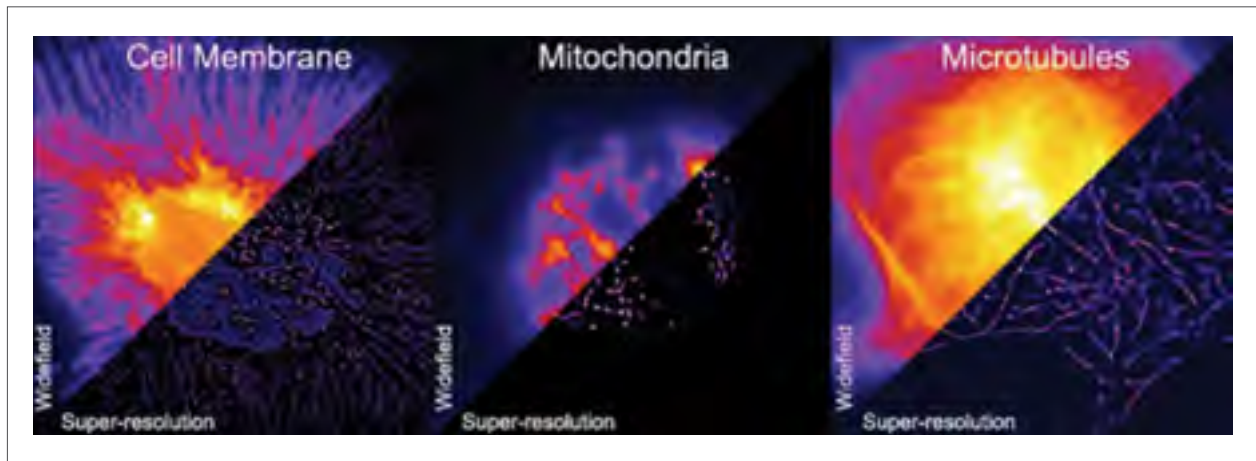


# Research Snapshots 2018-19



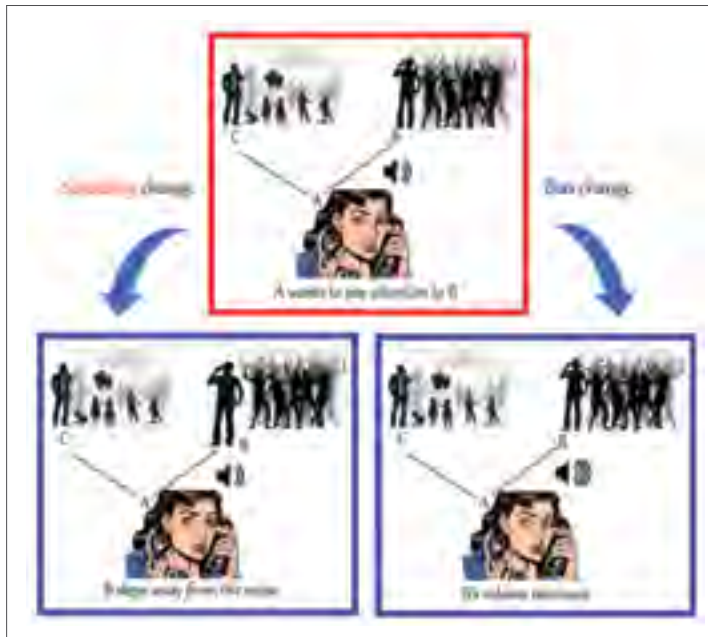
## Deepak Nair (CNS)

Fluorescence-Activating and absorption-Shifting Tag (FAST) is a novel genetically encoded optical highlighter probe. Since the fluorescence of FAST originates from the stochastic and reversible diffusive association of a fluorogenic ligand, we investigate the application of FAST using Super-Resolution Radial Fluctuations (SRRF) to achieve routine imaging below the diffraction limit in a widefield epifluorescence microscope. We show that intensity fluctuation analysis like SRRF allows the imaging of FAST-tagged proteins with sub – 100 nm resolution in live cells. FAST co-labeled with conventional fluorophores enables real time multicolour 2D and 3D super-resolution imaging, indicating that FAST can be used for observation of sub-diffraction limited structures in both living and fixed samples. The development of improved FAST variants with orthogonal fluorogen selectivity in the future could allow efficient, cost-effective, multicolour super-resolution imaging in any widefield epifluorescence microscope, improving our understanding of fundamental molecular organization in cell biology.

