8th RAMALINGASWAMI CONCLAVE
February 15-17, 2018

NATIONAL INSTITUTE OF PLANT GENOME RESEARCH

AND

DEPARTMENT OF BIOTECHNOLOGY

GOVERNMENT OF INDIA

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ABSTRACT BOOK

CELEBRATING 10TH ANNIVERSARY OF RAMALINGASWAMI FELLOWSHIP

Nurturing science... and Beyond!!

PROGRAM

8th CONCLAVE OF RAMALINGASWAMI FELLOWS

14th February : 12.00 noon onwards fellows can check in
The Ashok Hotel, New Delhi
Registration (5:00 – 7:00 pm): The Ashok Hotel

15th February : **Day -1**

7:30 - 8:30 am	**Breakfast:** Coffee shop, The Ashok Hotel
8:00 - 9:00 am	**Registration:** The Ashok Hotel

Inaugural Session (Venue: Banquette Hall)

9:00 - 9:10 am	Welcome Address: Dr. Ramesh V. Sonti, Director, National Institute of Plant Genome Research, New Delhi
9:10 - 9:25 am	Overview of the RLS fellowship program: Adviser, Dr. Meenakshi Munshi, Department of Biotechnology (DBT), Government of India.
9:25 - 9:40 am	Inaugural Address: Prof. Ashutosh Sharma, Secretary, Department of Biotechnology (DBT), Government of India
9:40 -10:00 am	Special Address: Prof. K. VijayRaghavan, former Secretary, Department of Biotechnology (DBT), Government of India
10:00 - 10:30 am	**Tea beak**
10:30 - 11:30 am	Keynote Address: Prof. M. K. Bhan former Secretary, Department of Biotechnology (DBT), Government of India

Experience of being a RLS Fellow

11.30 - 11.45 am	Dr. Deepak Gaur, Jawaharlal Nehru University (JNU), New Delhi
11.45 - 12.00 pm	Dr. Chetana Sachidanandan, Institute of Genomics & Integrative Biology (IGIB), New Delhi
12.00 - 12.15 pm	Dr. Arnab Mukhopadhyay, National Institute of Immunology (NII), New Delhi

Parallel talk Sessions: 12:30 - 1.30 pm

Session 1: Structural Biology, Biophysics, Bioengineering

Reviewers: Dr. Amit Sharma; Prof. Balasubramanian Gopal; Prof. Mukesh Doble; Prof. Sanjeev Galande

Session Venue: Suite 292

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
1.	12:30-12:45pm	Dr. Beena Krishnan Institute of Microbial Technology, Sector- 39A, Chandigarh - 160036	Molecular level understanding of folding/mis-folding and degradation of extracellular proteins implicated in conformational diseases	03
2.	12:45-1:00 pm	Dr. Parimal Kar Centre for Biosciences and Biomedical Engineering, Indian Institute of Technology, Indore - 452020	Multiscale simulations of protein-glycan complexes: Toward understanding the molecular basis of host-pathogen interactions and immune response	31
3.	1.00-1.15 pm	Dr. Ashok Kumar Patel Kusuma School of Biological Sciences, Indian Institute of Technology, Hauz Khas, New Delhi - 110016	Structurally understanding the mechanism of Pyruvate kinase M2 in tumor cell proliferation transcription of genes, cell-cycle progression and brain tumorogenesis	14
4.	1:15-1:30 pm	Dr. Gautam Vivek Soni, Raman Research Institute, C.V. Raman Avenue, Sadashivanagar, Bangalore - 560080	Epigenetic gene silencing by chromatin using nano-devices	34

Session 2: Plant Biology, Agriculture Biotechnology

Reviewers: Dr. Aijaz A. Wani; Dr. Ajay Parida; Prof. Nikhil Chrungoo; Prof. Sudhir Kumar Sopory

Session Venue: Suite 293

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
5.	12:30-12:45pm	Dr. Jagadis Gupta Kapuganti, National Institute of Plant Genome Research, Aruna Asaf Ali Marg, New Delhi - 110067	The role of hypoxia-induced nitric oxide in plant growth and flooding stress survival	29
6.	12:45-1:00pm	Dr. Ram Kishore Yadav, Indian Institute of Science Education and Research – Mohali, Sector- 81, Knowledge City, Mohali	Identification of transcriptional gene networks using genomic approaches	19
7.	1:00-1:15pm	Dr. Ravi Maruthachalam, School of Biology, Indian Institute of Science Education and Research Thiruvananthapuram - 695016	Generation and characterization of minichromosomal and neocentromere formation in plants	42
8.	1.15-1.30 pm	Dr. Vishwesha Guttal Indian Institute of Science, Bangalore - 560 012	Mobile organisms to patterned vegetation: Investigation of self-organization in ecological systems	39

Session 3: Cancer Biology

Reviewers: Prof. B. Ravindran; Dr. Guruprasad R. Medigeshi; Dr. Rakesh Kumar; Dr. Srikrishna Jayadev

Session Venue: Suite 294

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
9.	12:30-12:45pm	Dr. Rohit Saluja, All India Institute of Medical Sciences, Saket Nagar, Bhopal -462020	Mechanism and relevance of IL-33 mediated mast cell proliferation in asthma	25
10.	12:45-1:00pm	Dr. Arjun Guha, Institute for Stem Cell Biology and Regenerative Medicine, National Centre for Biological Sciences, GKVK, Bellary Road, Bangalore - 560065	Regulation of progenitor proliferation and cell fate in the airway epithelium	57
11.	1:00-1:15pm	Dr. Somesh Baranwal, Central University of Punjab, Bathinda, City Campus, Mansa Road, Bathinda - 151001,	Role of integrin binding protein, kindling in colon cancer progression inter-organ infection	46
12.	1.15-1.30 pm	Dr. Rashmi Mishra, Rajiv Gandhi Centre for Biotechnology, Poojappura, Thiruvananthapuram - 695014	Mechanotransduction through caveolae: Lipid rafts in homeostatic control of cell proliferation signaling and tumorigenesis	08

1:30 - 2:30 pm: Lunch at Banquette Hall

Parallel talk Sessions: 2:30 - 4:00 pm

Session 4: Immunology, Infection Disease Biology, Vaccination

Reviewers: Dr. Ayub Qadri; Dr. Himanshu Kumar; Dr. Rakesh Mishra; Prof. Ravinder Goswami

Session Venue: Suite 292

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
13.	2:30-2:45pm	Dr. Amit Kumar Pandey, Translational Health Science and Technology Institute, NCR Biotech Science Cluster, Faridabad - 121001	Regulation of cholesterol metabolism in *Mycobacterium tuberculosis*	21
14.	2:45-3:00pm	Dr. Amit Prasad School of Basic Sciences, Academic Block, Near Bus Stand, Indian Institute of Technology (IIT), Mandi - 175001	Immuno-modulating effect of *Taenia solium* cyst antigens on immune reactive cells and their role in pathogenesis	02
15.	3:00 – 3:15pm	Dr. Soma Rohatgi Department of Biotechnology, Indian Institute of Technology, Roorkee - 247667	Investigating the role or B cells and antibodies in *Candida albicans* and Chikungunya infections	01
16.	3:15-3:30pm	Dr. Prasenjit Bhaumik Department of Biosciences and Bioengineering, Indian Institute of Technology, Bombay, Mumbai - 400076	Development of antimalarial inhibitors targeting Plasmodium parasite plasmepsins	32
17.	3:30-3:45pm	Dr. Syed Mohd Faisal National Institute of Animal Biotechnology, Axis Clinicals Building, Miyapur, Hyderabad - 500049	Understanding the host response and molecular pathogenesis of *Leptospira interrogans* infection	15

S. No.	Time	Name & Address	Title	Page No.
18.	3:45-4:00 pm	Dr. Dhanasekaran Shanmugam Biochemical sciences division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pashan, Pune - 411008	Genetic, metabolomic and chemical interrogation of apicomplexan metabolism: Targeting pathways with essential role in growth and differentiation for drug discovery	40

Session 5: Cancer Biology, Cell Biology, Signal Transduction

Reviewers: Dr. Guruprasad R. Medigeshi; Dr. Rakesh Kumar; Prof. Sanjeev Galande; Prof. Shahid Jameel

Session Venue: Suite 293

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
19.	2:30-2:45 pm	Dr. Anindita Chakrabarty, Shiv Nadar University NH91, Tehsil Dadri, Gautam Buddha Nagar, Greater Noida - 201314	Deciphering the role of the phosphatidyl inositol 3-kinase oncogenic mutation in conferring anti HER2 therapy resistance by enriching for the stem-like tumor initiating cell population in HER2 oncogene-positive breast cancer	47
20.	2:45-3.00 pm	Dr. N. Ravi Sundaresan Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore - 560012	Control of cardiac fibrosis via sirtuin 2 inhibition	50
21	3:00-3:15 pm	Dr. Vikas Yadav Department of Biochemistry, Central University Haryana, Mahendergarh	Role of Nuclear Receptor coactivator PGC1β in diabetes mediated endothelial cell dysfunction and angiogenesis	48

S. No.	Time	Name & Address	Title	Page No.
22	3:15-3:30 pm	Dr. Mahavir Singh, Molecular Biophysics Unit, Indian Institute of Science, Bangalore - 560012	Role of long non-coding RNA TERRA in telomere maintenance and heterochromatin formation	35
23	3:30-3:45 pm	Dr. Sona Rajkumari Rajiv Gandhi Centre for Biotechnology, Poojappura Thiruvananthapuram -695014	Molecular regulation of Beige programming of adipocytes by Ebl2	-
24	3:45-4:00 pm	Dr. Sourav Banerjee National Brain Research Center NH-8, Nainwal Mode, Manesar - 122051	Mechanism of synaptic protein synthesis by selective miRNA decay and its implication in fear memory.	56

Session 6: Structural Biology, Biomaterials, Bioengineering

Reviewers: Dr. Amit Sharma; Prof. Balasubramanian Gopal; Prof. Mukesh Doble; Dr. Tasleem Arif)

Session Venue: Suite 294

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
25.	2:30-2:45 pm	Dr. Praveen Kumar Vemula, Institute for Stem Cell Biology and Regenerative Medicine, National Centre for Biological Sciences, GKVK, Bellary Road, Bangalore - 560065	Self-assembled amphiphilic prodrug-based gelators: A novel drug delivery platform approach for *glioblastoma multiforme* therapy	30
26.	2:45-3:00 pm	Dr. Hari. M. Verma, Department of Biosciences and Bioengineering Indian Institute of Technology, Powai, Mumbai	Laser speckle based three-dimensional tomographic imaging of blood flow during ischemic stroke: Theoretical framework based on experimental data from small animal ischemic stroke models	28

S. No.	Time	Name & Address	Title	Page No.
27	3:00-3:15 pm	Dr. Banani Chakraborty, Department of Chemical Engineering, Indian Institute of Science, Bangalore -560012	Parallel screening of multiple targets and testing protein functions using nano-gold as a reporter on DNA origami surface and apta-sensor controlled 3D-DNA-origami mediated drug delivery	33
28	3:15-3:30pm	Dr. Rudresh Acharya, School of Biological Sciences, National Institute of Science Education and Research, Bhubaneswar- 751005	Structural characterization of viral ion channels	-
29.	3:30-3:45 pm	Dr. Narendra Reddy, Centre for Incubation, Innovation Research and Consultancy, Jyothy Institute of Technology Campus, Tataguni off Kanakapura Road, Bangaluru-560082.	Developing high value biopolymeric materials for the food, fiber, biofuel, composites, medical and automotive industries using indigenous renewable resources	10

4:00 - 4:30 pm Tea Break at Banquette Hall

8th CONCLAVE OF RAMALINGASWAMI FELLOWS

Evening session (Venue: Banquette Hall)

4:30 - 5:15 pm **Mentor Talk:** Dr. Rajesh Gokhale, National Institute of Immunology (NII), New Delhi

Experience of being a RLS Fellow

5:15 - 5:30 pm Dr. Gobardan Das, Jawaharlal Nehru University (JNU), New Delhi

5:30 - 5:45 pm Dr. Shweta Tyagi, The Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad

5:45 - 6:00 pm Dr. Giridhari Lal, National Centre for Cell Science (NCCS), Pune

6:00 - 6:15 pm Dr. Senthil Venugopal, South Asian University (SAU), New Delhi

6:15 - 7:15 pm **Panel Discussion: How to set up lab/dealing with the system**

- Prof. Sanjeev Galande, IISER, Pune (Moderator)
- Prof. M.R.S. Rao, JNCASR, Bangalore
- Prof. M Radhakrishna Pillai, RGCB, Thiruvananthapuram
- Dr. Ramesh V. Sonti, NIPGR, New Delhi
- Dr. Rakesh Mishra, CCMB, Hyderabad
- Dr. Shekar Mande, NCCS, Pune
- Dr. Ajay Parida, ILS, Bhubaneswar
- Prof. Sudhanshu Vrati, RCB, Faridabad
- Dr. Amit Sharma, ICGEB, New Delhi
- Dr. Ayub Qadri, NII, New Delhi
- Dr. Meenakshi Munshi, DBT, New Delhi

7:15 - 8:00 pm **Interaction among fellows**

Dinner 8.00 PM onward at Banquette Hall

8th CONCLAVE OF RAMALINGASWAMI FELLOWS

16th February: Day -2

7:30 - 8:30 am	Breakfast: Coffee shop, The Ashok Hotel

Morning Session (Venue: Banquette Hall)

9:00 – 9:45 am	**Mentor Talk:** Dr. Vineet Ahuja, All India Institute of Medical Sciences (AIIMS), New Delhi

Experience of being a RLS Fellow

9:45 - 10:00 am	Dr. Zahoor Ahmad Parry, Indian Institute of Integrative Medicine (IIIM) Srinagar
10:00 - 10:15 am	Dr. Manideepa Banerjee, Indian Institute of Technology (IIT), New Delhi
10:15 - 10:30 am	Dr. Rajni Kant Dixit, National Institute of Malaria Research (NIMR), New Delhi
10.30 - 10.45 am	Dr. Swasti Tiwari, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow
10:45 - 11:00 am	**Tea Break at Banquette Hall**

