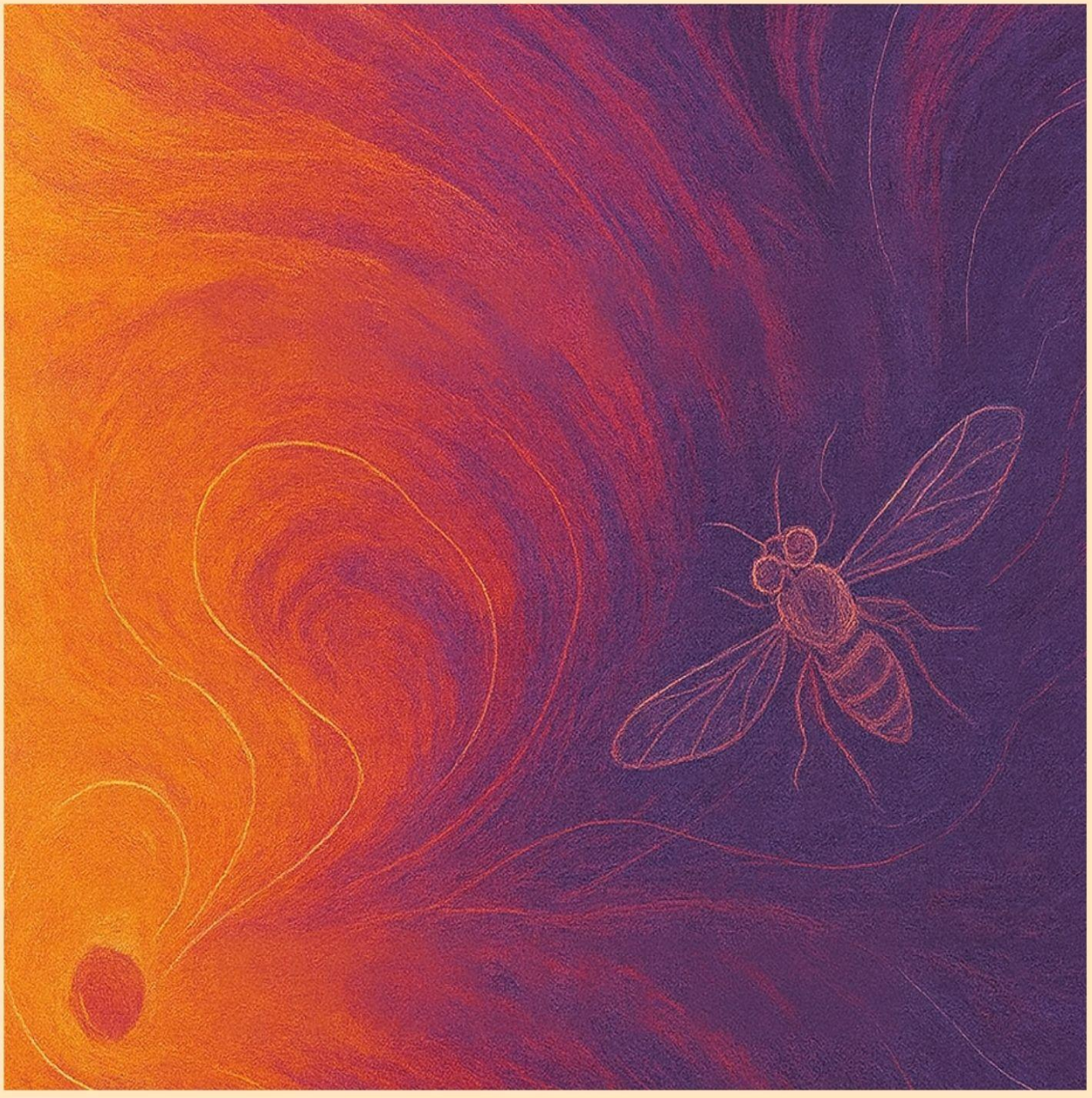

ABSTRACT BOOK

7th Indian Drosophila Research Conference

December 11-13 , 2025

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InDRC 2025 Schedule

7th Indian Drosophila Research Conference (InDRC2025)

December 11, 2025 (Thursday)

08.00 am to 09.30 am	Breakfast
09.00 am to 10.30 am	**Registration** (Foyer of Lecture Hall Complex)
10.00 am to 10.15 am	**Inaugural Session**
	Scientific Session 1 Chairperson: Dr. S. C. Lakhotia
10.18 am to 10.20 am	Opening remarks by Chairperson
10.20 am to 11.05 am	**Dr. Gaiti Hasan** Integration of neuromodulatory inputs by cellular Ca^{2+} signaling for systemic growth and behaviour
11.07 am to 11.32 am	**Dr. Jishy Verghese** Early-life nutritional stress reprograms insulin signalling and enhances starvation resilience in *Drosophila*
11.35 am to 12.00 pm	*Tea/Coffee Refreshment*
	Scientific Session 2 Chairperson: Dr. Ram Kumar Mishra
12.03 pm to 12.05 pm	Opening remarks by Chairperson
12.07 pm to 12.32 pm	**Dr. Sudipta Tung** Plastic and Adaptive Responses to Dietary Macronutrient Variation in *Drosophila melanogaster*
12.35 pm to 01.00 pm	**Dr. Varun Chaudhary** Regulation of the unfolded protein response pathways by Drosophila Rer1 and its importance in competitive cell survival
01.02 pm to 01.27 pm	**Dr. Rohit Joshi** Molecular basis of cell diversity generation in developing central nervous system of Drosophila.
01.30 pm to 01.45 pm	**Dr. Sveta Chakraborti** Drosophila blood cells bridge distant injury and gut homeostasis through Upd3-mediated inter-organ signaling
01.45 pm to 02.45 pm	*Lunch Break*
	Scientific Session 3 Chairperson: Dr. Geetanjali Chawla
02.50 pm to 02.52 pm	Opening remarks by Chairperson
02.55 pm to 03.30 pm	**Dr. Adam Chippindale**, An Evolutionary Battle of the Sexes: Arms Race or Arm Wrestle?
03.32 pm to 03.57 pm	**Dr. Girish Ratnaparkhi** VAPB at membrane contact sites: ALS at the crossroads of inflammation and lipid homeostasis
03.55 pm to 04.20 pm	**Dr. Bodhisatta Nandy**

	Life, death, and male fertility traits: a 1200 generation evolution experiment
04.22 pm to 04.37 pm	**Dr. Meghana Tare** Understanding cellular and molecular mechanisms involved in onset and progression of Parkinson's Disease
04.45 pm to 05.15 pm	*Tea/Coffee Refreshment*
04.45 pm to 6.45 pm	**Poster Session 1** *First floor of Lecture Hall Complex*
07.00 pm to 08.00 pm	**Cultural Program** *Auditorium, LHC*
08.00 pm to 09.30 pm	*Dinner*

December 12, 2025 (Friday)

08.00 am to 09.30 am	*Breakfast*
09.00 am to 10.30 am	**Registration** (Foyer of Lecture Hall Complex)
	Scientific Session 4 Chairperson: Dr. Jagat Kumar Roy
09.30 am to 09.32 am	Opening remarks by Chairperson
09.32 am to 10.07 am	**Dr. Amitabh Joshi** Re-examining the role of heritability in explaining selection responses
10.10 am to 10.35 am	**Dr. Sonal N Jaiswal** *Inseparable*: a new player in vesicle fusion
10.37 am to 11.03 am	**Dr. Surajit Sarkar** Bench to Bedside with Drosophila: A Snapshot of Our Experience
11.05 am to 11.25 am	**Dr. Dhananjay Chaturvedi** Acox function in peroxisomes and beyond is essential for Skeletal Muscle homeostasis
11.25 am to 11.45 am	*Tea/Coffee Refreshment*
	Student Scientific Session 1 Chairperson: Dr. Mohit Prasad
11.45 am to 11.47 am	Opening remarks by Chairperson
11.47 am to 11.57 am	**Ms. Medha Rao** Effect of generation length on population stability of *Drosophila* populations in the context of selection for rapid development and short breeding duration.(OP-1)
12.00 pm to 12.10 pm	**Ms. Sohela Sarkar** Tracheal cells on diet: How tracheal nutrition shapes the physiology and metabolism of the fruit fly (OP-2)
12.12 pm to 12.22 pm	**Ms. Ujjayita Chowdhury** Elucidating systemic signaling between epithelial tumor and the hematopoietic system: an inter-organ crosstalk in a *Drosophila* model of cancer cachexia (OP-3)
12.25 pm to 12.35 pm	**Ms. Sarani Dey**

	Developmental Spontaneous Neuronal Activity Alterations and its Connection with Autism Spectrum Disorder: Insights from the *Drosophila* Model (OP-4)
12.37 pm to 12.47 pm	**Mr. Joy Bose** Adaptation to Juvenile malnutrition associated with infection costs and increased disease transmission risk in *Drosophila* adults: a novel insight into Disease Ecology (OP-5)
12.50 pm to 01.00 pm	**Mr. Saurabh Chand Sagar** Rok, Arp2/3 and Gelsolin mediated microfilament disruption in absence of caspase-3 activity in *Drosophila* Malpighian tubules (MTs) (OP-6)
01.00 pm to 02.00 pm	*Lunch Break*
	Scientific Session 5 Chairperson: Dr. Pavan Agrawal
02.05 pm to 02.07 pm	Opening remarks by Chairperson
02.09 pm to 02.45 pm	**Dr. L S Shashidhara** Differential development of wing and haltere in *Drosophila*
02.48 pm to 03.13 pm	Dr. Mallikarjun Shakarad Healthy aging without tradeoffs: myth or reality
03.15 pm to 03.30 pm	**Dr. Anand Singh** The long noncoding RNA hsrω-n reduces neurotoxicity in the FUS-ALS model of *Drosophila*.
03.32 pm to 03.47 pm	**Dr. Shampa Ghosh** Sex-specific Effects of Temperature on Fitness Traits in *Drosophila melanogaster*
03.50 pm to 04.05 pm	**Dr. Harshvardhan Thyagarajan** The temporal dynamics of a balanced inversion polymorphism
04.10 pm to 04.40 pm	**Sponsor Talk** **Mr. Rishi Kant,** M/S Carl Zeiss India (Bangalore) Pvt. Ltd.
04.40 pm	**GROUP PHOTO**
04.50 pm to 05.15 pm	*Tea/ Coffee Refreshment*
04.50 pm to 6.50 pm	**Poster Session 2** *First floor of Lecture Hall Complex*
07.00 pm to 08.00 pm	
08.00 pm to 09.30 pm	*Dinner*

December 13, 2025 (Saturday)

08.00 am to 09.30 am	*Breakfast*
09.00 am to 10.30 am	**Registration** (Foyer of Lecture Hall Complex)
	Scientific Session 6 Chairperson: Dr. Carmen Coelho
09.30 am to 09.32 am	Opening remarks by Chairperson
09.32 am to 10.07 am	**Dr. Marco Milan** Chromosomal Instability in development and disease: beyond cancer evolution
10.10 am to 10.35 am	**Dr. Subhash Rajpurohit**

	Dynamic modulation of insect cuticular hydrocarbons under desiccation stress
10.37 am to 11.03 am	**Dr. Tina Mukherjee** The Immuno-Metabolic Control of Organismal Growth
11.05 am to 11.25 am	**Dr. Vanika Gupta** Single-cell resolution of fat body specialisation and immune constraints in *Drosophila*
11.25 am to 11.45 am	*Tea/Coffee Refreshment*
	Student Scientific Session 2 Chairperson: Dr. Anuradha Ratnaparkhi
11.45 am to 11.47 am	Opening remarks by Chairperson
11.47 am to 11.57 am	**Ms. Adhisree Sharma** Proteasomal Subunit Rpn7, Choreographs Group Cell Migration in *Drosophila* Oogenesis (OP-7)
12.00 pm to 12.10 pm	**Mr. Srikanth Pippadpally** E3 Ubiquitin Ligase Highwire/Phr1 Phase Separation Mediates Endocytic Control of JNK Signaling in *Drosophila* Neurons (OP-8)
12.12 pm to 12.22 pm	**Ms. Tsering Choton** Pathogen-driven selection shapes the *Drosophila* genome at specific loci while maintaining overall diversity (OP-9)
12.25 pm to 12.35 pm	**Ms. Devki** Usage of ACE Inhibitor triggers Oxidative Stress, Impairing Hematopoiesis and Immune Response (OP-10)
12.37 pm to 12.47 pm	**Mr. Abhijith Pradeep** Differentiating Blood Cells Define the Hematopoietic Niche Size in *Drosophila* larval lymph gland (OP-11)
12.50 pm to 01.00 pm	**Mr. Snehasish Samanta** Context-dependent differential neurotransmission from octopaminergic neurons drives distinct memory consolidation pathways (OP-12)
01.00 pm to 02.00 pm	*Lunch Break*
	Scientific Session 7 Chairperson: Dr. Vimlesh Kumar
02.03 pm to 02.05 pm	Opening remarks by Chairperson
02.07 pm to 02.45 pm	**Dr. Adrian Moore** Building Dendrites
02.50 pm to 03.15 pm	**Dr. Rhitobhan Raychoudhury** Integrated 'Weed' Management in Fungus-growing termites.
03.17 pm to 03.32 pm	**Dr. Debdeep Dutta** Genes and Mitochondria: Exploring Molecular Connections
03.35 pm to 03.50 pm	**Dr. Richa Arya** Canonical Cell Cycle Regulators and Their Impact on the Growth Dynamics of Cortex Glia in the Drosophila Central Nervous System
04.15 pm to 04.30 pm	**Valedictory Program**
04.30 pm to 05.30 pm	***High Tea***

PLENARY TALKS

PT-01

Building Dendrites

Adrian Moore

RIKEN Center for Brain Science, Japan.
Email: adrian.moore@riken.jp

Transcription factors specify neuronal subtypes, in part by controlling dendrite arbor diversification. We identify downstream effector networks through which transcription factor activity is translated into the stereotyped arbor patterns characteristic of each neuronal type. Some of these effector networks ultimately converge on microtubule nucleation, a critical determinant of the specialized microtubule networks that construct dendrite arbors. Through optimized long-term in vivo imaging of *Drosophila* dendrite differentiation coupled with computer vision-based analysis, we link individual subcellular microtubule nucleation events to emergent arbor architecture, establishing key pathways linking neuron subtype to arbor architecture.

PT-02

An Evolutionary Battle of the Sexes: Arms Race or Arm Wrestle?

Adam Chippindale

Department of Biology, Queen's University, Canada.
Email: chippind@queensu.ca

Females and males are caught in an evolutionary battle that cannot be won: famously "there's just too much fraternizing with the enemy". The conflict is played out in two distinct dynamics. First, adaptations by one sex to assert control over reproduction may illicit counter-adaptations in the other; an evolutionary "chase" or "arms race". Second, shared traits may be pulled in different directions by selection; an "armwrestle" created by genetic constraints. In this talk, I will focus on results from three decades of experimental investigation of sexual conflict with laboratory evolution in the fruit fly, Drosophila, showing evidence for both processes, but also the potentially temperamental nature of selection studies. I will argue that sexual conflict has profound implications for topics as diverse as the origin of species and human psychosocial disorders.

PT-03

Re-examining the role of heritability in explaining selection responses

Amitabh Joshi

Evolutionary and Organismal Biology Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru, India. E mail: ajoshi@jncasr.ac.in

Heritability is typically treated as a unitary concept in evolutionary genetics, depicted as a quantity ranging between zero and one that can be estimated through the ratio of additive genetic to phenotypic variance, or by offspring parent phenotypic regression, or as the ratio of selection response to selection differential. However, these three heritabilities are distinct, and converge only under very restrictive conditions. Two of them are not even constrained to lie between zero and one. I will discuss what exactly these three heritabilities are, when they do or do not coincide, and some implications for widely-held beliefs in evolution such as Sewall Wright's misplaced insistence that Fisher's Fundamental Theorem implies that populations can not move downhill on an adaptive landscape under the influence of selection. I will show that even for a simple one-locus two-allele model of viability selection - if we relax only the assumption that the previous generation underwent random mating - heritability exceeds one, or is negative, for large parts of the genotypic frequency simplex. These imply, respectively, that heredity can also amplify the mean fitness gains of selection, or move populations downhill on the fitness landscape from one generation to the next, in addition to playing its canonical role of slightly reducing the fitness gains through selection due to a return to Hardy-Weinberg frequencies upon reproduction. The canonical role of heredity actually manifests itself only in a small part of the genotypic frequency simplex, around the Hardy-Weinberg parabola.

PT-04

Integration of neuromodulatory inputs by cellular Ca^{2+} signaling for systemic growth and behaviour

Gaiti Hasan

National Centre for Biological Sciences, GKVK Campus Bengaluru 560 065, Karnataka, India.
Email: gaiti@ncbs.res.in

Behavioural plasticity is an essential requirement for organismal survival. The nervous system achieves this by altering cellular responses appropriately through neuromodulatory signals that are initiated by changes in the extracellular milieu. We work on understanding how neuromodulators change responses of neuronal cells. Both in vertebrates and invertebrates Inositol 1,4,5-trisphosphate (IP_3) is generated as a second messenger within cells in response to neuromodulatory signals. IP_3 in turn binds to the IP_3 receptor (IP_3R) present on intracellular Ca^{2+} stores to generate cellular Ca^{2+} signals. Our past work has shown that neuronal IP3/Ca^{2+} signals affect systemic physiology and behaviour in the fruit fly *Drosophila melanogaster*. I will discuss the molecular and cellular mechanisms underlying these changes followed by the relevance of these findings to human neurological conditions. Dysregulation of endoplasmic reticulum derived calcium signals and altered calcium homeostasis occurs in a range of neurodegenerative disorders including several Ataxias, Parkinson's and Alzheimer's disease emphasizing the importance of understanding how IP_3/Ca^{2+} signals affect nervous system function.

PT-05

Differential Development of wing and haltere in *Drosophila*

L.S. Shashidhara

National Centre for Biological Sciences, GKVK Campus Bengaluru 560 065, Karnataka, India.
Email: lsshashidhara@ncbs.res.in

In this talk, I will summarise our research, initiated in 1995, on how the Hox protein Ultrabithorax (Ubx) governs the differential development of the wing and haltere. We have focused on how Ubx, as a transcription factor, recognises its targets and regulates their expression, and how these regulatory interactions shape the small, bulbous haltere in contrast to the large, flat wing. By comparing Ubx function across *Drosophila*, *Apis*, and *Bombyx*, we uncovered an evolutionary mechanism through which key wing-patterning genes may have come under Ubx regulation in the Dipteran lineage. Beyond these developmental insights, we identified new regulatory steps in major signalling pathways such as Wg, Dpp, and Notch. More recently, we have extended this work to explore how these evolutionarily conserved mechanisms operate in human epithelial cancers.

PT-06

Chromosomal Instability in development and disease: beyond cancer evolution

Marco Milan

Institute for Reseach in Biomedicine (IRB) Barcelona, Spain.
Email: marco.milan@irbbarcelona.org

Chromosomal instability (CIN), an increased rate of changes in chromosome structure and number, has been classically associated with human disease as a way of evolving the cancer genome. In recent years, three additional research lines concerning the impact of CIN on human disease have been consolidated. First, beyond the generation of genomic copy number heterogeneity, CIN acts as a source of tumor growth, metastasis, and malignancy through additional mechanisms. Second, CIN is pervasive in early human development, and the resulting aneuploid cells are selectively removed from the fetus to give rise to healthy births. Third, CIN is associated with mosaic variegated aneuploidy, a rare familial disease that compromises brain development and contributes to tumor formation. In this seminar, I will summarize recent advances of our lab in these three topics, with a particular focus on the use of Drosophila to understand the increasing impact of CIN on human biology and disease.

INVITED TALKS

S-01

Life, death, and male fertility traits: a 1200 generation evolution experiment

Bodhisatta Nandy

Department of Biological Sciences, IISER Berhampur, Odisha 760003, India.
E mail: nandy@iiserbpr.ac.in

Experimental evolution of faster development and shorter lifespan have been successfully achieved in five replicate populations of fruit fly, *Drosophila melanogaster*. Over more than 1200 generations of evolution, a host of life history traits have been found to have evolved as direct and correlated responses to selection. We used these populations as a model to test the theory that life history should modulate the evolution of sexually selected traits through trade-offs, and its impact on breeding ecology. Through a series of controlled experiments, we show that evolution of faster life history was associated with the evolution of quite dramatic reduction in male reproductive investment, that resulted in almost complete amelioration of sexual conflict, and reduction in sperm size and sperm competitive ability. Yet, male fitness evolution was found to be more nuanced, and was found to be affected by age-specific selection pressure, and fertility constraints. We also found a range of clear signs of male-female coevolution. While some of these findings were clearly dependant on the evolution of body size, alteration in breeding ecology including extremely short breeding life appears to be a major driver of such evolution.

S-02

VAPB at membrane contact sites: ALS at the crossroads of inflammation and lipid homeostasis

Girish S Ratnaparkhi

Indian Institute of Science Education and Research, Pune, Maharashtra, India, 411008.
Email: girish@iiserpune.ac.in

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease marked by motor neuron loss leading to gradual paralysis and death 2-5 years post-diagnosis. 10% of ALS cases are familial, with ~18 independent genetic loci implicated in the onset of the disease. VAMP Associated Protein B (VAPB) is the 8 th ALS locus discovered, with the $VAPB^{P56S}$ mutation being the predominant variant. VAPB is a single-pass, ER-based, cytoplasmic-facing, transmembrane protein implicated in critical functions at the intracellular membrane contact sites (MCS) niche.

We utilized CRISPR-Cas9-based genome editing to develop a Drosophila model of ALS8. This ALS8/$VAPB^{P58S}$ fly line develops normally; however, adult animals exhibit a shortened lifespan, age-dependent progressive motor dysfunction, and defects in circadian and sleep patterns. In the adult $VAPB^{P58S}$ brain, we observe VAPB protein inclusions, accelerated inflammation and lipid dysbiosis. One allelic dose of $VAPB^{WT}$ in $VAPB^{P58S}$ flies can rescue all disease phenotypes.

The $VAPB^{P58S}$ brain exhibits age-dependent neuroinflammation, as measured by whole-transcriptome quantitative mRNA sequencing. Defence genes for all major immune pathways, Toll/NFκB, IMD-NFκB, JAK-STAT and JNK show higher levels of expression. We also find that the Janus Kinase (JNK) transcription factor, kayak (dFos), is a global negative regulator of neuroinflammation. Expression of Kayak in glia can reduce inflammation and suppress age-dependent motor dysfunction.

We also observe age-dependent accumulation of sphingolipids and cholesterol esters in the $VAPB^{P58S}$ adult brain, accompanied by a concomitant decrease in cholesterol. Lipid Droplet (LD) homeostasis is also disturbed, with glial VAP function linked to LD regulation. Moreover, our study highlights tissue-specific regulation of ceramide synthesis, and its transfer in the brain, where reducing ceramide in the neurons can improve motor function in ALS8 flies.

Our studies highlight the critical roles of VAPB-enriched membrane contact sites in both inflammation and lipid metabolism, which, in turn, affect cellular physiology. This points to a vital role for the lipid-inflammation axis in ALS pathogenesis.

S-03

Early-life nutritional stress reprograms insulin signalling and enhances starvation resilience in *Drosophila*

Jishy Varghese

Indian Institute of Science Education and Research (IISER-TVM), Maruthamala Post, Vithura, Thiruvananthapuram, Kerala, India 695551. Email: jishy@iisertvm.ac.in

Organisms often face unpredictable changes in their environment that can disrupt physiological balance, and they also have to deal with pathogens and toxins that act as additional stressors. Although many stressors are damaging or even deadly, mild exposure, especially early in life, can trigger adaptive adjustments that make individuals more resilient later on. This phenomenon, known as hormesis, has been linked to benefits for aging, immunity, and metabolism. In *Drosophila*, for instance, brief bouts of heat or oxidative stress can extend lifespan and improve tolerance to other stresses. Starvation is one of the most common and recurring environmental pressures, and prior exposure to food deprivation is known to affect survival, lifespan, and general stress resistance, though the underlying mechanisms are still not fully understood.

In our lab, we've been exploring how early mild stress shapes later-life resilience using two different models in *Drosophila*. In the first, we reared larvae on a diet with 50% of the normal food content and then examined the adults. This modest nutritional stress increased starvation resistance in adults, which appears to stem from better storage and utilization of fat reserves, a consequence of reduced insulin signalling during larval growth. In other words, larvae raised on limited food seem to "prepare" physiologically for a future of scarce resources. In our second study, we tested whether repeated short episodes of starvation in adults could improve their ability to withstand prolonged food deprivation. We found that this repeated mild stress leads to metabolic and transcriptomic changes that enhance survival, and that increased insulin sensitivity plays a key role in the response.

Together, these findings shed light on how hormesis operates at the molecular and metabolic levels, and they highlight broader themes in the evolution of stress resilience - topics that are becoming increasingly relevant in the context of environmental change and climate-related stress.

S-04

Healthy aging without tradeoffs: myth or reality

Mallikarjun N. Shakarad

Evolutionary Biology Laboratory, Department of Zoology, University of Delhi, India.
Email: mallik@zoology.du.ac.in

Evolution of increased lifespan is generally suggested to tradeoff with reproduction and its related traits, owing to physiological constraints on resource acquisition and allocation mechanisms. Several studies have supported this hypothesis while few have questioned. In this study, males from *Drosophila melanogaster* populations selected for faster pre-adult development and increased longevity (FLJ) emerge with fewer resources, yet live longer than their ancestral control (JB) males without compromising on reproductive performance. Across adult ages, FLJ males show courtship duration, copulation duration, fecundity and fertility comparable to JB males. Further, FLJ males mate with more number of females and show superior sperm competitive ability compared to JB males. They also have higher locomotor activity at late ages with comparable early life activity. The higher performance of FLJ males was due to better gut integrity, higher metabolic rate and more efficient resource utilization through adulthood. Collectively, these results suggest that FLJ males have evolved an extended healthy lifespan without apparent reproductive costs. The absence of detectable tradeoffs, despite reduced resources challenges the classical life history theory, which predicts that enhanced somatic maintenance and increased lifespan comes at the expense of reproduction.

S-05

Integrated 'Weed' Management in Fungus-growing termites

Rhitoban Ray Choudhury

Indian Institute of Science Education and Research Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli, PO 140306, Punjab, India. Email: rhitoban@iisermohali.ac.in

Social insect colonies represent great evolutionary success stories. Nevertheless, the high density of individuals, low genetic variability and confined space of these colonies attract several predators and parasites. Social insects must evolve sophisticated responses to deal with such threats. I will describe one such strategy in the fungus-growing termite *Odontotermes obesus*. These termites practice agriculture and cultivate a specific fungus as food. However, these crop fields are also prone to be invaded by weeds and parasites. Termites have to deal with such invasion in such a way which minimizes damage to their crop fields. I will elaborate how *O. obesus* termites solve this problem.

S-06

Molecular basis of cell diversity generation in developing central nervous system of *Drosophila*

Rohit Joshi

BRIC- Centre for DNA Fingerprinting and Diagnostics (CDFD), Inner Ring Road, Uppal, Hyderabad – 500 039, Telangana State. Email: rohit@cdfd.org.in

Generation of right Cell diversity is cardinal for assembly of a functional CNS. A fine coordination of neural stem cell proliferation, differentiation and apoptosis lies the heart of the generation of this cell diversity. We use Drosophila CNS to study molecular regulations controlling the cell diversity generation. I will be discussing our recent work giving insights into the molecular basis of the how Protein Phosphatase 1 play role in these phenomenon to regulate cell diversity generation in developing CNS of Drosophila.

S-07

Inseparable: a new player in vesicle fusion

Sonal Nagarkar Jaiswal

CSIR-Centre for Cellular and Molecular Biology (CCMB), Habsiguda, Uppal Road, Hyderabad - 500 007, Telangana, India. Email: sonalnj.ccmb@csir.res.in

De-regulated neural stem cell maintenance has profound consequences on brain development that can lead to neurodevelopmental disorders. To unveil the molecular players that maintain neural stem cell homeostasis, we conducted a genetic screen in *Drosophila* and isolated an uncharacterized gene that we named *Inseparable* (*Insep*). *Insep* is the *Drosophila* homologue of human *IER3IP1*, a gene associated with Microcephaly, Epilepsy, and Neonatal Diabetes Syndrome (MEDS-1). We show that *Insep* loss leads to early larval lethality with small brains and these phenotypes can be rescued by expressing IER3IP1 indicating that their biological function is conserved through evolution. Loss of *Insep* in flies and *IER3IP1* in human cells leads to cytokinesis failure. Insep and IER3IP1 localize to Rab11 vesicles and interact with Rab11, and their loss leads to an accumulation of Rab11 vesicles in the cytoplasm. Further, we found that Insep interacts with SNARE proteins. Overall, our results reveal a cellular function of Insep and IER3IP1 in advancing cytokinesis, possibly by regulating the fusion of Rab11 vesicles to the ingressing furrow during cytokinesis.

S-08

Dynamic modulation of insect cuticular hydrocarbons under desiccation stress

Subhash Rajpurohit

Ahmedabad University, Commerce Six Roads, Navrangpura, Ahmedabad – 380009, Gujarat, India.
Email: subhash.rajpurohit@ahduni.edu.in

Insects are vulnerable to desiccation as they are smaller in size and have a high surface area-to-volume ratio. To handle desiccation, insects maintain an outer waxy coating throughout their body. Insects lose over 80% of their body water through the cuticle and to combat water loss, specialised insect cells (i.e., oenocytes) synthesize hydrocarbons (CHCs), which form a hydrophobic waxy barrier between environment and body. This is especially crucial for small insects where spatiotemporal variations in abiotic factors can be drastic resulting in water loss. However, how rapidly CHCs are synthesized and transported across the cuticle under desiccating conditions remains poorly understood. To examine this, we exposed male *Drosophila melanogaster* to varying durations (hours) of desiccation (0, 2, 4, 6, 8, and 10 h) and compared CHC composition for each of these time-points. We uncovered significant variation in CHC composition over time, with a notable shift observed post 2 h, and becoming more pronounced at 6 h of progressive dehydration during desiccation. Concurrently, the rate of water loss increased by ~4% per hour of desiccation, leading to significant loss in total body water (0 to 10 h). The progressive water loss was tightly linked to rapid temporal shifts in CHC composition indicating dynamic CHC biosynthesis and deployment onto the cuticle.