*Live cell super resolution imaging by radial fluctuations using fluorogen binding tags*

M Venkatachalapathy, V Belapurkar, M Jose, A Gautier, D Nair *Nanoscale* 11 (8), 3626-3632, 2019





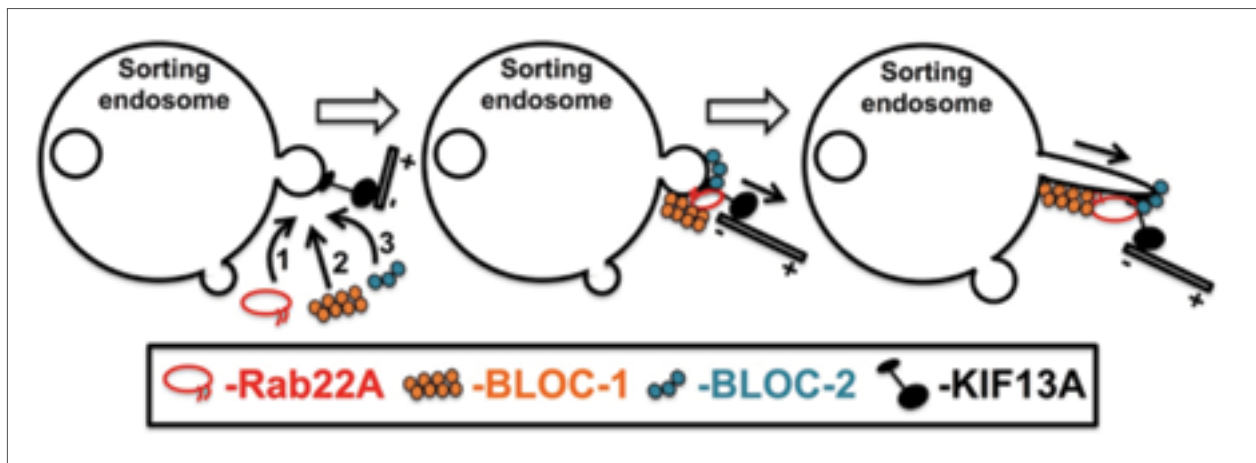
### Sridharan Devarajan (CNS)

Attention is the remarkable ability that allows us to selectively process relevant information from the world around us, but is “attention” a single (unitary) phenomenon? In two behavioral studies conducted with human participants we show that attention is not a unitary phenomenon, but can be divided up into two components: “sensitivity” (improving information encoding) and “bias” (enhancing information weightage). The cartoon alongside illustrates these concepts: Say, individual A is having two conversations (over two phones) simultaneously with individuals B and C, who are themselves in noisy environments. And say, A is more interested in hearing what B has to say, and wants to pay attention selectively to B’s voice. She could ask B to step away from the noisy dance floor to increase the clarity of B’s voice over his background noise (increasing “sensitivity”). Alternatively, she could increase the volume on the receiver over which she hears B’s voice, to make B’s voice (and his background noise) louder, and more audible, compared to C’s (increasing “bias”). We show that both of these mechanisms are at play regardless of whether participants pay attention voluntarily, instructed by an attention cue (“endogenous” attention, Banerjee et al, 2019) or have their attention captured automatically, by a bright flashing stimulus (“exogenous” attention, Sagar et al, 2019). These findings form the basis for future research on brain mechanisms of these components of attention.

Banerjee S, Grover S, Ganesh S and Sridharan D. Sensory and decisional components of endogenous attention are dissociable. *Journal of Neurophysiology* (in press). <https://doi.org/10.1152/jn.00257.2019>

Sagar V, Sengupta R, and Sridharan D. Dissociable sensitivity and bias mechanisms mediate behavioral effects of exogenous attention. *Scientific Reports* (in press). <https://doi.org/10.1038/s41598-019-42759-w>





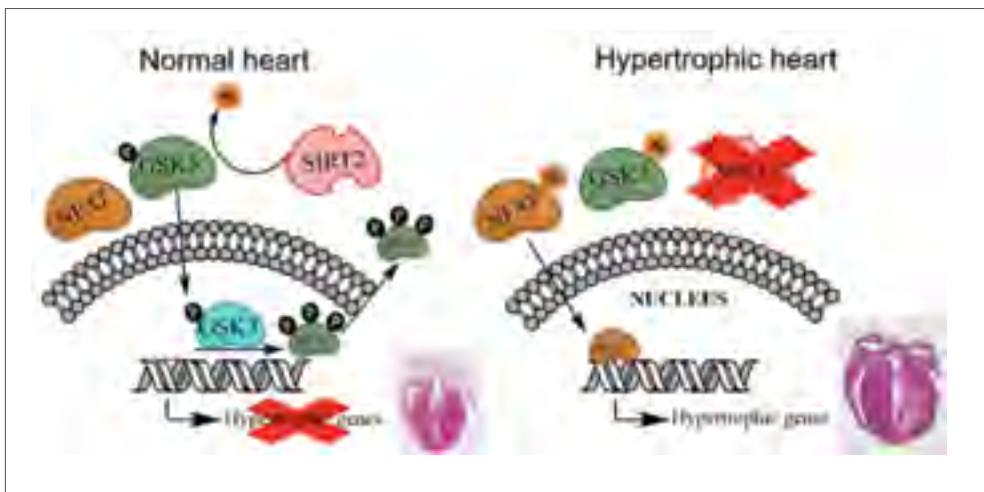
### Subba Rao Gangi Setty (MCB)

