IISER TVM FRONTIER SYMPOSIUM IN BIOLOGY (FS-BIO 2020)

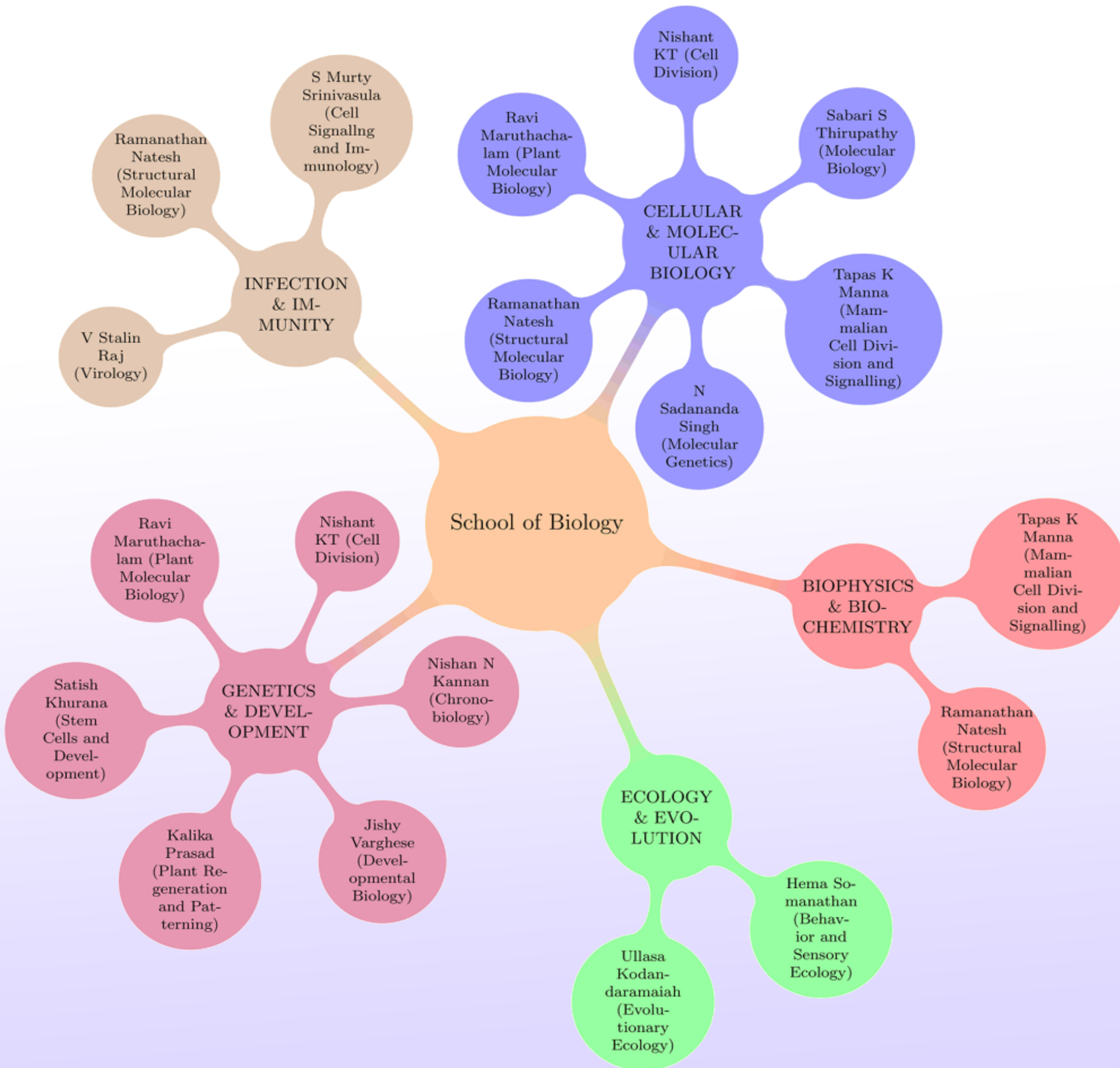
31 January - 1 February 2020

School of Biology
Indian Institute of Science Education and Research Thiruvananthapuram