S-09

Plastic and Adaptive Responses to Dietary Macronutrient Variation in *Drosophila melanogaster*

Sudipta Tung

Ashoka University, Plot No. 2, Rajiv Gandhi Education City, National Capital Region P.O. Rai, Sonepat Haryana-131029, India. E mail: sudipta.tung@ashoka.edu.in

How organisms respond and adapt to nutritional variation is a central question in evolutionary physiology. Using *Drosophila melanogaster*, we investigated the effects of isocaloric protein-rich and carbohydrate-rich diets across developmental and adult life stages in both short-term and long-term experiments. In single-generation assays, developmental exposure to a carbohydrate-rich diet increased male body size and lifespan, whereas protein-rich diets at either stage enhanced reproductive output. Adult carbohydrate-rich diets extended desiccation resistance but reduced lifespan in both sexes. Most life-history traits exhibited additive effects of larval and adult diet, with sex-specific differences in trait associations. In a parallel long-term experiment, populations evolved for over 60 generations under all four combinations of larval–adult diets exhibited distinct adaptive changes in metabolic reserves, stress resistance, and reproductive allocation. These evolutionary outcomes diverged from plastic responses, highlighting how chronic dietary environments shape novel physiological strategies. Together, our findings illustrate the interplay between nutritional plasticity and adaptation in shaping life-history evolution under macronutrient variation.

S-10

Bench to Bedside with *Drosophila*: A Snapshot of Our Experience

Surajit Sarkar

Department of Genetics, University of Delhi South Campus, Benito Juarez Road, New Delhi-110 021, India. E mail: sarkar@south.du.ac.in

We previously reported that the growth-promoting branch of the insulin pathway can serve as an effective drug target against polyglutamine [poly(Q)] disorders, including Huntington's disease (HD) and Spinocerebellar ataxias (SCA) 1, 2, and 3. Building on this, we investigated whether established insulin-stimulating drugs could mitigate poly(Q) pathology in Drosophila disease models. We found that glipizide, an FDA-approved and cost-effective anti-diabetic drug, enhances insulin signaling in poly(Q)-expressing tissues, reducing the formation of inclusion bodies and neurodegeneration. Notably, glipizide also restores chromatin architecture by improving histone acetylation, which is otherwise disrupted by poly(Q) toxicity. Given the functional conservation of the insulin signaling pathway between Drosophila and humans, these findings strongly suggest that glipizide could be repurposed as a therapeutic strategy for poly(Q) disorders. With further validation in mammalian models, glipizide may ultimately be considered for clinical trials in human patients.

S-11

The Immuno-Metabolic Control of Organismal Growth

Tina Mukherjee

Institute for Stem Cell Science and Regenerative Medicine (inStem), GKVK post, Bellary Road, Bangalore 560065, India. Email: tinam@instem.res.in

Understanding hematopoiesis has traditionally focused on how blood cells arise, diversify, and maintain immune competence. In this context, our work explores the metabolic underpinnings of blood development and reveals systemic influences that metabolically tune hematopoietic progenitor cells to ensure their proper maturation. A key finding from our study is the importance of sensory input in modulating blood formation. As immune cells meet their metabolic demands, they also contribute to systemic physiology, with growth emerging as a major developmental outcome of this regulation. Using *Drosophila* as a model, we show that developing immune cells, through amino acid uptake required for their own development, also act as active nutrient sensors. Through metabolic reprogramming, these cells exert systemic influence on organ growth and overall body size. Our findings demonstrate that hematopoietic metabolism interfaces with systemic signaling pathways to coordinate developmental growth with nutritional state. This cross-talk positions hematopoiesis and its metabolic demands as integral regulators, rather than passive responders, broadening the concept of developmental hematopoiesis from building an immune system to orchestrating whole-body growth and homeostasis.

S-12

Regulation of the unfolded protein response pathways by *Drosophila* Rer1 and its importance in competitive cell survival

Varun Chaudhary

Indian Institute of Science Education and Research (IISER) Bhopal, Madhya Pradesh, India.
E mail: varun.c@iiserb.ac.in

Cell competition, first identified in Drosophila epithelium, eliminates less fit cells via fitness–sensing mechanisms, thereby maintaining tissue integrity. A critical determinant of cellular fitness is endoplasmic reticulum (ER) proteostasis. Disruption of ER homeostasis leads to proteotoxic stress and activation of the unfolded protein response (UPR) pathways. Although UPR activation is typically associated with the elimination of stressed cells, it is paradoxically also observed in "super-competitor" cells such as those overexpressing Myc, which overgrow by eliminating wild-type neighbours, despite exhibiting elevated stress. The molecular mechanisms linking cell competition to proteostasis regulation remain poorly understood.

We identified the ER- and Golgi-localized protein Rer1 as a crucial regulator of competitive cell survival and Myc-driven overgrowth. Loss of Rer1 induced proteotoxic stress, marked by elevated phosphorylation of eIF2α, indicating enhanced PERK activity. We also observed the activation of IRE1α branch of the UPR, however interestingly, this activation occurred indirectly through PERK signalling. Importantly, in contrast to the typical cytoprotective role of UPR, its activation upon Rer1 loss was found to be cytotoxic. The mechanism by which UPR signalling switches from promoting survival to triggering cell death remains an intriguing open question.

SHORT TALKS

ST-01

The long noncoding RNA hsrω-n reduces neurotoxicity in the FUS-ALS model of *Drosophila*

Anand K Singh

Department of Biology, IISER Tirupati, Srinivasapuram, Venkatagiri Road, Jangalapalli Village, Panguru (G.P), Yerpedu Mandal, Tirupati District, Andhra Pradesh, India – 517619. E mail: anand@labs.iisertirupati.ac.in

Long noncoding RNAs (lncRNAs) have been extensively studied for their roles in regulating various neurodegenerative diseases. The hsrω is a developmentally active, noncoding gene involved in neurodegenerative diseases associated with polyglutamine (PolyQ) diseases and the amyotrophic lateral sclerosis (ALS) disease model in Drosophila. The hsrω-n lncRNA sequesters several heterogeneous nuclear ribonucleoproteins (hnRNPs) and related proteins, forming omega speckles within the nucleus. We observed that the expression of nucleus-limited hsrω-n lncRNAs is upregulated in the degenerating neurons of the FUS-ALS model in Drosophila. The FUS protein binds to the hsrω gene locus on polytene chromosomes, leading to the induction of its transcription. Additionally, the FUS protein associates with hsrω-n lncRNAs and their related hnRNPs, interfering with their role in processing newly transcribed mRNAs on chromosomes. Genetic interaction experiments showed that overexpression of hsrω-n lncRNA helps in suppressing the neurodegeneration caused by FUS expression. Overexpression of hsrω-n lncRNA leads to the formation of FUS aggregates and thus preventing FUS from disrupting the functions of other RBPs. This study indicates that hsrω-n lncRNAs sequester FUS, reducing its toxic effects and thus providing a protective role against FUS-ALS related neurotoxicity.

ST-02

Genes and Mitochondria: Exploring Molecular Connections

Debdeep Dutta

IIT Kanpur, Kalyanpur, Kanpur -208 016, Uttar Pradesh, India.
E mail: ddutta@iitk.ac.in

Mitochondrial disorders affect approximately one in every five thousand individuals globally. In India, it is estimated that a child is born with such a disorder every 20–30 minutes. Unfortunately, more than half of them remain undiagnosed for years, sometimes for their entire lives, causing a significant economic and social burden. Our research focuses on discovering new disease-causing genes in humans to improve diagnosis and to uncover the molecular basis of mitochondrial dysfunction and neurodegeneration. To this end, 'humanized' fruit flies serve as an efficient platform for quick functional analyses of patient-derived genetic variants. In this talk, I will discuss how this approach contributes to medical discoveries related to mitochondrial diseases.

ST-03

Acox function in peroxisomes and beyond is essential for Skeletal Muscle homeostasis

Dhananjay Chaturvedi

CSIR-Centre for Cellular and Molecular Biology (CCMB), Habsiguda, Uppal Road, Hyderabad - 500 007, Telangana, India. Email: dhananjay@ccmb.res.in

Skeletal muscles require fatty acid metabolism for energy production, maintaining organelle membrane composition and signalling. Peroxisomes and mitochondria are the sites of β-oxidation of long-chain and branched-chain fatty acids, the first step being catalysed by Acyl–CoA oxidase. Modelling human skeletal muscle in Drosophila flight muscles, we have identified the requirement of a putative Acyl CoA oxidase 3 (Acox3) homolog, CG17544, for homeostasis. Drosophila flight muscles and vertebrate skeletal muscles are similar in architecture and function. We observe that CG17544 knockdown in muscles causes severe muscle breakdown, highlighting the necessity of this single ACOX in muscles. We have found that CG17544 localises to peroxisomes, and the M-line of the sarcomere where ER is positioned, surrounding mitochondria and sporadic nuclei. Upon CG17544 knockdown, muscle mitochondria appear rounded, with free spaces inside. Further, lipids accumulate in vivo. LC-MS measurements from these muscles suggest a candidate list of substrates, many of which are atypical for Acox3. Our structural studies show that this enzyme is an obligate homodimer, where only a single constituent monomer is likely to be active. Further, we have uncovered an unreported shorter isoform, lacking the catalytic domain, capable of binding the full-length protein and other ACOXes, probably regulating all their activity. This raises the intriguing possibility of combinatorial regulation of substrate selectivity for beta oxidation. In a further twist, peroxisomal localisation of CG17544 may be inessential for muscle homeostasis. These results will help us navigate the complex function and regulation of fatty acid metabolism in skeletal muscles as our investigations proceed.

ST-04

The temporal dynamics of a balanced inversion polymorphism

Harshavardhan Thyagarajan

Department of Biology, University of Fribourg, Fribourg, Switzerland.
Email: harshavardhan.thyagarajan@unifr.ch

The selective maintenance of balanced inversion polymorphisms represents a classical puzzle in evolutionary genetics. Numerous inversion polymorphisms have been found to persist at intermediate frequencies and are thus thought to be maintained by strong selection. Yet, despite decades of study, the precise modes of balancing selection responsible for their persistence remain incompletely understood. A classical example is the cosmopolitan In(3R)Payne inversion polymorphism of *Drosophila melanogaster*. Previous work suggests that this long-term polymorphism is subject to strong spatially varying selection along latitudinal gradients on several continents, always being at intermediate frequencies in tropical or subtropical low-latitude areas but absent in cool high-latitude areas. As spatially varying (divergent) selection is expected to generate frequency clines that approach fixation of the alternative alleles at the cline ends, it is unclear why the inversion does not locally fix at one end. An intriguing possibility is that the loci captured by the inversion are subject to local balancing (e.g., negative frequency-dependent) selection independent of temperature yet at the same time happen to render the inversion susceptible to cool temperatures. Here, we have sought to explore this hypothesis by manipulating and tracking the dynamics of inversion frequencies in (i) outdoor mesocosms in Philadelphia from late summer through early winter, and (ii) laboratory cages with factorial variation in starting frequency and temperature. We find that the polymorphism is amenable to multiple equilibria, consistent with maintenance by negative frequency-dependent selection; in conjunction with selection against the inverted arrangement in cooler environments, along latitudinal gradients. These results indicate that the In(3R)Payne polymorphism is affected by multiple forms of balancing selection across space and time.

ST-05

Understanding cellular and molecular mechanisms involved in onset and progression of Parkinson's Disease

Meghana Tare

Birla Institute of Technology and Science Pilani, Vidya Vihar, Pilani, Rajasthan-333031, India.
Email: meghana.tare@pilani.bits-pilani.ac.in

Parkinson's disease (PD) is a prevalent neurodegenerative condition involving the loss of neurons because of protein aggregation, resulting in impaired motor and cognitive abilities. PD majorly occurs due to genetic alteration; referred to as genetic PD or it can be acquired during life, referred to as sporadic PD. PD is usually characterized by loss of dopaminergic neurons resulting in motor disabilities. In our lab, we use both genetic and sporadic models to understand the cellular and molecular mechanisms involved in onset and progression of PD. We are employing *Drosophila melanogaster* as a model organism to understand the cellular, genetic and molecular basis of PD. At cellular level, we have identified that PD affects mitochondrial morphology of dopaminergic neurons in the genetic models of PD in flies in spatio-temporal fashion.
Compounds like Rotenone have been found to cause toxicity by inhibiting cellular events and causing neuronal death. Rotenone feeding has been shown to cause neuronal death and has been used in mimicking sporadic form of PD. We have developed a novel model by feeding rotenone mixed with food, that mimics PD phenotypes. Interestingly, different strains of wild-type flies respond differentially to rotenone exposure. Furthermore, we have identified that flies respond in context to biological gender to the rotenone. Our data indicates that specific genders and populations may exhibit differential sensitivity for PD onset and progression, which is in-sync with the global population studies for PD. However, mechanistic insights are required to elucidate the mechanisms involved to cause this biased behaviour in the progression of PD.

ST-06

Canonical Cell Cycle Regulators and Their Impact on the Growth Dynamics of Cortex Glia in the *Drosophila* Central Nervous System

Richa Arya

Cytogenetics Laboratory, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005, India. Email: aryaricha@bhu.ac.in

Cortex glia in the Drosophila central nervous system (CNS) play a crucial role in supporting neural cells by forming a reticulated niche that facilitates communication with the surrounding environment. These glial cells exhibit unique growth patterns, utilizing endocycling and acytokinetic mitosis to increase their ploidy and generate extensive cytoplasmic extensions. We show that despite following a variant cell cycle, cortex glia are regulated by canonical cell cycle regulators, including various cyclin and cyclin-dependent kinase complexes, which significantly influence their nuclear division and growth. Spatially, cortical glia in different regions, such as the thoracic and abdominal areas, demonstrate distinct growth behaviors; while thoracic cortex glia form syncytial structures, abdominal glia remain arrested in the G2 phase, showing a readiness to divide only when M-phase regulators are ectopically expressed. We identified the homeodomain transcription factor Cut as a key regulator of cortex glia fate and growth. Cut is essential for proper glial development and for orchestrating the timing of DNA content increase through endocycling, impacting the overall formation of glial networks around NSCs. Currently, we are evaluating how various growth signaling cross-talk constructs a complex glial niche in the Drosophila nervous system. Understanding these mechanisms not only enhances our knowledge of glial development in Drosophila but also offers potential insights into similar processes in other organisms.

ST-07

Evolution and Development in Hot vs. Cold: How Temperature Shapes Life History Traits and Gene Expression in *Drosophila*

Shampa Ghosh

KIIT, School of Biotechnology, Campus XI, Patia, Bhubaneswar-751024. Odisha, India.
E mail: shubhra.dbs@presiuniv.ac.in

How organisms adapt to changes in their thermal environment is a question relevant to the current era of climate change. Temperature affects myriads of biological traits, especially in ectothermic animals like Drosophila. We have used experimental evolution to allow *Drosophila melanogaster* populations to evolve under warm, cold, and fluctuating temperatures for many generations. Using RNA-seq analysis of these laboratory evolved populations, we studied gene expression changes underlying both thermal plasticity (short term) and thermal evolution (long term). This led to some fascinating findings about the underlying genetic details of thermal adaptation in flies. I would highlight the findings made from this study during the first half of my talk. The second half of the talk is about a phenotypic study focusing on effects of thermal shifts on growth and development of the fly. Thermal fluctuations are common in nature, and in holometabolous insects like Drosophila, different life stages such as egg, larva, pupa, and adults are exposed to different microenvironments. In view of this, we studied how thermal shifts across life stages affect (a) subsequent developmental duration, and (b)body size of flies, as they develop through different pre-adult stages. This study provided some interesting insights about thermal plasticity of growth and development time in Drosophila.

ST-08

Drosophila blood cells bridge distant injury and gut homeostasis through Upd3-mediated inter-organ signaling

Sveta Chakrabarti

Manipal Institute of Regenerative Medicine, BSF Campus, Yelahanka, Govindapura, Bengaluru, Karnataka-560064, India. E mail: sveta.chakrabarti@manipal.edu

Inter-organ communication is a central feature of host defence and tissue repair. In Drosophila, hemocytes secrete the cytokine-like ligand Unpaired 3 (Upd3, an IL-6 homolog) to activate JAK/STAT signaling in the gut, yet why this axis is essential for survival after injury has remained unclear. Here we show that loss of hemocyte activation by reactive oxygen species (ROS) and the consequent failure to produce Upd3 leads to adherens junction disruption, intestinal barrier dysfunction, and increased lethality following clean injury. Hemocyte-derived Upd3 drives sustained STAT activation in the gut epithelium, promoting enterocyte turnover and survival after injury. Chronic STAT activity further modulates intestinal stem cell fate and differentiation, indicating that hemocyte–gut signaling shapes long-term epithelial homeostasis. Notably, hemocytes home to the gut after distant wounding, where their localized presence enhances resistance to enteric infection. Taken together, these findings reveal that Drosophila blood cells bridge distant injury and gut homeostasis through Upd3-mediated inter-organ signaling that links wound sensing to epithelial integrity and host survival.

ST-09

Single-cell resolution of fat body specialisation and immune constraints in *Drosophila*

Vanika Gupta

Department of Zoology, University of Delhi, New Delhi, India. Email: vgupta1@zoology.du.ac.in

The insect fat body integrates metabolic regulation, reproductive provisioning, and systemic immune defense. The mechanism by which polyfunctional tissues simultaneously execute multiple distinct physiological functions is generally unknown. Immunity and reproduction are observed to trade off in many organisms; however, the mechanistic basis for this tradeoff is typically unknown. Here, single-nucleus RNA sequencing of the Drosophila *melanogaster* fat body reveals heterogeneous cellular subpopulations that partition diverse basal functions, while acute immune activation mobilizes the entire tissue as an emergency response. We found that bacterially challenged, reproductively active females exhibited signatures of ER stress and an impaired capacity to synthesize new protein in response to infection, including a decreased ability to produce antimicrobial peptides. Transient provision of a reversible translation inhibitor to mated females prior to infection rescued general protein synthesis, specific production of antimicrobial peptides, and survival of infection. The commonly observed tradeoff between reproduction and immunity appears to be driven, *in D. melanogaster*, by the fat body's inability to concurrently meet the protein translation demands of both reproduction and immunity. These findings support a mechanistic model in which the intrinsic translational capacity of multifunctional tissues generates physiological tradeoffs, providing a potential general explanation for the widespread coupling of reproductive investment and immune competence across animals.

ORAL PRESENTATIONS

OP-01

Effect of generation length on population stability of *Drosophila* populations in the context of selection for rapid development and short breeding duration

Medha Rao[1], Chinmay Temura[1], Amitabh Joshi[1]

[1]*Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru, India*.

The ubiquity of stable populations in nature generates considerable interest in how population stability can evolve. One of the theories concerning the evolution of population stability suggested that stability could evolve as a correlated response to life-history evolution. Supporting this, earlier work showed that *D. melanogaster* populations selected for rapid development and short breeding duration (FEJs) evolved greater constancy stability than their ancestral controls, likely due to correlated reductions in fecundity and pre-adult survivorship. Subsequently, two sets of populations were derived from the FEJs by relaxation of selection pressures: one set was relaxed only for rapid development, while the other was relaxed for both selection pressures. The ancestral, forward selected, singly and doubly relaxed populations are routinely maintained on a 21-day, 10-day, 12-day and 17-day discrete generation cycles, respectively. However, the population dynamics are typically assessed based on the cycle length of the ancestral populations – i.e., a 21-day generation length. Therefore, the previously observed greater stability of the FEJs could be an artefact of the generation length at which stability was measured, and results could vary if tested on a shorter generation length. In this context, we examined the effects of generation length and its interaction with the selection pressures on the dynamics and stability of these populations. The experiment ran for 27 generations (across 2 years), during which we simultaneously tracked the dynamics of 320 single-vial, small populations. Contrary to the 21-day generation length study, when measured on a shorter generation length, the FEJs did not differ in their constancy stability from the ancestral controls. Our results highlight that life-cycle length could significantly influence the stability of populations, thereby underscoring the need to account for generation length when comparing stability across populations.

OP-02

Tracheal cells on diet: How tracheal nutrition shapes the physiology and metabolism of the fruit fly

Sohela Sarkar[1], Prajakta Baliram Bodkhe[2], Namitha V S[1], Josy Joseph[3], Jishy Varghese[1]*

[1]*Indian Institute of Science Education and Research Thiruvananthapuram, Kerala, India;*
[2]*University of Calgary, Calgary, Canada; 3Indiana University, Bloomington, USA*

The fruit fly, *Drosophila melanogaster*, modulates its own physiology to survive during nutrient scarcity. Such adaptations are brought about by inter-organ molecular biocommunications. Sensor tissues identify the status of nutrient availability and conveys them to insulin producing cells (IPCs) in the brain. IPCs then regulate overall tissue growth by modulating the synthesis and secretion of growth hormones (Drosophila insulin-like peptides [DILPs]) based on nutrient availability information. With a series of genetic and environmental perturbation experiments, we have identified that tracheal terminal cells (TTCs), previously considered primarily for respiratory functions, are extremely sensitive to changes in dietary nutrients, especially amino-acids. We also identify the pivotal role of mTOR signalling within tracheal cells as the key molecular mechanism responsible for this nutrient sensing.

Moreover, we uncover the systemic impact of tracheal nutrient sensing, demonstrating its ability to regulate the overall growth and metabolism of the organism by regulating DILP secretion from IPCs. This study provides unprecedented insights into the cross-talk between respiratory and endocrine systems. It also helps

expand our understanding of cellular versatility. Overall, this research not only advances our understanding of tracheal cell biology but also highlights the integration of respiratory and metabolic processes in shaping the organism's response to dietary challenges.

OP-03

Elucidating systemic signaling between epithelial tumor and the hematopoietic system: an inter-organ crosstalk in a *Drosophila* model of cancer cachexia

Ujjayita Chowdhury[1,2], Gauri Panzade[1] , Priya Karnik[1], and Rohan J. Khadilkar[1,2]*

[1]*Stem cell and Tissue Homeostasis lab, Cancer Research Institute, ACTREC – Tata Memorial Centre, Navi Mumbai – 410210, India*
[2]*Homi Bhabha National Institute, Anushaktinagar, Mumbai – 400094, India*

Cancer Cachexia is a multifactorial syndrome that involves the systemic deregulation of metabolic pathways in several organs. Muscle wasting, lipolysis, and inflammation are central to the pathology of cachexia.
Previous studies have uncovered various signaling pathways that regulate peripheral organ wasting using multiple larval and adult cachexia models in *Drosophila*. We utilized a larval cachexia model by inducing Yki^{3SA} mutation in the mid-gut using escargot-Gal4 and characterized cachexic phenotypes like hyperglycemia, lipolysis, insulin resistance, and muscle thinning.
One of the hallmarks of cachexia is chronic inflammation. However, the crosstalk of the epithelial tumor on the hematopoietic system and the immune cells is fairly underexplored. Hence, we performed bulk RNA-seq analysis on the hemocytes of the Yki^{3SA} larvae, and analyses show differential expression of molecules related to the Insulin signaling pathway. One such insulin antagonist, Imp-L2, which is a known cachexic ligand secreted by tumor, was one of the candidates that were significantly upregulated even in the hemocyte transcriptome from the larval cachexia model.
We find that niche size reduces in the larval lymph gland with a widespread increase in blood cell differentiation in the cachexia background. This phenotype is recapitulated when we genetically mimic systemic elevation of Imp-L2 levels in the larvae systemically in the fat body or gut. Our results indicate that Insulin signaling in the niche is perturbed, resulting in a decreased PSC/niche size. Our observations indicate that elevated Impl2 levels cause Insulin resistance systemically which perturbs the Insulin–Wingless signaling axis in the niche-progenitor micro-environment impacting blood cell homeostasis in the larval lymph gland. This study reveals mechanistic insights into how cellular immune response is heightened in cancer cachexia, with important clinical implications.

OP-04

Developmental Spontaneous Neuronal Activity Alterations and its Connection with Autism Spectrum Disorder: Insights from the *Drosophila* Model

Sarani Dey[1], Sharba Bandyopadhyay[2] and Abhijit Das[1]

[1]*Department of Bioscience and Biotechnology, Indian Institute of Technology Kharagpur, West Bengal, India*
[2]*Department of Electronics and Communications Engineering, Indian Institute of Technology Kharagpur, West Bengal, India*

Developmental *spontaneous neuronal activity* is required to establish precise synaptic connectivity during neuronal development. Any disruption of this activity hampers the maturation of synapses. We hypothesize that a disruption of spontaneous activity in developing neurons might have role in the origin of neurodevelopmental disorders like Autism Spectrum Disorder (ASD). In *Drosophila,* the maturation of adult neurons generally takes place during the pupal stage with unique spontaneous neuronal activity (SNA) signature. In this study, we spatio-temporally silenced and enhanced the pupal SNA patterns by optogenetic and thermogenetic tools in the dopaminergic neuronal subset and assessed the behavioural impact in adult flies. We found behavioural anomalies in these flies that are akin to the ASD symptoms in humans. We compared these phenotypes with two existing ASD models namely *Fragile-X Mental Retardation* (*FMR*) gene mutant model and Valproic acid (VPA) drug feeding model. We found that both these *Drosophila* ASD models showed increased repetitive behaviour and decreased social interaction and courtship preference along with altered aggressive behaviour, phenocopying activity-manipulated flies.

We took a bioinformatic approach to find the potential activity-responsive genes connecting the SNA with transcriptional regulation in developing neurons. We identified ASD-associated gene *Mef2* as one of the Activity Regulated Genes (ARG), knockdown of which mimicked the behavioral alterations of activity-manipulation. Changing the developmental SNA has been observed to change the expression level of Mef2, indicating a connection between developmental SNA and Mef2 expression. Finally, two-photon microscopy-based calcium imaging shows SNA defects in *dfmr1* mutant, VPA-pupae and *Mef2* knockdown models, confirming the contribution of developmental spontaneous activity with the origin of Autism-like behavioral anomalies.

OP-05

Adaptation to Juvenile malnutrition associated with infection costs and increased disease transmission risk in *Drosophila* adults: a novel insight into Disease Ecology

Joy Bose[1], Aritra Bhattacharya[2], Dipendra Nath Basu[1], Biswajit Shit[1], Tadeusz j. Kawecki[3] and Imroze Khan [11]

[1]Ashoka University, India; [2]Texas A&M University, 400 Bizzell St, College Station, Texas, X 77840, USA; [3]University of Lausanne, CH 1015 Lausanne, Switzerland

Malnutrition is a global concern in host-pathogen interaction and subsequent evolution. Mechanistically, malnutrition disrupts metabolic networking, depleting the energy budget allocated for pathogen defence. Moreover, an impaired host immunity facilitates optimum pathogen growth, which leads to disease spread. Previous studies in fruit flies have shown that adaptation to juvenile malnutrition rescues pre-adult viability at the expense of enhanced pathogen susceptibility. However, other major evolutionary and ecological consequences, such as fertility and disease transmission risk, are poorly understood. In this study, we combined infection phenotypes from both host & pathogen, followed by RNA sequencing & genomics to assess the evolutionary and ecological consequences of infection to *Drosophila melanogaster* selected for juvenile malnutrition. We used Providencia rettgeri, a bacterial pathogen, to infect control and selected populations, followed by testing the virulence of passaged pathogens against common fly lines. We identified a substantial fitness loss, followed by elevated pathogen load in selected populations. These results suggest that evolution against poor food entails a fitness cost due to elevated pathogen load. RNA-Sequencing analyses confirmed substantial upregulation of immune genes and downregulation of reproductive genes in selected populations, suggesting a reproductive cost upon high pathogen load. Moreover, the passaged pathogens from selected lines show substantially high virulence consistently against various fly lines, indicating that the selected host genotype facilitates pathogens to increase virulence, therefore, the disease transmission risk. Finally, bacterial genomics analyses identified several mutations associated with virulence factors of selected passaged pathogens, validating the virulence shift. Taken together, we show that adaptation against juvenile malnutrition fosters infection cost and disease spread.

OP-06

Rok, Arp2/3 and Gelsolin mediated microfilament disruption in absence of caspase-3 activity in *Drosophila* Malpighian tubules (MTs)

Saurabh Chand Sagar[1], Madhu G Tapadia[1*]

[1]*Cytogenetis Laboratory, Department of Zoology, Banaras Hindu University, Varanasi, India. Email: schand027@bhu.ac.in & madhu@bhu.ac.in*

Caspases are often associated with the programmed cell death overshadowing their other non-apoptotic functions at the cellular level. Lately, the non-apoptotic functions of the caspases like proliferation, differentiation, endocytic trafficking, cell polarity, morphogenesis, inflammatory response and immune response etc. are more in focus. Here, we report a novel function of caspases in regulating actin dynamics within the Malpighian tubules (MTs) of *Drosophila melanogaster*.

Earlier our lab discovered actin associated morphological defects in absence of the Caspase activity in the *Droosphhila* Malpighian tubules. Further studies revealed this actin driven morphological defects are due to an imbalance in the Rho1 signalling pathway. In the present study, we employed *Drice* (the *Drosophila* caspase-3 homologue) deletion mutants and RNAi-mediated knockdown to investigate the underlying mechanisms. We show that loss of Drice disrupts Rho1 GTPase signaling, leading to Cofilin/Twinstar and Arp2/3-driven hyper-polymerization of actin filaments. Moreover, in the absence of caspase activity, Gelsolin—an actin-severing and capping protein—fails to undergo cleavage and activation, resulting in impaired clearance of excess actin. Together, these defects culminate in striking morphological abnormalities of the MTs.

Our findings establish a critical non-apoptotic role for Drice in coordinating the Rho1–Rok, Arp2/3, and Gelsolin pathways to maintain actin homeostasis and ensure proper tubule morphogenesis. This work broadens the understanding of caspase biology, highlighting their significance beyond apoptosis and underscoring their contribution to cytoskeletal regulation, developmental morphogenesis, and physiological function.

OP-07

Proteasomal Subunit Rpn7, Choreographs Group Cell Migration in Drosophila Oogenesis

Adhisree Sharma, Mohit Prasad

IISER Kolkata, Mohanpur, Nadia - 741 246, West Bengal, India

Cell migration, especially collective cell migration, is an integral part of metazoan development. It is essential for a variety of developmental events, such as gastrulation, neural tube formation, organogenesis and limb bud formation. Unfortunately, it is also linked to pathological conditions like cancer. Cell migration, like other morphogenetic events, requires active turnover of proteins and thus precise modulation of protein degradation is mandatory to permit efficient cell movement. The major component of the protein degradation pathway in the eukaryotic system is the 26S proteasome. The 26S proteasome consists of two 19S regulatory particles and a cylindrical 20S core particle. The 19S regulatory particle is made up of a lid and a base. The underlying mechanism by which proteosomes modulate cell movement is not very clear. The gene of our interest, Rpn7, is a member of this lid complex. Here, we have identified Rpn7, a component of the lid complex, as a modulator of efficient border cell (BC) migration in Drosophila oogenesis. We have identified that the polarity of the BC cluster is completely disrupted when the Rpn7 function is downregulated in the BCs. Employing live cell imaging, we show that protrusion dynamics of the BC cluster are perturbed when Rpn7 function is downregulated. Since phospho-Jun levels are low in Rpn7-depleted BC, we believe Rpn7 functionsthrough JNK to mediate efficient movement of BCs. The results from the above will be presented.