Recycling endosomes (REs) are transient endosomal tubular intermediates of early/sorting endosomes (E/SEs) that function in cargo recycling to the cell surface and deliver cell type-specific cargo to lysosome-related organelles such as melanosomes in melanocytes. Members of Subba Rao's lab study the mechanism of RE biogenesis. By using an endosomal Rab-specific RNAi screen, they have identified Rab22A as a critical player during RE biogenesis. Rab22A-knockdown results in reduced RE dynamics and cargo accumulation in the E/SEs. Rab22A forms a complex with BLOC-1, BLOC-2 and the kinesin-3 family motor KIF13A on E/SEs. Consistently, the RE-dependent transport defects observed in Rab22A-depleted cells phenocopy those in BLOC-1-/BLOC-2-deficient cells. These findings suggest that Rab22A promotes the assembly of a BLOC-1-BLOC-2-KIF13A complex on E/SEs to generate REs that maintain cellular and organelle homeostasis.

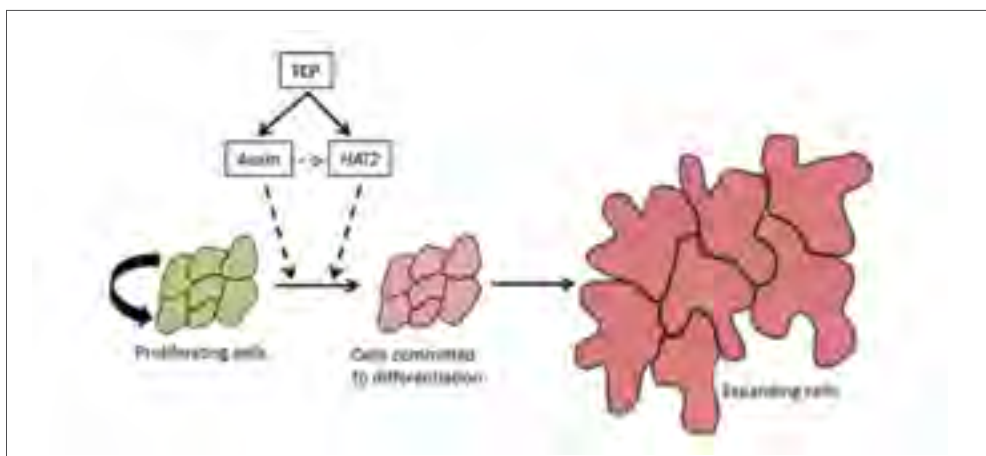
Shakya, S., Sharma, P., Bhatt, A. M., Jani, R. A., Delevoye, C. and Setty, S. R. (2018). Rab22A recruits BLOC-1 and BLOC-2 to promote the biogenesis of recycling endosomes. *EMBO Reports* 19, e45918.

### N. Ravi Sundaresan (MCB)

In humans, development of pathological cardiac hypertrophy involves complex molecular events occurring at the level of cardiac myocytes. Studies suggest that Glycogen synthase kinase 3 (GSK3) play a critical role in antagonizing the development of cardiac hypertrophy. Interestingly, the enzymatic activity of GSK3 isoforms is inhibited by phosphorylation-independent mechanisms during cardiac failure, although the mechanism(s) are not understood. Studies in Ravi Sundaresan's lab have identified acetylation as a novel modification of GSK3, which plays a critical role in the development of cardiac hypertrophy. Molecular modeling and/or molecular dynamics simulations indicate that acetylation of GSK3 would hinder both the adenosine binding and prevent stable interactions of the negatively charged phosphates. They found that SIRT2, a class III histone deacetylase blocks cardiac hypertrophy by deacetylating the GSK3 isoforms.



Sarikhani, M., Mishra, S., Maity, S., Kotyada, C., Wolfgeher, D., Gupta, M. P., Singh, M. and Sundaresan, N. R. (2018). SIRT2 deacetylase regulates the activity of GSK3 isoforms independent of inhibitory phosphorylation. *Elife*. 7. e32952.