FS-BIO 2020

IISER Thiruvananthapuram

SCHOOL OF BIOLOGY RESEARCH AREAS



Day 1, Session 1

Dr. Roop Mallik

09:30 - 10:05

Tata Institute of Fundamental Research(TIFR), Mumbai, India

Motor Proteins on Membranes : From Physics to Physiology

Molecular motors are force generators that sustain diverse biological activities in cells. Decades of research has provided insight into how these nano-machines work, but almost always with the motor divorced of an ancient partner. This partner is the lipid membrane, a dynamic substrate on which motors assemble to generate force inside cells, for example when membrane-bound motors transport vesicles or when motors on the cortical membrane pull on the mitotic spindle for cell division. Sadly, membranes are often viewed as a passive substrate for the motors. We believe that nothing could be farther from the truth, and that lipids and motors have profound impact on each other's function and fate. I will demonstrate this in the context of phagosome maturation and secretion of lipoproteins from the liver

Day 1, Session 1

Prof. Michael X. Zhu

10:05 - 10:40

McGovern Medical School, University of Texas Health Sciences Center, Houston, USA

TRPC4 in Dendritic Arborization of Hippocampal Neurons

Transient Receptor Potential Canonical (TRPC) channels are well known to be activated downstream from receptors that signal through phospholipase C (PLC), of which the Gq/11-PLCβ pathway constitutes the main mechanism of TRPC activation in neurons, causing slow and long-lasting membrane depolarization and Ca2+ influx. In addition, TRPC4 and TRPC5 are sensitive to stimulation of Gi/o proteins, making them not only mediators that convert inhibitory signals to excitation but also coincident detectors of metabotropic receptors that couple to Gq/11 and Gi/o proteins. We show that TRPC4 plays a critical role in dendrite development of hippocampal neurons in a manner that depends on costimulation of Gq/11 and Gi/o-coupled metabotropic glutamate receptors (mGluRs). Hippocampal neurons of young (P26) TRPC4 knockout (Trpc4-/-) mice exhibited decreased number of apical dendritic branches as compared to wild type littermates. In primary cultures of hippocampal neurons, dendritic arborization proceeded more slowly between days in vitro (DIV) 7 and 16 in Trpc4-/- than Trpc4+/+ neurons. Moreover, unlike wild type neurons, the Trpc4-/- neurons failed to show an increase in dendritic arborization in response to brain-derived neurotrophic factor (BDNF) or a low concentration (5 μM) of glutamate. Examination of intracellular Ca2+ concentration changes near plasma membrane in dendritic regions revealed that both group I and group III mGluRs are involved in generating the sustained Ca2+ signal in response to glutamate, which is largely missing in Trpc4-/- neurons. These mGluRs are also critical for TRPC4-mediated dendritic arborization. Using long-term (16 hrs) time-lapse live cell imaging, we observed that in response to 5 μM glutamate, dendrites of Trpc4+/+ neurons exhibited more persistent and longer-period extension than that of Trpc4-/- neurons. Mechanistically, the mGluR-mediated activation of TRPC4-containing channels provides the Ca2+ signal for myosin II interaction with actin cables to support podosome stabilization and maturation, which helps stabilize the newly formed dendrites. These findings suggest that downstream from coincident activation of Gq/11 ad Gi/o-coupled mGluRs, TRPC4 channels play an important role in dendritic arborization of hippocampal neurons during early development through regulation of actin-rich cytoskeleton.

Day 1, Session 1

Dr. Aldebaran M. Hofer

Harvard Medical School, Boston, USA

10:40 - 11:15

Signaling through GPCRs in the primary cilium

This presentation will describe optical approaches for interrogating cAMP signaling in the microdomain of the primary cilium, including calibrations of resting and stimulated second messenger levels. These tiny organelles sequester diverse GPCRs connected to cAMP signaling, such as receptors for dopamine (D1R), serotonin (5-HT6) and somatostatin (SSTR3). Our lab developed biosensors optimized for measuring ciliary cAMP and strategies to isolate signals in the cilium from the cell body and neighboring cells. Gα(s)-coupled GPCRs (e.g. 5-HT6 and D1R receptors) had reduced ability to generate cAMP upon trafficking to the ciliary membrane under control conditions. However, prior activation of another cilium based-signaling system, the sonic hedgehog (Hh) pathway, restored or amplified GPCR function to permit cAMP elevation selectively in the cilium. Hh therefore enables a local GPCR-dependent cAMP signaling circuit that is restricted wholly to the cilium. We discuss the untapped potential of ciliary GPCRs (many of which have well-defined pharmacology) in the modulation of cilia-based disease processes.