OP-08

E3 Ubiquitin Ligase Highwire/Phr1 Phase Separation Mediates Endocytic Control of JNK Signaling in *Drosophila* Neurons

Srikanth Pippadpally[1*], Anjali Bisht[1], Saumitra Dey Choudhury[1], Manish Kumar Dwivedi[1], Zeeshan Mushtaq[1], Suneel Reddy-Alla[1] and Vimlesh Kumar[1*]

[1]*Department of Biological Sciences, IISER Bhopal*

Synaptic growth and organization are orchestrated by pre- and post-synaptic signaling, neuronal activity, and environmental cues. Although endocytosis is known to attenuate synaptic growth, the underlying signaling mechanisms have remained elusive. Here, we uncover a previously unrecognized mechanism by which endocytosis constrains synaptic growth through regulation of the neuronal E3 ubiquitin ligase Highwire. We show that loss of endocytosis causes Highwire to accumulate in neuronal cell bodies, leading to elevated MAP3K Wallenda/DLK levels and hyperactivation of JNK signaling. The accumulated Highwire assembles into dynamic liquid–liquid phase-separated condensates, as revealed by their rapid and reversible dissolution with 1,6-hexanediol. Acute blockade of endocytosis using a temperature-sensitive dynamin mutant *Shibire*^{ts} similarly triggered robust Highwire phase separation. We further demonstrate that Rab11-positive recycling endosomes are essential for proper Highwire localization and turnover, directly linking endosomal trafficking to the control of JNK signaling. Finally, we show that both BMP and JNK signaling are necessary and sufficient to guide synaptic morphogenesis at the *Drosophila* NMJ, thereby integrating endocytic trafficking with synaptic growth signaling. Our findings establish endocytosis as a critical regulator of Highwire/Phr1-dependent JNK signaling via liquid–liquid phase separation, with implications that extend beyond synaptic morphogenesis to axon injury and degeneration pathways.

OP-09

Pathogen-driven selection shapes the *Drosophila* genome at specific loci while maintaining overall diversity

Tsering Choton [1], Rohit Kapila [1,2], Mayank Kashyap [1,3], NG Prasad [1*]

[1]*Indian Institute of Science Education and Research, Mohali, India*
[2]*Florida International University, Miami, Florida*
[3]*University of California, Riverside*

Long-term experimental evolution permits the direct observation of adaptive genomic change. We investigated genome-wide patterns in *Drosophila melanogaster* populations subjected to ~130 generations of selection for resistance to *Enterococcus faecalis*. The selected (E) population showed significantly higher infection survivorship compared to pseudoinfected (P) and unhandled (N) controls, confirming evolved resistance. Genome-wide nucleotide diversity (π) remained comparable across all populations, indicating that adaptation did not occur via a genome-wide sweep but was localized to specific loci. This was supported by population genomic signatures: Tajima's D values showed pronounced localized reductions in the E population, and pairwise FST analysis identified regions of elevated differentiation (>0.15) between E and controls, often coinciding with diversity dips. A composite likelihood ratio (CLR) scan identified 33 significant selective sweep peaks in each population; however, the E population was characterized by unique, high-amplitude peaks. Functional analysis revealed that the E population was distinctly enriched for mutations in immune and reproductive pathways. Gene Ontology terms included Wnt signaling, reproductive system development, sex differentiation, and cell cycle regulation. Our findings demonstrate that intense, pathogen-mediated selection drives predictable adaptation through repeatable, locus-specific sweeps associated with key biological functions, all while maintaining overall genomic diversity. This underscores a model of targeted, rather than genome-wide, evolutionary change under sustained experimental selection.

OP-10

Usage of ACE Inhibitor triggers Oxidative Stress, Impairing Hematopoiesis and Immune Response

Devki[1*], Suman Kumar Singh[1], Kriti Attri[1], Sudip Mandal[2], Lolitika Mandal[1]

[1]*Developmental Genetics Laboratory, Indian Institute of Science Education and Research Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli, PO 140306, Punjab. India*
[2]*Molecular and Development Biology Laboratory*

Hypertension is a growing global health crisis that significantly contributes to cardiovascular diseases, kidney dysfunction, and increased mortality rates. Anti-hypertensive drugs, such as Angiotensin-converting enzyme inhibitors (ACEIs), lower blood pressure via RAAS (Renin Angiotensin Aldosterone system. Few clinical reports suggest ACEI might disrupt cellular processes like blood cell homeostasis. However, the molecular mechanisms underlying these potential adverse effects in vertebrates are not well understood, largely due to the complex interactions between RAAS and ACE. To address this knowledge gap, we investigated the long-term effects of ACEI treatment using Drosophila blood cells which lacks a RAAS system but expresses Ance, a homolog of human ACE, making it an ideal model for studying the RAAS-independent effects of ACEIs on blood. We further validated our findings using human blood cell lines that express ACE but do not fully engage the RAAS pathway, ensuring the biomedical relevance of our results.

Data from both the Drosophila and human blood cell models indicate that ACEI treatment increases systemic levels of reactive oxygen species (ROS). These elevated ROS act as damage-associated molecular patterns (DAMPs), triggering stress-responsive JNK and Toll pathways. This interaction enhances the early differentiation of blood cell progenitors and boosts immune activation. However, despite the increased immune activity caused by ACEI treatment, there is a resulting impairment in cellular immunity, characterized by reduced phagocytosis and decreased production of infection-induced antimicrobial peptides (AMPs). While ACE inhibitors are known to manage hypertension, our findings reveal that they can trigger immune dysfunction and disrupt the normal regulation of blood cells with long-term use.

OP-11

Differentiating Blood Cells Define the Hematopoietic Niche Size in Drosophila larval lymph gland

Prerna Budakoti, **Abhijith Pradeep,** Lolitika Mandal, and Sudip Mandal

Developmental Genetics Laboratory, Indian Institute of Science Education and Research Mohali, Mohali, Punjab, INDIA

Stem cell niches are specialized microenvironments that serve as dynamic hubs, integrating both local and systemic signals to coordinate the maintenance, proliferation, and differentiation of stem and progenitor cells, thereby ensuring tissue homeostasis. While the mechanisms by which the niche regulates these cells are well understood, it is largely unknown whether signals from progenitor or differentiating cells can influence niche homeostasis. In this study, we demonstrate that JAK/STAT-dependent lactate synthesis and its release from differentiating cells in the Drosophila larval lymph gland are critical for regulating the hematopoietic niche. During the late third instar stages, the cytokine Upd2 is upregulated in differentiating cells, which leads to increased expression of lactate dehydrogenase (Ldh) and a gradual rise in lactate release. This lactate, released by the differentiating blood cells, suppresses niche proliferation by enhancing Dpp/BMP pathway activity. By limiting the size of the niche, this JAK/STAT-lactate-Dpp axis ensures proper progression of blood cell differentiation during development.
Notably, a leukemic model based on AML1-ETO exploits this signaling network to restrict niche proliferation, thus favoring the proliferation of differentiating blood cells that express AML1-ETO. Our findings reveal a metabolic feedback loop between lactate-producing differentiating blood cells and niche cells that impacts hematopoietic homeostasis in both normal and pathological conditions.

OP-12

Context-dependent differential neurotransmission from octopaminergic neurons drives distinct memory consolidation pathways

Snehasish Samanta[1], Varnika Bhardwaj[1], Nitin Singh Chouhan[1]

[1]Tata Institute of Fundamental Research, Mumbai

Sleep serves as a vital physiological process, playing a key role in maintaining homeostasis and enabling cognitive functions like memory consolidation. External cues- such as the availability of food- can regulate sleep-wake activity, prompting adaptive responses to changing environments.

Interestingly, *Drosophila melanogaster* can form two distinct types of appetitive olfactory memories: When flies are allowed to feed post-training, they form memories that are susceptible to sleep deprivation (Sleep -Dependent). However, in starved settings, they form a kind of memory that is resistant to sleep deprivation (Sleep-Independent). This behavioural plasticity allows flies to forage for food while also consolidating food-related memories, serving as an evolutionary adaptation. Together, this forms a tripartite interaction among sleep, internal state signals, and memory systems. While distinct mushroom body subsets and their output neurons have been characterised for these consolidation pathways, how these distinct mechanisms are recruited remains unexplored. Our findings illustrate the differential role of a subset of octopaminergic neurons in consolidating these two memory types. Octopamine and glutamate released from this subset facilitate the formation of sleep-dependent and sleep-independent memories, respectively. Octopamine integrates the perception of the reward component of food, in this case sweet taste, which is both necessary and sufficient for inducing sleep-dependent consolidation. Conversely, glutamate functions as a wake-promoting signal that enables sleep-independent memory consolidation. Hence, we see a context-specific release of neurotransmitters from a particular subset of octopaminergic neurons based on the internal state of the fly driving distinct memory consolidation pathways.

POSTER PRESENTATIONS

P001

Myb and CREB Coordinate Transcriptional Landscape for Long-Term Memory Formation

Papiya Mondal, Snehasis Majumder and **Abhijit Das**

Neuro-Epigenetics Lab. Department of Bioscience and Biotechnology, Indian Institute of Technology Kharagpur, Kharagpur, West Bengal, India- 721302

Long-term memory (LTM) arises from structural and functional modifications in neurons, collectively known as synaptic plasticity. The establishment of this plasticity relies on coordinated action among multiple memory-related proteins, whose synthesis requires transcriptional activation of specific genes. The transcription factor CREB (Cyclic AMP Response Element Binding protein) is a well-characterized regulator that drives memory-related gene expression during memory formation. In this study, we sought to identify additional transcriptional regulators with broad roles across memory paradigms and uncovered Myb proto-oncogene as a novel candidate shaping the transcriptional landscape of long-term memory. Myb, a SANT-Myb domain transcription factor, shares a common KIX domain with the CREB and interacts with its coactivator partner CREB Binding Protein (CBP) and is ubiquitously expressed in all fly brain neurons. We used Drosophila olfactory habituation memory paradigm and a novel long-term aversive olfactory memory paradigm to investigate the role of Myb as a global regulator of memory formation. Myb mutants are defective in forming both associative and non-associative forms of long-term olfactory memory, accompanied by the absence of corresponding synaptic plasticity. Using RNAi-mediated knockdown, mutational analysis and trans-heterozygote studies we find a genetic and functional interaction among Myb, CREB, and CBP. Transcriptomic profiling and genome-wide binding analyses using Targeted DamID in olfactory local interneurons during LTM induction show that Myb and CREB co-regulate key LTM-specific genes. Together, our findings establish Myb as a novel global regulator of long-term memory formation that cooperates with CREB to remodel the chromatin landscape and orchestrate transcriptional programs essential for long-term memory.

P002

Trade-off between immunity and reproduction in *Drosophila* males selected for faster development and longer lifespan

Abhishek Yadav[1], Nidhi Krishna Shrivastava[1], Adwait Mishra[2], Neha Rauhila[1], Abhishek Kumar Farand[1], Mallikarjun Shakarad[1*]

[1]Evolutionary Biology Laboratory, Department of Zoology, University of Delhi, Delhi-110007, India; [2]Evolutionary Genetics of Immunology Lab, Department of Zoology, University of Delhi-110007, India.

Trade-offs between growth, somatic maintenance and reproduction have been ubiquitous in biological systems due to common pool of resources being channelized for these traits. In biological systems such as insects and birds where sperms are stored for extended periods within the female body, sexual dimorphism in response to selection for extended lifespan should be more pronounced in favour of females. However, in *Drosophila melanogaster* populations under simultaneous selection for faster development and longer lifespan, the longevity of males was significantly higher than that of their ancestral controls. The increased longevity was due to robust immune response despite having reduced resources. The robust immune response was at a cost to investment in reproduction as shown by the significantly reduced number of females the male copulates with, suggesting a tradeoff between immunity, longevity and reproduction.

P003

Evolution of energy utilization during metamorphosis in rapid developing *Drosophila melanogaster*

Abhishek Kumar Farand[1], Adwait Mishra[1], Neha Rauhila[1], Surbhi Yadav[1], and Mallikarjun Shakarad[1*]

[1]Department of Zoology, University of Delhi, New Delhi, India

Maintenance of energy homeostasis is essential for survival. Reduced development time is often associated with tradeoffs among life history traits due to limited time in acquiring energy reserves. Late third instar larvae of *Drosophila melanogaster* selected for faster development and increased longevity (FLJs) had triacylglycerol comparable to their ancestral control (JBs) populations, despite their reduced larval duration. However, FLJ adults have non-significantly reduced lipid levels at emergence and significantly reduced starvation resistance post-emergence, indicating altered energy utilization during pupal stage. These findings suggest that the cost of rapid development arises not from energy acquisition, but from its utilization and deployment during metamorphosis.

P004

Impact of Pathogen Infection on Gut Microbiome and Host Resilience in an Outbred Drosophila Population

Adwait Mishra, Triveni Shelke, Soumyadeep Paul, Vanika Gupta

Department of Zoology, University of Delhi, New Delhi-110007, India; Department of Biochemical Engineering and Biotechnology, IIT Delhi-110016, India

"Insects like *Drosophila melanogaster* host a diverse array of commensal and symbiotic microbes that play an important role in modulating immune responses and maintaining gut homeostasis. Pathogenic infections can upset this fragile balance, leading to microbiome dysbiosis and influencing the evolutionary dynamics between the host and microbes. Most of our current understanding of dysbiosis comes from studies using inbred Drosophila strains, which lack genetic diversity and tend to show exaggerated infection outcomes. In this study, we used an outbred Drosophila population- with greater genetic variation and a closer resemblance to wild populations- to examine how bacterial pathogens of differing virulence affect microbiome composition and host physiology over time.
Using 16S rRNA gene sequencing, we characterised infection-induced shifts in microbial diversity, revealing changes in both alpha and beta diversity metrics, consistent with microbiome dysbiosis. Quantitative colony-forming unit (CFU) assays at 24 hours and 7 days post-infection demonstrated a significant decline in pathogen load ($p < 0.0001$), indicating effective immune clearance. Furthermore, gut barrier integrity, assessed via the smurf assay, remained intact even at 20 days post-infection, demonstrating strong resilience in this genetically diverse host population. These results reveal that genetically diverse Drosophila exhibit infection-induced shifts in microbiome structure and diversity and also effectively clear pathogens over time while maintaining stable gut barrier function."

P005

Drosophila TRAPPIII complex subunit TRAPPC8/Trs85 and its effector Rab1 regulate retrograde trafficking of Wnt/Wg and Evi/Wls

Satyam Sharma[1], Juilee Sabnis[1], **Aendrila Adhikary[1]** and Varun Chaudhary[1]

[1]*Indian Institute of Science Education and Research, Bhopal, Madhya Pradesh*

Wnt proteins are essential ligands that upon secretion from the Wnt-producing cells, activate Wnt signaling pathways that play essential roles in regulating major developmental processes like cell proliferation, cell migration and cell differentiation. In the Wnt-secreting cells, Wnts are post-translationally modified in the Endoplasmic reticulum (ER) via glycosylation and palmitoylation, the latter is carried out by an ER-

membrane protein Porcupine (Porc). This lipidation aids in the transfer of Wnt to its carrier protein Evi/Wntless. The Evi-Wg (Drosophila homologue of Wnt1) complex then travels to the plasma membrane (anterograde route), internalized together and their dissociation occurs in the acidic environment of sorting endosomes (retrograde route). The Wg is then secreted, either apically or basolaterally from the polarized cells of Drosophila wing imaginal disc, while Evi goes for retromer-mediated recycling to the ER via Golgi complex. A detailed understanding of the mechanisms involved in the intracellular trafficking of Evi-Wg complex is yet to be elucidated.
In this study, we identified a potential factor involved in regulating the intracellular trafficking of Evi-Wg complex, via RNAi screen – Trs85, a subunit of the TRAPPIII complex, which is known to be involved in essential intracellular trafficking processes. Loss of Trs85, via RNAi-mediated knockdown and generating Trs85 mutant clones, showed Wg and Evi accumulation in producing cells and impaired their retrograde transport. Since TRAPPIII functions as a Rab1-specific guanine nucleotide exchange factor (GEF), we also tested Rab1's role and found that its inhibition phenocopied Trs85 loss. Moreover, loss of both Trs85 and Rab1 led to accumulation of Wnt-unbound Evi, suggesting that they act downstream of Evi-Wg dissociation. Further study is required to understand specific mechanisms by which both Trs85 and Rab1 act towards mediating intracellular trafficking of Evi-Wg in the producing cells.

P006

Do reproductive traits and thermal fertility limits evolve in *Drosophila melanogaster* populations selected for resistance to extreme thermal stress?

Aindrila Das[1]*, Harisankar Durga[1], Sneha Saha[1], Debapriya Dari[1], Shivam Srivastava[1], Tsering Choton[1], Anmol Ratan2, Amey Rajendra Chandak [1]and N. G. Prasad [1]

[1]*Indian Institute of Science Education and Research Mohali, Knowledge City, Sector 81, SAS Nagar, PO Manauli, Punjab 140306, India; 2Indian Institute of Science Bangalore, CV Raman Road, Bengaluru, Karnataka-560012*

Global warming and rising temperature extremes threaten tropical ectotherms living near their upper thermal limits, making them especially vulnerable to climate change. Temperature strongly influences survival and reproduction in ectotherms. While stress responses like heat shock proteins may offer cross-tolerance, it remains unclear if adaptation to one thermal stress improves resilience to another. Notably, male fertility can be impaired by heat before lethality, highlighting the importance of fertility thermal limits (FTL). We investigated whether cold shock adaptation in *Drosophila melanogaster* enhances heat stress resistance in reproductive traits. Flies were exposed to heat shock across temperatures (35–38°C) and durations (30 min- 4 hrs); longer exposures (≥3 hrs) caused high mortality. After standardization, the selected and control populations were exposed to a 30-min heat shock at 38°C. Cold shock adaptation did not confer cross-tolerance in reproductive traits. Although heat-shocked flies showed increased mating within 24 hrs, no significant differences were observed in fecundity, survival, or

hatchability. However, only 50% of larvae from heat-shocked parents pupated, and eggs laid 24 hrs later developed more slowly. No evidence of male sterility before mortality was observed, suggesting minimal disparity between fertility and critical thermal limits (CTL). These findings highlight the stressor-specific nature of thermal adaptation and support treating FTL and CTL as distinct, species-specific thresholds.

P007

The Clock Within: How Circadian Rhythms Shape the Fly's Blood System

Aiswarya K P, Aditya Kanwal, Sujal Chede, Lolitika Mandal

Indian Institute of Science Education and Research, SAS Nagar, Mohali 140306, Punjab, India

Circadian rhythm, an endogenous 24-hour biological cycle, regulates diverse physiological and metabolic processes. Its synchronization depends on the interaction between intrinsic molecular oscillators and extrinsic environmental cues. Disruption of this rhythm—through factors such as shift work, social jet lag, or excessive screen exposure—has been linked to neurological, psychiatric, cardiometabolic, and immune disorders. However, how environmental cues are integrated into systemic signals that affect tissue homeostasis remains unclear.

Given the functional parallels between Drosophila hemocytes and vertebrate myeloid lineages, this study leverages Drosophila as a model to understand infection susceptibility associated with circadian misalignment. Throughout the investigation, experiments have been carried out by growing the larvae in a 12 hour light/12 hour dark cycle (LD) and constant light condition (LL). Our findings indicate that disruption of circadian rhythm induces precocious differentiation of blood progenitors in the lymph gland—an organ crucial for developmental and immune functions during later stages. Moreover, larvae reared under constant light conditions exhibited a marked reduction in the blood progenitor population. The underlying molecular circuitry responsible for these effects is currently being elucidated. In addition, while Drosophila blood cells are known to be influenced by an extrinsic clock located in the brain, ongoing investigations aim to determine whether an intrinsic clock exists within the lymph gland itself. In summary, this study explores how circadian rhythm disruption impacts Drosophila hematopoiesis and the regulatory mechanisms maintaining blood cell development and homeostasis.

P008

Effect of microbiome modulation on the neurodevelopmental gene expression profile and the associated phenotypes in the *Drosophila melanogaster*

Akanksha Singh, Dhruvi Bhandari

Center for Life Sciences, Mahindra University, Hyderabad, Telangana, India

The microbiome has a tremendous influence on human physiology, including the nervous system development. Here we showed that male and female Drosophila lacking microbiome has an effect on the neurodevelopment and circadian regulation. We develop conventional flies (with microbiome) and axenic flies (without microbiome) by rearing them on normal and tetracycline treated food. Through qPCR analysis we found significant sex specific gene expression changes in the heads of axenic flies compared to that of conventional. Axenic flies also show significant decrease in climbing behaviour and are found to be susceptible to the seizure assay. Using OrthoDB we found human orthologs of Drosophila genes and found they are associated synapse development, neuronal maturation as well as their dysfunction is associated with neurodevelopmental disorder. These findings suggest that microbiome regulates the normal brain function and development. Any alteration in microbiome through diet, antibiotic and drugs might leads to neurological disorder.

P009

A Three-in-One Strategy to Reduce the Pesticide Menace

Akansha Singh[1], Shimona Chaudhary[2], Deepak Kumar[3], Rajshri Bhattacharya[4], Dibyajyoti Banerjee[5]

Post Graduate Institute of Medical Education and Research, Chandigarh, 160012

Pesticide misuse remains a critical challenge to human health and environmental sustainability. Despite stringent legal regulations, the indiscriminate and excessive use of pesticides persists among farmers in India and other developing nations. This ongoing issue underscores the urgent need for innovative and sustainable alternatives beyond conventional law enforcement measures. We propose a novel three-in-one strategy that enables targeted pest control, even against resistant pest populations, while utilizing minimal pesticide doses. This integrated approach is designed to enhance pesticidal efficacy, reduce ecological contamination, and minimize associated health hazards. As a proof of concept, *Drosophila melanogaster* is employed as a model organism for developing a targeted starch-based nanopesticide. The findings and conceptual framework will be presented before the esteemed audience at the conference.

P010

Investigating sex-specific differences and drug responses in anxiety-like behaviour in *Drosophila melanogaster*

Aman gill, Geetanjali Chawla

Shiv Nadar Institute of Eminence, Uttar Pradesh, India

Anxiety-like behavior represents a conserved component of the stress response and is increasingly recognized as a sexually dimorphic trait across species, including *Drosophila melanogaster*. While the genetic basis of sex differences in anxiety remains poorly understood, Drosophila offers a robust system to dissect the interaction between genotype, stress exposure, and behavioral outcomes. To address this, we established a strong and quantifiable assay for anxiety-like states using the Drosophila Genetic Reference Panel (DGRP) lines to uncover sex-specific responses to acute stress. Our stress paradigm combined overcrowding, food deprivation, mechanical agitation, and transient cold exposure to mimic a multi-dimensional stress environment. Behavioral phenotyping was conducted using the open field test (OFT) to evaluate locomotor activity and wall-following behavior, both of which serve as reliable indicators of anxiety-like behavior. Under stress conditions, flies displayed reduced exploratory behavior and increased wall-following. Remarkably, stress exposure induced persistent behavioral changes even after recovery, suggesting prolonged modulation of neural circuits. Also, we found that dietary supplementation of Fluoxetine exerted resulted in alleviation of stress-induced locomotory defects as tested in OFT. Analysis of 50 DGRP lines indicates that males and females show distinct behavioral trajectories and magnitudes of stress-induced responses. Genome-wide association studies (GWAS) are underway to genetic variants that contribute to these sex-specific phenotypes. Preliminary findings suggest that anxiety is both sex- and genotype-dependent, supporting the notion that stress reactivity and behavioral plasticity are modulated through distinct molecular pathways. This framework provides evidence for the genetic and neurobehavioral basis of sexual dimorphism in anxiety, with implications for understanding conserved mechanisms underlying stress-related disorders.

P011

Convolvulus pluricaulis mediates its pharmacological effects via sod1, rdl, glut1, GABA-B-R1 and CG6293 orthologs in *Drosophila melanogaster*

Amit Kumar[1], Shreyasi Mitra[1], Aman Gill[1] and Geetanjali Chawla[1]

[1]*RNA Biology Laboratory, Department of Life Sciences, School of Natural Sciences, Shiv Nadar Institute of Eminence, Uttar Pradesh-201314, India*

Convolvulus pluricaulis, commonly known as Shankhpushpi, has been widely used to treat nervous system disorders, including depression and anxiety. In this study, we used the fruit fly *Drosophila melanogaster* to identify the metabolic and molecular targets that mediate the beneficial effects of dietary C. pluricaulis. Metabolomic analysis showed changes in ascorbic acid, glucose, and adenine monophosphate in the head tissue of flies fed C. pluricaulis for 20 days. Further gene expression analysis revealed significant changes in the expression of glut 1 (glucose transporter 1), CG6293 (ascorbate transporter), rdl (resistant to dieldrin), GABA-B-R1 (GABA-B receptor subtype 1), and sod 1 (superoxide dismutase 1) in the head tissue of adult flies exposed to different doses of C. pluricaulis. To identify downstream effectors responsible for the antidepressant effects, we tested the impact of dietary C. pluricaulis in a stress-induced depression model. Administering C. pluricaulis during development reduced depression-like behaviors in Drosophila. Wild-type adult flies fed C. pluricaulis showed elevated ascorbate levels in the head tissue, and knocking down the ascorbate transporter eliminated the antidepressant effect of C. pluricaulis in the stress model, indicating that C. pluricaulis's antidepressant effects are linked to increased ascorbate transport. Consistent with the gene expression data, knocking down sod 1, glut 1, GABA-B-R1, and CG6293 prevented C. pluricaulis from providing resistance to paraquat-induced oxidative stress. Administration of an L-Ascorbic-supplemented diet mimicked the antidepressant and antioxidant effects of C. pluricaulis. Overall, our findings reveal conserved downstream effectors that underlie the antioxidant and antidepressant activities of C. pluricaulis.

P012

Two sides of the same coin: Chemoattraction and Chemorepulsion employ Hedgehog to choreograph germ cell migration.

Amrita Roy[1], Adheena Elsa Roy[1], Airat Ibragimov[2], Paul Schedl[2], Girish Ratnaparkhi[1], Girish Deshpande[1], [2]

[1]Department of Biology, Indian Institute of Science Education and Research. Pune; [2]Department of Molecular Biology, Princeton University. Princeton

Migrating Primordial Germ Cells (PGCs) are guided by attractive and repulsive cues generated by HMGCoA-reductase (Hmgcr) and lipid phosphatases Wunen(s) respectively. Morphogenetic signaling ligand Hedgehog (Hh) serves as an attractive cue during PGC migration. While hmgcr potentiates Hh pathway, influence of wunen(s) on Hh signaling is unexplored thus far.
We demonstrate that wunen(s) inhibit Hh signaling including in the PGCs. Evidently, wunM- as well as wunZ- embryos display upregulation of Hh target genes (En, Wg, Ptc) in the ectoderm. Importantly, maternal depletion of wunen leads to an increase in endogenous overexpression of wunen mitigates the scattering of PGCs observed in elav-Gal4UAS-hmgcr embryos similar to hh depletion.
We will discuss the significance of phosphoinositides as critical targets of Wunen(s) and posit that reciprocal competitive influence of hmgcr and wunen upon Hh signaling dictates the precise path of PGCs.

P013

Investigating a developmentally crucial adipose tissue-derived factor in regulating nutritional homeostasis in *Drosophila melanogaster*

Anindita Rao, Anupama Krishna J, Anjana R, Gayathri Binu, Jishy Varghese

Indian Institute of Science Education and Research Thiruvananthapuram

Organisms employ a range of physiological and biochemical strategies to maintain nutrient balance when faced with environmental stressors—an essential process for survival and optimal function. These strategies involve diverse adaptive responses. The adipose tissue poses as a pivotal element in the organism's ability to mitigate such environmental fluctuations. We aim to identify crucial regulatory factors that govern nutrient equilibrium within the fat body through a targeted genetic screening approach. Our approach led to the identification of Larval Serum Proteins (LSPs), a member of the hexamerin family of storage proteins, as a key player in nutritional homeostasis. The Drosophila genome contains two hexamerin genes, Lsp1 and Lsp2, which are predominantly expressed in the larval fat body. These proteins function as amino acid reservoirs in insects, particularly

during metamorphosis, facilitating adult emergence. While much of the research on hexamerins has focused on their biochemical role, functional studies using genetic and molecular techniques remain limited. In our study, we specifically knockdown hexamerin synthesis in the larval fat body to examine its effects on development and metabolic status. Contrary to our expectations, reducing Lsp1 in the developing larval fat body results in increased organismal growth and an energy imbalance. Lsp1 also appears to play a role in responding to low nutrient conditions, and its downregulation triggers growth via TOR signaling activation. Additionally, Lsp1-deficient flies exhibit heightened survival rates under acute starvation, demonstrating resilience during dietary scarcity.
Our goal is to uncover the regulatory mechanisms by which hexamerins help manage alterations in the nutritional environment. This research will provide novel insights into hexamerin-mediated maintenance of nutrient homeostasis.

P014

Delineating role of insulin signaling in regulating dopaminergic neuron activity in *Drosophila*

Anindyo Paul[1,2], Gaurav Das[1]

[1]National Centre for Cell Science, Pune; [2]Regional Centre for Biotechnology, Faridabad

Growing evidence suggests a link between insulin signaling disruption and Parkinson's disease pathogenesis. However, the specific cellular mechanisms connecting the two, and how disrupted insulin signaling could make dopaminergic neurons more prone to degeneration, remain unclear.

We aim to address this gap by manipulating insulin signaling in a specific subset of dopaminergic neurons (DANs) that innervate the mushroom bodies and have been shown to affect flight and food-seeking behavior. In agreement with a previous study, knockdown of the insulin receptor in these DANs causes fed flies to seek food like hungry flies. We further show that FOXO and GSK3β overexpression recapitulate the same behavior in fed flies. We now intend to investigate how insulin signaling may regulate long-term cellular, behavioral, and gene-expression changes in these DANs as the flies age. We will also test whether changes in insulin signaling can make DANs susceptible or resilient to neural injury or damage.