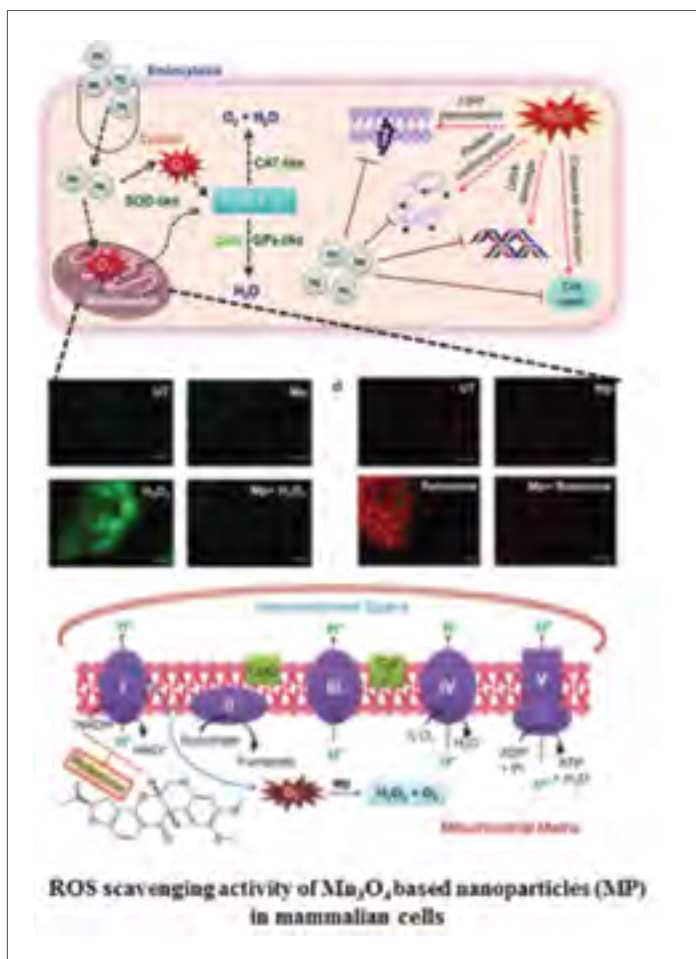


### Utpal Nath (MCB)

Cells in young organs undergo active proliferation at an early stage to generate sufficient number, before exiting proliferation and entering differentiation. How these proliferating cells acquire differentiation potential is unclear. Utpal Nath’s lab studies this process in plants by analyzing the role of TCP transcription factors which promote cell maturation. By inducing the activity of TCP4 at various developmental stages of Arabidopsis leaf primordium, they have shown that TCP4 acts as a switch for the transition from proliferation to differentiation. A 24-hour pulse of TCP4 activity is sufficient to impart irreversible differentiation competence to dividing cells. Possibly to ensure the transition, these proteins promote cell differentiation by a two-prong strategy; indirectly by promoting the maturity-inducing hormone auxin, and directly by activating another maturity protein, HAT2.

Challa, K. R., Rath, M. and Nath, U. (2019). The CIN-TCP transcription factors promote commitment to differentiation in Arabidopsis leaf pavement cells via both auxin-dependent and independent pathways. *PLoS Genet*. 15, e1007988.