Parallel Talk Sessions: 11:15 - 12:45 pm

Session 7: Cell and Molecular Biology

Reviewers: Dr. Amit Awasthi; Prof. Ashraf Ganie; Dr. Srikrishna Jayadev; Prof. V. Verma

Session Venue: Suite 292

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
1.	11:15-11:30 am	Dr. Durba Sengupta Physical Chemistry Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune - 411008	Effect of membrane composition on receptor association	41
2.	11:30-11:45 am	Dr. Tulika Prakash Srivastava, Indian Institute of Technology, Mandi - 175001	Exploring the human microbiome: A hunt for candidates for pre-and pro-biotics	04
3.	11:45-12:00 pm	Dr. Prabhanshu Tripathi, Translational Health Science and Technology Institute, NCR Biotech Science Cluster, Faridabad - 121001	Effect of environmental factors including diet and artificial sweeteners on gut microbiome and their consequences type 2 diabetes	36
4.	12.00-12:15 pm	Dr. Ranjith Kumar C.T. Translational Health Science and Technology Institute, NCR Biotech Science Cluster, Faridabad -121001	Modulation of innate immune response and characterization of viral polymerases for the development of potent vaccines	27
5.	12:15-12:30pm	Dr. Milan Surjit Translational Health Science and Technology Institute, NCR Biotech Science Cluster, Faridabad - 121001	Understanding the biology of Hepatitis E virus and development of vaccine and drugs against it	51
6.	12:30-12:45pm	Dr. Chandrima Das Biophysics Division, Saha Institute of Nuclear Physics, Bidhannagar, Kolkata- 700064	Prolyl Isomerization as a novel mode to regulate chromatin function	43

Session 8 : Biochemistry, Immunology, Molecular Biology

Reviewers: Dr. Himanhu Kumar; Prof. P.N. Rangarajan; Dr. Rahul Pal; Prof. Raies A Qadri

Session Venue: Suite 293

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
7.	11:15-11:30 am	Dr. Amrita Brajagopal Hazra, Indian Institute of Sciences Education and Research, Pune - 411 008	Exploring vitamins through chemical biology and enzymology: Discovery of new biosynthetic pathways and enzyme mechanisms	44
8.	11:30-11:45 am	Dr. Jagan Sundaram, Department of Biochemistry, University of Madras, Guindy Campus, Chennai-600025	Exploring the human microbiome: A hunt for candidates for pre-and pro-biotics	55
9.	11:45-12:00 pm	Dr. Nimesh Gupta, National Institute of Immunology (NII), New Delhi- 110057	Investigation of the dynamics of T-helper cell responses induced by a viral vaccine	17
10.	12.00-12:15 pm	Dr. Sudipta Basu Indian Institute of Sciences Education and Research, Pune- 411008	Chimeric nanoparticle: A novel nanoplatform for signaling pathway driven cancer chemotherapy	11
11.	12:15-12:30 pm	Dr. Tanmay Majumdar, Mucosal Immunocompetent Laboratory, Department of Zoology, University of Delhi, Delhi- 110007	Delineating the role of commensal microbial consortium in Wnt/β -catenin dependent tolerance vs immunity: small molecule-directed protection against drug-resistant parasite infection	49

Session 9: Neurology, Molecular Biology

Reviewers: Prof. Neeraj Jain; Prof. Tapas Kundu; Prof. Vijayalakshmi Ravindranath

Session Venue: Suite 294

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
12.	11:15-11:30 am	Dr. Arpan Banerjee, National Brain Research Centre, NH-8, Manesar- 122051	Neuro-cognitive networks underlying goal directed behavior	-
13.	11:30-11:45 am	Dr. Abrar Ahmad Quraishi, Department of Biotechnology, University of Kashmir, Hazratbal, Srinagar - 190006	Understanding the molecular basis of fragile X permutation rCGG mediated neurode generation	52
14.	11.45-12:00 pm	Dr. Dipanjan Roy National Brain Research Centre, NH-8, Manesar- 122051	Role of default mode brain network in normal cognitive functions	45
15.	12:00-12:15pm	Dr. Siva Sankar Koganti, Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar- Guntur- 522510 A.P	Exosome signaling via EBER-1 and EBER-2 and the regulatory role of host BTB/POZ domain containing Zinc finger proteins	54
16.	12:15-12:30 pm	Dr. Tina Mukherjee, Institute for Stem Cell Biology and Regenerative Medicine, National Centre for Biological Sciences, GKVK, Bellary Road, Bangalore- 560065	Identification of novel neuronal signals in stem/progenitor development and maintenance	38

12:45 - 1:45 pm Lunch at Banquette Hall

Parallel talk Sessions: 1:45 - 3:30 pm

Session 10: Neurobiology, Stem cell, Gene expression

Reviewers: Dr. Jyotsna Dhawan; Prof. Mukesh Doble; Prof. Neeraj Jain; Prof. Vijayalakshmi Ravindranath

Session Venue: Suite 292

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
17.	1:45 - 2:00 pm	Dr. Kommaddi Reddy Peera, Centre for Neuroscience, Indian Institute of Sciences, Bangalore - 560012	Ubiquitination of G-protein coupled receptors and betaarrestins: Implications in Alzheimer's disease	18
18	2:00-2:15 pm	Dr. Mirza Saqib Baig, Indian Institute of Technology, M-Block, IET-DAVV Campus Khandwa Road, Indore -452017	Neuronal nitric oxide synthase (NOS1) driven macrophage phenotype polarization	24
19.	2:15-2:30 pm	Dr. Bhupendra V. Shravage, Development Biology, Agharkar Research Institute, Agarkar Road, Pune - 411004	Autophagy is required for germline stem cell maintenance and delays their aging in Drosophila	23
20.	2:30-2:45 pm	Dr. Vidisha Tripathy, National Centre for Cell Science, P.B. No. 40, Ganeshkhind P.O. Pune - 411007	Investigating the role of long noncoding RNAs in mammalian gene expression regulation	09
21.	2:45-3:00 pm	Dr. Ramkumar Sambasivan, Institute for Stem Cell Biology and Regenerative Medicine, Bangalore	Gene circuits regulating stem cell fate and organogenesis	06

Session 11: Immunology, Infectious diseases, Vaccine

Reviewers: Dr. Amit Awasthi; Prof. Ashraf Ganie; Dr. Himanshu Kumar; Prof. Rana P. Singh,

Session Venue: Suite 293

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
22.	1:45-2:00 pm	Dr. Kajal Kanchan, School of Biotechnology, Jawaharlal Nehru University, New Delhi-110067.	Temperature sensing mechanism in *M. tuberculosis* and its role in pathogenesis	37
23.	2:00-2:15 pm	Dr. Somdeb Bose Dasgupta, School of Biomedical Engineering Indian Institute of Technology, Kharagpur	Identifying the host substrates for the Mycobacterial virulence factor Protein Kinase G, its functional characterization in context of mycobacterial survival	05
24.	2:15-2:30 pm	Dr. Chaithanya Madhurantakam, Department of Biotechnology, TERI University, 10, Institutional Area, Vasant Kunj, New Delhi-110070	Structural studies on proteins involved in synthesis and processing of mycolic acids in *Mycobacterium tuberculosis*	13
25.	2:30-2:45 pm	Dr. Jeya Marimuthu, Marine Biotechnology Division, National Institute of Ocean Technology, Pallikaranai, Chennai-600100	Discovery of new type II polyketide synthases for novel polyketide products	26
26.	2:45-3:00 pm	Dr. Ravindra P.V., Department of Biochemistry & Nutrition, Central Food Technological Research Institute, Mysore- 570 020	Exploring the effects of Diabetes on pathology of the lung	20
27.	3:00-3:15 pm	Dr. Varadharajan Sundaramurthy National Centre for Biological Sciences, Bangalore	Quantitative analysis of host determinants of intracellular mycobacterial infection	53

Session 12: Biofuel, Bio-energy

Reviewers: Dr. Amulya Panda; Prof. Dinabandhu Sahoo; Prof. Prashant S Phale; Prof. Sudhir Kumar Sopory

Session Venue: Suite 294

Each talk will be for 10 minutes + 5 minutes discussion

S. No.	Time	Name & Address	Title	Page No.
28.	1:45-2:00 pm	Dr. Ashish Bhattacharjee, Department of Biotechnology, National Institute of Technology, Durgapur, Mahatma Gandhi Avenue, Durgapur - 713209	Role of 15- Lipoxygenase (15-LOX) in the pathogenesis of several diseases	12
29.	2:00-2:15 pm	Dr. Sucheta Tripathy, Indian Institute of Chemical Biology, 4 Raja S.C. Mulick Road, Jadavpur, Kolkata - 700032	Development of comprehensive bioinformatics resource for newly sequenced genomes	16
30.	2.15-2.30 pm	Dr. Vivekanand, Centre for Energy and Environment, Malviya National Institute of Technology, JLN Marg, Jaipur - 302017	Breaking the lignocellulose barrier by two stages pretreatment for enhanced biogas production	58
31.	2.30-2:45 pm	Dr. Dhanashree Ashok Paranjpe, M.E.S. Abasaheb Garware College New Education Building Karve Road, Pune - 411004	The peacock's tail: can human-animal vicinity lead to sustainable mutual benefits and peaceful co-existence	07
32.	2.45-3.00 pm	Dr. Vijaykumar Krishnamurthy, International Centre for Theoretical Sciences, Tata Institute of Fundamental Research, Indian Institute of Sciences Campus, Bangalore - 560012	Mechanobiological patterns in morphogenesis	22
33.	3.00-3.15 pm	M. Rajkumar Department of Life Sciences Central University of Tamil Nadu, Thanjavur Road, Thiruvarur	Climate change and plant microbe interactions: consequences of phytoremediation of crude oil contaminated soils	-

3:00 - 3.30 pm Tea Break Banquette Hall

8th CONCLAVE OF RAMALINGASWAMI FELLOWS

Evening session (Venue: Banquette Hall)

3:30 - 4:15 pm	**Mentor talk:** Dr. Uma Rao, Indian Agricultural Research Institute, New Delhi
4:15 - 5:15 pm	**Funding Opportunities/ How to write a grant** Dr. Shahid Jameel, DBT-The Wellcome Trust, New Delhi Dr. Sanjeev Varshney, Department of Science and Technology, New Delhi
5:15 pm	Starting for NIPGR, New Delhi
6:00 pm	Reaching NIPGR, New Delhi
6:00 - 7:00 pm	**Refreshment will be served at NIPGR lawn** **Poster session by NIPGR students**
7:00 - 8:00 pm	Cultural Program at NIPGR auditorium
8:00 - 9:30 pm	**Dinner at NIPGR lawns**
9:30 pm	Bus for The Ashok Hotel

8th CONCLAVE OF RAMALINGASWAMI FELLOWS

17th February: Day-3

7:30 - 8:15 am	**Breakfast:** Coffee shop, The Ashok Hotel
8:15 am	Starting for NIPGR
9:15 am	Reaching NIPGR

Morning Session (Venue: NIPGR Auditorium)

9.30 - 10.15 am	**Mentor Talk:** Prof. Raghavan Varadarajan, Indian Institute of Science (IISc), Bangalore

Experience of being RLS Fellow

10:15 - 10:30 pm	Dr. Amit Asthana, Centre for Cellular & Molecular Biology (CCMB), Hyderabad
10:30 - 10:45 pm	Dr. Ananda Sarkar, National Institute of Plant Genome Research (NIPGR), New Delhi

High-Tea and interaction with Minister (Venue: NIPGR lawns)

11:00 - 11:30 am	High-Tea and informal interaction of Ramalingaswami Fellows with Dr. Harsh Vardhan, Honourable Minister of Science and Technology
11:30 - 11:35 am	Honourable Minister accompanied to NIPGR auditorium

Morning session continued (Venue: NIPGR Auditorium)

11:35 - 11:40 am	Inviting Honourable Minister and dignitaries on dais and lighting of lamp
11:40 - 11:45 am	Welcome address: Dr. Ramesh V. Sonti, Director, NIPGR, New Delhi
11:45 - 11:50 am	Update on 10 years of Ramalingaswami Fellowship: Dr. Meenakshi Munshi, Adviser, Department of Biotechnology, Government of India

11:50 - 12:05 pm	Special Address: Prof. Ashutosh Sharma, Secretary, Department of Biotechnology, Government of India
12:05 - 12:25 pm	Chief Guest Address: Dr. Harsh Vardhan, Honourable Minister of Science & Technology
12:25 - 12:30 pm	Vote of Thanks
12:30 - 1:30 pm	Meeting of Ramalingaswami Fellows with Directors, VCs, Deans/HoDs
1:00 - 2:00 pm	**Lunch at NIPGR lawns**
2:15 - 3:00 pm	**Mentor Talk:** Prof. Mukesh Doble, Indian Institute of Technology (IIT), Madras
3:00 - 4:00 pm	* Parallel Meeting among fellows (NIPGR Auditorium) * Parallel Meeting of expert committee members, mentors, directors, VCs, Heads (NIPGR Board Room)
4:00 - 4:30 pm	**Tea Break at NIPGR lawns**
4:30 - 5:30 pm	Final Wrap up and concluding remarks (Recommendations and Suggestions)
5:30 - 7:30 pm	Meeting of Fellows with Directors, VCs, Deans/HoD (Continued)
7:30 - 9:00 pm	**Dinner at NIPGR lawns**
9:30 pm	Bus will depart for The Ashok Hotel

ABSTRACTS

Investigating the role of B cells and Antibodies in *Candida albicans* and Chikungunya infections.