P015

Pfdn5 Integrates Mitochondrial Function and Oxidative Stress to Regulate Tracheal Cell Death and Plasticity in Drosophila

Anjali Bisht, Priyabrata Sarangi, P Srikanth, Vimlesh Kumar

Indian Institute of Science Education and Research Bhopal

Tissue plasticity enables organisms to adapt to physiological and environmental changes, and the tracheal system in Drosophila provides a powerful model to dissect these mechanisms. Here, we identify pfdn5 as a critical regulator of oxidative stress and tracheal-mediated plasticity, linking mitochondrial dynamics and cell survival to adaptive branching responses. Pfdn5 is tightly localized within the tracheal system and neurons, and tracheal-specific expression of a Pfdn5 transgene using Btl-Gal4 partially rescued mutant lethality from the third instar to the late pupal stage. Loss-of-function analysis showed that pfdn5 mutants exhibit impaired ganglionic and terminal tracheal branching, resembling hypoxia-induced tracheal phenotypes. Morphometric quantification revealed defective branch extension and the presence of ringlet-shaped branches, accompanied by abnormal mitochondrial morphology and distribution. Notably, ganglionic and lateral branches in pfdn5 mutants displayed increased apoptosis, as indicated by elevated cleaved Dcp1 staining, reflecting activation of cell death pathways. These findings suggest a failure to maintain cellular integrity under stress conditions. Genetic interaction studies further support a model in which pfdn5 coordinates mitochondrial function, cytoskeletal remodeling, and apoptosis to regulate tracheal plasticity. This work uncovers an uncharacterized role for pfdn5 in maintaining tracheal integrity and plasticity during oxidative stress response.

P016

hsrω lncRNAs modulate innate immunity in *Drosophila melanogaster* via JNK signalling pathway

Anjali Muraleedharan and S. C. Lakhotia

Cytogenetics Laboratory, Department of Zoology, Banaras Hindu University, Varanasi

The developmentally expressed and cell stress inducible heat shock RNA omega (hsrω) gene of *Drosophila melanogaster* produces multiple lncRNAs. Following our lab's earlier RNA sequencing data that hsrω down-regulation affects immune genes' expression, here we explore the mechanism. Upon down-regulation of hsrω, transcripts of anti-microbial peptides (AMPs) like Cecropin, Attacin, Diptericin and Drosomycin were downregulated. Immunostaining revealed that Relish, a transcription factor, and JNK, both of which positively regulate the Imd pathway, were also downregulated. Overexpression of hsrω

caused increase of the AMP transcripts along with enhanced levels of cytoplasmic and nuclear Relish. The p38a MAP kinase, which is a positive or negative regulator of different AMPs in flies, was also down- or up-regulated in hsrω down- or up-regulated condition, respectively. Other studies have also shown that in p38 mutants, the HSP60D is downregulated. Interestingly, we find that following hsrω down-regulation, all the four HSP60s (HSP60A, HSP60B, HSP60C, HSP60D) are downregulated. Our results thus connect, for the first time, the hsrω lncRNAs, Relish, JNK, p38 signalling pathway and HSP60s in the context of innate immunity response in Drosophila.

P017

G-protein signaling in the formation and regulation of the Blood-Brain-Barrier

Vrushali Katagade and **Anuradha Ratnaparkhi**

MACS-Agharkar Research Institute, G.G. Agarkar Road, Pune 411 004

The blood-brain barrier (BBB) is a protective structure that regulates prevents entry of molecules and pathogens into the brain. In vertebrates, the structure involves specialized endothelial cells that surround the capillaries along with pericytes and astrocytes to form a protective and selectively permeable barrier. In comparison, the BBB in Drosophila consists of a simple sheath of glial cells that tile with each other through septate junctions to ensheath the brain and ventral nerve cord. G-protein signaling mediated by the orphan receptor Moody is the one of the key signaling pathways identified as a major regulator of BBB development.

Folded gastrulation (Fog) is a secreted ligand that trigger apical constriction in epithelial cells during gastrulation. Fog activates a G protein signaling cascade mediated by the $G\alpha_{12/13}$. Fog is expressed in multiple glial subtypes including the subperineurial glia that give rise to the BBB. We are interested in understand the role of Fog signaling in regulating glial morphology. We will findings related to our current investigation aimed at understanding how Fog mediated G-protein signaling contributes glial tiling and barrier integrity of the BBB.

P018

Micro-managing the mind: Decoding the role of miR-996 in the fly brain

Aswathy BJ, Divyasree M Nair, Jishy Varghese

Indian Institute of Science Education and Research, Thiruvananthapuram (IISER-TVM)

MicroRNAs (miRNAs) are small, non-coding RNA molecules that post-transcriptionally regulate gene expression. They play a significant role in buffering fluctuations in gene activity, thereby preserving physiological stability. Their ability to simultaneously regulate multiple targets makes them key modulators of diverse biological processes, including development, metabolism, and lifespan. While the involvement of miRNAs in metabolic regulation is increasingly recognized, the specific roles of brain-derived endogenous miRNAs in regulating lifespan and metabolic homeostasis remain largely unexplored. To fill this lacuna, we performed an unbiased screen in adult *Drosophila melanogaster*, wherein 30 miRNAs were selectively downregulated in the neurons. From this screen, miR-996 emerged as a candidate of interest due to its physiological and metabolic relevance. Subsequent analyses investigated the effect of miR-996 on metabolic parameters, nutrient-responsive behavior, locomotion, and aging. Our results demonstrate that the absence of miR-996 enhances starvation resistance and is associated with significant alterations in energy metabolism and feeding behavior, indicating a central role in maintaining metabolic equilibrium. Conversely, neuronal overexpression of miR-996 leads to starvation sensitivity and accelerated aging. These findings underscore the pivotal role of miR-996 in orchestrating metabolic and longevity-related processes in the adult brain. Identification of miR-996 target genes will further elucidate the molecular mechanisms underlying the organismal response to nutrient stress and metabolic challenges.

P019

Regulation of amino acid-sensing mechanisms during developmental haematopoiesis in Drosophila

Atharva Anand Mahajan[1,2], Sumit Pande[1] and Rohan Jayant Khadilkar[1,2]

[1]Stem Cell and Tissue Homeostasis laboratory, ACTREC – Tata Memorial Centre, Kharghar, Navi Mumbai – 410210, Maharashtra, India [2]Homi Bhabha National Institute, Training School Complex, Anushakti Nagar, Mumbai – 400085, Maharashtra, India

Hematopoiesis, the process of generating mature blood cells, is tightly regulated by mechanisms that balance stem cell maintenance with differentiation. Nutrient sensing plays a critical role in this regulation, integrating environmental cues to control progenitor fate decisions. Among nutrients, amino acids are key modulators, and their sensing is mediated

by specialized pathways. Sestrins, a conserved family of proteins, act as leucine sensors and antioxidants, linking nutrient availability and stress responses to signaling outputs. One of their major targets is the mechanistic target of rapamycin (mTOR) pathway, central to cell growth, proliferation, and metabolism. Using Drosophila lymph gland (LG)—the primary hematopoietic organ comprising the Posterior Signaling Centre (PSC, niche), Medullary Zone (MZ, progenitors), and Cortical Zone (differentiated cells)—we investigated how Sestrin influences blood cell development. Our analyses reveal that sestrin null mutants show reduced PSC size, enhanced blood cell differentiation, and overall enlargement of the LG. A leucine-binding-deficient Sestrin mutant caused increased plasmatocyte differentiation but reduced crystal cell formation and smaller LG size, highlighting a distinct role of the leucine-sensing function. Progenitor-specific depletion of Sestrin promoted differentiation, whereas its overexpression preserved progenitors and restricted differentiation. In parallel, perturbation of branched-chain amino acid transporters in progenitors altered hematopoietic outcomes, further underscoring nutrient responsiveness in LG maintenance. These findings establish Sestrin as a critical regulator of hematopoietic homeostasis. Future studies will determine whether its effects derive mainly from leucine sensing, antioxidant activity, or both. Given its strong influence on blood cell fate, we also aim to assess Sestrin's role in malignant hematopoiesis to uncover conserved regulatory mechanisms.

P020

Validation of progressive neurometabolic disorder associated with DLST variants using the Drosophila model system

Vaishnavi Ashok Badiger[1], Priyanka Upadhyai[1], Michelle C do Rosario[1], **Ayesha Javed[2],** Priyanka Pandey[2,3], Puneeth H Somashekar[1], Katta Mohan Girisha[1,4], Marwan Shinawi[5], Daniel J Wegner[5], Sonal Nagarkar-Jaiswal[2,3], Anju Shukla[1]

[1]Department of Medical Genetics, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India; [2]CSIR-Centre for Cellular and Molecular Biology, Hyderabad,; [3]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, India [4]Department of Genetics, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman; [5]Edward Mallinckrodt Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, United States of America

The human 2-oxoglutarate dehydrogenase complex is a multi-subunit mitochondrial tricarboxylic acid cycle enzyme that catalyzes the decarboxylation of 2-oxoglutarate to succinyl-CoA, reducing NAD+ to NADH. It comprises multiple copies of three subunits, 2-oxoglutarate dehydrogenase, encoded by the OGDH gene, dihydrolipoyl succinyltransferase encoded by the DLST gene, and dihydrolipoamide dehydrogenase encoded by the DLD gene. We identified variants in the DLST gene in patients with global developmental delay (GDD), episodic decompensation, neuro-regression, metabolic, and lactic acidosis. In Drosophila, Dlst knockout/knockdown exhibited larval lethality. Mutant larvae show a developmental delay and a significant decrease in brain volume compared

to controls. Additionally, Dlst-deficient larvae have impaired locomotion, indicating neuromuscular dysfunction. We find that human DLST protein can rescue Dlst loss-of-function phenotypes in flies, suggesting the functional conservation between the two proteins in flies and humans. We are currently assessing how the variants, which we isolated, affect the protein function using flies.

P021

Drosophila polytene chromosome squashes using Feulgen stain – an innovative teaching tool

B Suneeta and Prachi Yadav

ICAR- Indian Agricultural Research Institute, New Delhi-110012

Polytene chromosomes are giant, multistranded chromosomal structures observed in the salivary glands of dipteran larvae, including *Drosophila melanogaster* and Chironomus species. Due to their remarkable size and structural details, polytene chromosomes in Drosophila serve as an excellent model for cytological studies, to understand chromatin structure, mapping genes, studying chromosomal rearrangements, etc. These chromosomes serve as a powerful tool in teaching chromosome cytology to students. Traditional method for polytene chromosome preparation uses 2% aceto-orcein, and chromosomes squash technique. Although widely used, this approach yields a limited number of well-spread polytene chromosomes per gland, and excessive cytoplasmic debris that obscures chromosomal details. Moreover, inconsistent chromosome spreading and suboptimal clarity restrict the efficiency and reproducibility, thereby posing challenges for high-resolution cytogenetic analysis and imaging. Our new protocol addresses the limitations associated with the traditional aceto-orcein method. We used controlled HCl treatment to hydrolyze and soften the salivary gland tissue, thereby facilitating optimal chromosome spreading. The use of the DNA-specific Feulgen stain ensures precise binding to DNA, resulting in a distinct and well-resolved banding pattern. Compared to conventional preparations, this method consistently yields a higher number of clearly spread polytene chromosomes per salivary gland and with minimal cellular debris.
This is a simple technique similar to chromosome squash preparation using Feulgen stain. This protocol is very easy to carry out even by school teachers with very basic knowledge of chromosome techniques. Overall, the protocol provides a novel, simple, and highly efficient technique for researchers working with polytene chromosomes, enabling the preparation of clean, well-differentiated, and high-quality chromosome spreads suitable for detailed cytogenetic analysis.

P022

A Tau-specific kinase inhibitor (TSKI-1) restricts human tau-mediated neurotoxicity by inhibiting the activity of GSK3β in Drosophila disease models

Barasa Rani Kalita, Surajit Sarkar

Department of Genetics, University of Delhi South Campus, Benito Juarez Road, New Delhi - 110 021, India.

Human neuronal tauopathies are devastating brain disorders marked by the accumulation of hyperphosphorylated tau protein aggregates in neurons. Under normal conditions, tau phosphorylation is tightly regulated by a balance between kinases and phosphatases. In tauopathies, this balance is disturbed, often due to genetic or epigenetic factors, leading to excessive tau phosphorylation. Among the kinases responsible for phosphorylating tau, Glycogen Synthase Kinase-3β (GSK-3β) plays a central role in promoting tau pathology. Consequently, GSK-3β is considered a key therapeutic target for treating tauopathies. However, despite its potential, few studies have directly tested drugs that inhibit GSK-3β to reduce tau-induced neurotoxicity. In this study, we evaluated several known GSK-3β inhibitors using Drosophila models expressing human tau. Remarkably, we found that TSKI-1, an FDA-approved anti-allergic drug, effectively inhibited GSK-3β by increasing its inactive form in tau-expressing tissues. This inhibition resulted in reduced pathogenic tau hyperphosphorylation and provided protection against neurodegeneration and the associated phenotypic abnormalities induced by human tau in Drosophila. Considering the functional conservation of GSK-3β between humans and flies, our findings highlight the potential of repurposing TSKI-1 as a promising therapeutic intervention for human tauopathies.

P023

Role of mitochondria in mediating infection driven immune signaling in *Drosophila melanogaster* model

Bharti Golchha[1], Biratal Wagle[1], Akshara Kulkarni[1], Kasturi Mitra[1,2]

[1]Ashoka University; [2]University of Alabama

"Mitochondria are multifaceted organelles central to ATP production, ROS generation, calcium signaling, and immune responses. Beyond energy metabolism, mitochondria modulate immune pathways, including the NF-κB-mediated innate immune signaling activated by cellular stress. In vertebrates, cytosolic mitochondrial DNA (mtDNA) acts as a DAMP, triggering cytokine production via the cGAS-STING-NF-κB axis. However, how mitochondrial dynamics influence immune signaling in invertebrates, and how mitochondrial morphology quantitatively relates to mtDNA release, remain poorly

understood. Drosophila, which lacks adaptive immune system, serves as a valuable model to study innate immunity. The Drosophila fat body, orchestrates systemic immune reactions through the NF-κB–dependent Toll and IMD pathways, driving the production of antimicrobial peptides (AMPs). Recent identification of cGAS-like receptors(cGLRs) in Drosophila raises the possibility of a parallel mtDNA-sensing mechanism akin to vertebrate systems. Here, we investigate how mitochondrial morphology and mtDNA influences AMP induction and, how ER-mitochondria contact sites are involved in these dynamic changes in the fat body following systemic infection with Providencia rettgeri. Using confocal microscopy, immunohistochemistry, and a customized computational image analysis pipeline, we identify early, infection-induced alterations in mitochondrial morphology that precede AMP expression. Ongoing analyses aim to map mtDNA distribution in 3D and determine whether mitochondrial morphology changes correlate with cytosolic mtDNA presence which may potentially be activating the cGLR–STING-NF-κB axis. Together, our findings aim to uncover a mechanistic and detailed quantitative link between mitochondrial dynamics, mtDNA, and immune activation through the cGLR–STING–NF-κB pathway in Drosophila, offering insights into the role of mitochondria in immunity."

P024

Fitness effects of adult crowding in Drosophila: The role of body size, density and evolutionary history

Bindya R S[1], Chinmay Temura[1], Medha Rao[1], Bhawna Mittal[1], Mohnish Singh[2], Aishwarya C S[1], Amitabh Joshi[1]

[1]Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru, Karnataka; [2]University of Lucknow, Lucknow, Uttar Pradesh

The theory of density-dependent selection assumes that fitnesses of different genotypes can vary based on population density. The effects of density-dependent selection on life history traits have been extensively studied in terms of larval crowding in Drosophila. A few studies examining the effects of adult crowding in Drosophila showed that adult crowding negatively impacts survivorship, longevity, and fecundity. Recent studies in our laboratory showed that the body size of the individuals influences the effects of adult crowding on mortality and fecundity, with smaller body size enabling the flies to mitigate the deleterious effects of adult crowding. Additionally, an earlier study suggests a trade-off between adaptations to larval versus adult crowding, with populations adapted to larval crowding being more susceptible to the deleterious effects of adult crowding than the ancestral controls. Here, using a full factorial design, we subjected flies of larval crowding adapted populations and ancestral controls, reared at varying larval densities (thereby differing in body size), to a broad range of adult densities and measured their survivorship and fecundity. We found that the smaller flies suffered lower survivorship costs. Additionally, we observed a hump-shaped relationship between adult density and fecundity

across the study populations, with a much broader peak for the smaller flies. Overall, these results highlight the nuanced relationship between adult density and fitness traits, which appears to be significantly influenced by the body size of the flies.

P025

A new model for organ size control based on growth-rate dependent negative feedback

Carmen Coelho, Varshitha Prabhakar, Jaya Anusha, Abhishek Sharma, Saher Chawla, Huimiwon Ramwung Shimrah

Centre for Human Genetics, Biotech Park, Electronic city phase I, Bangalore 560100

To reach reproducible body and organ size by the end of the developmental growth period, the time and rates of growth acceleration and deceleration need to be regulated. Most studies on organ size determination have focused on the phase of development when organs are approaching their final size. The start of the growth period has received little attention. If size variation due to stochastic variation in the starting rate and time of acceleration is not brought under control, reproducibility and symmetry will not be achieved. *Drosophila melanogaster* is an ideal system to address these questions. Growth starts in the larva shortly after hatching from the egg and slows markedly towards the end of larval life. Examining wing imaginal disc size in a large sample size of 1000 discs, we have observed high disc size variation in the middle of larval life, decreasing towards the end. We have also observed high fluctuating asymmetry (FA) in disc size within individual larvae during the first one third of the larval period, reducing by the end. To explain the reduction in size-variation towards the end of larval life, we have developed a mathematical model that utilizes growth-rate dependent negative feedback to regulate growth trajectories, in a manner that does not require size to be sensed. This model fits the data and is able to simulate the size variations. A prediction that this model makes is that alterations in size before the start of the growth period will not be compensated for, as the change in size is not sensed. In accordance, we find that an increase in size of wing discs before the larval period results in larger adult wings. However, increased growth rate at the start of the growth period is compensated for, without changing the length of the period, bringing size down to normal. Thus, faster growth rate stimulates faster slow down. Put together, our data strongly supports a model for growth-rate dependent feedback, without the need for sensing size.

P026

Impact of Developmental Nutrition on Adult Metabolism in *Drosophila melanogaster*

Chandrakanth M[1], Tanisha Kohli[1], Devashish Kumar[1], Chethan S[1], Chand S[1], Nishant Kumar[1], Sudipta Tung[1]

[1]*Ashoka University*

Nutritional conditions during juvenile stage can influence adult physiology, reproduction and metabolism, particularly shaping overall fitness. Although recent studies have highlighted the impact of juvenile diet on adult metabolism, its effects on freshly emerged adults remain largely unexplored. This study specifically investigated how variations in the larval protein-to-carbohydrate (P:C) ratio influence adult metabolism, reproduction and starvation resistance in *Drosophila melanogaster* under both virgin and mated conditions. The results revealed a complex, sex and mating-status-dependent interaction: virgin males reared on protein-rich diets exhibited increased starvation resistance, a dietary effect not observed in virgin females. Consistent with the metabolic costs of reproduction, mating uniformly reduced survival across both sexes. However, larval diet re-emerged as a critical factor in mated individuals: mated males displayed superior survival when developed on carbohydrate-rich diets, while mated females showed no difference. These findings underscore the critical role of early-life nutritional programming in shaping adult physiological trade-offs and subsequent resource allocation strategies, highlighting a sexually dimorphic mechanism where the fitness benefit of a larval diet depends heavily on reproductive status.

P027

Selection for rapid development and short breeding duration might reduce sexually antagonistic coevolution in Drosophila

Chinmay Temura[1], Medha Rao[1], RS Bindya[1], Bhawna Mittal[1], Mohnish Singh[2], Amitabh Joshi[1]

[1]*Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, Karnataka, India;* [2]*University of Lucknow, Lucknow, Uttar Pradesh, India*

In the absence of monogamy, factors maximizing male versus female fitness differ, leading to a 'tug-of-war' between them, termed sexual conflict. This can result in sexually antagonistic coevolution (SAC), with the evolution of adaptations (mate-harming traits) in males and counter-adaptations (mate-harm resistance traits) in females that are beneficial to themselves but detrimental to their partners. Evolution of reduced SAC has been reported in monogamous and female-biased sex ratio regimes, thereby linking lower SAC

to weaker male-male competition. In contrast, the collateral effects of life-history evolution on SAC remain poorly studied. To address this, we established populations of D. melanogaster selected for both rapid development and short breeding duration. Male-male competition in these populations evolved to be weaker, likely due to reduced body size and fewer re-mating opportunities. Additionally, to differentiate between the effects of the two selection pressures, we established populations relaxed for only rapid development selection and those that are relaxed for both selection pressures. These populations evolved to be slower-developing and larger in body size than forward-selected populations, with the responses being more prominent in the doubly relaxed populations. In the current study, we assessed males' mate-harming ability and females' mate-harm resistance in ancestral controls, forward-selected, singly and doubly relaxed selection regimes (16 populations). To do this, we quantified the post-mating mortality and fecundity of females when mated with males of their own selection regimes versus others. We show that both selection pressures resulted in a reduction of mate-harm and mate-harm resistance traits, thus highlighting that SAC might have been reduced substantially by both selection pressures, with reduced body size playing a prominent role in mediating these effects.

P028

Mutation Accumulation Affects Male Virility in Drosophila Selected for Later Reproduction

Daniel J. Borash, Michael R. Rose, and Laurence D. Mueller

An investigation of longevity, female fecundity, and male reproductive behavior in *Drosophila melanogaster* was undertaken in order to establish whether late-life fitness characters in short-lived populations is affected by an increase in deleterious alleles due to random genetic drift, and to determine whether selection for late-life fertility could eliminate alleles that produce a decline in later fitness components in short-lived populations, as predicted by the mutation accumulation hypothesis for the evolution of aging. Long-lived (O) populations, short-lived (B) populations, and hybrids made from crosses of replicate lines of these populations were employed. Longevity differences were not seen between hybrid B males and females and purebred B males and females. Reproduction in aged B purebred females was significantly less than in hybrid females at 3 wk of age only. A diallel cross of the five replicate B lines showed a steady increase in hybrid male reproductive performance after the first week of adult life, relative to parental lines. A diallel cross of the five replicate O lines revealed no significant increase in hybrid O age-specific male reproductive success compared with the purebred O lines when assayed over the first 5 wk of adult life. The male reproductive behavior results are consistent with the idea that relaxed age-specific selection in the B populations is accompanied by an increase in deleterious, recessive traits that exhibit age-specific expression. As a result, we conclude that a mutation accumulation process is at least partly responsible for the age-specific decline in male B virility relative to that of the O populations.

P029

Correlated responses of selection for thermal adaptation in Drosophila melanogaster: An interplay between directional selection and balancing selection

Joy Bose[1], **Dariya Tarangini Ghatak [1,2*]**, Imroz Alam[1], Biswajit Shit[1], & Imroze Khan[1**]

[1]Ashoka University, India, [2]St. Xavier's College, Kolkata.
[*] Presenting Author, [**]Correspondence

Detailed knowledge of organisms' adaptation to climate warming is a fundamental question in ecology and evolution. Climate warming negatively impacts a wide range of fitness traits by increasing metabolic rates associated with diverse body physiology whereas chronic exposure to thermal stress selects for thermal adaptation by rescuing fitness loss over an evolutionary timescale. To date, studies have primarily focused on fitness loss upon increasing temperature; however, the effect of thermal adaptation and associated life-history costs is poorly understood. In this study, we simulated chronic exposure to thermal stress by performing experimental evolution at 29°C over multiple generations using Drosophila melanogaster populations. Our key findings demonstrate that thermal adaptation rescues fertility loss. In contrast, unselected counterparts showed a substantial decline in fertility under high temperature, and that effect is substantially mediated by pre-adult adaptation to heat stress. The correlated responses to selection were observed in the absence of selection pressure (i.e., ambient temperature), only upon various other stress conditions. Depending on the nature of a stress condition, including starvation resistance, minimum critical feeding time, imbalanced diets, heat shock, etc, selected populations showed better competitive ability in terms of survival or fertility whereas, crowding, nitrogenous waste tolerance, bitypic competition, and cold shock mitigated the competitive ability of selected populations with respect to viability and fertility, therefore, postulated the 'maintenance cost' of thermal adaptation. Note, our 'cost' results entail the persistence of genetic variation at loci conferring thermal selection by the act of balancing selection inthe absence of selection pressure. Taken together, this study encompasses an empirical framework of the fitness advantages and disadvantages of thermal adaptation in response to climate warming.

P030

Glial Cells Unequally but Synergistically Shape Huntington's Disease Progression

Debalina Chatterjee*, Mansi Yadav, Jassika Gupta, Namita Agrawal, Anju Shrivastava

Department of Zoology, University of Delhi

Huntington's disease (HD) is a dominantly inherited neurodegenerative disorder caused by abnormal expansion of CAG repeats within exon 1 of the Huntingtin (htt) gene, leading to an extended polyglutamine (polyQ) stretch in the protein. Motor dysfunctions appear first, reflecting the high vulnerability of cortico-striatal neurons, followed by cognitive decline, psychiatric symptoms, and circadian disruptions as degeneration spreads across brain regions. While neuronal death has long been considered central to HD, growing evidence highlights the critical influence of glial cells in disease progression. Glia support neuronal survival, regulate immune activity, and maintain nervous system homeostasis. Importantly, mutant Huntingtin (mHTT) is expressed in all CNS cells, including glia. Our previous work in a Drosophila HD model showed that pan-glial mHTT expression alone reproduces HD-like traits—reduced survival and motor defects—but with delayed onset and milder behavior compared to neuronal expression. The mechanistic basis of these effects is currently under immunohistochemical investigation. To identify glial functions most sensitive to mHTT, we used the UAS/Gal4 system to drive its expression in distinct glial subtypes with specific CNS roles. Preliminary findings suggest that mHTT accumulation impacts survival and motor behavior in a glia-subtype-dependent manner, indicating unequal contributions of different glial populations to disease pathology. By dissecting these roles, our study seeks to clarify how neuron–glia interactions shape HD progression and to explore glial pathways as potential targets for immunomodulatory and neuroprotective therapies."

P031

Does co-infection affect host survival and starvation resistance differently than singular infections in *Drosophila melanogaster*?

Debapriya Dari[1], Aindrila Das[1], and Nagaraj Guru Prasad[1]

[1]*Evolutionary Biology Lab, Department of Biological Sciences, Indian Institute of Science Education and Research Mohali*

Hosts and pathogens exist as part of a community. Co-infections, where more than two pathogens simultaneously parasitize an individual host, are thus common in the wild. A co-infection is different from a singular pathogen challenge in various ways, including the costs incurred by the host to survive such challenges. Additionally, such costs are expected to be exacerbated when hosts are subjected to some form of nutritional deprivation, viz.,

starvation. We thus explore if the risk of mortality of *Drosophila melanogaster* is higher when co-infected with two common bacterial pathogens (*Enterococcus faecalis* and *Pseudomonas entomophila*) compared to when infected with either one of the pathogens, and if the mortality risk is further affected by whether the hosts are fed or starved. We find that flies subjected to co-infection exhibit significantly greater mortality during the acute phase of infection compared to flies infected with only one pathogen. Interestingly, starving the flies (from the point of infection onwards) does not further exacerbate mortality, either for co-infected or singly-infected flies.

P032

Functional assessment of dietary protein quality in *Drosophila melanogaster*

Debashis Rout[1], Megha[2], Gurmeet Singh[2]

The University of Trans-Disciplinary Health Sciences and Technology, Bengaluru, 560064

Protein is a vital macronutrient that supports growth, metabolism, and tissue maintenance, making its quality a critical determinant of nutritional adequacy. Presently, the most widely used indices to measure quality, such as PDCAAS and DIAAS, primarily quantify amino acid composition and digestibility without addressing the physiological processes that govern assimilation. Functional assays that bridge digestion with systemic utilization are therefore needed. Furthermore, these assays require higher mammals, thus limiting the scope of protein sources and modifications to be tested.

Here, we use *Drosophila melanogaster*–based functional assays to assess protein quality across dietary sources. Fecundity, a parameter highly responsive to dietary protein, showed that **whey protein (WP)** supported the highest reproductive output, followed by **soy (S)** and **soy isolate (SI)**. **Green gram (GG)**, **green gram isolate (GGI)**, and **peptone (P)** provided moderate fecundity, while **pea isolate (PI)** resulted in the lowest, comparable to the **negative control (NC, 1.25% yeast)**. To examine protein assimilation, we measured expression of *fit*, a gene responsive to dietary protein. WP elicited the strongest induction, followed by S, SI, and GGI, whereas GG and P produced moderate responses, and PI remained the lowest, similar to NC. *GCN2*, a marker of amino acid stress, was elevated in low-yeast diets but remained near baseline in flies fed WP, S, GG, and related sources, indicating sufficient amino acid availability. Protease activity followed a similar trend: S (5.4-fold) > WP (3.5-fold) > SI ≈ GG ≈ GGI ≈ P > PI ≈ NC. Overall, these functional outcomes reflect the relative assimilation and utilization of different dietary proteins and closely match established protein quality rankings based on *PDCAAS* and *DIAAS*.

Ongoing work includes standardizing total protein synthesis in adult muscle, total nitrogenous excretion to assess unused protein, and probing mTOR pathway activation via western blotting. Together, this framework establishes *Drosophila* as a scalable and physiologically aligned model to complement PDCAAS and DIAAS by linking digestion, nutrient signalling, and organismal outcomes as a pre-clinical model to assess protein quality.

P033

Deciphering the Role of Lipid Droplets in Drosophila Hematopoietic Stem Cell Homeostasis During Development

Deepak Jangra, Sudip Mandal, Lolitika Mandal

Department of Biological Sciences, Indian Institute of Science Education and Research Mohali, Knowledge City, Sector 81, SAS Nagar, Mohali

Hematopoietic stem cells (HSCs) sit at the apex of the blood cell lineage. They divide and differentiate to give rise to all mature blood cell types whilst maintaining their own pool. Two studies have reported the presence of HSCs in Drosophila 1-2. I aim to characterise the metabolic signatures of Drosophila HSCs, along with some molecular players. Our metabolic reporter screening has identified two crucial players that warrant further investigation. I am specifically examining the role of neutral lipid droplets (LDs) in HSC division and differentiation. Our compelling results indicate a strong correlation between reactive oxygen species (ROS) levels and lipid droplet content in HSCs, underscoring their critical role in HSC homeostasis. Our reporter and functional studies have conclusively demonstrated the essential role of lipid droplets in the maintenance of hematopoietic stem cells. For the next step, I intend to uncover the key signals that drive their timely differentiation. Results related to the above findings will be presented

P034

Investigating the Protective Role of PI3K/AKT Signaling in Neurodegeneration in Spinocerebellar Ataxia Type 3 Using the *Drosophila* Model System

Deepti Thapliyal[1], Naorem Tarundas Singh[1], Dr. Mayanglambam Dhruba Singh[1]

[1]*National Brain Research Institute, Haryana, India*

Spinocerebellar ataxia type 3 (SCA-3), also known as Machado-Joseph disease, is a progressive neurodegenerative disorder caused by polyglutamine (poly-Q) expansions in the Ataxin-3 gene. This leads to toxic protein aggregation and subsequent neuronal damage. SCA-3 pathogenesis is linked to disruptions in cellular processes, including mitochondrial dynamics and protein quality control pathways. Despite being the most prevalent form of ataxia globally, no effective treatments targeting these toxic aggregates have been identified. PTEN is a negative regulator of the PI3K/AKT signaling pathway, which plays a crucial role in regulating apoptosis, cell growth, and glucose metabolism. Our study investigates the neuroprotective potential of downregulating insulin signalling pathway via PTEN knockdown in a *Drosophila* model of SCA-3. We hypothesize that PTEN downregulation may modulate insulin signalling pathways to mitigate

neurodegeneration and could help alleviate neurodegenerative symptoms associated with SCA-3.
Our results indicate that PTEN knockdown substantially reduces morphological deficits in the *Drosophila* eye and brain. The observed rescue is linked to enhanced AKT signaling. These findings highlight the potential of PTEN as a therapeutic target for SCA-3, emphasizing the benefit of targeting multiple pathways to achieve enhanced outcomes.