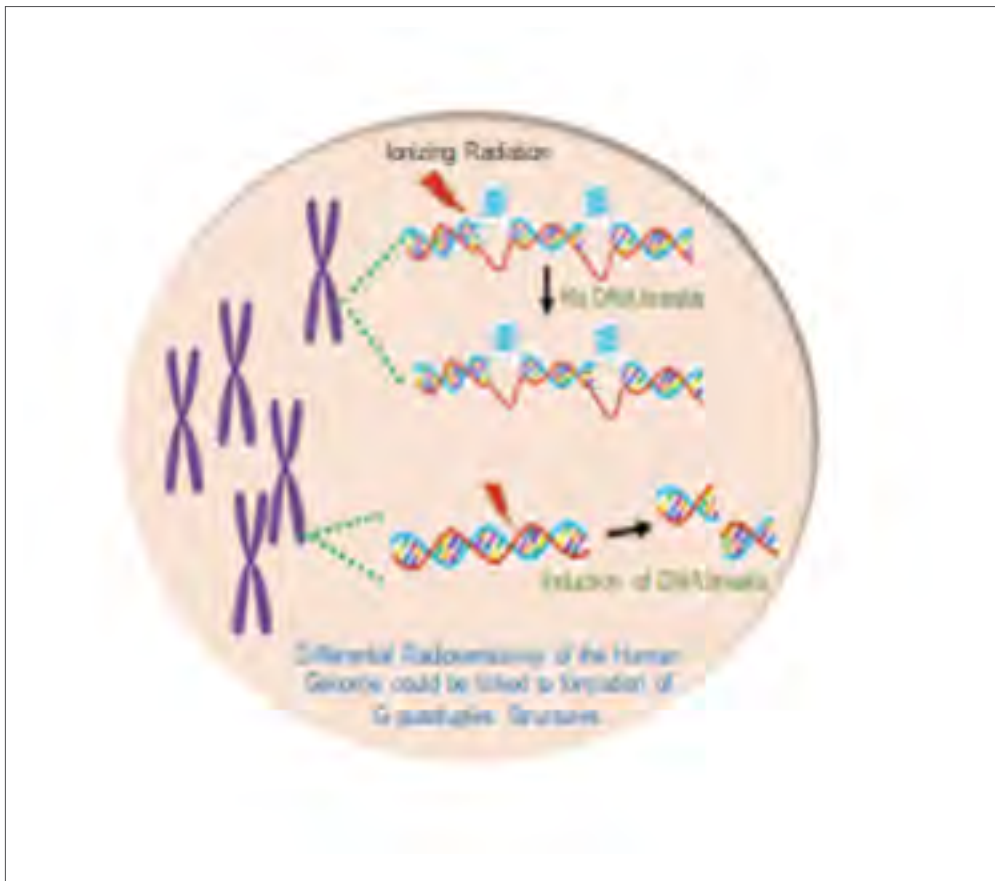


### Patrick D'Silva (BC)

The maintenance of an optimum level of reactive oxygen species (ROS) and their stringent regulation is the primary criteria for normal cellular health. The imbalance in the ROS levels due to either excessive production or inefficient in the antioxidant defense mechanism results in several pathological conditions, including cardiovascular, diabetes, cancer, and neurodegenerative diseases. This evokes the need for an efficient enzyme-mimic nanomaterial that can function under physiological conditions, circumventing the detrimental effects of excess ROS without perturbing the cellular machinery. We report here, the ability of Mn<sub>3</sub>O<sub>4</sub> nanoparticles to mimic the functions of three major antioxidant enzymes (catalase, glutathione peroxidase, and superoxide dismutase). The nanoparticle prevented the oxidative damage of cellular components such as DNA, protein, and lipids. Our observations highlight that the ROS-scavenging activity of Mn<sub>3</sub>O<sub>4</sub> nanoparticles functions synergistically with the endogenous antioxidant machinery. Based on our findings, we envisioned that the multienzyme mimic Mn<sub>3</sub>O<sub>4</sub> nanoparticles possess great potential in suppressing the oxidative stress-mediated pathophysiological conditions under which the antioxidant system is overwhelmed.

Singh N, Savanur MA, Srivastava S, D'Silva P\*, Mugesh G\*. (2019) "A manganese oxide nanozyme prevents the oxidative damage of biomolecules without affecting the endogenous antioxidant system". *Nanoscale*. 2019 Feb 28;11(9):3855-3863. doi: 10.1039/c8nr09397k.PMID:30758009 (\*Equal contribution).





### Sathees C Raghavan (BC)

DNA, the fundamental unit of human cell, generally exists in Watson-Crick base paired B-DNA form. Often, DNA folds into non-B forms, such as four stranded G-quadruplexes. It is generally believed that ionizing radiation (IR) induces DNA strand-breaks in a random manner. In an interesting new study, we observed that regions of DNA enriched in G-quadruplex structures are less sensitive to ionization radiations such as  $\gamma$ - or X-rays compared to B-DNA. Importantly, cells in S-phase of the cell cycle are less radiosensitive due to higher propensity of G-quadruplex formation. Thus, our results reveal that formation of G4 structures contribute towards differential radiosensitivity of the human genome and can be modulated in a cell cycle dependent manner.

Reference: Nitu Kumari\*, Supriya V. Vartak\*, Vidya Gopalakrishnan\*, Sumedha Dahal\*, Sagar S. Desai\*\*, Susmita Kumari\*\*, Bibha Choudhary and Sathees C. Raghavan# (2019). Differential Radiosensitivity of the Human Genome is linked to G-quadruplex Structures and could be modulated in a Cell Cycle Dependent Manner (To be published).





### Rohini Balakrishnan, Kavita Isvaran (CES)

Predation is considered a powerful force of natural selection, shaping the evolution of diverse traits, including signals and behaviours related to animal communication. In systems where males produce long-range acoustic signals to attract females from a distance, signal production increases conspicuousness and thereby the risk of predation. This has led to the assumption that the signaling male faces higher risk of predation than the silent female that moves to locate the signal. These assumptions have however rarely been tested empirically. Using a tree cricket species as a model system, Torsekar et al. (2019) provide one of the first empirical, quantitative estimates of the predation risk faced by signaling males and localising females in the wild. Given the difficulty of observing predation events in the wild, predation risk was estimated using a set of constituent probabilities, including co-occurrence with a predator on a bush, encounter and escape probabilities.

The results showed that predation risk was equivalent for signaling males and responding females, challenging the long-held idea that signaling is riskier than searching, and thereby that males are the sex taking the higher risk in the context of communication and mate-finding. This finding has implications for our understanding of sexual selection in the context of communication. In addition, the overall level of predation risk was low for both males and females, also questioning the role of predation as a major force shaping the evolution of signaling behaviour.