Day 1, Session 2
11:45 - 12:20

Prof. Donald Gill
Pennsylvania State University, USA

Calcium Signaling and Intracellular Communication

Ion channels transduce primary signals through gating mechanisms of extraordinary molecular precision. The widely expressed Orai1 plasma membrane (PM) calcium entry channel is gated by the endoplasmic reticulum (ER) Ca2+-sensing STIM proteins through a unique intermembrane conformational coupling mechanism. Triggered by ER calcium store release, STIM proteins migrate into ER-PM junctions where they tether and activate PM Orai1 channels. Orai1-mediated “store-operated” calcium signals control gene expression, growth, secretory, and motile responses universally among cells and are implicated in a spectrum of immunological, muscular and inflammatory disease states. Despite intense study, the molecular nature of the STIM-Orai1 coupling interface and the mechanism of Orai1 channel activation remain obscure. Our recent studies reveal that the STIM-Orai Activating Region (SOAR) of the STIM1 molecule contains a crucial phenylalanine residue. In STIM2, this residue is instead a leucine and accounts for the lower efficacy of STIM2. Mutated to histidine, the STIM1 molecule loses its ability to interact with Orai1 and gate its channel activity. The SOAR unit is STIM1 is a symmetrical dimer, yet only one of the two active sites is sufficient to fully activate the Orai1 channel. We propose a “unimolecular” coupling model whereby only one SOAR unit of the STIM1 dimer binds to an Orai1 channel subunit.

Day 1, Session 2

12:20 - 12:55

Prof. Natalia Prevarskaya

University of Lille, France

Calcium and calcium channels in initiation and progression of prostate cancer

Calcium permeable channels constitute a novel area of research in oncology. Malignant transformation of cells is the result of enhanced proliferation, aberrant differentiation, and impaired ability to die resulting in abnormal tissue growth, which can eventually turn into uncontrolled expansion and invasion, characteristic of cancer. Such transformation is often accompanied by changes in ion channel expression and, consequently, by abnormal progression of the cellular responses with which they are involved. At present, the expression profile of all calcium permeable channels and their isoforms in prostate carcinogenesis has not been yet completed while the specific functional roles for most of those are only just beginning to be understood. Here, we show that prostate cancer cells use ORAI and TRP protein redistribution as an oncogenic switch mechanism. In particular, ORAI3 and TRPV6 remodeling results from genomic and microenvironment perturbations that disrupt the equilibrium of channels and favors the formation of novel Ca2+ channels activated in a store-independent manner. Altogether, this remodeling of Ca2+ signaling in turn induces cell progression to a more aggressive pro-proliferative phenotype.

Finally, we explored the role of calcium channels in the regulation of the balance quiescence/activation in cancer stem cells (CSCs).Indeed, increasing evidence supports the idea that cancer is driven by CSCs and, according to this model, conventional therapies would only result in the elimination of actively dividing cancer cells with limited proliferation potential. The mechanisms controlling the quiescence/activation states of CSCs remain poorly understood. Here, we present the first evidence of the quiescence/activation regulation in prostate CSCs. We demonstrate that calcium signaling effectively regulates stemness, as defined by sphere-forming capacity, and expansion of the stem cell pool.

Our study specifically positions calcium permeable channels at the center of molecular machinery linking deregulated tumor metabolism, calcium homeostasis, and oncogenesis.