P035

Understanding the cause and consequences of neuronal RNA-binding protein Elav mislocalization in ALS pathologies

Srikanth Pippadpally[1], **Deshna Bankar[1]**, Vimlesh Kumar[1]

[1]*Department of Biological Sciences, IISER Bhopal*

Amyotrophic lateral sclerosis is a neurodegenerative disease caused by progressive loss of motor neurons and is characterized by the cytoplasmic aggregation of RNA-binding proteins (RBPs). Elav (embryonic lethal/abnormal vision) is one such RBP, predominantly located in the nucleus, where it is involved in mRNA processing in neurons. Previous studies have observed that Elav is mislocalized to the cytoplasm in ALS pathologies; however, the mechanisms or the consequences of this mislocalization are elusive. In this study, we aim to understand the cause of Elav mislocalization using the *Drosophila* ALS model and to determine its pathological consequences. Our preliminary analysis found that Elav mislocalization is a common pathological feature in several ALS models, such as Fus, TDP43, and Atxn2. We also show that mutations affecting the RRM motifs play a critical role in the mislocalization of Elav, but not the other intrinsically disordered regions present in these proteins. These results suggest that Elav mislocalization in multiple ALS pathologies is linked to their ability to interact with RNA and other RNA-binding proteins.

P036

Investigating the effect of dietary manipulation on stress and neuromuscular performance in *Drosophila melanogaster*

Devashish Kumar[1], Chandrakanth M[1], Chetan S[1], Nishant Kumar[1], Chand Sura[1], Sudipta Tung[1]

Ashoka University, Sonepat, Haryana

Aging results from the interplay of genetic, environmental, and metabolic factors, leading to a progressive decline in physiological function and increased disease susceptibility. Nutrition, particularly the balance of proteins and carbohydrates, plays a key role in

modulating lifespan and healthspan. However, integrated studies linking dietary composition to multiple aspects of aging, such as stress resilience and neuromuscular performance, remain limited. Moreover, previous work often confounds caloric intake with nutrient balance, limiting broader applicability. While caloric restriction can extend lifespan, it may cause malnutrition and is impractical; thus, adjusting macronutrient ratios at fixed caloric levels offers a more feasible approach. Nutritional requirements also differ across life stages, suggesting that stage-specific diets may differentially optimize performance.

In this study, I examine the plastic effects of stage-specific, isocaloric dietary manipulations varying in protein-to-carbohydrate ratios in outbred *Drosophila melanogaster* populations. Age-dependent performance was assessed at early, mid, and late life stages through stress assays (starvation, desiccation, thermal, cold, and osmotic tolerance) and neuromuscular assays (negative geotaxis and flight performance). To uncover biochemical correlates, triacylglyceride (TAG) and thoracic muscle protein levels were quantified. This work aims to link macronutrient balance with stress resistance, neuromuscular aging, and overall organismal performance across life stages.

P037

Ldh activity driven ROS generation in the pericardial cells regulate cardiac ECM remodelling in *Drosophila.*

Dheeraj Kumar[1], **Pooja Chaudhary**[1], Jayati Gera[1*], Lolitika Mandal[2], Sudip Mandal[1]

Molecular, Cell and Developmental Biology Laboratory[1]*, Indian Institute of Science Education and Research, Mohali (IISER Mohali), Developmental Genetics Laboratory*[2]*, Indian Institute of Science Education and Research, Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli PO 140306, Punjab, India. Neurobiology and Genetics, Theodor-Boveri-Institute, Biocenter, Julius-Maximilians-University of Würzburg, Würzburg, Germany*.*

Multicellular organisms rely on constant communication between their organs to maintain a balanced physiological state. Each organ has specialized functions, but these functions are closely coordinated to ensure overall health and well-being. When this communication is disrupted, it can result in systemic disorders, such as heart and metabolic diseases. Using *Drosophila melanogaster* as a model organism, we demonstrated that high levels of reactive oxygen species (ROS) in the adult pericardial cells (PCs) activate a signaling pathway involving Ask1, JNK, and p38 kinases, which in turn stimulates the expression of *upd3* in the PCs. Upd3 secreted by the PCs plays a role in regulating the composition of the cardiac extracellular matrix (ECM) by modulating the expression of *pericardin* (*prc*) from fat cells. However, the underlying cause of the physiological high levels of ROS in the PCs remained unclear.

In this study, we found that downregulation of Lactate dehydrogenase (Ldh), either through knocking down or knocking out the gene specifically in the PCs, led to a significant decrease in the physiological high levels of ROS. Additionally, we observed a considerable reduction in the levels of JNK and phospho-p38, as well as a decline in the *upd3* transcript

levels in the PCs following *ldh* downregulation. This was accompanied by a decrease in *prc* transcript levels in the fat cells and a reduction in Prc accumulation within the cardiac ECM. Based on these findings, we hypothesize that the physiological high levels of ROS in the PCs result from LDH-driven metabolism that supports NADPH oxidase activity. We are currently exploring this metabolic connection further.

P038

PTEN downregulation ameliorates Myotonic Dystrophy 1 by reducing autophagy in the Drosophila model

Dipti Chakraborty, NaoremTarundas Singh, Mayanglambam Dhruba Singh

i-BRIC-National Brain Research Centre (NBRC)

Myotonic Dystrophy 1 (DM1) is a debilitating, autosomal dominant multisystemic disorder caused by a CTG trinucleotide repeat expansion in the 3' untranslated region of the Dystrophia Myotonica Protein Kinase (DMPK) gene. This expansion leads to a complex cascade of downstream effects, including aberrant RNA metabolism, splicing defects, and, ultimately, progressive muscle wasting and neurodegeneration. There is no cure or specific treatment for DM1 beyond symptomatic management. We used a Drosophila model to investigate the role of PTEN (Phosphatase and Tensin Homolog), a negative regulator of the PI3K/Akt signaling pathway, in DM1 pathogenesis. The PI3K/Akt pathway is a critical regulator of cell growth, survival, and metabolism, and its dysregulation has been implicated in various diseases, including cancer and neurodegenerative disorders. Given the defect in alternative splicing of the insulin receptor (IR) and insulin resistance in DM1, we hypothesised that targeting PTEN could influence DM1 pathology. Drosophila expressing CTG270 repeats exhibited characteristic DM1-like phenotypes, including reduced eye size and pigmentation, muscle defects, and shortened lifespan. Furthermore, in CTG270 flies, a significant increase in autophagy was observed, and the genes regulating autophagy were significantly upregulated in CTG270 flies. PTEN downregulation rescued eye size and pigmentation, improved muscle defects, and extended lifespan. Also, the knockdown of PTEN reduced this aberrant autophagy. Our study suggests that upregulation of PI3K/Akt signaling by targeting PTEN expression suppressed the DM1 pathology.

P039

Ecdysone - Driven Epithelial Cell Shape Change in Developing Eggs

Gaurab Ghosh[1], Sudipta Halder[1], Aresh Sahu[2], Mohit Prasad[1]

[1]Department of Biological Sciences, Indian Institute of Science Education and Research (IISER) – Kolkata, Mohanpur Campus, Mohanpur, Nadia – 741246, West Bengal, India; [2] Department of Molecular and Behavioural Neuroscience Institute, University of Michigan, USA

Epithelial morphogenesis generates diversity in tissue organization and aids in the formation of various organs in the metazoans. At the cellular level, this process mediates change in the shape and organization of the epithelial cells. Given the wide importance of this process in multicellular development, we still lack clear understanding as to how epithelial morphogenesis is regulated in the metazoans. Employing the Drosophila oogenesis model, we have examined the role of Ecdysone (EcR) pathway in mediating the shape transition of epithelial follicle cells. Typically, a previtellogenic fly egg is enveloped by a layer of 750 somatic epithelial cells called the follicle cells. As the developing egg enters the vitellogenic phase, approximately 50 anterior follicle cells (AFCs) undergo shape transition from cuboidal to squamous fate. We demonstrate that the activity of EcR pathway in the AFCs coincides with the timing of cuboidal-to-squamous shape transition. Satisfying, depletion of the Ecdysone Receptor function impedes cuboidal to squamous shape transition of anterior follicle cells (AFCs) without affecting the fate of AFCs. Employing genetic tools, we show that EcR limits Notch signaling to facilitate the shape change of the AFCs. We suggest mechanistic model where Ecdysone signalling, with cooperative activity of the Notch pathway, finetunes the non-muscle myosin heavy chain zipper and neuroglian, prompting disassembly of adherens junction and lateral junction respectively during AFC shape transition. Over all, our work provides novel molecular insight as to how Ecdysone signalling mediates shape change in the epithelial follicle cells. Results from the above will be presented.

P040

Tollo/Toll8 signalling in peptidergic neurons drives lipid accumulation in response to mild oxidative stress in Drosophila.

Bhavna Pydah, Asmita Dogra, Tanaji Devkate Mirajul Islam, Rakesh Joshi, **Gaurav Das*** [1]

Department of Biophysics, BMS Block II, South Campus, Sector 25, Panjab University, Chandigarh, NCCS, Pune

While it is clear that severe stress is highly detrimental, the mechanisms by which organisms adapt to mild, chronic stressors that are more common are not well understood. We found that chronic exposure to mild oxidative stress induces systemic lipid accumulation in adult Drosophila, which renders them more resistant to starvation. Toll signalling pathways are known to be activated by oxidative stress and are expressed in multiple tissues, including the nervous system. Through a genetic screen, we identified that neuronal Tollo (Toll-8) modulates starvation resistance by affecting lipid accumulation. We narrowed down Tollo activity to a specific small cohort of neuropeptidergic neurons expressing the neuropeptide Leucokinin (LK), amongst others. Upstream Spätzle2 was the ligand responsible for activating Tollo under oxidative stress. Downstream of Tollo, the JNK pathway but not the NFKB pathway, was necessary for lipid accumulation and starvation resistance. Our evidence also suggests that IPCs act downstream of leucokinin to promote lipid accumulation and resistance to starvation. Our results implicate neuronal Toll signaling in adapting to mild oxidative stress by modulating systemic lipid metabolism, thereby lending the flies a greater ability to withstand starvation stress.

P041

Investigating the adult relevance of larval hexamerins in *Drosophila melanogaster*

Gayathri Binu[1], Aninditha Rao[1], Jishy Varghese[1]

[1]*Indian Institute of Science Education and Research, Thiruvananthapuram, Kerala*

The life cycle of holometabolous insects alternates non-feeding or “closed” periods (embryonic and pupal) with feeding or “open” ones (larval and adult). Therefore, the resources required to proceed through a closed developmental phase come from the stores made during the preceding open phase.
In *Drosophila*, larval **growth** is supported by nutrient intake, while the non-feeding pupal stage is fueled by vast reserves of **storage proteins**, primarily **hexamerins** known as Larval Serum Proteins (LSPs). Hexamerins are the storage proteins found in insects, known to reach a peak expression level during a specific developmental period. Larval

Serum Proteins(LSP) - 1 and 2 are the hexamerin protein complexes found in Drosophila. LSP complexes are maximally produced in the third instar larvae by the larval fat body, analogous to vertebrate liver and adipocytes. It gets released into the hemolymph, making up 70% of the total hemolymph protein. Prior to pupa formation, LSP is reuptaken from the hemolymph to the fat body for utilization throughout development. These proteins are synthesized by the fat body during feeding and sequestered to serve as a critical amino acid source for metamorphosis. The mobilization of these stores is not a simple passive process but is tightly regulated by a sophisticated interplay between developmental timing and systemic **nutrient-sensing mechanisms**. The fat body itself acts as a primary nutrient sensor, utilizing the Target of Rapamycin (TOR) pathway to assess amino acid availability. High nutrients activate TOR, promoting protein synthesis and suppressing autophagy.
In this study, we analyze the role of these hexamerins by tissue-specific genetic manipulations, tease apart their role in larvae versus adults, and try to elucidate the signalling mechanisms that may be involved in the regulation.

P042

Interplay between hypoxia and insulin signaling in regulating growth and metabolism in *Drosophila melanogaster*

Sohela Sarkar[1], **Gopika K.G.**[1*], Palak Khare[1], Prajakta Bodkhe[2], Siddharth Vidhu[1], Jishy Varghese[1#]

IISER TVM[1] ; University of Calgary[2]

Oxygen is vital for cellular metabolism, and reduced oxygen levels (hypoxia) activate the Hypoxia-Inducible Factor 1 (HIF) signaling pathway to maintain homeostasis. In *Drosophila melanogaster*, the HIF-α homolog Similar (Sima) and HIF-β homolog Tango (Tgo) mediate hypoxia responses, while Fatiga (Hph) promotes Sima degradation under normoxia. Although HIF signaling is well studied in hypoxic adaptation, the non-canonical regulation of Sima based on nutrient availability and its role in growth and metabolism remain poorly understood.
Our studies show that larvae exposed to 5% oxygen display delayed pupation and reduced body size, phenotypes mimicked by ubiquitous *sima* overexpression. Using tissue-specific GAL4 drivers, we found that *sima* activation in insulin-producing cells (IPCs) suppresses growth and delays development, while *sima* knockdown enhances growth. Reporter analyses (HRE-LacZ) revealed *sima* activity in IPCs even under normoxia, which increases under hypoxia. *sima* overexpression in IPCs causes DILP2 retention and reduced insulin signaling, indicating that Sima directly regulates insulin output in response to oxygen and nutrient cues.
Ongoing work aims to dissect tissue-specific Sima functions in IPCs and fat body using molecular reporters and physiological assays. This study will uncover how HIF signaling integrates oxygen and nutrient status to coordinate growth and metabolic balance in *Drosophila*.

P043

The role of miR-986 in the metabolism and lifespan of *Drosophila melanogaster*.

Hana Lukman, Aswathy BJ, Divyasree M Nair, Jishy Varghese

BS-MS Student at IISER TVM.

MicroRNAs (miRNAs) are small, non-coding RNAs that guide post-transcriptional gene regulation by targeting messenger RNAs. They are essential for maintaining metabolic homeostasis by modulating genes that control nutrient storage, energy use, and response to metabolic stress. In line with the growing awareness of miRNAs in metabolic regulation, we are investigating the specific contributions of miR-986 in controlling lifespan and metabolic adaptation in *Drosophila melanogaster*.Functional characterisation of the microRNA revealed that brain-specific knockdown and overexpression of miR-986 have significant roles in starvation resistance, accompanied by marked changes in metabolic profiles and feeding behaviours, thereby reinforcing its role in sustaining homeostasis.
Intriguingly, knockdown and overexpression of miR-986 in the fly brain yielded similar results instead of the expected opposite phenotypes and combining both the overexpression and downregulation of the miRNA in the same fly simultaneously rescues the phenotype, suggesting unexpected regulatory complexity. This also suggests the possible existence of compensatory pathways that only activate when both extremes (knockdown and overexpression) are present, allowing for a “rescue” of the phenotype, which warrants further investigation, such as target identification and pathway analysis, to clarify the underlying molecular mechanisms.
Ongoing efforts to identify downstream target genes of miR-986 aim to clarify the molecular circuitry responsible for organismal responses to nutrient stress and to investigate their potential role in neurodegeneration and ageing. By manipulating the miRNA levels, we highlight the novel role of miR-986 in orchestrating both metabolic homeostasis and lifespan. Understanding miRNA-mediated regulatory circuits in flies provides a robust framework for elucidating the molecular basis of ageing and metabolic diseases in higher organisms.

P044

Visual feature integration in approach detection in flies and humans

Harsh Vashistha, Natalia Matos, Heng Wu, Damon Clark

Yale University, USA

Detecting approaching objects is critical for survival and is classically attributed to detecting expanding visual stimuli. However, many visual cues beyond just expansion are

related to approach and can contribute to approach perception, yet their roles have remained poorly understood. Here, we employed a class of luminance-only visual stimuli that lack any expansion element yet evoke robust approach perception in humans. Strikingly, *Drosophila melanogaster* exhibits similar behavioral responses to these luminance-only approach stimuli that mirror their responses to classical looming objects. Using targeted neuronal silencing and two-photon calcium imaging, we identified two types of visual projection neurons that mediate fly behavioral responses to both classical looming stimuli and the luminance-only approach stimuli. This establishes these neurons as general 'approach sensors' in flies, responsible for integrating multiple cues of approach. Interestingly, it is inputs to these approach sensors from motion detecting neurons that confers the sensitivity to luminance-based approach stimuli, arising from the differential responses of motion detectors to local contrast dynamics. We further show that these approach-sensitive neurons perform nonlinear integration of expansion and luminance cues, enhancing responses when these cues are temporally ordered in a way that is consistent with the salience of these cues for an approaching object. Our results identify a visual computation in which expansion and luminance cues converge to enhance approach detection and provide a mechanistic account for how a visual system processes the luminance-only approach stimulus to lead to an approach percept, one that is shared by humans.

P045

Exploring biological functions of polyphosphates(polyP) in *Drosophila*

Harsha Sharma[1], Sunayana Sarkar[1], Manish Jaiswal[1]

[1] *Tata Institute of Fundamental Research Hyderabad, Hyderabad, Telengana*

Polyphosphate (polyP), a polymer of inorganic phosphates linked by phosphoanhydride bonds, is widely conserved across living organisms. While its biological roles are well-characterized in prokaryotes, the molecular and functional aspects of polyP in multicellular eukaryotes remain poorly understood. To identify the biological function of polyP in multicellular organisms, we have developed a *Drosophila* model to explore metazoan polyP functions. While investigating polyP in hemocytes, which are similar to blood cells in mammals, we observed large punctate structures at the periphery of cells that are labeled by polyP. We also found that polyP in hemocytes is required for hemolymph clotting. Further, depleting polyP leads to an increase in the number of hemocytes. These preliminary findings suggest that polyP may play a crucial role in maintaining hemocyte function and homeostasis.

P046

Role of nutrient sensitive non-coding RNAs in reproductive plasticity and inter-sexual communication of *Drosophila melanogaster*

Hrishita Pradhan, Utkarsh Bhore, Rabi Sankar Pal, Ruthrotha Selvi Bharathavikru, Bodhisatta Nandy

Indian Institute of Science Education and Research Berhampur, Odisha, 760003

Nutritional status profoundly influences reproductive physiology in *Drosophila melanogaster*, yet the molecular links between diet and reproduction remain poorly understood. Non-coding RNAs are key fertility regulators, acting via chromatin remodelling and post-transcriptional mechanisms. For instance, the miRNA let-7 has been proven to have a role in neuromuscular remodelling during larval to adult transition. Similarly, the lncRNA oskar is evident to play a role in germline development and embryonic patterning. Our research investigates the roles of two distinct non-coding RNAs in linking dietary status to reproduction. First, the microRNA let-7 and its axis with the RNA-binding protein Imp (IGF-II mRNA-binding protein) was explored in the female ovary. From experimental data, it was evident that yeast deprivation leads to shrunken ovaries and a significant reduction in mature oocytes. Further gene expression analysis revealed an unexpected yet significant upregulation of both pre-let-7 and Imp in yeast-deprived ovaries, and a strong positive correlation between them, providing evidence of a functional let-7-Imp axis in the Drosophila ovary that may mediate dietary effects on oogenesis. In parallel, we would explore the role of long non-coding RNA msa, which is expressed in the male accessory gland and modulates seminal fluid composition. We hypothesize that msa acts as a nutrient-sensitive trigger for sexual conflict, affecting its expression by dietary yeast. Furthermore, we aim to understand the effects of diet-mediated changes in msa on female post-mating responses and germline stem cell dynamics by mating nutritionally-manipulated males to females. Together, these studies would illuminate how nutrient-sensitive non-coding RNAs, operating in both sexes, fine-tune reproductive physiology and inter-sexual communication.

P047

Developing CRISPR-Cas9 based genome engineering technology for homology-independent genetic manipulation at endogenous genomic loci in a tissue specific manner

Devika TK[1], **Iqra Rizvi[2,3]**, Deepti Trivedi[1], Tina Mukherjee[3]

[1]*Drosophila Fly Facility, National Centre for Biological Science, Bengaluru, Karnataka -560065*
[2]*National Centre for Biological Science, Bengaluru, Karnataka -560065*
[3]*Institute For Stem Cell Science and Regenerative Medicine, Bengaluru, Karnataka – 560065*

Recent advances in CRISPR-Cas9 genome engineering have greatly facilitated the re-visit of homologous recombination (HR) in *Drosophila.* These techniques enable efficient generation of both whole-body/tissue-specific deletions as well as whole-body insertions in *Drosophila*. However, precise and tissue-specific insertions or targeted tagging remains a significant challenge. Here in this study, we combine CRISPR-Cas9, UAS-Gal4 system and fluorescent reporters to generate a genome editing tool termed "CRInsert". It is a modular system that enables **homology-independent, tissue-specific gene insertions** in *Drosophila*. This tool allows gene manipulation at endogenous genomic loci in a tissue specific manner. The system integrates CRISPR-Cas9 mediated double-strand breaks with the **Gal4/UAS system** for spatiotemporally restricted Cas9 expression. The donor construct, designed with dual gRNA target sites and fluorescent reporters (GFP and DsRed), facilitates cassette release and visual validation of successful integration via non-homologous end joining (NHEJ). CRInsert, thus, provides a versatile platform for **tissue-restricted, scalable, and marker-assisted genomic insertions**, expanding the toolkit for functional genomics and tissue/cell-specific studies in *Drosophila*.

P048

Nup133 Orchestrates Actin-dependent Synaptic morphology in *Drosophila melanogaster*

Ishita Jagtap[1], Nikita Sharma[1], and Ram Kumar Mishra[1]

[1]*Department of Biological Sciences, Indian Institute of Science Education and Research Bhopal, Madhya Pradesh, India.*

Nucleoporins (Nups) are proteins that form the nuclear pore complex (NPC), which regulates transport between the nucleus and cytoplasm. NPC is composed of ~30 different Nups organized into various sub-complexes, which influence gene expression, development, and neuronal function, beyond transport. Perturbations in the expression of any of these Nups result in both morphological and tissue-level functional defects. Among different Nups, Nup133, a member of the largest Y-complex subunit of NPC, is vital for

assembly and structure. Nup133 has been linked to impaired transport and hampers neuronal differentiation in mice. Moreover, Nup133 mutations are also associated with brain development anomalies in humans.
To develop further understanding of Nup133 functions, we generated a CRISPR-Cas9-mediated null mutant in *Drosophila melanogaster*. As anticipated, the loss of Nup133 in null mutants caused early pupal lethality and impaired movement. Examining the neuro-muscular junctions (NMJs) indicated impairment in synaptic morphology along with a reduction in active zones. Interestingly, Nup133 mutants exhibit disruption of actin bundling and levels were disrupted, leading to NMJ-associated defects affecting movement.
Collectively, these results demonstrate that Nup133 plays a critical role in maintaining cytoskeletal integrity, orchestrating synaptic plasticity and thus regulating neuronal and systemic development of Drosophila.

P049

Role of IP3 receptor in chromatin dynamics and gene regulation in Drosophila brain tissue

Jasmine Kaur Dhall, Nandashree Kasturacharya, Bharath Saravanan, Sundarraj Nidharshan, Syed Kavish Nizami, Dimple Notani and Gaiti Hasan

National Centre for Biological Sciences (NCBS) Bangalore, Karnataka, India

The role of 3D genome architecture and histone modifications have emerged as key players in gene regulation and expression (Marco et al., 2020). Furthermore, its role in neuronal function is pivotal owing to its crosstalk with neuronal stimulation and effect on neuronal circuitries (Marco et al., 2020; Grabowska et al., 2022). Importantly, it is well known that neuronal stimulation and synaptic activity are Ca2+ dependent (Zucker, 1999). Inositol 1,4,5-triphosphate (IP3) receptors regulate Ca2+ release from the endoplasmic reticulum to the cytosol. We have previously shown that a heteroallelic mutant of IP3 receptor (itprku) exhibits reduced store operated calcium entry in neurons in Drosophila (Joshi et al., 2004; Venkiteswaran et al., 2009). Furthermore, a positive feedback loop persists between IP3R and SET2 (methylatransferase) in glutaminergic and dopaminergic neurons in Drosophila (Mitra et al., 2021; Mitra et al., 2023). This prompted us to examine the role of IP3R in orchestrating chromatin dynamics and gene regulation in adult Drosophila brain tissue. To achieve this, changes in the chromatin accessibility and selected epigenetic modifications have been studied in adult itprku mutant brain. Furthermore, genome-wide changes in the transcriptome were examined. We found that the mutant exhibited widespread increase in the chromatin accessibility, reduced H3K36me3 enrichment, altered PolII CTD phosphorylations, and a widespread effect on the transcriptome. Conclusively, our study is a pioneering examination of the effect of IP3 receptor on chromatin dynamics and histone modifications in adult Drosophila brain tissue.

P050

Subduing of Huntington's disease symptoms by phytochemical Beta carotene in a transgenic model of *Drosophila*

Jassika Gupta[1], Mansi Yadav[1], Debalina Chatterjee[1], Namita Agrawal[1]

[1]*Department of Zoology, University of Delhi, Delhi-110007, India*

Huntington's disease (HD) is a progressive neurodegenerative disorder caused by an abnormal expansion of CAG repeats in the *huntingtin* (*HTT*) gene, resulting in motor dysfunction, cognitive decline, weight loss, and neuropsychiatric disturbances. Currently, no curative therapy exists for HD, and available treatments primarily manage symptoms, particularly chorea, with limited efficacy and considerable side effects. Given these limitations, phytochemicals have emerged as potential therapeutic agents owing to their antioxidant, anti-inflammatory, and neuroprotective properties, coupled with minimal toxicity. The present study explores the neuroprotective potential of beta-carotene in HD through an integrative approach combining *in silico* molecular docking and *in vivo* evaluation using a transgenic *Drosophila* HD model.

Molecular docking studies targeted key pathogenic target proteins, mutant huntingtin (mHttQ128), histone deacetylase 3 (HDAC3), and caspase-8, implicated in protein aggregation, epigenetic dysregulation, and apoptosis, respectively. Beta-carotene exhibited strong binding affinities of −8.6, −7.5, and −7.5 kcal/mol for these targets, suggesting its potential to modulate critical molecular pathways in HD pathology. Complementary *in vivo* assays revealed significant dose-dependent improvements in motor performance, including larval crawling, adult climbing, and flight ability, alongside modest lifespan enhancement in beta-carotene-treated HD flies compared to untreated controls. Among the tested doses, 30 µM emerged as the most effective concentration.
To further substantiate these findings, immunohistochemical analysis for elav (neuronal integrity) and huntingtin aggregation are underway to evaluate cellular correlates of neuroprotection. Collectively, these results highlight beta-carotene as a promising phytochemical candidate capable of mitigating HD-associated motor deficits and molecular dysregulation.

P051

Developmental and neurological effects of acute exposure to arsenic on *Drosophila melanogaster*

Jawaid Ahsan, Anushree, Md Zeeshan Ali, Shubham Gudadhe, Sushma Kumari Singh

Drosophila Behavior Lab, Department of Biotechnology, Central University of South Bihar, Panchanpur, Gaya, Bihar

The prevalence and toxicity of arsenic (As) afflict millions of people worldwide including developing countries like India. The exposure to arsenic-contaminated food and drinking water, continuous increase in industrial usage, and a number of other occupational conditions have all contributed to the harmful effects of arsenic on humans. The trivalent forms of inorganic arsenic (iAs) are particularly dangerous to living things because of their enhanced cellular absorption and capacity to cross the blood–brain barrier (BBB). Toxic levels of arsenic adversely affect an organism's various tissues and organs, leading to diseases of the central nervous system, circulatory system and skin cancer. To explore and better understand the mechanism of the effects of acute exposure to arsenic on the nervous system including cognitive functions, a useful and powerful model system is required. *Drosophila melanogaster* (common fruit fly or vinegar fly), with its short generation time, genomic and systemic similarities with humans, and availability for robust behavioral paradigms, may be considered an ideal model for studying arsenic toxicity. We studied the adverse effects of acute exposure to arsenic on Drosophila fecundity, development, locomotion, behavior, learning and memory in a dose and time dependent manner. We found that exposure to arsenic leads to reduced egg-laying, smaller pupae size, compromised motor skills, reduced olfaction, and also reduced learning and memory, indicating involvement of the nervous system. Thus, our studies show that the fruit fly (*Drosophila melanogaster*) could be used as a potential useful model system to study the mechanism of these neurological changes due to exposure to arsenic, at different levels of complexities including anatomical, molecular and biochemical levels. These studies could also be extended to mitigate these adverse effects by employing suitable interventions including common herbal formulations.

P052

Protein phosphatase 1(PP1) in Drosophila neural stem cell maintenance and neuronal diversity.

Jiban Barman[1, 2], Asif Bakshi[1,2], Rashmi Sipani[1, 2], and Rohit Joshi[1,]

[1]*Laboratory of Neuroscience and Cell Biology, (BRIC-CDFD), Hyderabad-500039. India.*
[2]*Graduate Studies, Manipal Academy of Higher Education, Manipal 576104.*
Contact: jbarman@cdfd.org.in; rohit@cdfd.org.in

Drosophila central nervous system (CNS) is generated by neural stem cells called Neuroblast (NBs). NBs have the ability to self-renew in order to maintain themselves and differentiate to give rise to neurons and glial cells. Proper CNS development and generation of neuronal diversity depends upon the balance between the proliferation and differentiation of NBs which is maintained by various factors. During CNS development the Notch signalling pathway known to be involved in maintaining tissue homeostasis and generating cell diversity by regulating cell proliferation, differentiation, and apoptosis. I will be discussing our recent work about identification of Protein Phosphatase 1-alpha (PP1-α) as a novel regulator of the Notch signalling pathway.