Torsekar, V. R., Isvaran, K. & Balakrishnan, R. (2019) *Evolutionary Ecology* 33: 329-343. <https://doi.org/10.1007/s10682-019-09982-3>





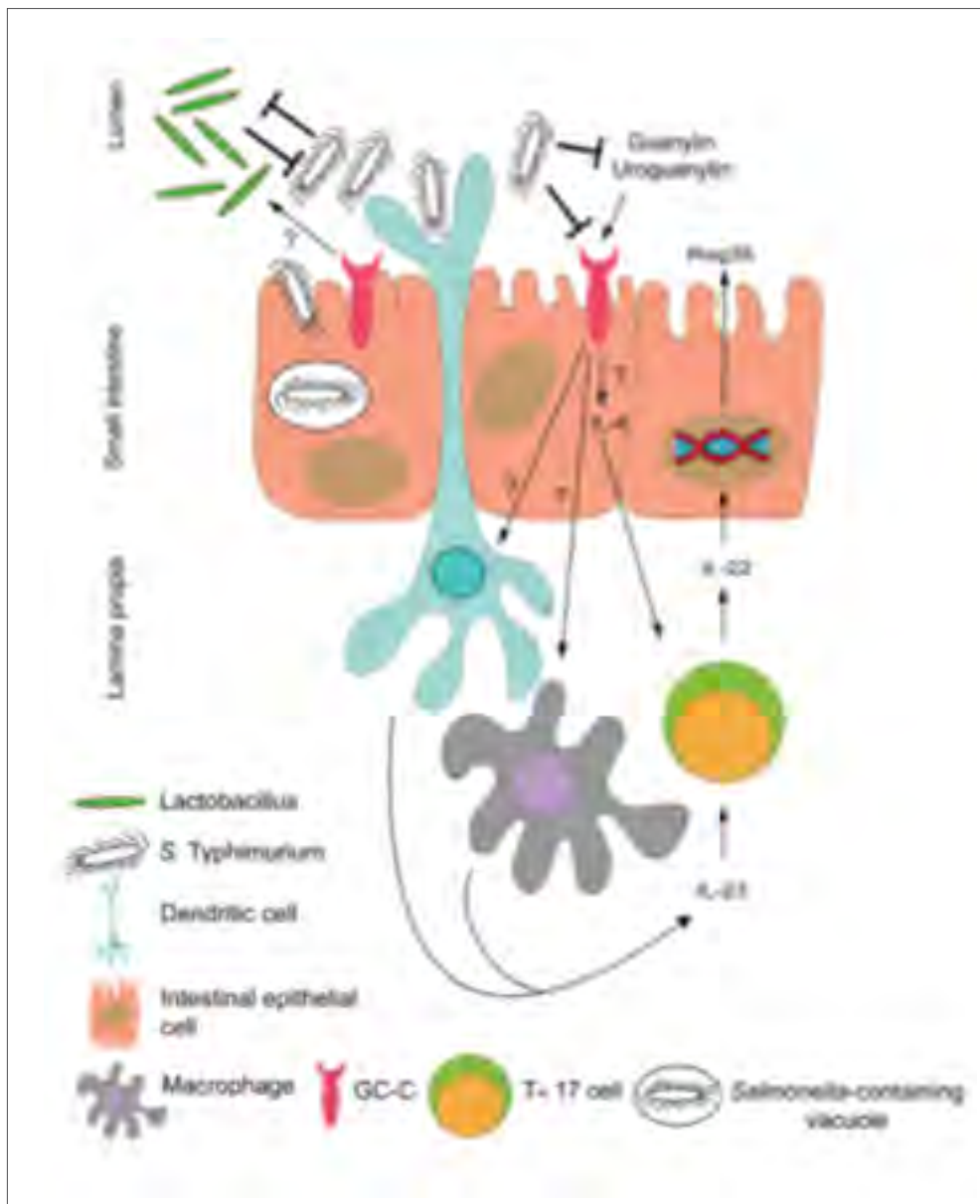
### **Maria Thaker (CES)**

Bright and conspicuous colours are used by many animals to attract mates and to communicate with each other. However, these conspicuous colours can also attract the attention of unintended audience, such as predators. Therefore, expressing bright colours may be risky to animals. In the Indian rock agama lizard (*Psammophilus dorsalis*), males dramatically change their colours and display different colour combinations when they are fighting with other males, and when they are courting females. Though visual modelling, we discover that the courtship colours of males are highly conspicuous not only to lizards, but also their predators such as birds, dogs and snakes. On the other hand, colours displayed by males when fighting and the colours of females are comparatively less conspicuous. We then placed lizard-shaped models in the wild and found that the courtship-coloured male models were attacked more than models of any other colour combination. Together, these results indicate that the courtship colour combination of males is risky to them. Therefore, colour change in these animals may have evolved as an elegant solution for the males to gain the advantages of bright colours for communication but still reduce the risk of being noticed by predators at other times.