Day 1, Session 2

12:55 - 13:30

Prof. Khaled Machacha

Weill Cornell Medicine, Qatar

Calcium teleporting/tunneling: signaling in the cell cortex

Exposure of cells to agonists linked to Ca2+ mobilization results in Ca2+ store depletion and Store-Operated Calcium Entry (SOCE), which is spatially restricted to microdomains at ER-plasma membrane contact sites (MCS). However, some Ca2+-dependent effectors that localize away from SOCE microdomains, are activated downstream of SOCE by mechanisms that remain obscure. I will discuss recent development in a Ca2+ tunneling/teleporting pathway that allows transmission of the SOCE Ca-dependent signal through uptake of Ca entering the cell by the SERCA pump and release through IP3Rs at distal sites to activate specific effectors without inducing a global Ca rise. This Ca signaling mechanism is adapted to mediate a spatially restricted Ca2+ rise within the cortical region of the cell to activate a specific subset of effectors.

Day 1, Session 3
16:00 - 16:35

Prof. Kumaravel Somasundaram
Indian Institute of Science (IISc), Bengaluru, India

Cancer stem-like cells are the tumor initiating cells: How important the differentiated bulk cells?

The drawback of the current cancer therapy is tumor adapting several mechanisms which selectively evolve resistance against the therapy. While there are many reasons for the therapy resistance, one major reason is the existence of cancer stem cells, which are present in small proportions and show resistance to most therapies. The cancer stem cell hypothesis proposes that organisation of cell lineage in tumors is hierarchical and only a subpopulation of cells termed "tumor initiating cells" or "cancer stem cells" is responsible for tumor expansion. They have the ability to self-renew, divide to give rise to another malignant stem cell and a progenitor cell by asymmetric cell division. These progenitor cells have high proliferative potential, and differentiate further to form the bulk of the tumor. Tumor cells lacking stem cell properties will not be able to initiate self-propagating tumors regardless of their differentiation status or proliferative capacity which makes cancer stem cells a probable drug target. Since the studies based on whole the tumor cannot provide information about the molecular mechanisms at cancer stem cells level, efforts are underway to purify cancer stem cells and study them, which will pave way to study the molecules and signaling pathways regulating cancer stem cells for better understanding and developing targeted therapies.

We study Glioblastoma (GBM; grade IV glioma), the most common and malignant primary adult brain tumor, as a model cancer in our laboratory. GBM patients usually undergo surgical resection (maximal near safe surgery) with complementary concomitant radiotherapy and Temozolomide chemotherapy followed by five cycles of Temozolomide chemotherapy. However, this treatment never acts as a cure. While glioma cancer stem cells GSCs were isolated originally by their selective expression of stem cell markers like CD133, glioma derived cells grown as neurosphere in stem cell medium with defined growth factors under non-adherent condition have been shown to be enriched with GSCs.

Picture Credits: Yash Bhale

A view of the hostel blocks

Further, the GSCs in the neurosphere can be made to differentiate to form a monolayer which consists of differentiated glioma cells (DGCs). The DGCs are capable of forming GSCs if they are allowed to dedifferentiate or reprogramme in stem cell medium to form neurospheres. For these reasons, GSCs has been our focus of investigation in the last several years.

In one of the investigations looking at the secreted proteins with differential abundance between GSC and DG, we identified several proteins with high abundance in the GSC secretome. While many of these proteins are under investigation, another protein Fibromodulin (FMOD) that showed high abundance in DGC secretome caught our attention. We have previously shown that FMOD, a small leucin-rich repeat proteoglycan, is a secreted protein up-regulated in glioblastoma (GBM) due to the loss of CpG methylation in its promoter orchestrated by TGF-β1-dependent epigenetic modulation (Mondal et al., 2016, 36; 71 Oncogene). This study also demonstrated that secreted FMOD induces integrin-FAK-Src-Rho GTPase-ROCK signalling and actin cytoskeleton remodeling to promote glioma cell migration. In addition, FMOD was found to have no role in colony formation, growth (on soft agar), chemosensitivity or proliferation of GBM cells. Further investigation revealed that the silencing FMOD inhibited tumor growth completely in an intracranial orthotopic mouse model and DGC secreted FMOD induced angiogenesis by activating Notch pathway through Integrin signalling pathway. We also found that FMOD is not needed for GSC growth and dedifferentiation/reprogramming of DGCs. The question now is that why DGCs, which cannot form tumors by themselves, should secrete factors like FMOD which is a potent inducer of angiogenesis. Based on these facts, we proposed a model wherein differentiation is an essential for GSCs during the process of tumor formation partly to make factors like FMOD which would help in angiogenesis to supply nutrients to bulk of the tumor.