P053

Essential role for Nup43 in Drosophila fertility and spermiogenesis through Myosin-VI dependent actin cone assembly dynamics

Jyotsna Kawadkar, Ashley Suraj Hermon, Rohit Kumar and Ram Kumar Mishra

Indian Institute of Science Education and Research (IISER), Bhopal, Madhya Pradesh, India

Nuclear pore complexes, critical for nucleocytoplasmic transport, are composed of nucleoporins (Nups). Recent studies have uncovered roles for different Nups in processes like cellular differentiation, contributing richly to organismal development. Intriguingly, the Nup107 complex member, Nup43, is linked with premature ovarian insufficiency (POI) in humans. We report that Nup43 is integral to the maintenance of Drosophila fertility. Nup43 null mutant (Nup43KO) generated by CRISPR-Cas9 causes sterility in both females and males. While oocyte development is halted at the first division stage, the Nup43KO males are sterile due to defective spermatogenesis, which is arrested at the canoe stage of development in Nup43KO mutants. The nuclear elongation, shaping, and actin cone formation steps of individualization complex (IC) formation are adversely affected, suspending sperm maturation. All these defects were rescued by the expression of the Nup43 transgene in null mutants, suggesting the criticality of Nup43 function in spermatogenesis. Myosin VI (jar), an actin cone modulator, and Nup43 interactor can partially rescue the actin cone formation but not the sterility defects. We propose that Nup43 facilitates sperm individualization along with jar by promoting actin cone formation

during spermatogenesis. These observations uncover a novel yet critical function for Nup43 in Drosophila gonad development and spermatogenesis.

P054

Synergistic effect of Leucine and Glutamine to restore metabolic homeostasis and redox balance by targeting chico-Akt axis in a High Sucrose Diet-induced Drosophila model of Type 2 Diabetes

Kalpanarani Dash, Monalisa Mishra

Neural Developmental Biology Lab, Department of Life Sciences, National Institute of Technology, Rourkela, Sundergarh, Odisha, India, 769008

Type 2 diabetes(T2D) continues to be a global health concern due to its rising prevalence and severe socioeconomic consequences. While existing pharmacotherapies attempt to control blood glucose levels and minimize complications, challenges come with their high cost, side effects, and narrow therapeutic window. Hence, there is a pressing need for novel treatment options to address the disease's intricate pathogenesis. In that scenario, the role of amino acids in insulin signalling and type 2 diabetes is yet to be explored. The current study highlights the synergistic role of leucine and glutamine as an anti-diabetic regimen in a high sucrose diet-induced Drosophila model of T2D. Biochemical analysis revealed that supplementation alleviates hyperglycemia and hyperlipidaemia, indicating metabolic restoration. Improved redox balance is indicated by decreased protein carbonylation, increased thiol levels, enhanced DPPH radical scavenging, elevated antioxidant enzyme activity, and decreased lipid peroxidation. Histological assessment found reduced reactive oxygen species (ROS) accumulation, restoration of actin filament architecture, and decreased apoptotic cell death in the gut and malpighian tubules. Furthermore, Malpighian tubule efflux activity was notably enhanced following treatment. At the molecular level, the supplementation predominantly targets downstream components of insulin signaling pathways, chico and Akt, while secondarily stimulating insulin secretion, which typically diminishes in the later stages of chronic hyperglycemia. Upregulation of cytoskeletal genes and nephrocyte markers further highlighted the multi-targeted effects of the treatment. Together, these findings identify leucine and glutamine co-supplementation as a promising and multifaceted strategy to counteract metabolic, oxidative, and cytoskeletal impairments associated with T2D, offering a potential nutraceutical intervention for diabetes management.

P055

Unravelling Mechanisms of Membrane Crumpling–Driven Exocytosis in Exocrine Secretion

Danisha Ahmed[1], Eyal Schejter[2], Ori Avinoam[2], Ben-Zion Shilo[2], **Kamalesh Kumari[1]**

[1] *Shiv Nadar Institution of Eminence, NCR, India*
[2] *Weizmann Institution of Science, Rehovot, Israel*

Exocrine secretory organs are essential to human physiology, releasing components critical for cell signaling, metabolism, and immune protection. Exocrine secretion relies on giant micron-sized vesicles that fuse with the apical surface; this poses a formidable challenge to maintaining plasma membrane size, shape, and composition. Despite their importance, the mechanisms that preserve membrane homeostasis during such secretion remained unclear. We addressed this fundamental problem using live-cell super-resolution imaging and correlative light and electron microscopy (CLEM) in *Drosophila* larval salivary glands and mouse pancreatic acinar cells. Our work uncovered a novel pathway of exocytosis that we call – the **Membrane Crumpling-mediated Exocytosis (Mem-CruX)**. During Mem-CruX, vesicle membranes undergo actomyosin-driven progressive crumpling, enabling both content extrusion and mechanochemical sequestration of the vesicle membrane from the apical surface. This prevents surface expansion and is subsequently coupled to targeted endocytic recycling (Kamalesh, K. et al., Dev Cell 2021). We further investigated how the spatiotemporal recruitment and organization of the actomyosin cytoskeleton orchestrate Mem-CruX. We found that myosin-II assembles into an anisotropic, cage-like meshwork on the F-actin coat that uniformly envelops the vesicle, generating the contractile forces required for crumpling. We also identified RhoGEF2 as a key regulator of myosin-II recruitment and organization (Kamalesh, K. et al., JCS 2024). More recently, we have identified lipid modulators critical for the membrane remodelling during Mem-CruX, providing new molecular entry points to understand and eventually target the pathophysiology of exocrine secretory disorders.

P056

Caspar, a bi-modal primordial germ cell fate regulator influencing both Oskar and centrosomal dynamics

Subhradip Das[1], Adheena Elsa Roy[1], **Kanika[1]**, Girish Deshpande[1*], Girish Ratnaparkhi[1*]

[1]*Indian Institute of Science Education and Research Pune, Pune, Maharashtra, India.*

Formation of primordial germ cells (PGCs) is central for the future development of germline stem cells (GSCs) in *Drosophila*, being their progenitors. The proper specification and formation of PGCs is thus essential for propagating life. The PGC fate,

in *Drosophila*, is controlled by Oskar which is deposited by the mother, and proper segregation of germplasm by the centrosomes. Caspar, a homolog of human Fas-associated factor 1 (FAF1), controls the PGC fate via controlling both the Oskar levels, and also modulating germplasm segregation by influencing centrosomal dynamics. Caspar potentially does so by influencing Smaug which is a translational repressor of Oskar and other germplasm components.

P057

Evolution of Host Resistance to Pathogens Under Laboratory-Stimulated Climate Warming Elevates Deleterious Mutation Rate

Kanishk Tomar[2], Biswajit Shit[1], Pallavi Jaswal[1], Selah Makinishi[1], Imroze Khan[1]

[1]Ashoka University, Sonipat, Haryana; [2]Indian Institute of Science Education and Research (IISER), Mohali, Punjab

Climate warming may enhance susceptibility to novel pathogenic infections by compromising several features of the immune system. Conversely, climate warming can also trigger an overreactive immune response, leading to cytotoxic effects and damage to germline DNA repair mechanisms, thereby elevating the mutation load and fitness costs in future generations. Can organisms adapt to chronic thermal stress to lessen these fitness costs? To answer this question, we first experimentally evolved *Drosophila melanogaster* populations under high temperature (29°C) for over 70 generations, followed by systemic infection with the bacterial pathogen *Pseudomonas entomophila*. While ancestral populations remained highly susceptible to bacterial infections under warmer conditions, experimentally evolved populations could completely mitigate such infection costs. Within-host bacterial growth dynamics revealed that selected populations could achieve this by evolving stronger pathogen resistance mechanisms. However, this was in stark contrast to ancestral populations, which, in fact, tolerated pathogenic infections without effectively clearing them when reared under ambient conditions. Also, selected populations transmitted more deleterious mutations into the next generations, revealing their poor germline maintenance as a potential cost of increased pathogen resistance. Finally, we found that selected flies accumulated deleterious recessive mutations more rapidly than ambient-maintained flies, as evidenced by increased inbreeding depression and higher extinction rates, which served as proxies for the accumulation of deleterious mutations. In summary, our experiments thus revealed a novel condition-dependent rise in mutation load during adaptation to chronic thermal stress and exposure to novel pathogenic infections.

P058

Role of PPIases in VAP aggregate dynamics in the *ALS8* model of *Drosophila*

Karthik H[1], Kriti Chaplot[1], Lovleen Garg[1], Lokesh Pimpale[1], Girish Ratnaparkhi[1,*]

[1]*Indian Institute of Science Education and Research, Pune.*

Amyotrophic Lateral Sclerosis (ALS) is a lethal neurodegenerative disease characterised by the loss of motor neurons, leading to paralysis and death of the patient. Most cases are sporadic, while 10% of cases are familial. At least 18 genes have been identified as definitive loci to cause ALS. VAMP-Associated Protein B (*VAPB*) is the 8th locus discovered with a Proline to Serine mutation at the 56th position that can cause fALS. VAPB is an ER membrane protein that acts as a docking site for various proteins that bind to its MSP(Major Sperm Protein) Domain. VAPB is thus involved in multiple contact site-specific functions, including vesicle fission, membrane trafficking, lipid transport regulation, etc. Our lab has generated an orthologous mutation (P58S) in *Drosophila* using genome-based CRISPR-Cas9 editing, which exhibits *ALS8*-like phenotypes, including motor and lifespan defects, ER stress, inflammation, and perturbed lipid metabolism.
VAP^{P58S} aggregation in neurons is one of the distinct features of the ALS8 neurodegeneration model. Proline residues are unique in that they can stably exist in both cis and trans conformations, and this isomerisation is intrinsically slow and rate-limiting. In the VAPB-MSP domain, of total 7 Prolines, 3 are in cis conformation. Since the conserved proline in the 58th position is in cis conformation, but the substitution with serine forces a trans conformation, we investigated whether the loss of cis conformation contributes to the observed misfolded protein aggregation. Preliminary study suggest loss of cis conformation leads to insoluble aggregates. We further attempt to shift the aggregation kinetics of the VAP protein by targeting a family of proteins called Peptidyl Prolyl isomerases (PPIases). PPIases are a superfamily of chaperones which help in proline cis-trans isomerisation. Our study helps identify specific PPIases that may contribute to this process and understand the underlying mechanism of disease progression.

P059

Glial cells not the passive bystander but as active participants in the pathogenesis of Tauopathies.

Khushboo Sharma[1], Neha Tiwari[1], Saurabh Chand Sagar[1] and Madhu G. Tapadia[1,*]

*1-Cytogenetics Laboratory, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi 221005, Uttar Pradesh, India. email- khushboo.zoology@bhu.ac.in; *Corresponding author: madhu@bhu.ac.in*

Glial cytoskeletal regulation is essential for maintaining neuronal health through axonal support, nutrient delivery, and waste clearance. Autophagy, a critical cellular maintenance process, relies on intact cytoskeletal dynamics and trafficking pathways. Tau, a microtubule-associated protein, stabilizes the cytoskeleton under normal conditions. In Alzheimer's disease and related tauopathies, Tau becomes hyperphosphorylated, detaches from microtubules, and forms toxic aggregates. While neuronal Tau toxicity has been extensively characterized, its effects on glial cells remain poorly understood. We used a *Drosophila* model (*RepoGAL4 > UASTau LacZ*) to express human Tau specifically in glia. Unlike neuron-specific models that show progressive degeneration, glial Tau expression resulted in complete developmental lethality, indicating early disruption of essential cellular processes. We observed significant upregulation of Rab5, early endosome marker, and the downregulation of Rab7, a key regulator of late endosomal trafficking and autophagosome maturation. This was accompanied by impaired autophagy, accumulation of undegraded proteins, and cytoskeletal disorganization. These findings suggest that Tau disrupts glial autophagic trafficking by suppressing Rab7, leading to systemic failure in cellular clearance and structural integrity. Our study suggests the crucial role of glial cells as active contributors to Tau-mediated neurotoxicity.

P060

Mechanisms of sleep-plasticity and sleep dependent plasticity

Krishna Melnattur

Ashoka University

Across diverse animals, sleep is plastic (i.e. modifiable by environmental circumstances and ecological niches) and supports plasticity. Two stories from our recent work in Drosophila yield mechanistic insight into these processes.
First, we have been studying socialization induced sleep as a model of sleep-plasticity. Group-housed socially enriched flies sleep more following the period of social enrichment than their singly housed counterparts. We conducted a circuit inactivation screen to identify the circuit basis of this phenomenon. These behaviour data were complemented by

measurements of changes in excitability and of the strength of connections using the GRASP technique. Together, our data suggest a model whereby socialization increases sleep through 3 mechanisms – 1) inhibition of arousal promoting circuits, 2) activation of sleep promoting circuits and 3) recruitment of learning and learning induced sleep circuits. Second, to study sleep dependent processes, we evaluated sleep-plasticity and sleep-dependent plasticity in mutants with altered sleep. Towards this end, we acquired mutants in different classes of anti microbial peptides (AMPs) – Group A,B,C and Bomanins. AMP mutants exhibit reduced sleep, and a longer sleep latency. Sleep homeostasis was not impaired in these mutants. GroupC mutants interestingly, exhibited an exaggerated sleep rebound. Finally, most classes of AMP mutants were impaired in learning and memory. GroupC mutants, that sleep the least, however retained normal learning and memory. GroupC mutants also uniquely exhibited lower synapse abundance. GroupC mutants thus appear to be able to carry out some sleep functions despite their reduced sleep. The mechanisms underlying these effects are the subject of active inquiry.

P061

Investigating the Fz2-mediated mechanism of cell survival in *Drosophila* wing epithelium

Kritika Verma[1], Swapnil Hingole[1], Varun Chaudhary[1]

[1] *Indian Institute of Science Education and Research, Bhopal, Madhya Pradesh*

Wnts are highly conserved lipid-modified glycoproteins that function as morphogens by forming concentration gradients from producing to receiving cells. In the *Drosophila* wing imaginal disc, Wingless (Wnt1 in vertebrates) is secreted from the dorsoventral (D/V) boundary cell layers and forms a gradient towards the dorsal and ventral sides of the wing pouch. Upon reaching the receiving cells, Wingless (Wg) activates canonical Wnt signaling through the Frizzled receptors. Fz1 and Fz2 both can activate canonical Wnt signaling. However, Fz2, not Fz1, is upregulated in low-Wg regions to maintain canonical signaling (Chaudhary et al., 2019). We recently showed that Fz2 knockdown, in low Wg conditions, severely compromises cell survival (Hingole et al., 2025). The redundancy between Fz1 and Fz2 is not supported. Moreover, our findings indicate that higher Fz2 expression enhances cell survival in a mosaic competitive environment and significantly contributes to clonal growth. We aim to understand the mechanism by which Fz2 mediates competitive cell survival and whether higher levels of Fz2 provide a competitive advantage to the cell.

P062

Interaction between RRM-domain containing ALS-prone proteins and chaperones mediates the neurotoxicity in ALS and FTD

Srikanth Pippadpally[1], **Leishangthem Biteshwari Devi[1]**, Chandan Sahi[1], Vimlesh Kumar[1]

[1]*Department of Biological Sciences, IISER Bhopal.*

RNA metabolism plays a crucial role in the functioning of neurons. RNA-binding proteins (RBPs) are vital proteins involved in RNA metabolism that are bound to RNA through their characteristic RRM motif. The disruption in RBPs can lead to the impairment of neuronal function and contribute to the progression of neurodegenerative diseases. One of the key aspects of neurodegeneration is the accumulation of RBPs in the cytoplasm, which further leads to the degeneration of the synapses. We identified CG17187, an Hsp40 type-C family protein, as a regulator of synaptic structure and eye morphogenesis. CG17187 is an ortholog of yeast Cwc23, involved in the spliceosome disassembly, and is essential for survival in yeast and *Drosophila*. Furthermore, we have also shown that dCwc23 genetically interacts with the RRM-containing ALS (amyotrophic lateral sclerosis) prone proteins, such as Fus (*Drosophila* Caz) and TDP-43 (*Drosophila* TBPH). Importantly, deletion of a single copy of *dcwc23* results in the dissolution of the Fus/TDP43 aggregates in the neuronal nuclei, but surprisingly leads to early lethality, suggesting that the increased availability of soluble Fus/TDP-43 may enhance its mislocalization to the cytoplasm, where it forms toxic aggregates. We therefore propose that dCwc23 functions as an essential chaperone in *Drosophila*, promoting the dissolution of nuclear TDP-43 aggregates but, in doing so, increasing the pool of soluble TDP-43 that can mislocalize to the cytoplasm, ultimately enhancing its toxicity.

P063

Dissecting Role of Nucleoporins in Autophagy of Drosophila larval fat body

Lisupriya Baral[1], Jyotsna Kawadkar[1], Samir Merabet[2], Ram Kumar Mishra[1]

[1]*Indian Institute of Science Education and Research, Bhopal;* [2]*Institute Genomics Functional De Lyon, ENS Lyon*

Autophagy is a conserved process that maintains cellular homeostasis by recycling the degraded proteins and organelles of the cell. It also plays a crucial role in the metamorphosis of Drosophila larvae into pupae by degrading old larval tissues, such as fat body, salivary glands,etc. Prior research has demonstrated that during the larval feeding phase, nuclear Hox proteins inhibit autophagy. When the larvae enter the wandering stage, repression is removed by the transport of Hox protein out of the nucleus, which initiates the formation of autophagosomes with the help of the Atg family of proteins.

Nucleocytoplasmic transport and nuclear integrity are crucial for regulating autophagy, therefore our study aims to investigate the role of nucleoporins in autophagy. Utilizing Drosophila genetics, namely the UAS-GAL4 and FLP-FRT systems, we conducted the knockdown of nucleoporins and generated mosaic clones, subsequently employing fluorescence microscopy based cell-visualization to evaluate autophagic activity in each instance. We evaluated all nucleoporins of the Nup107 complex to assess their role in autophagy. Interestingly, RNAi-mediated knockdown of Nup43, Nup107, and Seh1 led to the development of ectopic autophagosome vesicles during the feeding phase. Nonetheless, the depletion of Nup43 resulted in a substantial accumulation of autophagosomes during the feeding and wandering phases of larvae, suggesting a regulatory function in the initiation of autophagy. Our study further examines whether the regulation of nucleoporins on autophagy adheres to the conventional Hox-dependent pathway or a distinct Hox-independent pathway. The present investigation indicates that autophagy may be regulated by nucleoporins, thereby establishing a new research domain.

P064

Ribose-induced advanced glycation end products reduce the lifespan in *Drosophila melanogaster* by changing the redox state and down-regulating the *Sirtuin* genes

Lokanath Mishra[1], Monalisa Mishra[1]

[1]*Neural Developmental Biology Lab, Department of Life Science, NIT Rourkela, Rourkela, 769008, India.*

Advanced Glycation End (AGE) products are one such factor that accumulates during aging and age-related diseases. However, the mechanisms by which exogenous AGE compounds contribute to aging are an area that requires further exploration. Specifically, how an organ undergoes aging and aging-related phenomena that need further investigation. The intestine is the most exposed area to food substances. The impact of AGEs on the intestine in relation to aging requires further exploration. *Drosophila melanogaster*, a well-established model organism, was utilized to elucidate the mechanisms of aging and age-related phenomena. In this study, we fed Ribose-induced Advanced Glycation End-products (Rib-AGE) to *D. melanogaster* to investigate the aging mechanism. A series of changes was found in Rib-AGE-fed flies. Reactive oxygen species (ROS) and nitric oxide species (NOs) were higher in the Rib-AGE-fed flies, and the antioxidant level was lower. The intestinal permeability was altered. The microorganism load was higher inside the gut. The structural arrangement of the gut's microfilament was found to be damaged, and the nuclear shape was found to be irregular. Cell death within the gut was elevated in comparison to the control. The food intake was found to be reduced. The relative mRNA expression of the *Sirtuin 2* and *Sirtuin 6* genes of *D. melanogaster* was downregulated in Rib-AGE-fed flies compared to the control. All these findings strongly suggest that Rib-AGE accelerates aging and age-related disorders in *D. melanogaster*.

P065

Mechanistic Insights into Oxaliplatin-Induced Neurotoxicity: Role of Oxidative Stress, Apoptosis, and Neurobehavioral Impairments in *Drosophila melanogaster*

Lopamudra Mishra[1], Monalisa Mishra[1]

[1]*Neural Developmental Biology Lab, Department of Life Sciences*
National Institute of Technology, Rourkela, Odisha, India,769008

Cancer is a major global health burden and the second leading cause of death worldwide. The notable increase in life expectancy rates can be attributed to recent advancements in adjuvant antineoplastic therapy. Oxaliplatin is a widely used platinum-based drug for colorectal cancer treatment. However, long-term use of these medications is associated with neurotoxicity, which is regarded as one of the side effects that limits dosage. *Drosophila melanogaster* is an ideal model organism due to its short generation time, low maintenance costs, and well-characterized genome and is extensively employed to investigate neurological disorders, DNA damage, oxidative stress, and apoptosis-like mechanisms are analogous to mammalian systems. We aimed to examine the toxic effects of Oxaliplatin on *Drosophila* model in larva and adult. Behavioral alterations, developmental cycle, and biochemical changes were monitored. In adult flies, there was pharmacological toxicity by platinum-DNA adduct formation, gut cytoskeletal disruptions, and DNA damage. Reactive Oxygen Species accumulation and apoptosis were identified in the adult flies' gut and brain. In case of *Drosophila* larva, oxidative stress in the brain imaginal disc and gut was accompanied by abnormalities in their crawling, righting, and cold tolerance behaviors. Dysregulated mRNA levels of antioxidant genes and apoptotic genes was found according to age. Our results strive to understand the thorough toxicity of Oxaliplatin not described in earlier studies.

P066

Uncovering the role of *VAPB* in lipid homeostasis and its implications in a *Drosophila* model of ALS

Lovleen Garg[1], Kriti Chaplot[1], Shweta Tendulkar[1], Siddhesh Kamat[1], Girish Ratnaparkhi[1]

[1]*Indian Institute of Science Education and Research (IISER) Pune, Maharashtra, India, 411008.*

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease marked by motor neuron loss leading to gradual paralysis and death within 2-5 years post-diagnosis. 10% of ALS cases are familial, with ~18 independent genetic loci implicated in the onset of the disease. VAMP Associated Protein B (*VAPB/VAP*) is the 8th ALS locus discovered, with the VAP^{P56S} mutation being the predominant variant. An orthologous mutation VAP^{P58S} is used in *Drosophila* to study ALS8 pathogenesis.

VAP is a single-pass, ER-based, cytoplasmic-facing, transmembrane protein implicated in critical functions at the intracellular membrane contact sites (MCS) niche. Earlier we showed VAP^{P58S} flies develops normally; however, adult animals exhibit a shortened lifespan and age-dependent progressive motor dysfunction. In the adult VAP^{P58S} brain, we observe mutant protein inclusions, ER stress and increased inflammation. Expression of VAP^{WT} can rescue all disease phenotypes. As *VAP* interacts with a number of lipid transfer proteins, we investigated lipid dysbiosis in the VAP^{P58S} brain using a combination of lipid mass spectrometry and genetic analysis. We observed an age dependent accumulation of ceramides and cholesterol esters, accompanied by a concomitant decrease in cholesterol, all of which can be rescued by VAP^{WT}. Modulating *VAP* in glia perturbs lipid droplet (LD) homeostasis of the brain which is also affected in *ALS8* mutant. Removing mutant copy from the glia of adult brain leads to increase in LD density and also significantly delays the motor defects. On the other hand, lowering ceramide levels in the neurons at the adult stage of *ALS8* flies delays the motor defects reinforcing the role of lipids in the progression of ALS.

Our study highlights the importance of *VAP* in lipid homeostasis of the brain and give new insights on its role in LD regulation. Further studies can help understand the precise role of *VAP* in the glial LD homeostasis.

P067

Y-Box proteins as conserved regulators of microRNA biogenesis

Majid Ali[1], Aman Gill[1], Amit Kumar[1], Geetanjali Chawla[1]

[1]*RNA Biology Laboratory, Department of Life Sciences, Shiv Nadar Institution of Eminence, Greater Noida, Uttar Pradesh.*

Aberrant microRNA (miRNA) expression has been implicated in numerous age-associated disorders, including diabetes and cancer. Such dysregulation often arises from alterations in miRNA processing or activity. RNA-binding proteins (RBPs) are central to controlling miRNA biogenesis and function in response to various cellular cues.

The *Drosophila let-7-Complex* locus encodes three evolutionarily conserved and differentially regulated miRNAs—miR-100, let-7, and miR-125. Previous work from our laboratory has demonstrated that cis-regulatory elements, such as terminal loops and stem-base regions, contribute to the differential expression of these polycistronic miRNAs. Here, we characterize *Ypsilon schachtel* (Yps), an RNA-binding protein identified through proteomic screening as a terminal-loop binding factor for all three *let-7-Complex* precursor miRNAs. Yps and its vertebrate homolog YB-1 are multifunctional RBPs containing a conserved cold shock domain, which facilitates interactions with both RNA and DNA and mediates roles in stress adaptation and disease.

Given the established involvement of *let-7-Complex* miRNAs in aging, we investigated the role of Yps in lifespan regulation. Neuronal overexpression of Yps extended lifespan in female flies, whereas neuronal knockdown reduced lifespan in both sexes, indicating an essential role in neuronal maintenance and aging. Reducing one copy of *Yps* significantly shortened lifespan, implicating a dose-dependent effect on aging. Notably, neuronal knockdown of Yps elevated levels of let-7, suggesting that Yps may influence aging by modulating miRNA-mediated regulatory pathways.

We validated Yps–RNA interactions through gel shift assays and miRNA northern blotting, and are currently investigating whether Yps differentially affects the processing kinetics of *let-7-Complex* miRNAs. Taken together, our findings reveal Yps as a conserved regulator that integrates miRNA biogenesis with lifespan control in *Drosophila*.

P068

Impact of altered Immune-Metabolic repartee in Circulating Plasmatocytes in Huntington's Disease Progression

Mansi Yadav[1], Debalina Chatterjee[1], Jassika Gupta[1], Namita Agrawal[1]

[1]*Department of Zoology, University of Delhi, New Delhi - 110007, India*

Huntington's Disease (HD) is a fatal, inherited neurodegenerative disorder caused by CAG repeat expansion in the *HTT* gene, leading to mutant huntingtin protein accumulation. In HD, the central nervous system has been the traditional focus, however, emerging evidence highlights involvement of peripheral system—particularly immune and metabolic pathways—in disease onset and progression. In the present study, we have explored the crosstalk between peripheral immunity and metabolism in HD using transgenic *Drosophila* model expressing human mutant *HTTex1pQ93* under a neuron-specific GAL4 driver.

Our investigations throughout the disease to evaluate functional and molecular alterations in peripheral immune cells (plasmatocytes) revealed dynamic fluctuations in circulating plasmatocytes number during HD progression, particularly an increase in small-cell populations at advanced stage of the disease. Monitoring ROS showed a transient oxidative burst highest at day 7 post-eclosion, implicating early immune activation, followed by a sharp decline suggestive of mitochondrial dysfunction. Phagocytosis assay, a measure of immune cell function demonstrated consistent decline in HD flies, pointing towards an early and sustained innate immune impairment. Furthermore, lipid accumulation analysis using Nile Red staining indicated metabolic dysfunction within plasmatocytes, hinting at a disrupted immuno-metabolic balance.

These findings support the hypothesis that peripheral immune dysfunction is closely linked to metabolic irregularities and may represent an early manifestation of HD pathology. By delineating the temporal dynamics of immune and metabolic dysregulation in HD, our study provides mechanistic insights into how peripheral alterations might contribute to systemic disease progression, thereby opening new avenues for therapeutic targeting beyond the brain.

P069

Upregulation of PI3K/Akt signalling suppresses Myotonic Dystrophy 1 in the Drosophila model

Dipti Chakraborty[1], Naorem Tarundas Singh[1], **Mayanglambam Dhruba Singh[1]**

[1]BRIC-National Brain Research Centre, Gurgaon, Haryana, India

Myotonic Dystrophy Type 1 (DM1) is a progressive disorder characterized by muscle weakness and Myotonia. It affects several parts of the body, including skeletal muscles, smooth muscle, the heart, and the central nervous system, specifically the brain. The prevalence of DM1 is approximately 9 per 100,000 Individuals. The DM1 is caused by the expansion of CTG repeats in the 3' UTR of the Myotonic Dystrophy Protein Kinase (DMPK) gene. Abnormal repeats, ranging from 37 to thousands, have been observed in DM1 patients. The expanded CUG repeats transcribed from the mutant DMPK gene forms RNA foci that sequester RNA-binding proteins, including Muscleblind-like protein (MBNL), CUG-BP, and ETR-3-like factors (CELF). These RNA-binding proteins play a crucial role in splicing, and their depletion leads to misregulation of alternate splicing, resulting in different protein isoforms. For example, mis-splicing leads to the formation of the non-muscle isoform of the Insulin receptor (InR), which has reduced insulin signalling and metabolic responses. In our study, we screened the downstream pathway genes of the insulin signalling pathway. We expressed the Drosophila DM1 model, which contains 270 CTG repeats, in a tissue-specific manner. We observed that upregulation of the PI3K/Akt signalling pathway could significantly improve the DM1 phenotypes. We focused on the Drosophila *diminutive* (dMyc) gene. We observed that dMyc expression significantly improves the DM1 phenotype in both eye and muscle tissues. dMyc significantly enhanced the longevity and motor ability of the DM1 flies. Furthermore, we observed a significant reduction in autophagy and cell death in the Drosophila thoracic muscle. Our study highlights the potential application of dMyc modulation in DM1 therapeutics.