SOMA ROHATGI
Email: soma.rohatgi@gmail.com

IIT ROORKEE

This project proposed to investigate the role of B-cell and antibodies in *Candida albicans* and Chikungunya infections using animal models (mice) and patient samples. *Candida albicans* is a dimorphic fungus: the yeast form being associated withcommensalism, whereas the pathogenic hyphal form causes systemic candidiasis. Three hyphal-specific antigenic determinants: Secreted aspartyl proteinase 2 (SAP2), Agglutinin like sequence gene 3 (ALS3) and Hyphally regulated gene 1 (HYR1) were selected as vaccine candidates for the proposed study. Fungal strains were procured from National databases. We report successful cloning and expression of SAP2, ALS3 and HYR1 as purified recombinant proteins. Further, for developing glyco-conjugates of Candida-specific polysachharides, CRM197 protein expression was optimized. A mice model of systemic candidiasis was established in the laboratory. Optimal dose for fungal infection was decided using survival curve and organ fungal burden analysis. We are currently investigating the role of SAP2 immunization in mice during systemic candidiasis. Further studies will be initiated to characterize the murine SAP2-specific B-cell and antibody response in detail. Chikungunya virus (CHIKV) is a mosquito-borne alphavirus, causing sporadic epidemics in Asia and Africa. For Chikungunya studies, the project proposed to use envelop protein E2 from CHIKV, for studying B-cell and antibody responses in mice. Total RNA was extracted from an Indian CHIKV strain lysate, followed by cDNA synthesis and PCR amplification of E2 gene using gene-specific primers. We report successful cloning of E2 gene in histidine-tagged vector and further experiments are ongoing for protein purification. In order to initiate human studies pertaining to systemic candidiasis and CHIKV infections, flow cytometry staining strategies are currently being optimized in the laboratory. Patient blood samples are awaited to begin case-control studies. Further experiments are required to address the serological, molecular and functional studies proposed in the project, which are planned to be performed subsequently.

Immuno-modulating effect of *Taenia solium* cyst antigens on immune reactive cells and their role in pathogenesis

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Objective: *Taenia solium* is one of the most common parasitic infections of central nervous system, causing neurocysticercosis (NCC). The antigenic properties of parasitic cyst proteins are still not well characterized. Although cyst fluid (CF) had been identified as having major antigenic properties. Material & Methods: CF was isolated from cyst isolated from infected swine and insoluble part was separated. The soluble CF parts were further purified by FPLC on AKTA prime using filtration column, Superose 12. Different fractions were collected and run on 5% native page. The CF protein (30ug) sample was prepared for LC-MS analysis by in-gel tryptic digestion and the protein spectra obtained was annotated. Simultaneously, Blast2GO was used to perform BlastP, protein annotation and KEGG mapping. We further characterized these fractions for their humoral and cellular antigenicity. Results: We could identify five bands on native gel for CF and four of them were purified by FPLC. The two of them (fraction 2 and 3, strongly reacted with patient sera and significantly stimulated macrophages during MTT assay. Fraction 1 was cell proliferation inhibiotr in nature and had shown decreased pAKT activation and bacterial killing capability of macrophages when treated. T. solium proteome consist of ~12000 proteins, of which 355 mapped to global metabolic pathways of which 8 were related with PI3K pathway. LC-MS analysis of in vitro cultured CF protein annotated 307 proteins and eight were related with PI3K regulation. The cells treated with fraction 1 proteins had significantly less activation of pAKT and bacterial killing capability. Conclusion: CF proteins are important for immune modulation of host by T. solium, and CF proteins target PI3K/AKT pathway by down regulating it and thus suppressing the immune response.

Molecular Level Understanding of Folding/ Mis-folding and Degradation of Extracellular Proteins Implicated in Conformational Diseases

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Proteins are critical to understanding cellular processes, and yet many elementary questions relating to how a polypeptide chain assumes its final functional form still remain elusive. There is also a need to understand off-pathway protein misfolding as is evident from an increasing knowledge on protein conformational diseases. In my RLS project proposal, I had proposed to address molecular-level understanding of folding, function and degradation of a specific class of extracellular proteins, serpins that cause genetically-linked conformational disorder in humans. The choice of serpins as model protein was also due to these proteins existing in metastable native states, and using the stored energy to cause protease inhibition in the case of inhibitory serpins. Transitioning to their thermodynamically stable state is common to both function and mis-folding in these proteins. In my presentation, I will describe experiments on two of the important plasma serpins, alpha-1 antitrypsin (A1AT) and Plasminogen Activator Inhibitor-1 (PAI1). Our work on PAI1 has provided insights into the significance of packing interactions of β – sheets B and C in restraining serpins in native confirmation. In order to understand the protease specificity of serpins, we have designed and successfully made chimeric constructs of both PAI1 and A1AT, which exhibit switched protease inhibition specificities. An interesting off-shoot from our work on understanding the significance of specific sequence and conserved residues specifically at the termini of A1AT has revealed role of aminoacid sequence stretches at the protein termini, both N-and C-terminus, in the protein expression and folding of serpins. This work has further led us to study such similar effects in other proteins in general.

Exploring the Human Microbiome: A hunt for the candidates for Pre- and Pro-biotics.

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The endogenous microbial flora plays a fundamentally important role in human health and disease. Recent advancements in metagenomic approaches demonstrated that human body is co-housed by a community of trillions of diverse microbial species. The microbial products are involved in a crosstalk with the host genetic components and trigger phenotypic responses. Therefore, some members of the human microbiome have been used as Probiotics for several years. However, there is limited evidence supporting the use of these species and more scientific knowledge is needed about probiotics. There are three main objectives of my research: (1) to explore the "Enterotypes" in healthy individuals of one ethnic group, (2) to explore the correlation between the enterotypes and "Prakriti" of individuals as classified by ancient Ayurvedic system, and (3) to elucidate the role of microbiota in maintaining the gut associated immunity. Towards the first objective, analysis of 16S rRNA gene sequences from 597 healthy individuals of 15 countries showed significant differences in the human gut microbiome of different geographical regions. The study also revealed that geographical location is responsible for upto 40% of the overall variation observed in the human gut microbiome. Towards the second objective, analysis of healthy male and female gut metagenomic samples (16S rRNA), separated into three Prakriti classes, viz., Vata, Pitta, and Kapha, showed some minor variations in the taxonomic compositions of the Prakriti classes. Analysis of the core gut microbiome present in each Prakriti class with respect to male and female helped in elucidating the communities' specific to "Prakriti" classes which gave us deeper insights into the behavior, function and interrelationship among the co-occurring bacterial taxa. Towards the third objective, we calculated the imputed metagenome from the 16S rRNA based analysis which indicated significantly altered functions in Kapha and Pitta Prakriti. In to providing better insights about the roles of microbiota in maintaining human health, the direct application of this study is in the advancement of pharmabiotics leading to the development of better probiotics for maintaining and enhancing our immune system which will be extremely beneficial for human health.

Identifying the novel macrophage substrates for the Mycobacteria secreted virulence factor Protein Kinase G

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Tuberculosis, a dreadful disease caused by *M. tuberculosis* is a major cause of global mortality and more so in the developing countries with the advent of extreme and total drug resistant mycobacteria. Mycobacteria are adept at hindering phagosome maturation once inside the macrophages and can effectively subvert the host immune response. It utilizes several host and also secretes a number of virulence factors for this process. One such virulence factor secreted by Protein kinase G (PknG), expressed only by pathogenic mycobacteria and released into macrophage cytosol during infection. PknG is secreted out of mycobacteria via the SecA2 secretion system and it prevents phagosome-lysosome fusion during early mycobacterial pathogenesis. PknG has also been implicated in reducing the level of PKA during early mycobacterial infection. The rubridoxin domain present at the N-terminus of PknG has been predicted to be involved in the activation of its kinase activity other that its autophosphorylation. Being a crucial virulence factor, inhibitors such as AX20017 and Sclerotiorin has been identified as specific inhibitors of PknG. Despite several allied studies, it still needs to be determined what are the macrophage substrates of PknG, which when phosphorylated by the protein, creates an environment favorable for early mycobacterial infection. Therefore we carried out a phosphoproteomic screen of non-infected or mycobacteria infected macrophages, which were untreated or pre-treated with PknG inhibitors. Three key proteins that emanated above the significant threshold in this screen were PSMD9, HIF1a and L13a. PSMD9 is a regulatory subunit of the 26S proteasome, which gets activated upon phosphorylation, HIF1a is an hypoxia inducible transcription factor, which gets degraded upon phosphorylation and L13a is a small ribosomal subunit whose mycobacterial counterpart has been shown to be phosphorylated by PknG. We are in the process of further identifying the role of PSMD9 phosphorylation in mycobacterial pathogenesis.

Cell fate commitment in early mesoderm populations in vertebrates

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During development functional identity of cell populations are specified according to their embryonic coordinates along the body axes. Knowledge of these developmental mechanisms is key for differentiation strategies aimed at generating organoids and stem cells, and therefore, would impact advances in regenerative medicine. Cardiopharyngeal mesoderm, which gives rise to heart and head muscles is a clinically important cell type. Using mouse genetics, embryonic stem cell differentiation as well as mouse embryology approaches, we reveal the mechanism specifying this mesoderm subtype. We show that the regulatory network governing cardiopharyngeal mesoderm is controlled by inhibition of Wnt / beta-catenin as well as Nodal (TGF-beta) signaling. Importantly, leveraging this finding, we have directed the differentiation of pluripotent stem cells into bipotent progenitors, which differentiate efficiently into heart and skeletal muscle. Our current efforts are to improve the generation of skeletal muscle stem cells in culture, which will help in modeling and treating muscle-wasting diseases. Another cell type that has attracted a lot of attention in the field is neuromesoderm. It contributes to the spinal cord as well as into paraxial mesoderm, which forms muscle-skeleton below the forelimbs. Our work has revealed the fate choice mechanism of this bipotent stem cell pool. Our findings have underscored the role of Tbx6, a T-box transcription factor, as a mesoderm fate switch in this population. Currently, we are dissecting the global function of Tbx6 in driving paraxial mesoderm fate. In summary, we are uncovering fundamental regulatory mechanisms underlying specification of distinct mesoderm subtypes as well as exploiting this knowledge to develop methods for deriving clinically relevant cell types from pluripotent stem cells.

The Peacock's tale: consequences of human-animal vicinity and interactions

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Natural habitats for animals are shrinking at an increasing rate 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 leading to more human-animal interactions and conflicts. The impact of local human population on animal populations living close to human population 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 and food given by humans might changefeeding habits, inter-individual competition and demographics of a species. The nature of humanpeafowl interactions was studied using questionnaire based survey. Conclusions emerging from survey responses about preference of peafowl for various crops, stages of crops eaten by peafowl, social customs and beliefs that contribute to treatment of peafowl by local community will be presented. Quantity and types of grains offered to peafowls by local community were estimated. People's perception of crop loss due to peafowl changed according to stages of crop season. Most people estimated crop loss due to peafowl in the range of 5-20%, especially around March-April harvest season. To understand the effects of interactions with humans on Indian Peafowl populations, time budget and feeding ecology was studied in two areas in Maharashtra and one in Rajasthan which differed in the extent of human- peafowl interactions. Time budget and diet composition of peafowl varied systematically across field sites as amount of grains offered by local people varied. Frequency of feeding bouts differed according to grains offered and risks/ disturbances from humans/ predators. The results can help us design strategies/ guidelines for Peafowl population management and conservation with community participation.

Mechanotransduction through Caveolae: Role of lipid rafts in homeostatic control of cell signaling and proliferation control.

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Caveolae are very specialized cholesterol-sphingolipid enriched domains that are recently evidenced to serve as an excess membrane reservoirs in buffering the cellular changes from the micro-environmental physical forces such as the changes in osmotic pressure, imposition of the stiffening forces and due to the shear stress caused by the fluid flow. Both pro and anti-tumorigenic roles of caveolae or rather caveolin-1 protein have been documented however the exact mechanistic insights on caveolae and cell proliferation is lacking. Here, I will present our study how caveolar disassembled vs. assembled states in stiffening forces may trigger differential signal transduction in normal glial progenitors which may eventually be a seed to cancerous transformation.

Investigating the role of long noncoding RNAs in mammalian gene expression regulation

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Recent transcriptome analyses have revealed a large subset of RNAs, defined as long non-coding RNAs (lncRNAs), which execute various structural or regulatory functions without being translated into proteins. Characterization of these novel lncRNAs in mammalian cells is expected to unravel important gene-regulatory functions and roles associated with the complexity observed in multicellular organisms. Several lncRNAs are differentially expressed in various cancers suggesting their critical function in the tumorigenesis. We have identified a novel lncRNA [miR100HG] that serves as a host gene for encoding a class of miRNAs, i.e. miR100 family. This lncRNA is differentially regulated during cell cycle progression with elevated levels during G1 phase. Depletion of this RNA from cells leads to a slower S-phase progression with concomitant G2 arrest. Interestingly, depletion of this lncRNAs doesn't alter the levels of the miRNAs that it encodes. Further, this lncRNA interacts with several RNA binding proteins including HuR and regulates the binding of HuR to its target mRNAs during cell cycle progression. So far, our studies have revealed a unique cell cycle regulatory role of a long noncoding RNA in mammalian cells.

Developing Bioproducts and Biomaterials from Agricultural Residues

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Agricultural residues are available in large quantities at low cost. In India, residues are usually burnt or buried leading to considerable environmental pollution. Our laboratory focuses on developing biobased materials from these agricultural residues. Currently, we have developed bioproducts from coir, banana fibers, sugarcane bagasse for food, electronic, packaging and other applications. Prototypes of these products have been made and we are looking to develop the products on a commercial scale. In addition, we are also working on using proteins in oil meals to develop films,fibers and 3D scaffolds for tissue engineering and controlled drug release applications. Another aspect of our research is to develop biosorbents for pollution control. Unique aspect of our products are that the raw materials are used in their native form without any chemical of physical treatment. This approach preserves the properties of the raw material and also reduces cost.

