilized with TPGS (D-alpha tocopheryl polyethylene glycol 1000 succinate) and Poloxamer 188. Developed LF-SLNs were characterized for particle size distribution, zeta potential, entrapment efficiency, solid state properties and biopharmaceutical properties including *in situ* intestinal permeability and oral bioavailability. The particle size distribution, zeta potential and entrapment efficiency of optimized batch (LF-SLN7) was found to be 357.7±43.27nm, 25.29±1.15mV and 97.35±0.30%, respectively. DSC thermographs showed loss of crystalline nature of lumefantrine in LF-SLNs. *In situ* single pass intestinal permeability study (SPIP) indicated significant enhancement in the effective intestinal permeability of LF from LF-SLN7 as compared to that of control. Pharmacokinetic study also showed significant increase in Cmax and area under curve (AUC0-∞) from LF-SLN7 (3860±521ng/mL and 43181±2557h×ng/mL, respectively) as compared to that of LF-control suspension (1425±563ng/mL and 19586±1537h×ng/mL, respectively). Thus, developed LF-SLNs can be promising to overcome P-gp efflux pump and enhance the oral bioavailability of lumefantrine.

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