Amdekar, M. S., & Thaker, M. (2019). *Risk of social colours in an agamid lizard: implications for the evolution of dynamic signals. Biology Letters, 15(5), 20190207.*





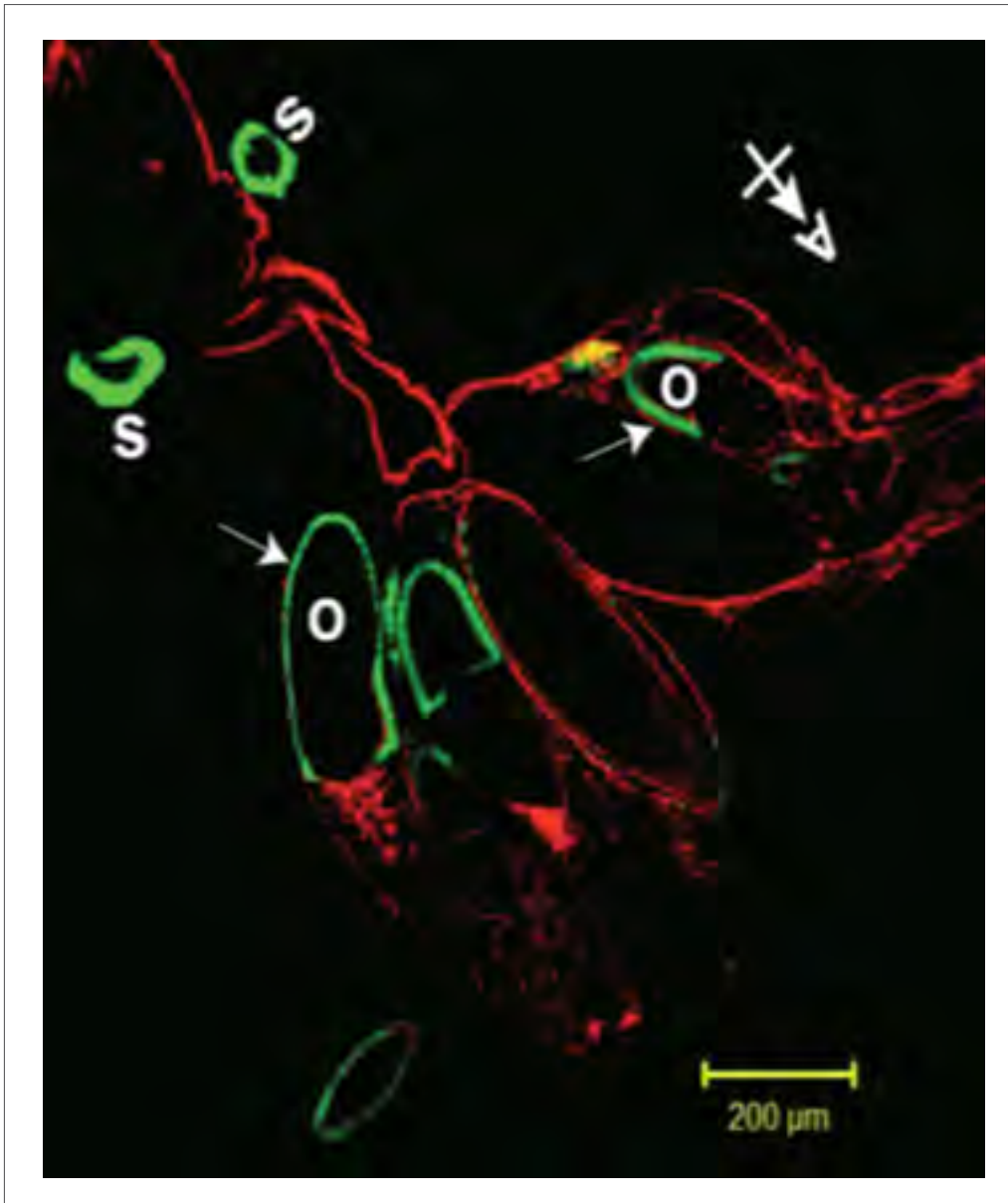


## Sandhya Visweswaraiah (MRDG)

The group of Prof. Sandhya S. Visweswaraiah is interested in understanding the role of receptor guanylyl cyclase C in the gut of mammals. Using knock out mice and working in collaboration with Prof. Dipankar Nandi and his group from the Department of Biochemistry, it appears that this receptor is involved in providing protection from infection by the gut pathogen, Salmonella Typhimurium. Mechanisms underlying this protection include a poorer immune response generated in the intestine as a result of lower cytokine production by immune cells in the gut.