Chimeric Nanoparticle: A Novel Nanoplatform for Signaling Pathway Driven Cancer Chemotherapy

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Colon cancer has emerged as one of the devastating diseases in the whole world. MAPK-PI3K signaling hub has gained lots of attention due to its deregulation in colon cancer cells. However, selective targeting of oncogenic MAPK-PI3K hub in colon cancer remained highly challenging, hence mostly unexplored. To address this, we have engineered hyaluronic acid layered lipid-based chimeric nanoparticle (HA-CNP) consisting of AZD6244 (MAPK inhibitor), PI103 (PI3K inhibitor) and cisplatin (DNA impairing drug) ratio-metrically in a single particle. Electron microscopy (FESEM and AFM) and dynamic light scattering (DLS) were utilized to characterize the size, shape, morphology and surface charge of the HA-CNPs. Fluorescent confocal laser scanning microscopy (CLSM) and flow cytometry analysis confirmed that HA-CNPs were taken up by HCT-116 colon cancer cells by merging of clathrin and CD44 receptor-mediated endocytosis along with macropinocytosis to home into acidic organelles (lysosomes) within 1 h. Gel electrophoresis study evidently established that HA-CNPs simultaneously inhibited MAPK-PI3K signaling hub with DNA damage in HCT-116 cells. These HA-CNPs stalled cell cycle into G0/G1 phase leading to induction of apoptosis (early and late) in colon cancer cells. Finally, these HA-CNPs exerted remarkable cytotoxicity in HCT-116 colon cancer cells at 24 h compared to free triple drug cocktail as well as HA-coated dual drug loaded nanoparticles without showing any cell death in healthy L929 fibroblast cells. These HA-coated CNPs have prospective to be translated into clinics as novel platform to perturb various oncogenic signaling hubs concomitantly towards next-generation targeted colon cancer therapy.

15-Lipoxygenase (15-LO) dependent gene expression and function in IL-13-activated cells.

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Monocytes/macrophages are innate immune cells that play a crucial role in the resolution of inflammation. IL-13-mediated activation of monocytes/macrophages upregulate several gene products involved in inflammatory resolution. Among the most strongly upregulated genes in IL-13-activated monocytes/macrophages with potential anti-inflammatory properties are 15-lipoxygenase (15-LO), monoamine oxidase A (MAO-A), fibronectin etc. During monocyte/macrophage activation, IL-13 interacts with a specific (Type II IL-4R) receptor. Our data show the involvement of the receptor-associated Jaks (Jak2 and Tyk2) and the Jak kinase-mediated activation of Stats (Stat1, Stat3 and Stat6) during IL-13 activation of monocytes/macrophages. We presented evidence that Stat transcription factors, that control 15-LO gene expression, are also involved in regulating MAO-A expression in response to IL-13 stimulation. Other than the Jak-Stat pathway we also investigated the role of Egr1 and CREB transcription factors in regulating the expression of both 15-LO and MAO-A. The existence of Stat binding sequences in the promoter of 15-LO gene (not in the promoter of MAO-A gene) led us to speculate that MAO-A gene expression can be directly controlled by 15-LO. We demonstrated significant inhibition of MAO-A gene expression and function by transfecting 15-LO antisense ODNs in IL-13-stimulated monocytes and A549 lung carcinoma cells thus suggesting the novel regulation of MAO-A gene expression by 15-LO. Collectively, these results have major implications for understanding the mechanism and function of IL-13-activated cells and add novel insights into the pathogenesis and potential treatment of various inflammatory diseases.

Structural studies on proteins involved in synthesis and processing of mycolic acids in *Mycobacterium tuberculosis*

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Mycolic acids form a major component of the cell envelope and had been specific targets for anti-tubercular drugs. The enzymes which are involved in synthesis and processing of mycolic acids as such represent an important class of proteins for targeted drug designing strategies. *M. tuberculosis* exhibit alpha-alkyl and beta hydroxyl fatty acids (75 to 80 C- length) and are classified as alpha-, methoxy-, and keto-mycolates. Further, pathogenic mycobacterium species produce high levels of mycolic acids with cyclo-propane rings that helps in expanding the meromycolate chain. The *M. tuberculosis* genome constitutes S-adenosyl methionine (SAM) dependent methyl-transferases (MmaA1, MmaA2, MmaA3 and MmaA4) which are implicated in modification of mycolic acids with methyl chains and cyclo-propane rings. The importance of MmaA1 had been highlighted by the deletion of mmaA1 from *M. tuberculosis* resulting in hindrance to trans- cyclopropanation without accumulating trans-unsaturated oxygenated mycolates before CmaA2 in the mycolate cycle. This indicates a redundancy of function between MmaA2 and CmaA2. The Specific Objectives of our study were primarily crystal structure determination of MmaA1 methyl transferase and finally, a structure based inhibitor design against MmaA1. The proposed activity will result in understanding the pathogenesis of multi-drug resistant *M. tuberculosis* strains.

Structurally understanding the mechanism of Pyruvate M2 in tumor cell proliferation, transcription of genes, cell cycle progression

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Pyruvate kinase is a glycolytic enzyme with a key role in the Warburg effect and non-metabolic functions and thus it plays a critical role in regulating gene transcription. However, the structural and functional mechanisms underlying PKM2-regulated transcription of gene expression are not known. In the proposed project, we would like to understand the role of PKM2, it's functioning as a protein kinase, the interaction of PKM2 with nuclear proteins, histones and promoter genes may be involved transcription. The goal is to understand the mechanism underlying the nonmetabolic function of protein kinase in gene transcription and tumor cell proliferation. In this direction we have generated the recombinant constructs of PKM2 in *E.coli* (pET28 vector) as well as mammalian expression system (pEGFPN1 vector). We have generated PKM1 also for control experiments. To study the interaction with nuclear proteins we are studying in HepG2, HEK293 cells and A549 cells. Additionally, We are understanding activation of PKM2 or transition from non functional non-metabolic form to active metabolic form. The research outcome may help in understanding the role of PKM2 in tumor development and may be some possible molecules against tumor.

Understanding the host immune response and molecular pathogenesis of Leptospira infection

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Leptospirosis is zoonotic and emerging infectious disease of global importance. It is caused by gram negative bacteria Leptospira, which infects variety of domestic and farm animals which become major source of infection to humans. Leptospira is known to disrupt Toll-like receptor (TLR) signaling by varying Lipopolysaccharide (LPS) expression or downregulating expression of surface proteins to evade host immune attack and quickly disseminate and establish infection in various organs. In present work we have tried to understand how leptospira modulates the host innate immune response via TLRs by exploiting its surface proteins. We screened several Leptospira outer membrane/surface proteins viz. LipL32, LipL45, 21 kDa Leptospira surface adhesin (Lsa21)and Leptospira immunoglobulin like proteins (LigA and LigB) for their ability to activate/inhibit TLR2/4 signaling in HEK293 cell lines. Of these Lsa21 showed strong TLR2 and TLR4 activity leading to production of proinflammatory cytokines (IL-6, TNF-α), expression of costimulatory molecules (CD80, CD86, CD40), and maturation marker (MHCII) in mouse macrophages. We published the data in Nature Scientific Reports (Faisal et. al. Scientific Reports 2016, Dec 20;6: 39530). In continuation of search for identifying more proteins having TLR activity we showed that LigA and LigB were also able to activate mouse macrophages and induce production of proinflammatory cytokines (IL-6, TNF-α). Out of various portions of Lig proteins viz, conversed region (Ligcon), variable region of LigA (LigAvar) and variable region of LigB (LigBvar) tested, LigAvar was most potent. We are now trying to identify the domain involved in TLR activity. In conclusion, we have identified surface proteins which activates strong innate and need to be tested as subunit vaccine candidates in animal model (experiments are ongoing as part of second objective).

Development of comprehensive bioinformatics resource for newly sequenced genomes

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Scientific data is generated at much faster rate now than it was ever before! In the last 2 years we have produced the same amount of scientific data as that in last 50 years. Now the big bottleneck we face is to translate this information into knowledge. In recent years, the sequencing technology has undergone huge metamorphosis from humble Sanger sequencing methods to whole genome shut gun sequencing using 2nd and 3rdgeneration sequencing. Quick profiling of transcript expressions can be easily quantified with RNAseq leading to major discoveries. The cost of sequencing also has fallen substantially making it affordable to small labs. At IICB our research group is currently focusing on large scale transcript discovery via whole genome de novo sequencing of indigenous organisms using novel computational tools. We have already characterized and published an indigenous Lactobacillus sp. from guts of Indian individuals and sequenced and characterized transcriptomes of an eukaryotic mutualist, *Arthrinium malaysianum* that has huge commercial significance. We have also isolated several Cyanobacteria species from monuments in India and have undertaken whole genome de novo sequencing of those species using Ion Torrent and Illumina Hiseq platforms. Several commercially significant genes have been discovered for the first time that can be eventually used for over production of economically important metabolites. These platforms provide an uniq opportunity for comparative and evolutionary genomics. In addition we have developed a new computational analytic pipeline for whole genome sequences which is extremely light weight. We have named the product as GAL(Genome Annotator Lite) and is an open source product. Based on GAL, two genome analysis and data ware house platforms are created for two distinct clades of life e.g; Cyanobacteria (Prokaryotes) and Oomycetes (Eukaryotes). The Cyanobacterial resource includes comparative and functional genomics data for 69 complete Cyanobacterial genomes and the portal is available at http://bgagenomics.iicb.res.in. The Oomycetes functional genomics portal is available at www.eumicrobedbd.org. We have also created several pipelines for complete genome assembly and recently we completed assembly of 2 Leishmania genomes. Alongside, we also work on 3rd generation sequencing data including PacBio data for *Phytophthora ramorum*.

Investigation of the Dynamics of T-helper Cell Responses Induced by A Viral Vaccine

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Emergence and geographical expansion of Flaviviruses is a growing concern throughout the globe. The positive attributes of human vaccine may serve as the rational for designing efficient immunization strategies. Empirically developed live attenuated Japanese encephalitis (JE) vaccine provides an opportunity to identify the immune correlates of long-term protective antibody (Ab) responses. By providing help to B-cells, Follicular T helper (TFH) cells are limiting for devising the magnitude and quality of germinal center derived Ab responses. Here, employing JE vaccine as a model, we are attempting to identify and characterize the preferentially induced TFH-cell subset for its function in long-term protective immunity.

Perturbation of GPCRs and beta-arrestins occurs prior to onset of pathophysiological hallmarks of Alzheimer's disease

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Synaptic dysfunction is considered to occur prior to the appearance of pathophysiological and behavioral symptoms of Alzheimer's disease (AD). G-protein coupled receptors (GPCR), including mGluRs, and β -adrenergic receptors have been associated with synaptic dysfunction. GPCRs function through β-arrestins, which regulate receptor desensitization and activation of G protein-independent signaling pathways. Previous studies have shown anomalies in β-arrestin2 and β2-adrenergic receptor expression in both AD patients and AD mice. However, it is unclear whether GPCRs and β -arrestins contribute to early synaptic dysfunction seen in AD pathogenesis, and therefore, we examined whether altered GPCRs and their interacting molecules at mRNA and protein level could contribute to synaptic deficits in AD. We used APPSwe/PS1deltaE9 mice (APP/PS1) and litter mate WT controls for our experiments. We isolated synaptosomes from cortices of 1 month old (pre-plaque phase) and 9 month old APP/PS1 mice and age matched controls. We found significant decrease in β -arrestin1, mGluR5 levels in the synaptosomes from 1 month old APP/PS1 mice and this reduction was sustained until 9 months when overt symptoms are observed. While, β -arrestin2 levels increased significantly in the synaptosomes from 1 and 9 old APP/PS1 mice. β-arrestins were localized predominantly in retrosplenial area, entorhinal area of cerebral cortex, and pyramidal neurons of the hippocampus. Here we also report that Adrb1, Adrb2, Arrb1, Arrb2, Nedd4 and Usp33 mRNAs levels are down regulated in one month old APP/PS1 mouse brain hippocampus whereas Arrb1 mRNA is elevated and mGluR5 is diminished in cortex. Interestingly, Adrb2 and Usp33 mRNAs show sustained down regulation until three months in APP/PS1 mouse brain hippocampus. Further, Arrb1 and Usp20 mRNAs are up regulated and Adrb1 is down regulated in cortex of APP/PS1 mice (3 months). Intriguingly, at 13-14 months of age, levels of specific mRNAs (Arrb1, Arrb2, Adrb2, Mdm2 and Grm1) are significantly higher in synaptosomes of APP/PS1 mice compared to the wild type mice. Collectively, we demonstrate that the GPCRs and interacting proteins are perturbed in synaptic compartment early in AD and which may lead to behavioral deficits. Our results indicate that mGluR5 and beta-arrestins are potential early targets in the pathogenesis of AD.

Gene regulatory network of epidermal and sub-epidermal cell population enriched transcription factors revealed regulatory hierarchies underlying the cell proliferation and differentiation

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Elucidating the transcriptional gene regulation that underlie the development of multicellular organism is fundamental for understanding the mechanisms of cell and tissue specialization. Arabidopsis shoot apical meristem (SAM) is comprises of ~500 cells that are organized into three distinct zones. Stem cells reside in the central zone (CZ) and self-renew; however, their progenitors undergo cell proliferation and differentiation in the peripheral zone and underneath the CZ in the rib meristem, respectively. One of the key challenge is to decipher the gene regulatory networks (GRNs) that direct the selfrenewal and differentiation of stem cells into distinct cell types in SAM. We have identified sixty-five transcription factors (TFs) from the epidermal and sub-epidermal cell types of SAM stem cell niche and characterized them to build a comprehensive GRN. In situ hybridization and promoter reporter studies revealed predominate spatiotemporal expression pattern of the TFs. To systematically map the interactions among the TFs (proteins) and their TF promoter DNA elements, a high throughput yeast-one-hybrid assay was developed. In total, 16250 protein-DNA interactions were setup involving 47 DNA baits and 327 TFs, we found 165 interactions between 37 regulatory elements and 53 TFs. Majority of the TFs that interacted with target promoters are broadly expressed. To determine the regulatory hierarchy and their function in development, we used both genetics and molecular biology approaches. We identified molecular phenotype for 75% of the interactions. In one GRN, we identified GROWTH REGULATING FACOTR3 (GRF3) binding on the HDG12 promoter. In grf123 mutant HDG12 transcript level was reduced in comparison to WT. Analysis of hdg12 mutant plants revealed smaller leaves, as has been shown earlier for grf123 mutants. Taken together, the systems biology approach taken in this study elucidate role of GRFs GRN in regulating the HDG12 expression, and explain how GRFs exert their influence on the leaf and SAM size.