Picture Credits: Yash Bhale

A view of the hostel blocks

Day 1, Session 3
16:35 - 17:10

Prof. Colin W Taylor
University of Cambridge, UK

Signalling to and from IP3 receptors

IP3 receptors are intracellular Ca2+ channels expressed in the ER of all animal cells, where they mediate Ca2+ release in response to the many extracellular stimuli that evoke IP3 formation. Since IP3 receptors deliver Ca2+ to both the cytosol and the surface of closely apposed organelles, and they control Ca2+ entry across the plasma membrane by causing loss of Ca2+ from the ER, we can regard IP3 receptors as hubs that initiate most receptor-evoked Ca2+ signals. In this talk, I will discuss our recent work suggesting that only a small subset of the IP3 receptors within a cell are competent to respond to IP3 and evoke cytosolic Ca2+ signals. I will discuss the mechanisms responsible for this additional level of regulation, which we have described as IP3 receptor 'licensing'.

The other unit in the dimer is able to interact with another Orai1 channel unit on a separate channel molecule. In this way, STIM1 can cross-link between Orai1 channels and cause them to cluster, with important consequences for the generation of calcium signals. In our new studies, we define a discrete segment in the Orai1 protein that creates a critical nexus between the peripheral C-terminal STIM1-binding site and the inner core helices surrounding the central N-terminal pore. The nexus comprises a flexible "hinge" and hydrophobic "hinge plate" attaching it to the channel body. Mutation of four critical amino acids in the nexus transforms the Orai1 channel into a persistently open state, virtually identical to the STIM1-activated state. Yet, the mutant is independent of STIM1 and still fully active after removal of the entire STIM1-binding site adjacent to the nexus. The results militate against a complex and widely-held two-site gating model involving direct STIM1 binding to the N-terminal pore-forming helix to open the channel. Instead, we conclude that binding of STIM1 to gate the channel is restricted to the peripheral C-terminal extension helix which remotely controls gating of the Orai1 pore through a simple conformational switch mediated by the nexus and transduced through the core helices to rearrange the pore mouth and open the channel.

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Day 1, Session 4
17:40 - 18:15

Dr. Ranjan Sen
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, India

Bacterial transcription terminator, Rho, is a pleiotropic regulator of bacterial physiology and a potential therapeutic target

Bacterial transcription terminator, Rho, is a hexameric RNA-dependent helicase that upon binding to the nascent RNA dislodges transcription elongation complexes. Genomic data suggest that about 30-40% of the operons are under the control of Rho-dependent termination, which enables Rho to function as a pleotropic “master regulator” of gene expression regulating a wide range of diverse physiological processes (1).
Here, we describe two such unrelated physiological processes that are under the control of Rho-dependent termination. I) Transcription-coupled DNA repair pathway, where Rho could augment the function of the DNA-helicase, Mfd, facilitating the dissociation of RNA polymerase stalled at a DNA-lesion (2). II) The broad-spectrum antibiotic sensitivity in *E.coli* is regulated by Rho-dependent termination in a TolC efflux-pump dependent manner (3).
As multiple pathways are under the control of this master regulator, Rho, it could be a highly effective therapeutic target in many bacterial pathogens. We have earlier characterized a bacteriophage protein, Psu that functions as an antagonist of Rho by direct interaction (4). Here, we describe design of anti-Rho peptides from the Psu protein by a directed evolution method. These peptides could function as precursors of antimicrobial peptides (AMPs) targeting the Rho protein.