P070

Fuelling the Bloodline: Insulin-Dependent Glycolysis Sustains Hemocyte Progenitors' Proliferation in *Drosophila*

Md Kaizer, Akshara Babu, Kaustuv Ghosh, Sudip Mandal, Lolitika Mandal

Developmental Genetics Laboratory, Indian Institute of Science Education and Research Mohali, Punjab, India

The *Drosophila* larval lymph gland harbors hemocyte progenitors that transition from a proliferative to a differentiation-competent state as it ages. In late third instar progenitors, we observe G_2/M arrest accompanied by an essential reliance on fatty acid β-oxidation

(FAO) for differentiation. However, the metabolic mechanisms underlying the rapid proliferation of early-stage progenitors have been insufficiently addressed – until now. Using pharmacological and molecular genetic tools, we uncover that insulin signaling is instrumental in orchestrating the development of hematopoietic progenitors in *Drosophila* by regulating their metabolic state. In the early stages, insulin signaling actively promotes glycolysis-driven proliferation while suppressing the ROS-JNK-FAO pathway to prevent quiescence. As insulin signaling wanes in later stages, there is a deliberate shift toward FAO, leading to progenitor arrest and enabling their differentiation. Further, we demonstrate that the burst of proliferation observed in early progenitors results from a dual regulatory action of insulin signaling. On one hand, insulin signaling pulls the strings of glycolysis to sustain rapid proliferation. At the same time, it restrains the activation of FOXO, a transcription factor that ordinarily suppresses proliferation, by inhibiting its nuclear entry.
This research has far-reaching implications, paving new avenues to investigate how progenitor metabolism adapts to immune challenges during development.

P071

Human poly(Q) mediated neurotoxicity alters the global metabolic status in Drosophila disease models

Meenu Mor, Surajit Sarkar

University of Delhi

Human polyglutamine [poly(Q)] disorders, such as Huntington's disease, Spinocerebellar ataxias, and Spinal and Bulbar Muscular Atrophy, are a group of age-onset neurodegenerative diseases characterized by abnormal expansion of CAG trinucleotide repeats within the coding regions of their respective genes. This expansion results in proteins with an aberrantly extended glutamine tract, leading to their misfolding. The aggregation and progressive accumulation of these misfolded proteins as neurotoxic inclusion bodies in brain cells is a hallmark of poly(Q) pathology. These inclusion bodies migrate through various cytoplasmic compartments and eventually reach the nucleus, triggering multiple pathogenic processes including mitochondrial dysfunction, reactive oxygen species (ROS) generation, transcriptional dysregulation, and apoptosis. We have utilized Drosophila disease models to investigate whether the expression of pathogenic human poly(Q) causes significant global metabolic changes. We observed a major alteration in the metabolic profile associated with pathogenic poly(Q) expression. Our preliminary observations further suggest that restoring the altered metabolic state alleviates poly(Q)-mediated neurotoxicity in these models. These findings provide valuable insights into metabolic dysregulation in poly(Q) diseases and highlight a promising future approach for treatment.

P072

Adaptation to elevated temperature increases lifespan in fruit flies

Mousumee Das[1], Prabhu Kaibalya Das[1], Rabi Sankar Pal[1], Bodhisatta Nandy[1]

[1]*Indian Institute of Science Education and Research Berhampur, Odisha, 760003*

Concern over the long-term survival of various species with the rising average global temperature is real. Organisms are expected to adapt to the elevated temperature or become extinct over time. How thermal selection can shape adaptation is thus key to understanding the changing biodiversity in response to climate change. Here, we use laboratory-adapted populations of *Drosophila melanogaster* to investigate thermal adaptation. Four replicate populations were subjected to maintenance at higher ambient temperature. As the first set of investigations, we measured the divergence in key life history and fitness components. Experimentally evolved females (i.e., higher-temperature females) were found to have evolved increased early-life reproductive output, especially at high temperature - clearly indicating adaptation. Interestingly, high-temperature flies evolved longer mean lifespan regardless of temperature in which they are reared. Other life-history traits - egg-to-adult development time, and egg-to-adult survivorship showed no effect of selection indicating that the primary adaptive evolution in adult traits. While increased lifespan and reproductive output may appear counterintuitive, life-time reproduction remains to be measured for a more complete test of the life history theory.

P073

A screen to identify the role of novel microRNAs in the Drosophila prothoracic gland

Muhammed Naseem K[1], Nithin K A[1], Jervis Fernandes[1], Jishy Varghese

[1]*Indian Institute of Science Education and Research Thiruvananthapuram*

The prothoracic gland, an endocrine organ responsible for producing the molting hormone ecdysone, plays a critical role in insect larvae's growth and developmental transitions. Coordinated growth and development of the prothoracic gland and the timely release of ecdysone are essential for ensuring proper organismal development. Various external signaling factors, along with intrinsic factors, are known to regulate both the growth of the prothoracic gland and the release of ecdysone. Among the intrinsic factors, microRNAs (miRNAs), i.e., 21-23 nucleotide-long short noncoding RNAs, that regulate the expression of their target mRNAs could play a crucial role in the prothoracic gland. Thus, we conducted a microRNA (miRNA) knock-out screen and identified several miRNAs that cause delays in development. Target prediction analyses suggest that these miRNAs may

be involved in regulating various downstream signaling cascades and the growth of the prothoracic gland, with further investigation being carried out to confirm these findings.

P074

Kayaking the neuroinflammatory storm: Insights from a *Drosophila* ALS8 model

Namrata Pramod Kulkarni[1], Pulkit Goel[1], Amarendranath Soory[1], Girish Ratnaparkhi[1]

[1]*Indian Institute of Science Education and Research, Pune*

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by progressive loss of motor function. A Proline to Serine point mutation in vesicle-associated membrane protein-associated protein B (VAPB/ALS8) causes ALS in humans. We have developed an equivalent *Drosophila* model (VAP^{P58S}) using CRISPR/Cas9 gene-editing. VAP^{P58S} flies show progressive motor deficits and a short lifespan (~50%).
The adult VAP^{P58S} brain exhibits age-dependent neuroinflammation, as measured by whole-transcriptome quantitative mRNA sequencing. We have identified the Janus Kinase (JNK) transcription factor, Kayak (dFos), as a novel modulator of neuroinflammation. Overexpression of Kayak in glia reduces inflammation and, concomitantly, improves motor function. In contrast, knockdown of glial Kayak accelerates age-dependent deterioration of motor function and enhances inflammation. Overexpression of a dominant-active variant, $Kayak^{K357R}$, in glia, also improves motor function and reduces inflammation. Our study underscores the roles of glial-modulated brain inflammation in dictating the progression of ALS. We also identify Kayak as a major regulator of inflammation in disease.

P075

Neuromodulatory Control of Metabolic Homeostasis by miR-100 in *Drosophila melanogaster*

Nandana Rajeev Nair[1], Bhavya Binoy[1], Reshma V Menon[1], Jishy Varghese[1]

[1]*Indian Institute of Science Education and Research, Thiruvananthapuram, Kerala - 695551*

MicroRNAs (miRNAs) are short, single-stranded, non-coding fragments of RNA that function as post-transcriptional gene expression regulators. They play a pivotal role in modulating essential cellular processes such as cell division, development, differentiation, apoptosis, inflammation, and response to viral infections. In particular, miRNA-mediated metabolic fine-tuning is important to maintain energy homeostasis and overall health of the organism. In this study, we investigate miR-100, a microRNA conserved across

bilaterians, with a focus on its role in the neuromodulation of stress-dependent metabolic changes. In *Drosophila melanogaster*, miR-100 is encoded within the polycistronic let-7 complex and has been implicated in cancer and immune regulation in mammalian systems. Through tissue-specific screening, we observed that pan-neuronal downregulation of miR-100 enhances stress resistance. Further experiments revealed that reduced miR-100 expression leads to altered metabolic profiles. Our findings reveal a previously uncharacterized role for miR-100 in neuromodulatory regulation of metabolism under stress, providing new insights into the post-transcriptional control of stress-related metabolic adaptations.

P076

A gut-brain axis for aversive interoception drives innate and anticipatory emesis in *Drosophila*.

Rashmi Karunakaran[1, 2] , Prerana Choudhary[1, 2, #] , **Neena Baburaj**[1, 3], Meghna Sawant[1], Zeyu Chang[4], Meet Zandawala[4, 5], and Gaurav Das[1, 2, 3*]

[1]*Brain and Feeding Behaviour Laboratory, National Centre for Cell Science, S.P. Pune University Campus, Ganeshkhind, Pune 411007, India*
[2]*Savitribai Phule Pune University, Ganeshkhind, Pune 411007, India*
[#]*Current address: Department of Neurobiology, Harvard Medical School, Boston, MA 02115, USA*
[3]*Regional Centre for Biotechnology, Faridabad*
[4]*University of Nevada, Reno, Reno, NV, USA*
[5]*University of Würzburg, Würzburg, Germany*

Signals from the gut are increasingly recognized as modulators of brain function and behavior. However, the pathways through which the gut conveys adverse or unpleasant information to the brain are still not well understood. In this study, we identify an aversive gut-brain axis in *Drosophila melanogaster* that detects toxin-induced gut damage and triggers both innate and learned anticipatory emesis (vomiting). After toxin ingestion, reactive oxygen species are produced by midgut enterocytes and detected by the transient receptor potential channel TrpA1 on nearby enteroendocrine cells. This sensing stimulates the release of neuropeptides from enteroendocrine cells, likely representing the gastric malaise flies experience after eating. We show that these neuropeptides act on specific serotonergic and dopaminergic neurons in the brain. These neurons interact with each other and signal to the downstream memory-related mushroom bodies to promote emesis. This circuit not only drives an immediate emetic response but also represents a malaise-driven aversive signal. The signal manifests as the persistent activity of dopaminergic neurons, which reinforces aversive valence to odor cues in the mushroom bodies. Thus, the flies learn that a specific odor predicts the presence of a toxin in food and exhibit anticipatory emesis upon re-exposure to the same odor. Taken together, we have identified an interoceptive signaling pathway that may be conserved for detecting harmful gut conditions and for remembering how to avoid them. Our work offers a mechanistic

framework for studying aversive gut-brain communication involved in feeding, metabolism, depression, brain injury, and neurodegenerative diseases.

P077

Delayed neuronal senescence in *Drosophila melanogaster* selected for faster development and extended longevity

Neha Rauhila[1], Abhishek Kumar Farand[1], Abhishek Yadav[1], Surbhi Yadav[1], Mallikarjun Shakarad[1,*]

[1]*Evolutionary Biology Laboratory, Department of Zoology, University of Delhi, Delhi-110007*

A well-formed organism is quintessential for a healthy life and maximizing Darwinian fitness. A robust nervous system is the centrepiece of a well-formed organism as effective motor neuronal control is essential for survival and reproductive success. However, the gradual decline in motor activity with age is a well-established relationship that is observed across several taxa. All iteroparous and long-lived organisms are required to maintain robust motor neurons throughout their lifespan in order to maximize fitness. We used *Drosophila melanogaster* populations that are under simultaneous selection for faster pre-adult development and extended longevity (FLJs) and their ancestral controls (JBs) to assess motor neuron function across different ages. Age specific climbing activity and flight behaviour were assessed as proxy of motor neurons health. Our results show that FLJs maintain higher locomotor activity in late life compared to control populations, without reducing locomotor activity in early ages. These findings suggest improved maintenance or delayed degeneration of motor neuron system in FLJs, indicating an overall enhanced neuronal health, which may contribute to their extended longevity.

P078

Tau maintains epithelial architecture by coupling cytoskeletal stability with endocytic regulation of Notch signaling

Tiwari, Neha[1]; Tapadia, Madhu*

[1*]*Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005*

Using the Drosophila Malpighian tubule as a model system, we investigated how Tau contributes to epithelial morphogenesis and signalling. Loss of Tau led to striking morphological abnormalities, including cystic dilations, shortened tubules, and disrupted cell arrangement, underscoring its essential role in maintaining epithelial architecture. High-resolution mass spectrometry–based proteomic profiling of Tau knockout (KO) and wild-type tubules revealed widespread molecular alterations. Cytoskeletal regulators such

as MAP205, Jupiter, Comb over, and Myofilin were significantly downregulated, while actin modulator Rho1 was upregulated, indicating disrupted cytoskeletal homeostasis. Notably, the endocytic adaptor Liquid facets (Lqf)—crucial for Notch receptor internalization and activation—was also reduced in Tau KO, suggesting impaired endocytic trafficking. Functional enrichment and STRING analyses highlighted affected pathways related to cytoskeletal organization, vesicle transport, and signal transduction. Consistent with these findings, Notch signalling activity was markedly reduced in Tau-deficient tubules, as evidenced by decreased Notch intracellular domain (NICD) staining and lower transcript and protein levels. Together, our results identify Tau as a key coordinator of cytoskeletal stability and endocytic machinery, essential for sustaining Notch signalling and epithelial morphogenesis. These findings uncover a previously unrecognized, non-neuronal role of Tau in maintaining epithelial tissue organization.

P079

Targeting Neurodegeneration: Plumbagin as a Protective Agent in *Drosophila* Alzheimer's Models

Nikhil Raj S[1], Parvathy Venugopal[1], Rajaguru Aradhya[1], Chinchu Bose[1], Bipin Nair[1]

[1]*Amrita School of Biotechnology, Amrita Vishwa Vidyapeetham, Kollam*

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by amyloid-beta (Aβ) aggregation, tau pathology, oxidative stress, and progressive cognitive decline. This study investigates the neuroprotective effects of plumbagin in *Drosophila melanogaster* models expressing human Aβ42 in neuronal tissues and tau in eye tissues. Transgenic flies treated with plumbagin exhibited significant improvements in locomotor activity, extended lifespan, and reduced reactive oxygen species (ROS) levels compared to untreated controls. Thioflavin T staining revealed decreased amyloid and tau aggregation in plumbagin-treated flies. The nail polish imprint technique demonstrated preserved neuronal structural integrity. These findings suggest that plumbagin confers neuroprotection in both Aβ42- and tau-mediated AD models by mitigating oxidative stress, preserving neuronal function, and limiting protein aggregation. This study highlights plumbagin as a promising candidate for further mechanistic investigations and potential therapeutic development in Alzheimer's disease.

P080

Nup133 Orchaestrates Nuclear Pore Integrity and Notch-Dependent Muscle Development in *Drosophila*

Nikita Sharma[1], Ishita Jagtap[1] and Ram Kumar Mishra[1]

[1]Department of Biological Sciences, Indian Institute of Science Education and Research Bhopal, Madhya Pradesh, India.

A multitude of nucleoporins (Nups) come together to assemble the nuclear pore complex (NPC), which mediates vital nucleocytoplasmic transport processes. Recent advances in NPC biology have linked several Nups to diverse cellular functions including gene regulation, signaling, and development, underscoring their importance in cellular homeostasis and organismal growth. Recent studies have implicated several nucleoporins in the regulation of myogenesis, neuronal development, chromatin organization, transcriptional control, and signal transduction, revealing novel functions beyond their traditional transport roles. Disruptions in these tightly coordinated events result in structural and functional abnormalities.

Recent studies have linked nucleoporins to myogenesis and differentiation. Nup210 is required for myoblast formation, Nup358 depletion disrupts myotube development, and Nup133, a Y-complex component within the NPC, influences neuronal differentiation in mice.

To investigate the functional role of Nup133, we have used the *Drosophila melanogaster* model and generated a null-mutant using CRISPR-cas9. Expectedly, Nup133 null mutants exhibited early developmental arrest and failed to progress beyond the larval stages, indicating the essentiality of Nup133 for viability. We therefore utilized ubiquitous and tissue-specific RNAi-mediated depletion to assess its functional requirement. Nup133-depleted flies showed defective thoracic muscle patterning and pupal lethality due to eclosion failure. Further, loss of Nup133 impaired the incorporation and stability of Y-complex Nups, suggesting its broader role in maintaining NPC integrity. Reduced Nup133 levels also led to mislocalization of Delta and Cut, key proteins in the Notch signaling pathway involved in muscle progenitor specification.

Together, our findings establish that Nup133 is essential for myoblast differentiation, functioning of signaling pathways, and myogenesis that dictate muscle patterning and growth.

P081

Elucidating the role of Gprk2 in *Drosophila* ovarian nurse cell death

Partha Protim Karmakar[1], Mohit Prasad[1]

[1]*Indian Institute of Science Education and Research- Kolkata, Campus Rd, Mohanpur, Haringhata Farm, West Bengal 741246.*

To maintain overall tissue homeostasis, undesired, superfluous or damaged cells must be eliminated. Phagoptosis is a programmed tissue homeostasis mechanism observed in metazoans. In this process, viable cells display "eat me" signals and are subsequently engulfed and destroyed by phagocytes. Though phagoptosis is commonly observed in different metazoan contexts, the underlying mechanism is not very well understood. We are using the Drosophila ovary model to examine how, in the later stages of oogenesis (stages 11 to 14), somatic anterior follicular epithelial cells phagoptose and clear unwanted germline nurse cells. Here, we report that downregulation of G-protein-coupled receptor kinase 2 (Gprk2) in anterior follicle cells inhibits the removal of nurse cell (NC) in late stages of oogenesis. The migration of anterior follicle cells between NC-NC junctions, the envelopment of underlying NCs by these cells, and subsequent acidification assist in the nuclear degradation of nurse cell nuclei. Our results indicate that engulfment receptor Draper acts downstream of Gprk2. We have also used live imaging of late-stage egg chambers to uncover that Gprk2-depleted stretched follicle cells exhibit defects in the clearance of NC nuclei. Further, we observed that Gprk2-depleted stretch follicle cells are unable to promote the permeabilisation of germline NC nuclei. Since overexpression of lysosomal cathepsin L1 (CP1) in the stretch follicle cells rescues the NC clearance defect associated with Gprk2 depletion, it suggests that Gprk2 functions through CP1 to mediate efficient NC removal in late-stage egg chambers. The results from the above will be presented.

P082

DANCE of solitary flies: supervised machine learning and low-cost hardware for high-throughput genetic and neural screens.

R Sai Prathap Yadav[1], Paulami Dey[1], Faizah Ansari[1], Tanvi Kottat[1], P Pallavi Prabhu[1], Manohar Vasam[1], Shrinivas Ayyangar[1], Swathi Bhaskar S[1], Krishnananda Prabhu[2], Monalisa Ghosh[1], **Pavan Agrawal**[1]

[1]Centre for Molecular Neurosciences, Kasturba Medical College, Manipal; Manipal Academy of Higher Education, Udupi, 576104, India.
[2]Department of Biochemistry, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Udupi, 576104, India.

Social isolation profoundly affects mental health and behavior, as highlighted during recent global lockdowns. We model social isolation in *Drosophila melanogaster*, which, similar to mammals, shows disrupted sleep and increased aggression when isolated.
To probe the neuronal basis of these changes, we developed DANCE (Drosophila Aggression and Courtship Evaluator), a high-throughput, cost-effective platform that pairs supervised machine-learning classifiers (trained using JAABA) with an easy-to-assemble behaioral rig. Our setup uses easily sourced parts and low-cost Android smartphone cameras, bringing the cost to under ₹30 per arena, in stark contrast to commercial systems priced above ₹3 lakh. DANCE classifiers outperform existing methods and enable large-scale genetic and neural screens in resource-limited labs. Using DANCE we implicated aminergic neurons in regulating isolation driven aggression. These assays demonstrate how environmental stressors produce behavioral changes through specific neuronal and molecular mechanisms. By pairing inexpensive consumer hardware with frugal machine-learning tools, DANCE makes mechanistic behavioral neuroscience more accessible.

P083

Crosstalk between PolyP and DYRK1A in regulating blood clotting

Payal Agarwal[1], Sunayana Sarkar[1], Harsha Sharma[1], Manish Jaiswal[1]

[1]Tata Institute of Fundamental Research, Hyderabad.

Inorganic polyphosphates (PolyP) are a chain of orthophosphates linked together by the phosphoanhydride bond. Recent studies have associated PolyP with various physiological processes like immunity, blood clotting, neurodegeneration, stress survival, etc. A recent study identified that PolyP can bind to DYRK1A, a well-known neuronal kinase implicated in Down Syndrome. DYRK1A overexpression reduces platelet count and bleeding time in mice, while its inhibition enhances megakaryocyte maturation, suggesting its broader role in hematopoiesis and immunity. In this work, we hypothesized that PolyP and DYRK1A

interaction may regulate blood clotting. We tested this hypothesis in flies by manipulating minibrain (Mnb), which is a homolog of DYRK1A. Interestingly, *mnb* mutants show enhanced clot fibre formation and low levels of PolyP in hemocytes. In contrast, *mnb* overexpression shows a reduction in clot fibers and an increase in PolyP levels within hemocytes. These observations highlight a potential PolyP-dependent regulatory mechanism and provide a foundation to explore its relevance in DYRK1A/Mnb-associated clotting disorders.

P084

Experimental evolution of spontaneous dispersal in fruit flies

Prabhu Kaibalya Das[1], Mousumee Das[1], Rabi Sankar Pal[1], Bodhisatta Nandy[1]

[1]*Indian Institute of Science Education Research Berhampur, Odisha, 760003*

In spatially structured habitats, animals often disperse between neighbouring habitat patches, without being driven by a dire situation necessitating movement. Such spontaneous dispersal is typically exploratory in nature, and may allow animals to assess nearby habitable patches, exploit ephemeral resources, escape antagonistic mates or other ecological enemies. Female-biased spontaneous dispersal tendency is well-characterised in the laboratory populations of *Drosophila melanogaster*. Yet it is not known if this trait is heritable, and if yes, to what extent a population harbours genetic variation in this trait. We addressed both these questions by subjecting four replicate populations of *D. melanogaster* to experimental selection for increased spontaneous dispersal. In experimental populations, individuals that showed spontaneous dispersal in a two-patch setup were allowed to constitute the breeding cohort. Such screening was done every generation, allowing selection on dispersal traits. All the replicate populations responded to the selection after five generations, showing a significant increase in dispersal tendency (proportion of individuals dispersed within a fixed time window). After ten generations, we found a clear sign of stronger response in males than in females. These results clearly indicate a non-zero heritability of spontaneous dispersal in these populations.

P085

Prolonged exposure to Tetracycline Hydrochloride delays the developmental cycle and alters the expression of lipid transporter vps 13 in *Drosophila melanogaster*

Priyatama Behera[1], Monalisa Mishra[1]

Neural Developmental Biology Lab, Department of Life Science, National Institute of Technology Rourkela, Rourkela – 769008, Odisha, India

Antibiotics are frequently found in the environment in high amounts due to their widespread use in medicine, fishing, and animal husbandry. The role of antibiotics has significantly expanded in the post-COVID-19 era, with improper waste disposal contributing to the persistence of these compounds as environmental pollutants. Among different antibiotics, tetracycline (TC) has emerged as a major environmental contaminant. The toxicity of TC exposure to humans and animals is a growing concern, as the indiscriminate use of antibiotics promotes bacterial resistance through genetic mutations. However, little is known about the broader environmental and health impacts of TC. To investigate the toxicological effects of TC, we employed *Drosophila melanogaster* as a model organism. Our study revealed that long-term exposure to TC delayed the larval-to-pupal transition by approximately two days**,** likely due to a reduction in 20-hydroxyecdysone levels. Furthermore, TC exposure decreased female fecundity**,** resulting in fewer offspring. TC also increased body weight by elevating glucose levels and inducing lipid droplet accumulation. In addition, TC exposure altered the lipid transporter gene vps13 expression and reduced locomotor activity in both larvae and adults in an age-dependent manner**.** Our in-silico analysis demonstrated that TC binds to the Vps13 protein with a binding energy of −6.4, stronger than lipid binding (−4.2). To our knowledge, this is the first study to report that prolonged TC exposure promotes lipid droplet accumulation through the upregulation of *vps13* expression in *Drosophila melanogaster*.

P086

Oxidative Stress–Driven Retinal Neurotoxicity in *Drosophila melanogaster*: Insights into Glial-Like Cell Involvement

Puja Karmakar[1], Janmejaya Bag[1], Seekha Naik[1], Monalisa Mishra[1].

[1] *Department of Life Science, Neurodevelopment Biology Lab, NIT Rourkela, Rourkela, 769008*
[*]*Corresponding Author: mishramo@nitrkl.ac.in, monalisam@nitrkl.ac.in*

Oxidative stress plays a key role in neurotoxicity and retinal degeneration, but the early responses of glial-like cells remain unclear. Using *Drosophila melanogaster*, we investigated how cobalt chloride ($CoCl_2$)-induced oxidative imbalance affects retinal

development and neuron–support cell interactions. $CoCl_2$ exposure reduced pupal yield and caused cellular degeneration in eye-imaginal discs, along with cytoskeletal fragmentation in glial-like retinal regions. Treated flies showed impaired locomotion, phototaxis, and survivability, accompanied by elevated oxidative load and altered redox homeostasis. Molecular analyses revealed activation of stress-response pathways linked to protection and repair. These findings position *Drosophila* as a valuable model for studying redox-driven glia–neuron interactions and the cellular basis of oxidative retinopathy.

P087

Mutations in antimicrobial peptides differently affect sleep and plasticity

Rahul Kumar[1], Gokul Madhav[1,3], Priyanka Balasubramanian[1], Rhea Lakhiani[1], Mugdha Joshi[2], Vibhu Jaggi[2,4], Anushna Pal[1,2,5], Imroze Khan[1] and Krishna Melnattur[1,2]

[1] Department of Biology, Trivedi School of Biosciences, Ashoka University, Sonepat, India
[2] Department of Psychology, Ashoka University, Sonepat, India
[3] Department of Developmental Biology, RWTH Aachen University, Germany
[4] Department of Philosophy. Ashoka University, Sonepat, India
[5] Sloan Program of Health Administration, Jeb E. Brooks School of Public Policy, Cornell University, Ithaca, NY, USA

Sleep and immunity are closely linked. Sleep loss is associated with decreased immunity, whereas activating the immune system increases sleep. Sleep loss also impacts learning and memory. In *Drosophila*, infection stimulates the systemic release of a battery of anti-microbial peptides (AMPs). These fly immune effectors have been understudied as sleep modulators. We have been studying flies carrying mutations in anti-microbial peptides (AMPs) to understand the link between sleep and immunity. We find that AMP mutants sleep less. Different AMP knockouts cause sex-specific sleep perturbations, with males and females exhibiting distinct patterns of daytime and nighttime sleep. Group C mutant flies, combined mutant for the anti-fungal peptides Metchinikowin (Mtk) and Drosomycin (Drs), showed the greatest impairments. These Group C mutants also showed an exaggerated sleep rebound. Sleep rebound was unaltered in other mutants. Different sets of AMP mutants exhibited specific disruptions in socialization and rocking-induced sleep. These data are a detailed characterization of sleep regulation in AMP mutants. We also evaluated sleep functions. Group C mutants uniquely exhibited normal learning and memory, and lower synapse abundance, despite sleeping the least. Group C mutants are thus able to carry out some sleep functions without sleeping much. Glial knockdown of Metchnikowin and Drosomycin mimicked the sleep phenotypes of the null mutants, indicating that these genes act via glia. Sleep and memory defects in AMP mutants were found to be reversible, and enhancing sleep of short-sleeping Bomanin mutants pharmacologically or behaviourally improved learning and memory. Together, these data suggest that AMPs are potent sleep modulators and that different classes of AMPs differently affect sleep and sleep-dependent outcomes.

P088

Role of Rer1 in UPR-mediated cell survival in coordination with autophagy

Rajni Kumari, Shruti Umarvaish, Varun Chaudhary

Indian Institute of Science Education and Research, Bhopal, Madhya Pradesh

Cell competition is a tissue surveillance mechanism in which the loser cells get eliminated by the winner cells in a heterotypic population. Maintenance of proper protein homeostasis is essential for healthy cellular physiology Mammalian cells and tissues respond to chemical and physical stress by inducing mechanisms that are either adaptive or protective, thereby enhancing their survival potential. Autophagy is one such conserved pathway essential in maintaining homeostasis and promoting cell survival in different conditions such as protein aggregate induced stress and ER stress. Our previous work has demonstrated that an endoplasmic reticulum (ER) resident protein Rer1 is essential for protein homeostasis and competitive cell survival. We have further observed that loss of *rer1* results in increased autolysosomal load without directly effecting autophagic route. It is only when there is disruption in the UPR mediated PERK-Atf4 axis which results in accumulation of autophagic cargo p62 (Ref2P in *Drosophila*) thereby disrupting autophagy. This highlights the importance of coordinated signaling between UPR and autophagy. However, the role of PERK and autophagy whether cytoprotective or maladaptive requires requires further investigation. Further, the involvement of other parallel ER-stress responsive pathways under conditions of loss of *rer1* such as ERAD and ER-Phagy can be insightful in understanding the signaling crosstalks.

P089

InR/Akt signaling regulates the cortex glia cell cycle in the *Drosophila v*entral nerve cord

Ramkrishna Mishra[1], Richa Arya[1]

[1]*Cytogenetics laboraty, Department of Zoology, Institute of Science,Banaras Hindu University, Varanasi, India-221005*
Correspondence: mishraramkrishna2@gmail.com, aryaricha@bhu.ac.in

Cortex glia (CG) in the *Drosophila* CNS primarily provide trophic support, acting as a niche for all neural stem cells and their progeny neurons. To do this, the nuclei of CG become hyperploid, and the cells transform into syncytium, creating a honeycomb-like cellular architecture around neural cells. Earlier studies have shown that CG nuclear division and growth depend on Htl and InR signaling; however, the exact mechanism by which these signals regulate cortex glia development remains unknown. These signals are

also linked to the regulation of G1/S and G2/M transitions in various tissues. We investigated the role of InR/Akt signaling in controlling the hyperploidy and cellular complexity of CG in the thoracic and abdominal regions of the ventral nerve cord (tVNC and aVNC, respectively). Knocking down InR, PI3K, and Akt limited the formation of syncytial CG in tVNC and also reduced their cellular complexity compared to controls at the LL3 larval stage. Additionally, knockdown of PI3K and Akt decreased the DNA content in CG in both tVNC and aVNC, indicating that InR/Akt signaling is necessary for CG to become hyperploid. Overexpression of the constitutively active form of these transducers restricted nuclear division but increased DNA content in tVNC CG, further supporting their role in promoting hyperploidy. Studies on aVNC are ongoing. Overall, these findings suggest that InR/Akt signaling plays a crucial role in regulating hyperploidy and syncytium formation of CG in the developing VNC. Additional research continues to explore the detailed functions of various growth signaling pathways and their interactions in CG development.

P090

Nup43 is indispensable for fertility and regulates sperm individualization-related events during Drosophila spermatogenesis

Jyotsna Kawadkar[1], Ashley S. Hermon, Rohit Kumar[1], **Ram Kumar Mishra[1]**

1 Indian Institute of Science Education and Research (IISER) Bhopal, Bhopal, Madhya Pradesh
2 International Max Planck Research Schools (IMPRS), Munster, Germany

Nuclear pores allow bidirectional nucleo-cytoplasmic transport of biomolecules. Constituent members of nuclear pores called nucleoporins (Nup) are assembled into sub-complexes located at different faces of the nuclear pores. Nup-mediated nucleo-cytoplasmic transport is integral to carrying out homeostatic functions by a cell. The Nup107-160 complex is symmetrically located on both sides of the nuclear membrane and mediates mRNA export. Different members of the Nup107-160 complex are known to bind to active chromatin regions, regulate transcription, localize to the kinetochore, and assist in cell division. Accordingly, loss-of-function mutants of several Nups exhibit embryonic lethality. We have reported that Nup107, an integral member of the Nup107-160 complex, is crucial for metamorphic transformation in *Drosophila melanogaster*. A loss-of-function mutation in human Nup43 is associated with premature ovarian insufficiency.