Diabetes induces pulmonary fibrosis through TGF-β1-activated epithelial-tomesenchymal transition (EMT) pathways

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Objective: 1.To investigate the hypotheses that diabetes may also induce long-term pathological changes in the lung similar to other organs. 2.To elucidate the signaling pathways contributing to diabetes-induced pathological changes in the lung. 3.To explore reasons for delayed response of the lung for effects of diabetes. Results and interpretations: The bronchoalveolar lavage fluid (BALF) of diabetic patients showed a substantial increase in MIP-1δ, IP-10, RANTES, TNF-α, MIP-1β, and TGF-β1 compared to the controls. The diabetic rat lung showed intense cell infiltration, collagen accumulation, and significant levels fibronectin, α-SMA both in the tissue and in cultured cells. The lung also showed significant upregulation of TGF-β1, vimentin, Twist, N-cadherin, and decreases in E-cadherin suggesting induction of the EMT process. Further, a substantial increase in the levels of the TGF-β 1 receptor, phospho(p)-SMAD2/3, pERK, pp38, RAGE, TGF-β 1 promoter activity, nuclear localization of SMAD3 and substantial decrease in the levels of SMAD7 suggested that diabetes-induced EMT was mediated through the activation of both SMAD-dependent and SMAD-independent signaling pathways. Additionally, glucose restriction (5mM) of diabetic cells suppressed the expression levels of inflammatory and fibrotic genes indicating that diabetes-induced EMT was mediated through the effects of hyperglycemia and glucose restriction promoted the mesenchymal-to-epithelial transition (MET). Results also show that SMAD7 levels were substantially more in the lung compared to the kidney from 4 through 12 Wk. post-diabetes induction suggesting that SMAD7 delayed the diabetes-induced pulmonary fibrosis. Additionally, persistent exposure of diabetic cells to higher glucose concentration (25mM) promoted the upregulation of caveolin1, N-cadherin, SIRT3, SIRT7 and lactate levels suggesting that diabetes in the long-term may promote cell proliferation. Conclusions: Our results report for the first time that diabetes induces pulmonary fibrosis by TGF-β1-activated EMT pathways. SMAD7 in part protects the lung during the initial stages of diabetes.

Regulation of cholesterol metabolism in *Mycobacterium tuberculosis* and its implications on mycobacterial persistence

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Tuberculosis (TB) remains one of the world's most important infectious diseases, with an estimated 10 million cases and 2 million deaths per year. Although the current treatment of drug-susceptible TB is effective, treatment duration is exhaustively long (6-9 months). The long treatment regimen is attributed to a subset of slow growing, non-replicating, metabolically inactive "persisters" population. Studies shows that targeting these persisters by altering the metabolic state of dormant *Mycobacterium tuberculosis* (Mtb) could increase the effectiveness of antibiotics and shorten treatment duration that ultimately could lead to a decrease in the frequency of MDR/XDR form of infection. We have earlier demonstrated that *Mycobacterium tuberculosis* (Mtb) could survive on media containing cholesterol as a sole carbon source and that cholesterol utilization is essential for Mtb to persist inside the host. We hypothesize that host cholesterol utilization during tuberculosis infection makes Mtb to persist by modulating critical metabolic and signaling pathways in a way that significantly decreases both the replication rate and the metabolic activity. These metabolically arrested non-replicating persisters are refractory to anti-mycobacterial treatment and predicted to be the main reason behind mycobacterial persistence. RNAseq based transcriptional profiling experiments revealed Mtb grown in cholesterol i) generates a transcription signature indicating reduced growth rate ii) up regulates genes required for growth in low oxygen (hypoxia) condition iii) differentially regulate genes of unknown function possibly regulating cholesterol mediated persistence in Mtb. We have scientific evidence that shows, Mtb culture when exposed to cholesterol rich environment modulates its own growth and selectively enriches slow growing persister population. Our long-term interest is to further expand our knowledge and identify novel metabolic and signaling networks involved in mycobacterial persistence. Besides identifying the mechanism, the current study provides opportunity of targeting persister, a new paradigm facilitating tuberculosis drug development.

Mechanobiological patterns in morphogenesis

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Morphogenesis-- the emergence of the three-dimensional shape and functional form in developing embryos, involves a strong interplay between active mechanochemical forces and biochemical signaling. Mechanical forces in cells and tissues arise from the adenosine-triphosphate (ATP) consuming activity of molecular motors in the cellular cytoskeleton. We will discuss the generic physical principles of the establishment of active mechanochemical patterns in the actomyosin cytoskeleton. This self-organization of the cytoskeleton can couple to signaling proteins that are involved in various morphogenetic processes, like the establishment of cell polarity and the emergence of body axes in developing embryos. We will discuss our recent and ongoing work on studying active cytoskeletal patterns on curved deformable surfaces, and show how this can explain alignment of geometrical and chemical axis in the establishment of cell polarity.

Autophagy is required for germline stem cell maintenance and delays their aging in Drosophila

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In multicellular organisms, the production of gametes is dependent on the continuous activity of specialized stem cells called "germline stem cells (GSCs)". The prolonged persistence of these stem cells in the gonadal niche renders them susceptible to cellular damage including oxidative damage which affects their aging and eventually death. Damaged GSCs are eliminated from the niche which subsequently leads to their loss. This results in the decline in production of gametes and eventually reproductive failure. Macro-autophagy (henceforth called autophagy) is a conserved degradative process that influences aging and is implicated in age-associated disorders. To investigate the role of autophagy in GSC maintenance and aging, we are studying the female GSCs of Drosophila as a model. To study the effect of autophagy on GSCs aging, we assessed the loss of GSCs in Atg7-/- mutant and Atg1 mutant GSC mosaics. Atg7-/- GSCs exhibited accelerated aging as compared to control GSCs. Atg1-/- GSCs are lost at a significantly faster rate as compared to the control GSCs. In contrast, moderately increasing autophagy levels through the expression of Atg8a or Atg5 specifically in the GSCs slowed down their aging significantly. Atg7-/- and Atg1-/- GSCs showed reduced phosphorylation of Mad indicative of decreased self-renewalsignaling within the niche. On the contrary, pMad levels were maintained at significantly higher levels in both Atg8a and Atg5 expressing GSCs. Similar trends were observed for E-cadherin and Armadillo, components of adherens junction complex, that are crucial for maintaining GSC within the germarium. Currently, we are exploring the relationship between Atg1, Atg7 (autophagy), pMad and E-cadherin signaling within the GSCs. Further studies are being carried out to determine the status of mitochondria in Atg null GSCs. Our work will lay a foundation that will be crucial for further studies in the field of reproductive biology, stem cell biology and regenerative medicine.

Role of neuronal nitric oxide synthase (NOS1) in LPS-mediated inflammation

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Nitric oxide (NO) is a signaling molecule generated when L-arginine is converted to L-citrulline by the enzyme nitric oxide synthase. Among the three isoforms of nitric oxide synthase, NOS2 (inducible NOS or iNOS) and NOS3 (endothelial NOS or eNOS) have already been appreciated as mediators of inflammatory processes. However, considerably less is known about the role of NOS1 (neuronal NOS or nNOS) in inflammation. We have investigated the role of Neuronal nitric oxide synthase (NOS1)-mediated regulation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and Activator protein 1 (AP1) transcription factors in macrophages. We demonstrate that the low-output NOS1 plays a critical role in the inflammatory response by promoting the activity of NF-κ B and AP1. NOS1-derived NO production in macrophages leads to the proteolysis of suppressor of cytokine signaling 1 (SOCS1), which results in the repression of NF-κB and AP1 transcriptional activity, resulting in a decreased proinflammatory cytokine production. Taken together, our results demonstrate that NOS1 is a fundamental regulator of gene transcription of the inflammatory response thereby heavily impacting the course, type and duration of the inflammatory process.

Mechanism and Relevance of IL-33 Mediated Mast Cell Proliferation in Asthma

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Interleukin-33 (IL-33), a member of the IL-1 cytokine family, is emerging as a new modulator of immune and inflammatory responses. Although IL-33 and its associated receptor ST2 are reportedly expressed in mast cells (MCs), the precise role of IL-33 in modulating MC function has not been determined. The objective of the project is to explore "Mechanism and Relevance of IL-33 Mediated Mast Cell Proliferation in Asthma". Our hypothesis is that IL-33 increases mast cells (MCs) numbers by the induction of MC proliferation, and this is relevant for the pathogenesis of asthma. In the present studies, we explored IL-33 effects on MCs in vivo and in vitro. IL-33 increased the number of peritoneal and skin MCs in vivo. IL-33 also resulted in increased proliferation of MCs in vitro, as explored by WST assay. IL-33 did not induce degranulation and was not cytotoxic for MCs. IL-33 induces MC proliferation further defines the role of IL-33 in MC-dependent diseases including allergies and may help to develop novel approaches for the treatment of these disorders.

Discovery of new type III polyketide synthases for novel polyketide products

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Polyketides belong to a diverse group of natural products with potent biological characteristics, like antibacterial and antitumor properties. They are synthesized by polyketide synthases (PKSs), a family of enzymes and multi-enzyme complexes, which vary according to their sequences, structures and catalytic mechanisms. Type III PKSs are simple homodimeric enzymes that produce a wide array of compounds, including pyrones, acridones, chalcones, stilbenes, phloroglucinols and alkyl resorcinols. With an aim to identify new type III PKSs producing novel polyketide products, genomes of several fungi were mined. Putative type III PKS from fungi belonging to Sordariomycetes class were cloned and expressed in *E. coli*. The substrate specificity and product profile of purified recombinant proteins (SmPKS from *Sordaria macrospora* and CtPKS from *Cheatomium thermophilum*) were analysed by HPLC method. The structure and moleculer weight of products were confirmed by HRMS. Both the enzymes synthesized tri, tetraketide pyrones, resorcylic acid and resorcinol compounds from various fatty acyl-CoA starter units. CtPKS was shown to exhibit high catalytic efficiency of 7.4 X104 s-1 M-1 towards arachidoyl-CoA. In another approach using CODEHOP (Consensus Degenerate Hybrid Oligonuceotide Primer) strategy, target PKS genes from the endophytic fungi (isolated from Bacopa monnieri, Abrus precatorius, Citrus aurantifolia and Datura wrightii) have been amplified. Eight fungal strains showed positive amplification for type III PKS. A new type III PKS, Fipks from Fusarium incarnatum BMER1 was amplified by TAIL-PCR and the predicted putative FiPKS showed 64% identity towards oxoalkylresorcylic acid synthase of Neurospora crassa. Attempts are being made to characterize this protein by heterologous expression in E. coli. Deep-sea microbes exist under harsh environmental conditions, which may trigger them to produce metabolites that help the microbes to survive in high pressure and low temperature conditions. Metagenomic DNA was extracted from deep-sea sediments obtained from the Bay of Bengal and Arabian Sea. Subsequently, PCR with degenerate primers specific for fungal type III PKS was carried out. Sequence analyses of partial fragment of 510 bp revealed similarity towards putative PKS from Fusarium (86%) and Neonectria sp. (80%). Further, new PKS from unexplored bacteria/fungi, Penicillium citrinum, Cladosporium sp. isolated from deep-sea sediment sample are exploited in the present study to identify and characterize type III PKSs that produce novel polyketide products/drugs with potent biomedical significance. Alternatively, functional metagenomic approaches are being employed to identify novel type III PKSs from deepsea sediment samples and deep-sea water samples available at Marine Biotechnology, NIOT. Further, metabolic engineering approaches are being initiated to produce aromatic polyketide in significant levels in *Saccharomyces cerevisiae.*

Modulation of innate immune response and characterization of viral polymerases for the development of potent vaccines and antivirals

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Hepatitis C virus (HCV) is a global pathogen and hence a serious health issue for the entire world in general and for India in particular. The newly developed direct acting antivirals (DAA) have shown significant improvement in HCV treatment. HCV genotype 3, the most prevalent form of HCV in India, continues to show inferior response to DAAs. HCV RNA dependent RNA polymerase (RdRp) is an important drug target as it is the catalytic subunit of the viral RNA replication complex. To identify novel small molecule inhibitors specific to the HCV RdRp, we established a high-throughput cell-based assay for HCV genotype 3a RdRp. The assay was used to screen small molecule libraries and a compound that specifically inhibited HCV genotype 3a RdRp was identified. The inhibition of HCV replication was further confirmed using genotype 3a replicon. Furthermore, the compound inhibited RdRp activity from all the six major genotypes of HCV suggesting that it could be potential pan genomic inhibitor of HCV. In addition, our lead compound could successfully inhibit other viruses including, hepatitis E virus (HEV) and Dengue (DENV) suggesting that it could be a broad-spectrum antiviral. Innate immune response forms the first line of defense against pathogen infection and viruses are known to modulate innate immune responses to establish successful infection. We investigated the role of HEV proteins in interfering with innate immune responses. We found that the HEV encoded papain-like cysteine protease (PCP) inhibited signaling from the innate immune receptor RIG-I through its interaction with the adaptor protein, IPS-1. Further characterization revealed that the N-terminal region of PCP is important for the interaction with IPS-1. In the presence of PCP, IPS-1 was unable to oligomerize and interact with othersignaling partners upon activation of RIG-I signaling.