References:

1). Mitra, P., Ghosh, G., Hafeezunnisa, M. and Sen, R. (2017). Rho protein: mechanism and action. Annual Review of Microbiology, 71, 687-709.
2). Jain, S., Gupta, R, and Sen, R. (2019). Rho-dependent transcription termination in bacteria recycles RNA polymerases stalled at the DNA lesions. Nature Communications, Mar 14; 10(1):1207.
3). Hafeezaunnisa, M. Shashni, R. and Sen, R. (2019). Rho-dependent transcription termination regulates broad-spectrum antibiotic sensitivity in Escherichia coli via a multipartite network of pathways. Submitted.
4). Ranjan, A., Sharma, S., Banerjee, R., Sen, U. and Sen, R. (2013). Structural and mechanistic basis of antitermination of Rho-dependent transcription termination by a bacteriophage capsid protein. Nucleic Acids Research, 41 (14):6839-6856

Day 1, Session 4
18:15 - 18:50

Dr. Ullas Kolthur Seetharam
Tata Institute of Fundamental Research(TIFR), Mumbai, India

Metabolic roller-coaster rides: make it a fun but safe ride!

Science of aging has revealed that reduced intake of calories determines lifespan and in addition provides resistance to several stresses including infections. It is now well regarded that calorie restriction is primarily driven through key genetic/metabolic factors that couple metabolism to molecular functions of cells. Dietary and metabolic inputs have long been regarded as being inconsequential except for generating energy to life. However, emerging literature has established that they play deterministic roles and are causally associated with almost all cellular processes. In this talk I will provide a brief overview of the field and importance of metabolic sensing in mediating organismal physiology. Our research brings together fundamental insights from mitochondrial functions and nuclear epigenomic mechanisms.

Further, based on our recent work we propose that modern day diseases emerge due to a discord between evolutionary history and our life history vis-à-vis fed-fast cycles. This is relevant Failure to mediate efficient fed-fast-refed transitions has been known to be one of the primary causes of metabolic diseases and tissue inflammation, specifically in the liver. Although much is known about metabolic pathways, molecular mechanisms that act in a relay to bring about rapid and efficient state reversals are relatively less understood. Emerging literature has also shown that there is an interplay between metabolic and circadian inputs, which are necessary to bring about a coordinated change in gene expression. However, despite these studies, a systems level understanding of the interplay between metabolic signalling and gene expression mechanisms is less understood especially under normal fed-fast cycles, which is in a continuum. We have discovered mechanisms that govern efficient and dynamic physiological transitions and perturbing these mechanisms lead to metabolic diseases and aging. Our current efforts have led to mathematical modelling the contributions of various molecular players that maintain frequency and amplitude of oscillations, mediated by nuclear-mitochondrial cross talk. We propose that age-associated onset of diseases is contributed by aberrant oscillations and metabolic deficits during aberrant fed-fast cycles.

Picture Credits: Aswathy BJ

Hostel blocks at night reflected in the river

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Day 1, Session 4

18:50 - 19:25

Dr. Rakesh Kumar Mishra

Centre for Cellular and Molecular Biology (CCMB), Hyderabad, India

Regulation of homeotic genes and evolution of complexity in animals

Information encoded in the genomes of organisms determines their shape, size and functionality. Large scale genome analysis in a variety of organisms suggests that the evolution of complexity is based on not a greater number of genes, but on the non-coding part of the genome that presumably leads to a more sophisticated regulation of genes. One of the most fascinating examples of such gene regulation is that of homeotic or hox genes that determine the anterior-posterior body axis in animals. Hox genes exist in clusters and their arrangement in the genome reflects the order in which they regulate the body axis. This colinearity of organization and function of is conserved from fly to mammals. We study the mechanisms of regulation of hox genes in this context and their implication in the evolution of complexity in animals. We have also analyzed the functionally conserved aspects of the regulatory elements in the Hox complexes. These studies provide insights into the complex regulatory processes that control expression of homeotic genes and, thereby, development of body structures along the A-P body axis.