Majumdar, S., Mishra, V., Nandi, S., Abdullah, M., Barman, A., Raghavan, A., Nandi, D. and Visweswaraiah, S.S. (2018) Absence of receptor guanylyl cyclase C enhances ileal damage and reduces cytokine and antimicrobial peptide production during oral Salmonella Typhimurium infection. *Infect. Immun.* 86: 799-817



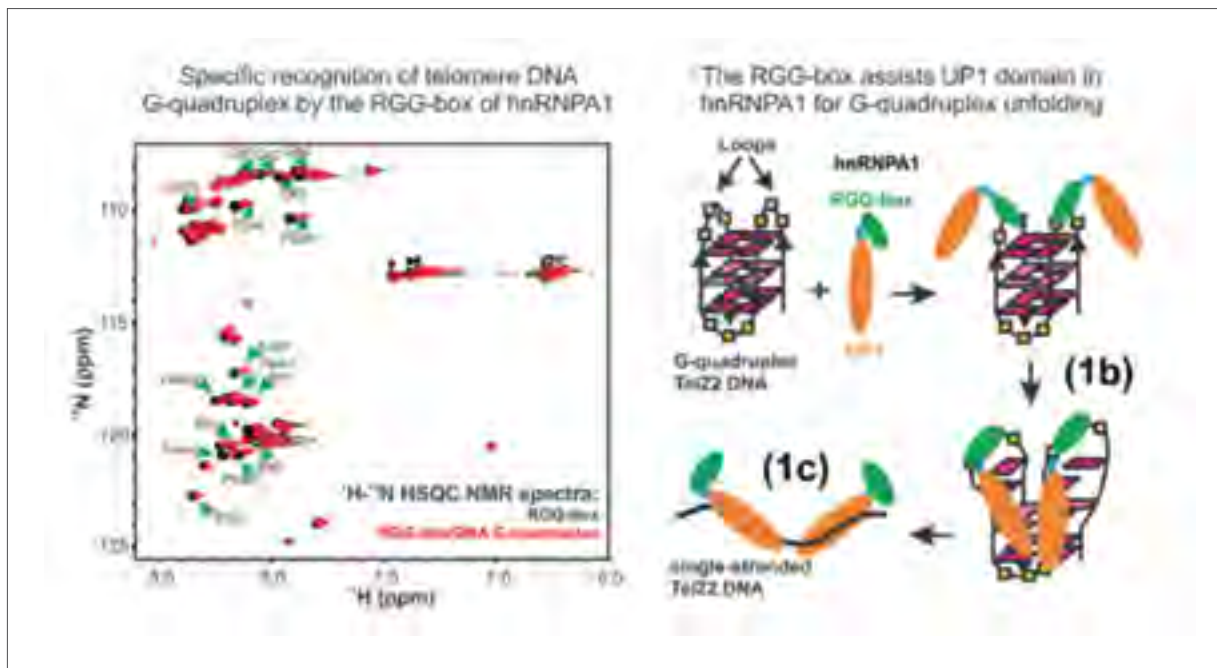


### Upendra Nongthomba (MRDG)

Bx function in follicle cells is important for normal egg development and fecundity in *Drosophila*. Two enhancer trap Gal4 lines, c323a and c204, which were reported to be expressed in follicle cells were selected to knock down Bx in follicle cells. These drivers show GFP expression in follicle cells (white arrow in A) surrounding oocyte (O), and also in the cells of spermathecae (S). Beadex is essential for egg development and fertility.

Subhash Kairamkonda, Upendra Nongthomba, Beadex, a *Drosophila* LIM domain only protein, function in follicle cells is essential for egg development and fertility, *Experimental Cell Research* 367 (2018) 97–103





## Mahavir Singh (MBU)

Maintenance of telomere DNA has implications in both cellular aging and cancer. Controlled remodeling of highly ordered and organized telomere nucleoprotein structure is critical during DNA replication. Several proteins (e.g. hnRNPA1, TRF2, RTEL1 etc.) and a non-coding RNA called TERRA (telomere repeat containing non-coding RNA) play important roles in telomere DNA remodeling, however the precise mechanism of the process is not well understood. Mahavir Singh's lab focuses on understanding the interplay of various proteins, telomere DNA and TERRA RNA that is critical for coordinated telomere DNA remodeling. Recently, Mahavir Singh's lab has shown that an intrinsically disordered, arginine and glycine rich domain (RGG-box) of hnRNPA1 specifically recognizes the higher order telomere DNA and TERRA RNA G-quadruplex structures but not the single-stranded DNA or RNA. This helps adjacent the UP1 domain in hnRNPA1 to unfold G-quadruplex structures more efficiently. The lab is currently pursuing the understanding of role of arginine methylation the structure of the RGG-box and G-quadruplex binding.

Ghosh, M. and Singh, M. "RGG-box in hnRNPA1 specifically recognizes the telomere G-quadruplex DNA and enhances the G-quadruplex unfolding ability of UP1 domain". *Nucleic Acids Research*. (2018). 46(19):10246-10261. doi: 10.1093/nar/gky854.