LASER speckle based three dimensional tomographic imaging of blood flow during ischemic stroke: Theoretical framework based on experimental data from small animal ischemic stroke models

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To achieve a non-invasive 3-d tomographic imaging of blood flow by utilising dynamic laser speckles.

The role of Alternative oxidase in increasing energy efficiency under hypoxia

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Plant mitochondria contain Alternative oxidase (AOX) which is an integral part of the mitochondrial electron transport and can prevent reactive oxygen species (ROS) and nitric oxide (NO) production under non-stressed, normoxic conditions. Here we assessed the roles of AOX by imposing stress under normoxia in comparison to hypoxic conditions using AOX over expressing (AOX OE) and anti-sense (AOX AS) transgenic Arabidopsis seedling roots. Under normoxic conditions stress was induced with the defence elicitor flagellin (flg22). AOX OE reduced NO production whilst this was increased in AOX AS. Moreover AOX AS also exhibited an increase in superoxide and therefore peroxynitrite, tyrosine nitration suggesting that scavenging of NO by AOX can prevent toxic peroxynitrite formation under normoxia. In contrast, during hypoxia interestingly we found that AOX is a generator of NO. Thus, the NO produced during hypoxia, was enhanced in AOX OE and suppressed in AOX AS. Additionally, treatment of WT or AOX OE with the AOX inhibitor SHAM inhibited hypoxic NO production. The enhanced levels of NO correlated with expression of non-symbiotic haemoglobin, increased NR activity and ATP production. The ATP generation was suppressed in nia1,2 mutant and non symbiotic haemoglobin antisense line treated with SHAM. Taken together these results suggest that hypoxic NO generation mediated by AOX has a discrete role by feeding into the haemoglobin-NO cycle to drive energy efficiency under conditions of low oxygen tension.

Self-assembled amphiphilic prodrug-based gelators: A novel drug delivery platform approach for *glioblastoma multiforme* therapy

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A significant leap in drug delivery is an autonomous system that titrates the amount of drug released in response to a disease, for instance, tumor growth, ensuring the drug is released only when needed at therapeutically relevant concentration. Diseases have inherently fluctuated in nature such as tumor growth, inflammatory and autoimmune diseases, in particular, pose an enormous challenge to deliver drugs in safe, efficient and compliant manner. We have developed an injectable hydrogel with biocompatible amphiphile. A detailed characterization of the hydrogel that can release the drugs in response to tumor growth has been carried out. Additionally, we have evaluated the cytotoxicity of chemotherapeutic agent (camptothecin, CPT) and PARP- inhibitor (AG014699), using a series of in vitro studies. Additionally, I will discuss about how disease-responsive and disease-targeting biomaterials have developed to i) improve the lifetime of the transplanted organs and ii) inflammation-targeted drug delivery to alleviate inflammatory bowel diseases.

Multiscale modeling of glycosylation

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Glycosylation produces an abundant, diverse, and highly regulated repertoire of glycans (oligosaccharides) that are frequently attached to proteins and lipids. Carbohydrates remain the least structurally characterized among the major classes of biological molecules. They are challenging because glycans are not templated. Unlike proteins, nucleic acids or lipids, carbohydrates are typically associated with a high extent of conformational heterogeneity resulting from the high number of monosaccharides and possible glycosidic linkages and also because of their intrinsic flexibility. Furthermore, glycans can be highly branched. Consequently, carbohydrates arguably represent the most challenging class of biomolecules in terms of experimental characterization and elucidation of dynamics of structure-function relationships. On the other hand, their flexibility and dynamics frequently play a key role in biological activity and must be taken into account. Furthermore, to be able to predict a glycan's impact on the protein function, it is critical to understand its impacts on protein structure and dynamics. Additional knowledge of glycobiology in the context of 3-dimensional structures is crucial for the fundamental understanding of biology and pharmaceutical development. We have used predictive application of computational methods such as molecular dynamics (MD) simulations to 3D structure predictions of glycans and revealing the binding mechanism of glycans to proteins.

Development of antimalarial inhibitors targeting Plasmodium parasite plasmepsins

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Malaria is a deadly disease killing hundreds of thousands people each year worldwide. The disease has acquired resistance against the available drug combinations, which urgently demands the development of novel and potent antimalarial drugs. The four vacuolar plasmepsins (PMs) in P. falciparum involved in the hemoglobin catabolism represent promising targets to fight against drug resistant malaria parasites. High antimalarial activities can be achieved by simultaneously inhibiting all four vacuolar PMs. However, developing a single drug targeting all these enzymes remains a challenge. In this study, plasmepsin II (PMII) is explored as a model system for structure-guided drug discovery using inhibitors from a KNI-series. Compounds used in this study (KNI-10742, 10743, 10395, 10333, and 10343) exhibit low nanomolar inhibition against PMII. The high resolution crystal structures of PMII–KNI-inhibitor complexes reveal crucial interactions modulating their potency. Important individual characteristics of the inhibitors and its importance in potency have been established. The alkylamino analog, KNI-10743 has an intrinsic flexibility at P2 position that potentiates its interactions with Asp132 and Leu133. While in the phenylacetyl tripeptides, KNI-10333 and KNI-10343 accommodating different p-substituents at phenylacetyl ring at P3 position, determines the orientation of the ring making novel hydrogen bonding contacts, responsible for their differential potency. KNI-10333 and KNI-10743 possess considerable antimalarial activity and lack of cytotoxicity, and are also effective in blocking the activities of other vacuolar PMs. Therefore, these inhibitors are promising candidates for future clinical trials. Further modifications to KNI-10333 and KNI-10743 could generate derivatives with improved antimalarial activity for clinical use.

DNA aptamer based functional DNA origami with various nanostructures

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With the latest advancement of DNA nanotechnology, specially with the introduction of DNA origami, researchers have widely demonstrated the structural diversity that can be programmed and visualized with various single molecule techniques such as Atomic Force Microscopy (AFM), SEM, TEM, Fluorescence and very recently with single molecule FRET. Recently the functionalizing aspect of DNA origami is being in focus. Here we plan to detect multiple targets such as adenosine, thrombin, lysozyme, kanamycin etc. on a single DNA origami platform. DNA origami surface and will be characterised using atomic force microscopy. We have also been working on different shapes of Origami Aptamer combination for detection of target and delivery of drugs in one step. We are also modifying the origami with different nanoparticles for multiple applications.

Nanopore and AFM Platform to study Chromatin Structure

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We are interested in understanding structural and functional aspects of inter-nucleosomal and inter-chromatin fiber interactions. These interactions lead to small and large scale chromatin condensation. Regulation of these interactions is primary to local chromatin condensation, higher order chromatin folding as well as a prime mechanism for gene silencing. Effects of these interactions and local condensations are evident in developmental as well as genetic disorders systems. This makes it imperative to understand the role of magnitude, time dependence and regulation of these inter-nucleosomal interactions. However, the magnitudes of these biophysical interactions are extremely small (few picoNewtons) and their range is only a few nanometers (nm). We are developing biophysical tools sensitive to single molecule resolution. I will present data on detecting octameric states of nucleosomes and CENPA-nucleosomes using nanopore platform. Further we will also present preliminary data on AFM measurements of molecular forces.

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Interplay of hnRNPA1, telomere DNA, and TERRA RNA in telomere maintenance and structurefunction analysis of BAF250a

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hnRNPA1 has been shown to promote the telomere elongation apart from its general roles is in RNA transport and alternative splicing. It is a modular protein with two RNA Recognition Motifs (RRMs) domains (RRM1 and RRM2, collectively called UP1) and an RGG-box (rich in Arg and Gly residues) containing C-terminal region that constitutes additional nucleic acid and protein binding motif in hnRNPA1. UP1 has been shown to specifically bind and destabilize telomeric G-quadruplex structures and participate in telomere remodeling. However, the role of RGG-box in telomere ssDNA and G-quadruplex recognition and unfolding remain unexplored. Here we report the binding and unfolding of telomere G-quadruplexes by UP1 with RGG motif (UP1+RGG) using various biophysical methods including NMR spectroscopy. Our results show that RGG box enhances the binding and G-quadruplex unwinding activity of UP1. Further, our results suggest that the unfolding of TERRA RNA by UP1 is structure dependent. BAF250a (also known as ARID1a) is a subunit of BAF-A chromatin remodeling complex that was also found to associate with TERRA RNA in a proteomic screen. BAF250a contains an N-terminal DNA binding ARID (~110 residues) and C-terminal folded region (~250 residues) of unknown structure and function, recently annotated as BAF250_C. In spite of being a central subunit of BAF-A complex, the exact contribution of ARID and BAF250_C in BAF-A functions have not been established. Here, using hydrophobic core analysis, fold prediction, and comparative modeling we have associated a β-catenin like ARM-repeat fold to BAF250_C. Further, we have probed the interaction of ARID with dsDNA sequences using ITC and NMR methods. Using NMR chemical shift perturbation experiments we have mapped residues interacting with different DNA sequences on the structure of ARID and generated the data driven models of ARID-DNA complexes.

Artificial sweeteners increased intestinal permeability, altered expression of tight junction proteins and glucose transporters in human intestinal Caco-2 cell line.

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Urban lifestyle promotes artificial sweeteners (AS) consumption to prevent the increasing prevalence of metabolic disorders such as obesity and type 2 diabetes (T2D). These AS helps to limit the caloric intake and easily available in market such as diet foods, ice creams, chocolates and beverages like soda drinks. The prime concern has been raised about the safety and possible long-term effect of these substitutes for human health. It is a well-known fact that AS seem to be active in the gastrointestinal tract and seem to affect the intestinal functions which might eventually lead to many complicated conditions such as increased insulin secretion, effect on weight, appetite and glycaemia. The Food and Drug Administration (FDA) have approved the AS consumption but there usage is still controversial. Among them the presence of large amounts of sucralose within the gastrointestinal tract was found to be associated with histo-pathological changes in colon of rats. Saccharin is generally considered to be safe, remains un-metabolized by human body but eliminated rapidly in the urine. Subsequently it is also known to cause liver inflammation and alters the mouse gut microbiota Similarly, aspartame is a dipeptide derivative (L-aspartyl L-phenylalanine methyl ester) absorbed from the intestinal lumen and hydrolyzed mainly to phenylalanine and aspartic acid and small amount of methanol which is oxidized to cytotoxic formaldehyde and formic acid. To best of our knowledge, there are no elaborated studies investigating the cellular and molecular mechanisms of AS on biomarkers related to hyperglycemia and its influence on intestinal barrier integrity. We investigated the influence of three different AS on the integrity of Caco-2 cell monolayers as an in-vitro model of absorption and metabolism. Our results indicated first time that AS has capability to dysfunction the TJ assembly via increased membrane permeability, changes in levels of TJs proteins and glucose transporters.

Temperature sensing mechanism in Mycobacterium and its role in pathogenesis

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The success of MTB is tied to the adaptive repertoire of the bacilli in the face of varying and hostile environments within the host. Therefore, we need to explore novel strategies to combat mycobacterium, which can be achieved by having a through understanding about how mycobacterium adapts to the adverse environmental factors encountered inside the host for its survival and persistence. Once such factor is its exceptional adaptability to the change in the host body temperature after microbe invasion. Therefore, by understanding how mycobacteria maintain its pathogenicity while adapting to the changing temperature could provide important clues for developing new drug targets. Consequently, major objective of this proposal is to understand how change in the host body temperature during MTB infection reprograms the transcriptional machinery of the bacilli and how it regulates MTB pathogenesis. I am using genomics, proteomics a d computational approaches to model transcriptional, post-transcriptional and translational regulation of this pathogen in the hope to find novel molecular strategies to interfere with the unique regulatory pathways of MTB and treat this costly disease. To this end, I have created an in vivo mycobacterial temperature reporter, which can be used for functional genetic screening. Additionally, I have identified the presence of RNA thermometers in mycobacterium at whole genome level. Furthermore, to study the effect of temperature change on transcriptional and translational regulation, I have generated mycobacterial sigma factor mutant strains as well as FLAG tagged sigma factor overexpression lines to be used for transcriptome analysis upon temperature change in wild type and mutants using RNA Seq and regulators of transcriptional changes using ChIP Seq.

Identification of novel neuronal signals in stem/progenitor development and maintenance.

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We have proposed to identify neuronal signals influencing blood progenitor cell development and maintenance with the focus on identifying secreted entities from the brain.With specific emphasis on identifying new neuronal circuitry, the upstream physiological inputs and the systemic cue mediating this long range signalling in hematopoiesis. The presentation will encompass the significant progress achieved in each of these aspects and discuss an interesting avenue where in the use of odors in controlling blood progenitor immune-potential has been identified.

Mobile organisms to patterned vegetation: Investigation of self-organisation in ecological

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Various ecological and other complex dynamical systems exhibit self-organisation and critical dynamics in space and time. One such example of dynamics is abrupt regime shifts or critical transitions, wherein they reorganize from one stable state to another over relatively short time scales. Because of potential losses to ecosystem services, forecasting such unexpected shifts would be valuable. Using mathematical models of regime shifts, ecologists have proposed various early warning signals of imminent shifts. In our research, we have investigated a number of questions related to spatial selforganisation as well as early warning signals of critical dynamics of ecosystems. In this talk, we summarise the ones that were part of Ramalingaswamy-Fellowship research support below. Our work has led to six publications and one more currently in advanced stages of completion.

Genetic, metabolomic and chemical interrogation of apicomplexan metabolism: Targeting pathways with essential role in growth and differentiation for drug discovery.