Day 2, Session 5
09:00 - 09:35

Prof. Grant Jay Jensen
HHMI, CalTech, USA

Electron cryotomography: present capabilities and future potential

In the last ten years electron cryotomography (cryo-ET) has made it possible to visualize large macromolecular assemblies inside intact cells in a near-native, "frozen-hydrated" state in 3-D to a few nanometers resolution. Increasingly, atomic models of individual proteins and smaller complexes obtained by X-ray crystallography, NMR spectroscopy, or other methods can be fit into cryotomograms to reveal how the various pieces work together inside cells. A few good pictures is therefore sometimes all that is really needed to distinguish between competing models. To illustrate these points, I will present examples of current results from our recent work on bacterial secretion systems and eukaryotic stress responses. The range of cellular samples that cryo-ET can reveal is dramatically expanding with FIB-milling, and will likely soon become dramatically more useful with correlated light and electron microscopy (CLEM) targeting. Two major developments in cryo-ET technology further suggest that cryo-ET will become an important new method for determining the structures of single particles and small proteins as well. First, highly eucentric stages are now allowing tilt-series to be recorded in seconds rather than minutes, opening the possibility of high resolution single particle tomography. Second, cryo-ET of very small crystals (“nanocrystals”) offers compelling potential advantages over X-ray crystallography. I will explain these advances and their projected implications with examples from our work.

Day 2, Session 5
09:35 - 10:10

Dr. Brent Lane Nannenga
Arizona State University, USA

MicroED: High-resolution structure determination by microcrystal electron diffraction

A common barrier to high-resolution structure determination is the growth of large well-ordered crystals. Electron diffraction is capable of producing high-quality diffraction data from crystals that are orders of magnitude smaller than those needed for conventional X-ray crystallographic experiments, and 3D electron diffraction methods have recently begun to yield high-resolution structures from extremely small microcrystals. In this presentation, the cryo-electron microscopy technique of microcrystal electron diffraction, or MicroED, will be described in detail along with representative structures determined by the method. Additionally, current work in our lab, which is focused on improving MicroED methodology and extending this technique to new samples will be presented.

Day 2, Session 5
10:10 - 10:45

Prof. Elizabeth R Wright
University of Wisconsin, Madison, USA

Structural studies of bacterial appendages by correlative light and electron microscopy

The bacterial flagellum is a complex propeller and is composed of three major units: the motor (basal body), the hook, and the filament. As a whole, the components work together to drive the bacterium through its environment. A number of studies of bacterial species indicate that flagellar filaments are assembled from several flagellin proteins as opposed to a singular flagellin. Many of the flagellins are differentially regulated, redundant in molecular weight, and function. While there may be some redundancy, there appears to be evidence that a single flagellin is essential for flagellar filament synthesis, motility, and virulence. *Caulobacter crescentus* expresses six flagellin proteins, and all the flagellins are present along the length of the flagellar filament. In this discussion of our structural study of the *Caulobacter* flagellum, we will highlight how we sought to ascertain which flagellin was essential and determine the high-resolution structure of both the full-length flagellum and the flagellin protein. We used a combination of mutagenesis experiments, (cryo-)fluorescence microscopy, and cryo-electron microscopy (cryo-EM) to generate and identify the appropriate mutants for structure determination.

Day 2, Session 7

15:30 - 16:05

Dr. Dmitry Lyumkis

Salk Institute for Biological Studies, California, USA

Structural Basis for Strand Transfer Inhibitor Binding to HIV Intasomes

Exposure of cells to agonists linked to Ca2+ mobilization results in Ca2+ store depletion and Store-Operated Calcium Entry (SOCE), which is spatially restricted to microdomains at ER-plasma membrane contact sites (MCS). However, some Ca2+-dependent effectors that localize away from SOCE microdomains, are activated downstream of SOCE by mechanisms that remain obscure. I will discuss recent development in a Ca2+ tunneling/teleporting pathway that allows transmission of the SOCE Ca-dependent signal through uptake of Ca entering the cell by the SERCA pump and release through IP3Rs at distal sites to activate specific effectors without inducing a global Ca rise. This Ca signaling mechanism is adapted to mediate a spatially restricted Ca2+ rise within the cortical region of the cell to activate a specific subset of effectors.

Picture Credits: Anumit Saralkar

Day 2, Session 7
16:05 - 16:40

Prof. Raghavan Varadarajan
Indian Institute of Science (IISc), Bengaluru, India

HIV-1 immunogen design and evaluation

Human immunodeficiency virus 1 (HIV-1) is an important human pathogen which causes over a million deaths annually. Despite extensive efforts for several decades, we are far from an HIV-1 vaccine. While some infected people have antibodies that can neutralize many different strains of HIV-1, it has so far not been possible to elicit such antibodies through vaccination. We have used structure guided protein design to develop immunogens derived from Env, the major surface protein of the virus. One such design successfully elicited antibodies that could protect non-human primates against HIV-1 infection. We have also developed a novel epitope mapping approach that uses a combination of scanning mutagenesis, chemical labeling and deep sequencing to map neutralizing epitopes targeted by monoclonal antibodies and in polyclonal sera, that can be used for vaccine evaluation.