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Understanding essential metabolic pathways in parasitic organisms facilitates the development of anti-parasitic drugs. Towards this we have carried out biochemical and genetic validation of key pathways pertaining to nutrient and energy metabolism. Using a combination of nutrient depletion, genetic manipulation, pharmacological intervention, and metabolic labeling studies, we have dissected the plasticity of central carbon and energy metabolism in both *Plasmodium falciparum* (malaria parasite) and *Toxoplasma* gondii (toxoplasmosis parasite). In experiments carried out with *P. falciparum*, we have studied the kinetics of drug action by monitoring glycolytic flux in a parasite stage specific manner using NMR metabolomics and demonstrate the use of this method for identifying fast acting drugs targeting ring stage parasite. We also demonstrate how metabolic studies can help in validating the mechanism of action of inhibitors and their analogs in wild type and drug resistant parasites using the mitochondrial inhibitor atovaquone as an example. Finally, we demonstrate the versatility of parasite metabolism in using alternate nutrients to assimilate carbon and obtain energy, using *T. gondii* as a model. The unique aspects of parasite metabolism revealed by our work will facilitate future studies on discovering specific metabolic inhibitors as anti-parasitic agents.

Effect of Membrane Composition on Receptor Association

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The association of single transmembrane receptors, such as the ErbB receptors is a key event in initiating cell signaling networks. The interactions between these receptors have been well characterized for both ligand-driven and pre-formed dimers. However, the role of the membrane in modulating association is less well understood and assumes greater importance in light of altered membrane composition in diseased states. In this talk, I will discuss how membrane composition has been observed to induce both structural and dynamic differences in receptor association. Computational studies, especially those using coarse-grain simulations have been successful in predicting the role of the membrane and calculating the related free energy landscapes. Membrane perturbations and differences in lipid chain order, related to the lipophobic effect, have been shown to play a large role in driving membrane protein association. Understanding the role of the membrane in receptor association will provide general design principles driving receptor organization, as well as help to identify novel therapeutic strategies.

Generation and characterization of minichrosomes and neocentromere formation in Plants

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IISER THIRUVANANTHAPURAM

Minichromosomes in plants represent extra chromosomal genetic entities analogous to plasmids in bacteria that are dispensable for normal growth and reproduction in plants. They are mostly heterochromatic, supernumerary in nature, reported to increase over generations and are known to influence meiotic recombination. Further in some plant and animal species, minichromosomes (B chromosomes) are known to influence meiotic drive, directing its own preferential transmission in gametes that give rise to next generation. Other than this, there are no reports of minichromosomes inducing any heritable mutation in the otherwise normal chromosomes of host species. Here, we report our observation where in a ring minichromosome produced as a result of centromere specific histone H3 (CenH3) mediated genome elimination process underwent recombination to double its size and upon further transmission to next generation yielded a novel mutant phenotype that shows a characteristic long lived, bushy phenotype with multiple plantlets arising from a single mutant plant. The mutant phenotype is stably transmitted and segregates in a Mendelian fashion. In this presentation, I will present the identification, meiotic behaviour and efforts made towards molecular characterization of the mutant phenotype most likely induced by the minichromosome.

Decoding the Epigenetic Landscape of chromatin by the dual activity proteins CBP and CBX4/PC2

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Epigenetic modifications in DNA and core histone proteins of chromatin fine-tune the underlying gene expression programs, genome repair as well as replication. The epigenetic modifications are operated through a class of proteins termed as "chromatin reader/effector" which lead to differential recruitment of other regulatory factors. The research focus of Chromatin Dynamics Laboratory is to understand some of these epigenetic readers in the context of cellular functions and their possible connection to the disease. In this context we were interested to understand the epigenetic cross-talk between dual activityproteins (i) a general transcription coactivator, Creb binding protein (CBP) and (ii) a canonical Polycomb repressor complex (cPRC1) component, a chromobox protein, CBX4/PC2 which has both chromatin writing and reading functions. CBP is a Histone Acetyl Transferase (HAT) and can mediate multi-protein interactions. We have been able to demonstrate that bromodomain of CBP binds to histone H3K56Ac in an autoacetylation-dependent manner. This interaction has been proposed to be due to an autoacetylation induced conformational switch of CBP. We further show that CBP bromodomain interacts with histone chaperone Asf1 and this interaction is instrumental in delivering the histones to the HAT domain of CBP to promote H3K56Ac. CBX4/PC2, an integral component of cPRC1 complex, is a SUMO E3 ligase of several factors implicated in DNA damage response. We have identified it to be a novel regulator of telomerase activity. We observed an association of CBX4 and hTERT, the catalytic component of the telomerase enzyme, in cellular context. Through several cell biological assays we establish CBX4/PC2 as a novel SUMO E3 ligase for hTERT. We also identified SENP2/3, as the desumoylase for hTERT. Telomerase has already been reported to have role in transcriptional regulation of selective subsets of genes and we identify that CBX4 is able to epigenetically regulate their expression. Thus we have been able to relate the chromatin reading and writing activities of two individual dual activity proteins and their consequent role in cellular functions.

Investigating the enzymology of methylations in anaerobic Vitamin B12 biosynthesis

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Vitamin B12 (cobalamin) is an essential cofactor for humans and several other living organisms(1). Structurally, B12 and other cobamide cofactors consist of a tetrapyrrolic corrin ring containing a cobalt ion, coordinated to an upper and a lower ligand, and are synthesized in the environment exclusively by prokaryotes via an aerobic or an anaerobic pathway (1). The anaerobic biosynthesis of 5,6-dimethylbenzimidazole (DMB), the lower ligand of B12, branches out from the purine biosynthesis pathway and is catalyzed by the bza operon, consisting of genes bzaA-E(2). The formation of DMB occurs through consequent methylations of 5-hydroxybenzimidazole (5-OHBza) and the intermediates 5-methoxybenzimidazole (5-OMeBza) and 5-hydroxy-6-methoxybenzimidazole (5-OMe-6-MeBza) are also lower ligands of other naturally occurring cobamide cofactors. The conversion of 5-OHBza to 5-OMeBza is predicted to be catalyzed by the gene product of bzaC, annotated to be a class-I SAM-dependent methyltransferase (3). Our study involves characterization of the activity and mechanism of the enzyme BzaC from two anaerobes, Eubacterium limosum and Moorella thermoacetica. We have purified the BzaC homologs, and in vitro reconstitution of their methyltransferase activity is currently underway. We also find that the two homologs are highly similar, except that the E. limosum BzaC consists of an additional domain of unknown function, DUF2284. We are examining the role of the DUF2284 domain through bioinformatics, biochemical and structural studies. The study of the role of BzaC, the first of the three methyltransferases in the anaerobic biosynthesis of DMB, will help us to better understand the activity of the other enzymes of the bza operon and their role in the overall process of cobamide cofactor biosynthesis.

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Accurate Prediction and Recovery of Human Resting State Brain Connectivity and Dynamics

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Computational modelling of the spontaneous dynamics over the whole brain provides a critical window in understanding the spatiotemporal brain dynamics that unfolds on a given anatomical connections. These connections in the healthy brain exhibits gradual eterioration or dysfunction of structure (e.g. in diseased states, aging, across individuals). Recent, experimental evidence further suggests that the adverse effect of such dysfunction is clearly visible on spontaneous dynamics characterized in particular by changes in resting state functional connectivity and its graph theoretical properties (e.g. modularity, hub classification, rich club index). These changes originate from altered neural dynamics in individual brain areas that are otherwise poised towards a homeostatic equilibrium to maintain a stable excitatory and inhibitory activity. Using a mean-field network model that operates close to criticality we show excitation-inhibition (E/I) balance (that is the local Glutamate/GABA ratio) has the potential to provide substantial recovery and restore the functional connectivity in the higher order neurocognitive networks. Further, recent findings suggest that these cognitive networks e.g. Saliency network (SN), Default Mode Network (DMN) and Dorsal Attention Network (DAN) are hubs of the brain and important for cognitive functions. Their dysfunction also lead to a variety of neurological disorders and pathological spatiotemporal brain dynamics. We show that local homeostatic plasticity provides a functional recovery by re-establishing excitation–inhibition balance in all areas that are affected by lesion. We systematically compare the extent of recovery in the primary hub areas and demonstrate that stability, richness similar to normal resting state is achievable.

Kindlin isoform regulates cell migration and proliferation in Colon Cancer Cells

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Gastrointestinal malignancies are the leading cause of cancer-related mortality worldwide. Changes in the function of the target gene that regulates cell-cell and cell-extracellular matrix interaction have been implicated in the progression of colorectal cancer metastasis. Integrin's and integrin-associated proteins, component of extracellular matrix, play an important roles in cell invasion and tumorigenesis through modulations of integrin expression and their downstream signaling. Kindlin, the member of the focal adhesion family, regulates integrin activation and involved in the regulation of cell-matrix adhesion. I propose to determine the molecular mechanism of the roles of Kindlin isoform in the colon cancer progression and selfrenewal of Colon Cancer Stem Cells. Our preliminary result shows the significant downregulation of Kindlin 1 in the colonosphere as determined by both QPCR and western blot. Further, Kindlin isoform regulates cell proliferation and migration of the colon cancer cells. Future studies will delineate the exact role of this important family in the progression of colon cancer progression.

Deciphering the role of the phosphatidylinositol 3-kinase oncogenic mutation in conferring anti- HER2 therapy resistance by enriching for the stem-like tumor initiating cell population in HER2 oncogene-positive breast cancer

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HER2 (Human Epidermal Receptor 2) oncogene is amplified in about one-fifth of all breast cancers (BC) characterized by their aggressive nature, propensity to metastasize and resistance toward chemotherapeutic agents. HER2+ BC cells are critically dependent on the phosphatidylinositol 3-kinase (PI3K) signaling for tumorigenesis, metastatic progression and tumor stem cell maintenance. In fact, success of FDA-approved anti-HER2 agents, like HER2 monoclonal antibody herceptin is dependent on its ability to effectively inhibit the PI3K signaling. Herceptin-resistant tumors often bypass anti-tumor effect of the drug by hyper activating the PI3K signaling by multiple mechanisms including gain of oncogenic mutation in the catalytic subunit of PI3K enzyme itself. Herein, we have aimed to decipher the exact mechanism by which H1047R PI3K mutant tumors develop herceptin resistance. We proposed that this could be due to enrichment of cancer stem-like cell (CSC) population. Indeed, we have conclusively demonstrated that the co-existence of H1047R PI3K in HER2 overexpressing mammary epithelial or BC cells increases the number of cells having phenotypic and function properties of BCSC. This is directly associated with mutant PI3K, since genetic knock-down or pharmacological inhibition of p110 , the subunit of PI3K bearing the oncogenic mutation, drastically diminishes such properties of HER2+ BC cells. Part of these could also be correlated with a plethora of molecules secreted by the mutant cells due to their pro-senescent nature. The secretory phenotype of mutant expressing HER2+ cells acutely sensitizes them to inhibition of molecular chaperone machinery HSP90. Thus, direct inhibition of HSP90 could be used as a therapeutic modality for tumors bearing both HER2 and H1047R mutant PI3K. Furthermore, lapatinib, a small molecule HER family kinase inhibitor sensitizes HER2+ cells bearing H1047R mutation despite of their lack of sensitivity to herceptin. Therefore, lapatinib can also be considered as a successful therapeutic option for PI3K mutant, herceptin resistant HER2+ breast tumors.

Role of Nuclear Receptor Coactivator PGC1β in Angiogenesis in Endothelial cells.

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Impaired angiogenesis is a major problem in would healing and cardiovascular complications in diseases like diabetes. The reason behind this impaired angiogenesis is endothelial cell dysfunction (ECD) because of prolonged exposure to hyperglycemia. There are several reasons for ECD at cellular level and among them, the excessive production of ROS in endothelial cells is one of the major role for ECD. Here, we have postulated that nuclear receptor co-activator PGC1β might ease the ROS management in ECs and thus protect the endothelial cells (ECs) to become dysfunctional. To validate out hypothesis, we have investigated the role of PGC1β in angiogenesis in ECs. We observed that expression of PGC1β in various ECs was lower than PGC1α. since PGC1αis pro-angiogenic thus we speculate for our expression studies that PGC1β might antagonize PGC1α effect in ECs. Further we did gain-of PGC1β functional studies to assess the angiogenic potential of PGC1β in HUVEC cells using wound scratch assay and tube formation assays. In wound scratch assay, we observed that PGC1β over expressing (OE) HUVEC cells migrates slower (in both number and distance) compare to vector control cells. In tube formation assay, PGC1β OE cells rearrange in tube like structure slower compare to vector control cells. These findings, taken together with migration assay, so far reveals that PGC1β is an antiangiogenic gene in ECs. In future, we will evaluate its role of PGC1βin ROS management in diabetic ECs.

Delineation of Wnt/b-catenin pathway in IRF3 mediated innate immunity in Toxoplasma gondii infection.

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The Wnt/ß-catenin pathway plays a critical role in cellular development, survival, proliferation, but the role of this pathway in immunity is still under surveillance. Our current research is focused to find the role of Wnt/ß-catenin pathway in innate immunity during the infection of protozoan parasite *Toxoplasma gondii*. *T. gondii* is an obligate intracellular pathogen that normally facilitates host survival for encystment within the cells. Recently, we reported the pro-Toxoplasma role of interferon regulatory factor 3 (IRF3) which is an essential transcription factor for the expression of antiviral genes, including type I interferons and several interferon stimulating genes (ISGs). We showed the phosphorylation of IRF3 facilitates parasite replication. In the present study, we sought to find out the role of Wnt/ß-catenin pathway on IRF3 mediated innate immunity against Toxoplasma infection. Here, we report that phospho-ß-catenin-TCF4 complex binds at the promoter region of IRF3, and triggers transcription of tolerogenic molecule, indoleamine-2,3- dioxygenase (IDO). We also observed the parasite replication negatively regulates IDO1 expression by depleting reactive oxygen species (ROS) and over-expression of IDO1 in presence of IFN-γ abrogates parasite replication. In absence of IDO1, tryptophan, one of the essential amino acids was metabolised via melatonin pathway. There was burgeoned parasite growth in presence of higher level of melatonin which helps to suppress ROS. Again, the treatment with tert-butyl hydroperoxide (tBHP), a ROS inducer, could impede parasite replication. It implies that T. gondii utilizes tryptophan to produce antioxidant melatonin which keeps cells alive for better parasite replication.

Role of SIRT2 in cardiac fibrosis

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Cardiac fibrosis is a major complication associated with age related diseases like diabetes mellitus and hypertension. There is no definitive therapy available for development of cardiac fibrosis. The objective of this study is to elucidate mechanism of regulation of cardiac fibrosis by SIRT2. Methods: Fibroblasts isolated from mouse hearts were over expressed with SIRT2, and then fibrosis and TGFβ1 signalling were evaluated by western blotting. Neonatal cardiac fibroblasts and HEK cells were used for in vitro experiments. Role of SIRT2 in JNK signalling was studied. SIRT2 and JNK interaction was studied by coimmunoprecipitation. Also, the role of SIRT2 in development of diabetic conditions was also studied. Results: Western blot and Confocal analysis revealed increased expression of fibrotic markers like fibronectin, collagen 1a and α-SMA in SIRT2 overexpressed fibroblasts. Further molecular analysis indicated that the TGF-β signalling pathway was not activated in SIRT2 over expressed fibroblasts. Instead, we found that SIRT2 overexpression activate JNK, a stress responsive kinase involved in the development of fibrosis. Co-immunoprecipitation showed that SIRT2 interact with JNK and deacetylates it. Western blotting results showed that SIRT2 over expression increases JNK activity, while SIRT2 depletion and SIRT2 mutant decrease its activity. Deacetylation of JNK by SIRT2 promotes oxidative stress-induced cell death. Conversely, SIRT2 inhibition attenuates H2O2-mediated cell death in HeLa cells. SIRT2 deficient (SIRT2-KO) mice exhibit increased acetylationof JNK, which is associated with markedly reduced catalytic activity in liver. Interestingly, SIRT2-deficient mice were resistant to acetaminophen-induced liver toxicity. SIRT2-KO mice show lower cell death, minimal degenerative changes, improved liver function and survival following acetaminophen treatment Conclusion: We can postulate that SIRT2 induces fibrosis through activation of JNK pathway. SIRT2 may be a potential therapeutic target for the treatment of cardiac fibrosis. our work identifies SIRT2-mediated deacetylation of JNK as a critical regulator of cell survival during oxidative stress.

Understanding the biology of Hepatitis E virus and development of vaccine and drugs against it.

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Hepatitis E virus (HEV) causes acute hepatitis, accounting for~ 50% of viral hepatitis in human. In India and many other developing countries, lack of proper hygiene & sanitary facilities, which are crucial prophylactic measures against HEV, as well as unavailability of specific drugs & vaccine has allowed HEV to become a major public health concern. My research efforts are directed at establishing a laboratory model for studying the life cycle of genotype-1 HEV and identifying the molecular mechanism(s) controlling the release of HEV from infected cells. We followed a trans-encapsidation strategy to establish a human hepatoma stable cell line based laboratory model of genotype-1 HEV, in which an EGFP chimeric viral genomic RNA is constitutively synthesized by ribozyme mediated processing of a precursor transcript. These RNA are able to replicate and assemble into new virions utilizing the capsid protein produced in trans. Analysis of various stress inducing agents revealed a positive role of endoplasmic reticulum stress in enhancing viral replication. Further investigations led to the discovery of a new stress regulated virus encoded factor, named ORF4, which mediates the assembly of a multiprotein complex consisting of several viral and host factors and also stimulate the activity of viral RdRp and promote viral replication. Towards identifying the molecular mechanism(s) of HEV release, a Yeast two hybrid library screening approach was followed. 164 host proteins were identified and the host-virus protein interaction network was generated. Proteins involved in different processes such as host metabolism, immune response and cell signaling pathways were dominantly represented in the network. Remarkably, we have also obtained several proteins involved in host translation regulation and few proteins known to play important roles in the release of other viruses. Ongoing studies aim at obtaining a definitive answer regarding the role of these proteins in virus replication/release.

Fragile X premutation rCGG repeats induce early defects in larval neuromuscular junction (NMJ) likely due to attenuation of mGluR signaling.

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Fragile X-associated tremor/ataxia syndrome (FXTAS) is a progressive neurodegenerative disorder recognized in older patients carrying fragile X premutation (CGG)55-200. We have established a Drosophila model that ectopically expresses the human FMR1 5′-UTR containing either normal- or premutation-length rCGG-repeats. We showed that fragile X premutation rCGG repeats alone is sufficient to cause neurodegeneration in a dosage and repeatlength dependent manner, and induce the formation of inclusions. Here we are utilizing this FXTAS fly model to identify small molecules that can ameliorate rCGGmediated neuronal toxicity and lethality. Of particular interest among screened compounds are Glutamate receptor agonists. Further, we also found that rCGG repeats leads to significant decrease in the number of active zones at larval glutamatergic neuromuscular junction (NMJ). Through genetic interaction experiment, we have identified a dRep2 (DNA fragmentation factor-related protein 2) that specifically modulates rCGG repeat induced phenotypes at NMJ. dRep-2 is a synaptic protein that colocalizes with metabotropic glutamate receptors (mGluRs) at larval Neuromuscular junction. At translational level dRep-2 level is reduced upon rCGG expression. These results together suggest that premutation rCGG repeats interferes larval NMJ development likely due to attenuation of mGluR signaling.

Quantitive analysis of host determinants of intracellular mycobacterial survival

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The success of *M. tuberculosis* depends on its ability to evade the host cell defence mechanisms. It is well known that Mtb arrests the maturation of phagosomes, thereby preventing delivery to lysosomes. While the mechanisms underlying the phagosome maturation arrest is well-studied, the consequence of presence of arrested phagosome for the host cell is not known. In our work, we report global changes to the host endo-lysosomal landscape during Mtb infection. Perturbation of this axis by chemical and genetic means results in altered intracellular growth patterns of mycobacteria. We further show that these alterations are driven both by host and the pathogen and identify the pathogen component mediating the change. Our results underline the host endo-lysosomal pathway as a key determinant in the maintenence of the balance between the host cell and Mtb in its intracellular stage.

Host STAT3 regulates EBER1 expression via ZBTB1 in EBV infected B-cells

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EBER1 is a long non-coding RNA produced abundantly in EBV infected B-cells that proliferate indefinitely as Lymphoblastoid cell lines invivo. EBER1 has found to affect host cell signal transduction which leads to oncogenesis. So firstly by In-silico analysis we searched for regulatory gene signatures in EBER1 and found that EBER1 promoter region has binding sites for ZBTB1, a BTB/POZ domain containing C2H2 class zinc finger proteins. From our previous findings we know that STAT3 has regulatory role on C2H2 class zinc finger proteins, so we further checked whether ZBTB1 is subjected to regulation by STAT3. We found that STAT3 knock down by siRNA has shown a decrease in expression of ZBTB1 both at mRNA and protein levels. In turn EBER1 levels were found to be decreased when STAT3 and ZBTB1 levels were down regulated. This is a part of our main objective to understand EBER1 associated signaling via EBV generated exosomes and regulate EBER1 upload from cell to exosome.This finding confirms the association of STAT3,ZBTB1 and EBER1 and facilitates in further understanding of its role in signaling via EBV generated exosomes.

Role of Class A Macrophage Scavenging Receptor in Sepsis

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Macrophage provide initial surveillance for pathogenic glycopeptides via scavenger receptors (SRs) and for viruses via Tolllike receptors (TLRs) which trigger pro-inflammatory response. On the onset of sepsis, endotoxins in the case of Gramnegative bacteria and in the case of Gram-positive bacteria exotoxins of different types bind to specific pattern recognition receptors (PRR), members of the so-called toll-like receptor family (TLR) expressed on monocytes/macrophages. This leads to transcriptional activation of a number of genes, mediated mainly by nuclear factor (NFkB) and the accumulation of proinflammatory cytokines, tumor necrosis factor TNFα, and interleukin (IL)1β. In addition, a number of anti-inflammatory mediators are activated in an attempt to restore immunological homeostasis. Eventually, the immunological imbalances and coagulopathies lead to vascular instability and microvascular occlusions that have serious consequences, resulting in hypoxia, widespread ischemia, and organ dysfunction and failure. It is known that LPS, the specific constituent in Gramnegative bacteria, induces the expression of at least 100 different genes in human monocytes, and the induction of 38 genes in endothelial cells has been reported. The induced transcripts code, e.g., for cytokines, chemokines, proteases and protease inhibitors, proteins involved in lipid metabolism and iron homeostasis, and proteins involved in antigen presentation. LPS, in addition to binding to TLRs, also bind macrophage class A scavenging receptor on macrophages. Rather than eliciting proinflammatory responses, LPS bound to MSR get internalized and then partially degraded The role of Macrophage Class A scavenging receptor role in sepsis is unknown. At the same time why our host immune system facilitates TOLL like receptor mediated pro inflammatory response instead of trigger the macrophage Scavenging receptor endocytosis pathway thereby less proinflammatory mediators/ or less tissue damage. The role of Macrophage Class A scavenging receptor role in sepsis is unknown. The aim of this study was to investigate Class A Macrophage Scavenging Receptor in a cell culture model of endotoxemia and whole blood model of sepsis

Mechanism of synaptic protein synthesis by selective miRNA decay and its implication in fear memory.

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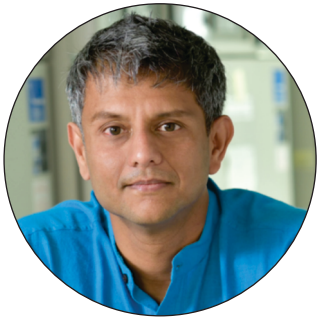
Local gene expression makes persistent changes at the synapse that governs vital cognitive functions such as memory formation and storage. Among various gene regulatory control at the synapse, localized protein synthesis emerged as a key modulator of long-term synaptic modification or plasticity. microRNAs (miRNAs) have emerged as one of the most important classes of regulators of translation within local subcellular contexts. However, our knowledge is very limited about how miRNAs selectively regulates the local protein synthesis at the synapse and its importance in memory formation. To address mechanistic control of miRNA –mediated control of localized protein synthesis at the synapse, using genome wide sequencing approach we have identified synapse-enriched miRNAs from isolated synaptic fraction or synaptoneurosome. Glutamate stimulation of synaptoneurosome resulted in rapid degradation of subset of synapse-enriched miRNAs. Focal stimulation of synapses by photo-uncaging of CNB-caged glutamate combined with time-lapse imaging of hippocampal neurons transduced with miRNA sensors revealed that synaptic activation leads to significant degradation of miRNAs within ~10 minute and continues through 30 minute imaging period. Furthermore, our data also demonstrated that this degradation is NMDA dependent and selectively regulated by exribonulease, XRN1. We have identified target transcripts of respective miRNAs using reporter assay and endogenous expression of these targets was analyzed by western blot after loss of respective miRNA function. Furthermore, our in situ hybridization data confirmed synaptic localization of miRNAs and their respective target transcripts. To gain a mechanistic insight into localized protein synthesis by activated regulated decay of miRNAs, we have focally stimulated hippocampal neurons transduced with respective 3'UTR of miRNA targets fused to photoconvertible Dendra. Similar time scale of miR degradation and new protein synthesis (~10 minutes) at the synapses clearly demonstrates that selective degradation of miRNAs release translation suppression of target transcripts containing respective miRNA binding sites. Furthermore, we observed that contextual fear conditioning of mice lead to rapid selective degradation of synapse-enriched miRNAs. Experiments are in progress to evaluate implication miRNA decay -mediated control of protein synthesis at the synapse in modulation of fear memory formation.



Regulation of Progenitor Proliferation and Cell Fate in the Airway Epithelium

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We are broadly interested in the processes that protect and repair the respiratory tract. Differences in the efficacy of these processes can lead to distinct health outcomes and our goal is to elucidate these at cellular and molecular scales. The lab currently focuses on the mechanisms by which the epithelial lining of the respiratory tract copes with damage caused by exposure to chemical and biological toxicants. While most of our research is conducted in mice and cells lines of murine and human origin, we also utilize other model organisms like fruit flies and Planaria. Under the auspices of the Ramalingaswami fellowship we are investigating the regulation of proliferation and cell fate. More specifically, our studies on the regulation of the G2-M transition and on the role of the Notch singling pathway.

Breaking the lignocellulose barried by two stage pretreatment for enhanced biogas production

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Our global economic system is dependent on the use of fossil energy sources for the production of fuels and chemicals. However, fossil fuels are limited resources and its depletion is inevitable. Escalating world population and living standards will lead to higher global energy consumption and demand. It is predicted to increase dramatically over the next half century; at least, from the current 17.7 TW to 28 TW by 2050. As a solution to this challenge renewable energy sources (Biomass, wind, solar etc) may meet the energy demand in a secure, sustainable and eco-friendly way. Agro-industrial residual resources and non-food plant biomass represent sustainable, renewable and alternative feedstock(s) for production of energy and chemicals in emerging Bioeconomy. In this regard, efficient technologies for biomass conversion as well as sustainable biomass production systems will be key technologies. Lignocellulosic biomass has inherent recalcitrance due to its chemical composition; despite recent improvements in enzyme technology, it’s processing usually requires physic-o-chemical pretreatment for optimal biochemical conversion. Thermal hydrolysis/steam explosion is one of the most efficient and environment friendly pretreatment methods for lignocellulosic biomass. It works well on marine as well as terrestrial biomass. Intense research is on the way to understand the underlying mechanisms of lignocellulose breakdown by pretreatment that will allow us to extract more sugar/energy. The fundamental insight of biomass (viz. lignocellulose, seaweed and agricultural residual material), its saccharification efficiency, biomethane potential and microbial consortia composition are under investigation to realize the potential of biomass for energy applications in future bioeconomy.

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