Day 2, Session 8

17:10 - 17:45

Prof. Elena Orlova

Birkbeck College, University of London, UK

Study of the Barley stripe mosaic virus using cryo electron microscopy

Barley stripe mosaic virus (BSMV, genus *Hordeivirus*) is a rod-shaped single-stranded RNA virus similar to viruses of the structurally characterized and well-studied genus Tobamovirus. We discovered that BSMV forms two types of virion that differ in the number of coat protein (CP) subunits per turn and interactions between the CP subunits. BSMV and tobacco mosaic virus CP subunits have a similar fold and interact with RNA using conserved residues, the axial contacts between the CP of these two viral groups are considerably different.

Day 2, Session 8
17:45 - 18:20

Dr. Rajendra Kumar Agrawal
Wadsworth Center, University at Albany, New York, USA

Unraveling the mysteries of translation in human mitochondria using single-particle cryo-EM

Human immunodeficiency virus 1 (HIV-1) is an important human pathogen which causes over a million deaths annually. Despite extensive efforts for several decades, we are far from an HIV-1 vaccine. While some infected people have antibodies that can neutralize many different strains of HIV-1, it has so far not been possible to elicit such antibodies through vaccination. We have used structure guided protein design to develop immunogens derived from Env, the major surface protein of the virus. One such design successfully elicited antibodies that could protect non-human primates against HIV-1 infection. We have also developed a novel epitope mapping approach that uses a combination of scanning mutagenesis, chemical labeling and deep sequencing to map neutralizing epitopes targeted by monoclonal antibodies and in polyclonal sera, that can be used for vaccine evaluation.

Day 2, Session 8

18:20 - 18:55

Prof. P. N. Rangarajan

Indian Institute of Science (IISc), Bengaluru, India

My adventures with Pichia pastoris

Pichia pastoris, a methylotrophic yeast is widely used as a host for the commercial production of recombinant proteins such as insulin and Hepatitis B virus surface antigen. Our own laboratory developed a recombinant *P. pastoris* strain expressing Hepatitis B surface antigen which is being used for the commercial production of monovalent (BEVAC, Elovac-B) and pentavalent (ComBE Five, Vaxtar-5) vaccines. Being a respiratory yeast, *P. pastoris* harbours metabolic and regulatory pathways that are different from those of Saccharomyces cerevisiae. Studies in our laboratory during the past decade have led to the identification of unique metabolic enzymes, transcription factors and post-transcriptional regulators of *P. pastoris*. An overview of these studies as well as the possibility of developing a novel expression vector will be presented.

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Hall Arrangement

Vinayak G Kamath, T.M Tejas, Riya Sheokand, Yash Bhale, Swetha G,
Devika Radhakrishnan, Gifty Alin Jacob.

Abstract Book

Azmi Sheriff, Reshma Menon, Uthpala

Transport

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Allipra Sreejith, Ankit Kumar Pradhan

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Aishwarya Hatekar

Food

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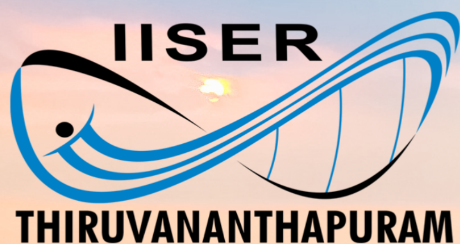

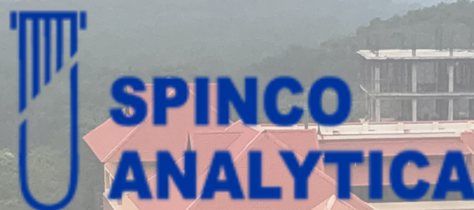

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