Here, we report the importance of Nup43 in *Drosophila* fertility and spermatogenesis. Although the Nup43 null mutants have normal nuclear pore morphology and function and survive till adulthood, both males and females are sterile. The spermatogenesis in Nup43 null mutants proceeds normally but is halted at the early canoe stage of development, affecting sperm individualization, resulting in empty seminal vesicles. Expression of the Nup43 transgene in a germline-specific manner rescues these spermatogenesis defects. While the mandatory histone to protamine exchange in developing sperm is unaffected, the

Nup43 mutants fail to assemble the actin and myosin-rich cone required for sperm individualization. The stagnation of spermatogenesis at the early canoe stage is rescued, but only partially, by the expression of Jar (Myosin VI ortholog) in the Nup43 null background.

We propose that Nup43 is required for the proper assembly of the actin-myosin-rich individualization complex, thus affecting spermatogenesis and fertility in *Drosophila*.

P091

Multi-targeted Phytotherapeutic Approach for Friedreich's Ataxia using a *Drosophila* Model.

Ravi Kant Yadav[1], Dipesh Talukdar[1], Vikas Kumar[2], Anami Ahuja[2], Vishnu Swarup[2], Achal Srivastava[2] and Prachi Yadav[1]*

[1]*ICAR-Indian Agricultural Research Institute, New Delhi*
[2]*All India Institute of Medical Sciences (AIIMS), New Delhi*

Friedreich's ataxia (FRDA) is a progressive neurodegenerative disorder caused by frataxin deficiency, leading to mitochondrial dysfunction, oxidative stress, and impaired locomotor activity. The multifactorial nature of Friedreich's ataxia (FRDA) pathophysiology has stalled the development of effective therapeutic interventions that can stop or reverse the disease's progression. Hence, there is an urgent need to identify new therapeutic targets. The *Drosophila melanogaster* model of FRDA offers a powerful genetic system to dissect the molecular mechanisms of the disease and evaluate potential therapeutics.
We are trying to utilize the potential of medicinal herbs and their phytochemicals in FRDA pathophysiology simultaneously targeting various aspects of FRDA, such as dysregulated mitochondrial iron homeostasis, oxidative stress, and Nrf2 signalling. In this study, we employ both larval and adult *Drosophila* FRDA models to study the beneficial effects of medicinal herbs and their phytochemicals on behavioral and physiological phenotypes associated with mitochondrial dysfunction.

P092

Impact of DRP1-Mediated Mitochondrial Dynamics on Dietary Regulation of Ovarian Stem Cells in *Drosophila melanogaster*

Yoshita Sriramkumar[1], **Rhea Wali[1]**, Kasturi Mitra[1*]

[1] Department of Biology, Trivedi School of Biological Sciences, Ashoka University, New Delhi (NCR), India
**Corresponding author: Kasturi Mitra*

Cellular metabolism, tuned by its mitochondrial state, regulates stem cell function. This organelle, through its processes of fission and fusion, affects stem cell maintenance, proliferation and differentiation. As an adaptation to changing dietary conditions, the mitochondria provides the plasticity to a cell to meet the altering metabolic demands. Previous studies from our lab indicate that repression of Drp1(Dynamin-related protein 1), a major fission regulator, has been implicated in mitochondria primed stem cell state that enhances its self-renewal ability. The complete downregulation of this protein also disrupts the cell cycle and causes excessive proliferation of the ovarian epithelial layer. Additional factors such as nutrient availability can further cause morphological changes that affect stem cell functionality. Building on the lab's prior expertise on ovarian stem cell model, we aim to investigate how mitochondrial structure proteins regulate stem cell behaviour in ovarian development. Our preliminary findings using egg laying assays and lineage tracing tools indicate that protein rich diet creates distinct patterns of follicle and germline stem cell behaviour. We further wish to test how high sugar and specific amino acids using a defined diet influence stem cell functionality in the context of altered mitochondrial dynamics. Further, utilising confocal and ex vivo microscopy, we want to understand how these altered mitochondrial dynamics impact its redox state under various dietary modulations. By elucidating the mechanisms underlying these interactions, we can gain valuable insights into how nutrition impacts stem cell behaviour and function, which has implications in cancer and other metabolic disorders.

P093

Effects of Sleep Modulation on Alcohol Addiction and Associated Life History Traits in *Drosophila melanogaster*

Rishita

Indian Institute of Science Education and Research, Mohali, Punjab

This study investigates the effect of sleep quality modulation (enhancement vs deprivation) on alcohol addiction susceptibility and associated life history traits in *Drosophila melanogaster*. While existing literature suggests a strong link between sleep deprivation

and increased vulnerability to addictive substances, the role of sleep quality enhancement in mitigating alcohol addiction remains poorly defined. We utilized the Canton-S strain of *D. melanogaster* to assess developmental time, egg-to-adult viability, and adult morphology. Flies were divided into six experimental groups receiving either control food or alcohol-containing food, paired with three sleep conditions: normal sleep, enhanced sleep, or deprived sleep. After five days of exposure, addiction was quantified using a Y-maze and a two-choice preference test. The findings indicate that sleep modulation significantly impacts susceptibility to alcohol addiction, with specific effects observed on the number of addicted flies across the different sleep conditions. Furthermore, the study provides quantified baseline data on the influence of alcohol and sleep on developmental metrics and adult body size. These results elucidate the regulatory role of sleep quality in the development of substance use disorders and suggest potential behavioural interventions for reducing addiction vulnerability.

P094

Macrophage metabolic reprogramming during dietary stress influences adult body size in Drosophila

Anusree Mahanta, **Sajad Ahmad Najar**, Nivedita Hariharan, Ajit Bhowmick, Syed Iqra Rizvi, Manisha Goyal, Preethi Parupalli, Ramaswamy Subraman, Angela Giangrande, Dasaradhi Palakodeti and Tina Mukherjee

*[1] Institute for Stem Cell Science and Regenerative Medicine (inStem), GKVK post, Bellary Road, Bangalore 560065, India. a The Shanmugha Arts, Science, Technology & Research Academy (SASTRA), Thanjavur, Tamil Nadu 613401, India. b The University of Trans Disciplinary Health Sciences & Technology (TDU), Bengaluru, Karnataka, 560064, India. [2] Department of Biological Sciences, University of Texas, Dallas, USA. [3] Department of Biological Science, Purdue University, West Lafayette, Indiana, USA. [4] Bindley Biosciences Centre, Purdue University, West Lafayette, Indiana, USA. [5] Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg, France. # Co first authors. * Co corresponding authors*.

Immune cells are increasingly recognized as nutrient sensors; however, their developmental role in regulating growth under homeostasis or dietary stress remains elusive. Here, we show that Drosophila larval macrophages, in response to excessive dietary sugar (HSD), reprogram their metabolic state by activating glycolysis, thereby enhancing TCA-cycle flux, and increasing lipogenesis—while concurrently maintaining a lipolytic state. Although this immune-metabolic configuration correlates with growth retardation under HSD, our genetic analyses reveal that enhanced lipogenesis supports growth, whereas glycolysis and lipolysis are growth-inhibitory. Notably, promoting immune-driven lipogenesis offsets early growth inhibition in imaginal discs caused by glycolytic and lipolytic immune-metabolic states. Our findings reveal a model of immune-metabolic imbalance, where growth-suppressive states (glycolysis, lipolysis) dominate over a growth-supportive lipogenic state, thereby impairing early organ size control and ultimately affecting adult size. Overall, this study provides important insights into dietary

stress-induced immune-metabolic reprogramming and its link to organ size regulation and early developmental plasticity.

P095

G4C2-mediated transsynaptic signaling regulates cytoskeleton organization in *Drosophila*

Srikanth Pippadpally[1], **Sakshi Dunakhe**[1], Athulya T Gopi[1], Vimlesh Kumar[1]

[1]*Department of Biological Sciences, IISER Bhopal*

Intronic GGGGCC (G4C2) hexanucleotide repeat expansions (HRE) in the C9orf72 gene are one of the primary causes of amyotrophic lateral sclerosis and frontotemporal dementia. These repeats range from 2 to 30 units in the normal physiological state, whereas a pathogenic expression constitutes several hundred to several thousand repeats. Prior studies have shown that defective organelle trafficking in neurons is a key feature of the repeat expansion pathologies; however, the underlying mechanisms are elusive. In this study, we aim to investigate the effect of HREs on the cytoskeletal organization through a *Drosophila* model of G4C2 repeat expansion. Our results suggest that the actin and microtubule cytoskeletons are hyperstabilized without affecting their monomer levels in the repeat expansion pathologies. Intriguingly, we also found that neuronal expression of these repeats showed defective network formation in muscle, suggesting a transsynaptic cytoskeletal effect. Further analysis revealed an involvement of BMP signaling in HRE pathologies. Our data indicate that HRE causes hyper-stabilization of the microtubule cytoskeleton both in cell-autonomous and cell-non-autonomous manners, possibly leading to organelle transport defects in neurons.

P096

Analysis of *Spodoptera frugiperda* sialotranscriptome and protein interaction studies for the identification of effector candidates and their cognate plant partners

Sakshi Pandey[1], Sundaram Shilpi[2], Jayendra Nath Shukla[1]

[1]*Central University of Rajasthan*

Pest insects release oral secretions while feeding on plants. This oral secretion contains effector proteins that help them to suppress the plant's defence system and successfully infest the host. *Spodoptera frugiperda* is a devastating pest affecting more than 300 crop species. However, little is known about the effector candidates produced by this insect.

To identify *S. frugiperda* effector candidates, the salivary transcriptome of its larvae reared on an artificial diet, as well as those fed on Tomato plants, was generated. A reference-based analysis was performed. This led to the identification of several upregulated genes in the salivary glands of tomato-plant diet induced larvae, compared to artificial diet-fed larvae. Using an in-silico secretome prediction pipeline, we identified which of these upregulated genes code for secretory proteins.
We hypothesized that these upregulated secretory proteins might act as effector proteins of *S. frugiperda*. Hence, to identify their possible plant targets, in-*silico* protein-protein interaction studies were conducted between the putative effectors of *S. frugiperda* and immune pathway proteins of tomato plant using Alphapulldown. It is python package that predicts protein-protein interactions and models protein complexes using AlphaFold-Multimer, enabling fast screening of interaction partners.
This computational approach helped identify potential interactions between *S. frugiperda* effectors and tomato defence proteins. These findings provide valuable insights into how this pest manipulates its host plants and lay the foundation for developing targeted strategies to disrupt pest–plant interactions and enhanced crop protection.

P097

Deciphering the role of high sugar diet–induced metabolic alterations in fat cells in the maintenance of ovarian germline stem cells in Drosophila.

Gunjan Chauhan[1], **Sameeksha Verma**[1], Akanksha Singh[1], Lolitika Mandal[12] and Sudip Mandal[1]

[1]Molecular Cell and Developmental Laboratory, Indian Institute of Science Education and Research Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli, PO 140306, Punjab. India
[12]Developmental Genetics Laboratory, Indian Institute of Science Education and Research Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli, PO 140306, Punjab. India

The diet of an organism significantly impacts tissue homeostasis and health in mammals. Numerous studies have demonstrated the negative effects of a high-calorie diet on various organs, leading to obesity, metabolic dysfunction, oxidative stress, and inflammation. These systemic consequences disrupt overall metabolism and impair the homeostasis of Adult Stem Cells (ASCs). The Drosophila ovarian germline stem cell (GSC) system has emerged as an excellent model for understanding how systemic, metabolic, and environmental factors regulate the maintenance of ASCs. Our research shows that a high sugar diet (HSD) affects the maintenance of ovarian GSCs, causing these cells to become unresponsive to niche-derived *Dpp* signaling. Systemic metabolic analyses revealed that flies fed an HSD exhibit key features of type 2 diabetes, including hyperglycemia, hyperinsulinemia, and hyperlipidemia. Specifically, the fat cells in HSD-fed flies show reduced sugar uptake, compromised glycolytic flux, and increased lipid metabolism. Notably, high dietary sugar activates ROS-dependent JNK signaling, which promotes fatty acid oxidation (FAO) in the fat cells. Most intriguingly, the activation of the ROS-JNK-FAO pathway in the fat cells of HSD-fed flies is responsible for the loss of GSC

maintenance. Genetic manipulations targeting components of this pathway can rescue the loss of GSCs. The molecular genetic basis of this mechanism will be discussed. Thus, our study reveals the complex interplay between diet, metabolism, and stem cell maintenance, highlighting how the altered metabolic landscape of fat cells can influence adult stem cells in a distant tissue.

P098

Developmental Spontaneous Neuronal Activity Alterations and its Connection with Autism Spectrum Disorder: Insights from the *Drosophila* Model

Sarani Dey[1], Sharba Bandyopadhyay[2] and Abhijit Das[1]

[1]*Department of Bioscience and Biotechnology, Indian Institute of Technology Kharagpur, West Bengal, India*
[2]*Department of Electronics and Communications Engineering, Indian Institute of Technology Kharagpur, West Bengal, India*

Developmental *spontaneous neuronal activity* is required to establish precise synaptic connectivity during neuronal development. Any disruption of this activity hampers the maturation of synapses. We hypothesize that a disruption of spontaneous activity in developing neurons might have role in the origin of neurodevelopmental disorders like Autism Spectrum Disorder (ASD). In *Drosophila,* the maturation of adult neurons generally takes place during the pupal stage with unique spontaneous neuronal activity (SNA) signature. In this study, we spatio-temporally silenced and enhanced the pupal SNA patterns by optogenetic and thermogenetic tools in the dopaminergic neuronal subset and assessed the behavioural impact in adult flies. We found behavioural anomalies in these flies that are akin to the ASD symptoms in humans. We compared these phenotypes with two existing ASD models namely *Fragile-X Mental Retardation* (*FMR*) gene mutant model and Valproic acid (VPA) drug feeding model. We found that both these *Drosophila* ASD models showed increased repetitive behaviour and decreased social interaction and courtship preference along with altered aggressive behaviour, phenocopying activity-manipulated flies.

We took a bioinformatic approach to find the potential activity-responsive genes connecting the SNA with transcriptional regulation in developing neurons. We identified ASD-associated gene *Mef2* as one of the Activity Regulated Genes (ARG), knockdown of which mimicked the behavioral alterations of activity-manipulation. Changing the developmental SNA has been observed to change the expression level of Mef2, indicating a connection between developmental SNA and Mef2 expression. Finally, two-photon microscopy-based calcium imaging shows SNA defects in *dfmr1* mutant, VPA-pupae and *Mef2* knockdown models, confirming the contribution of developmental spontaneous activity with the origin of Autism-like behavioral anomalies.

P099

The mechanism behind the therapeutic role of Alpha-tocopherol in mitigating hypobaric hypoxia-induced eye defect in *Drosophila melanogaster*

Seekha Naik[1], Smruti Sudha Biswal[1], Monalisa Mishra[1*]

Neural Developmental Biology Lab, Department of Life Science, NIT Rourkela, Rourkela, Odisha 769008, India

Hypoxia, or low oxygen levels, is linked to several pathological disorders, including retinopathies. Retina, being a metabolically active tissue, low oxygen levels resulted in retinal degradation. The developmental perspective of hypobaric hypoxia-induced eye development remains elusive. Drosophila is used as our model organism to investigate the impact of hypobaric hypoxia on eye development and Alpha-tocopherol as a potential inhibitor. To induce the hypoxic condition, we exposed the Drosophila to hypobaric pressure(120mbar). Hypoxia induces eye defects in different developmental stages of Drosophila as revealed by histological staining. Biochemical estimation disclosed the presence of reactive oxygen species (ROS) during hypoxia, which led to cellular injury and DNA damage. Quantitative PCR reveals the upregulation of *Puf*, *Wge,* and *Twr* genes and the downregulation of *Rh1* and *Rh6* involved in eye development. All these defects are brought back to normal levels after treatment with Alpha-tocopherol. This research provides a foundation for understanding ocular developmental problems caused due to oxygen deprivation and Alpha-tocopherol as a crucial therapeutic approach to the treatment of hypobaric hypoxia.

P100

Optimization of a High-sugar Diet Induced Model of Parkinson's Disease in *Drosophila melanogaster*

Shiva Chaudhary[1], PR Deepa[1], and Meghana Tare[1]

[1]*Biochemistry and Enzymology Lab, Department of Biological Sciences, Birla Institute of Technology and Sciences, Pilani, Pilani Campus, Rajasthan, 333031*

Parkinson's disease (PD) is a multifactorial neurodegenerative disorder characterized by the aggregation of pathogenic proteins leading to neuronal cell death. PD is further categorized as sporadic, where the onset of PD is attributed to exposure to certain environmental toxins, and familial, where the PD is induced due to inheritable genetic factors. Some symptoms of PD include, restless tremor, bradykinesia, cognitive impairment, and gut dysbiosis. In addition to genetic and sporadic forms, metabolic dysfunction has emerged as a potential contributor to PD onset and progression. Recently, it has been reported that obesity and other metabolic conditions may lead to increased risk

of developing PD and exacerbate its symptoms, causing early PD onset and progression. To investigate molecular links between metabolic stress and PD, we utilized *Drosophila melanogaster* exposed to high-sugar diets of various sucrose concentrations and compared the phenotypes of these flies to those in a rotenone-induced sporadic model of PD. These phenotypes include, affected overall survival, locomotory defects, and reduced body weight. A decrease in overall survival was observed in both sugar- and rotenone-induced models compared to control. Further, to assess the locomotory dysfunction which ensue in PD these flies were subjected to rapid iterative negative geotaxis assay, which showed that high sugar-induced model showed locomotory defects similar to those observed in the rotenone-induced model. An age-related reduction of body weight in both sugar- and rotenone-induced models was also observed. The optimum sugar concentration for a high-sugar induced PD model was identified as the dietary sugar concentration that most closely recapitulated rotenone-induced PD-like phenotypes. These findings suggest that metabolic stress induced by high-sugar diets can elicit PD-like phenotypes providing a tractable model for dissecting the interplay between insulin resistance and neurodegeneration.

P0101

Drosophila melanogaster tackles gastro-oral infections by stimulating pathogen expulsion

Shreya Verma[1], Sushovan Bhattacharyya[1], Meghana Tare[1], Sandhya Amol Marathe[1]

[1]*Department of Biological Sciences, Birla Institute of Technology and Science, Rajasthan, 333031*

A coordinated set of antimicrobial defenses acts to counteract the invading bacteria, with some variations depending on the entry route into the host. In our study, we tracked the dynamics of Enterobacteriaceae pathogens, *Salmonella enterica* subspecies *enterica* serovar Typhimurium*, Klebsiella pneumoniae,* and *Enterobacter cloacae* in *Drosophila melanogaster* using a natural mode of oral infection. Notably, most bacterial species were cleared effectively within 48 hours post-infection (hpi), except for *E. cloacae*, which persisted within the fly up to 72 hpi. Despite the bacterial persistence in the flies, we did not observe any significant mortality in the infected flies, indicating robust infection control. At four hpi, a substantial increase in the production of reactive oxygen species (ROS) was observed, followed by a decrease at 24 hpi and a resurgence at 48 hpi. This suggests that ROS plays an important role in bacterial clearance. However, flies lacking the dual oxidase (*duox*) gene showed unchanged survival rates, suggesting ROS alone is not enough for infection control. In line with previous reports, we observed expulsion of these pathogens from the fly gut. We further show that the ROS-sensing receptor, TRPA1, which triggers intestinal contractions, was induced in flies infected with *S.* Typhimurium and *E. cloacae.* Thus, the shedding of these bacterial species could be attributed to increased *TRPA1* expression. Our findings reveal that the host can distinguish and respond to various bacterial species in a well-synchronized, gut-localized, and pathogen-specific

manner. This also illustrates the reliability of natural infection route models in unravelling and understanding the complexities of host-pathogen interaction.

P102

Understanding cellular and molecular mechanisms involved in onset and progression of Parkinson's Disease

Shreyas Iyer, Sonia Narwal, Shiva Chaudhary, Meghana Tare

Birla Institute of Technology and Science Pilani, Pilani, Rajasthan 333031

Parkinson's disease (PD) is a prevalent neurodegenerative condition involving the loss of neurons because of protein aggregation, resulting in impaired motor and cognitive abilities. PD majorly occurs due to genetic alteration; referred to as genetic PD or it can be acquired during life, referred to as sporadic PD. PD is usually characterized by loss of dopaminergic neurons resulting in motor disabilities. In our lab, we use both genetic and sporadic models to understand the cellular and molecular mechanisms involved in onset and progression of PD. We are employing *Drosophila melanogaster* as a model organism to understand the cellular, genetic and molecular basis of PD. At cellular level, we have identified that PD affects mitochondrial morphology of dopaminergic neurons in the genetic models of PD in flies in spatio-temporal fashion.
Compounds like Rotenone have been found to cause toxicity by inhibiting cellular events and causing neuronal death. Rotenone feeding has been shown to cause neuronal death and has been used in mimicking sporadic form of PD. We have developed a novel model by feeding rotenone mixed with food, that mimics PD phenotypes. Interestingly, different strains of wild-type flies respond differentially to rotenone exposure. Furthermore, we have identified that flies respond in context to biological gender to the rotenone. Our data indicates that specific genders and populations may exhibit differential sensitivity for PD onset and progression, which is *in-sync* with the global population studies for PD. However, mechanistic insights are required to elucidate the mechanisms involved to cause this biased behaviour in the progression of PD.

P103

Divergent Roles of *Drosophila* Orthologs of Sis1 in Mitigating Tauopathies

Tanvi Saksena[1], **Shruti Tyagi[1]**, Priyabrata Sarangi[1], Parth Chaddha [1], Chandan Sahi[1], Vimlesh kumar[1]

[1] *Department of Biological Sciences, IISER Bhopal*.

Molecular chaperones act as a frontline defense system during neurodegenerative diseases such as Tauopathies and ALS (amyotrophic lateral sclerosis) by assisting in the mitigation of toxic aggregations. Although it is the most abundant protein family among the HSP families, Hsp40s are underappreciated for their roles in the modulation of neuronal pathophysiology. The Hsp40 family plays a critical role in protein quality control by cooperating with HSP70 through its conserved J-domain. Independent of their structural similarity, individual Hsp40s often exhibit distinct cellular functions in diverse neurological conditions. To explore this diversity, we aimed to investigate the structural and functional variability between the *Drosophila* orthologs of the yeast Sis1 protein: CG5001, CG12020, Droj1, and CG2887. Co-expression of these orthologs along with hTau in *Drosophila* eyes revealed variable interaction of these orthologs with the hTau despite their structural conservation. For instance, CG5001 was found to enhance the Tau toxicity and exacerbate the rough eye phenotype and increase the percentage of degenerated area in both hTauWT and hTauV337M backgrounds, while CG2887 failed to suppress tau-induced phenotypes, even though they show similar identity to Yeast Sis1. In support of this, both CG5001 and CG12020, unlike Droj1, failed to complement the Sis1 loss-of-function phenotype in yeast and exhibited a slow-growth defect. These results suggest that evolutionary conservation of Hsp40 family proteins does not comply with their functional conservation, and may have additionally acquired newer functions in the higher organisms.

P104

Investigating the role of Rer1 in the maintenance of protein homeostasis and Myc-driven overgrowth in developing *Drosophila* wing epithelium

Shruti Umarvaish [1], Pranab Kumar Paul [1], Shivani Bajaj [1], Rishana Farin S [1], Hrudya Mohan [1], Wim Annaert [2], Varun Chaudhary [1]

[1] *Cell and developmental signaling laboratory, Department of Biological Sciences, Indian Institute of Science Education and Research Bhopal, Bhopal, Madhya Pradesh, India.*
[2] *Laboratory for Membrane Trafficking, VIB-Center for Brain and Disease Research, KU Leuven, Leuven, Belgium, and Department of Neurosciences, KU Leuven, Gasthuisberg, Leuven, Belgium.*

The precise maintenance of tissue homeostasis is essential for the development of a healthy multicellular organism. To protect the growing tissues from harbouring unfit or aberrant cells, multicellular organisms have evolved various tissue-intrinsic mechanisms, one of which is known as "cell competition". In this process, cells with reduced fitness acquire the loser status and are eliminated by the fitter(winner) neighboring cells via contact-dependent cell-cell interactions. In this study, we have explored the role of an ER and cis-Golgi localized protein known as Retention in the endoplasmic reticulum 1 (Rer1) in the competitive survival of the developing *Drosophila* wing epithelial cells. We demonstrate that the loss of Rer1 induces proteotoxic stress, activating the PERK pathway. This activation increases phosphorylated eIF2α levels, which causes cytotoxicity and the elimination of mutant cells by their neighboring normal cells.
Interestingly, proteotoxic stress is also observed in super-competitor cells such as Myc overexpressing cells, which proliferate at the expense of neighboring wild-type cells. Thus, Myc-driven overgrowth relies on the activation of cytoprotective unfolded protein response (UPR) pathways. Furthermore, we find that Rer1 levels are upregulated in response to Myc overexpression, and this increase in Rer1 provides cytoprotection to Myc-overexpressing cells, thereby supporting their overgrowth. These findings uncover a dynamic interplay between Myc, Rer1, and the unfolded protein response (UPR), highlighting how developing tissues harness stress-response pathways not only to maintain protein homeostasis but also to shape competitive cell behaviors that determine cellular fitness and tissue composition.

P105

Ataxin-2 mediated regulation of Zfh1 and its role in neuronal development and maintenance in *Drosophila melanogaster*

Shweta Tandon[1], Shiva Kumar[1], Omkar Koppaka[1], Baskar Bakthavachalu[1]

[1] *School of Biosciences and Bioengineering, Indian Institute of Technology Mandi, Himachal Pradesh.*

Ataxin-2, an evolutionarily conserved RNA Binding Protein (RBP), plays important roles in nervous system development, regulation of circadian rhythm and behaviour. It is associated with polyribosomes and stress granules, where it regulates translation. Mutations in Ataxin-2 lead to neurodegenerative diseases like Spinocerebellar ataxia 2 and Amyotrophic lateral sclerosis. Therefore, understanding the molecular functions of Ataxin-2 is essential to elucidate its physiological function and understand its role in neurodegenerative disorders.
Search for mRNA targets of Ataxin-2 using TRIBE (Targets of RNA Binding proteins Identified By Editing) technique identified *zfh1* mRNA as a strongly interacting target in the *Drosophila* S2 cells. Zfh1 or Zinc finger homeodomain 1 (homologous to mammalian ZEB1/2), is a transcription factor expressed in stem cell precursors across various tissues. It plays a critical role in the normal development of brain and muscles.
To verify the *in vivo* interaction between Ataxin-2 and *zfh1* mRNA in *Drosophila*, we are employing the modified TRIBE technique by conducting cell type specific Gal4 screens to identify the precise brain cell types.
Our study aims to understand the physiological significance of Ataxin-2 interaction with *zfh1* mRNA and elucidate its regulatory mechanism in *Drosophila*. Our results show that modulating Ataxin-2 expression in cell type specific manner in the CNS, impacts Zfh1 expression resulting in morphological defects in the third instar larvae. Our ongoing studies aim to understand mechanism of this regulation and its consequences on the behaviour of the organism.

P106

Transgenerational Immune Priming in *Drosophila melanogaster*

Simran, Tsering Choton

Indian Institute of Science Education and Research, Mohali, Punjab

Transgenerational immune priming (TGIP) describes the phenomenon where parental immune experience shapes offspring immunity, despite the absence of classical adaptive memory in invertebrates. In this study, we examined TGIP in the BRB baseline population of *Drosophila melanogaster* using a fully factorial parental-priming design. Parents (F_0)

were subjected to four treatments using heat-killed *Enterococcus faecalis* (Ef): (1) both sexes primed, (2) only females primed, (3) only males primed, and (4) unprimed controls. Offspring (F_1) were collected at three post-infection time points—24 h, 48 h, and 96 h—to capture temporal effects. All F_1 flies were then challenged with live *E. faecalis* (OD 2.8), and survivorship, larval crystal cell number, and adult fecundity were quantified.
Our results reveal significant time-dependent variation in survivorship across the three collection points, whereas differences among the four parental treatments were minimal, suggesting a limited or transient TGIP effect under the tested conditions. Fecundity also showed time-dependent fluctuations, indicating that parental immune experience or offspring developmental timing may influence reproductive output. Crystal cell counts varied across time points but did not differ consistently across treatments.
Overall, this study provides a detailed temporal evaluation of TGIP in Drosophila, highlighting the importance of developmental timing in shaping immune and fitness outcomes across generations.

P107

Molecular Insights into Prip Aquaporin–Mediated Hydrogen Peroxide Transport during the Innate Immune Response

Soumyadip Sarkar, Sveta Chakrabarti

Manipal Institute of Regenerative Medicine (MIRM),
Manipal Academy of Higher Education, Bengaluru Campus, 560065

Innate immunity forms the first line of defense against pathogens through rapid, nonspecific responses. Reactive oxygen species (ROS) play a central role in this process, acting not only as antimicrobial agents but also as signaling molecules that regulate immune pathways, such as NF-κB (Hong et al., 2024) and MAPK (Son et al., 2010). In *Drosophila melanogaster*, ROS activates the Toll pathway to induce the production of antimicrobial peptides and coordinate hemocyte migration to infection or injury sites (Chakrabarti & Visweswariah, 2020). Aquaporins have been reported to transport hydrogen peroxide, in addition to their traditional role in facilitating the transport of water molecules. The Drosophila aquaporin Prip, a primarily water-selective channel, has been reported to transport hydrogen peroxide (H_2O_2), thereby linking aquaporin function to immune signaling in Drosophila (Chakrabarti & Visweswariah, 2020). However, the mechanistic basis of this hydrogen peroxide transport and its impact on the downstream immune pathways remains unexplored. This study aims to (1) elucidate the selectivity of Prip aquaporin for water and H_2O_2, (2) assess the functionality of mutants of Prip proteins lacking H_2O_2 transport through *in vitro* assays in S2 cells, and (3) investigate the *in vivo* role of Prip-mediated ROS signalling during immune activation in Drosophila. Understanding Prip's dual transport function will provide insight into how aquaporins regulate oxidative signalling during innate immune response. These findings could have

broad implications for ROS-associated disorders and immune dysregulation in higher organisms.
Our preliminary findings show that Prip is predominantly expressed in hemocytes, the female ovary, and the Malpighian tubules. It has also been observed that Aquaporins are highly expressed in the post-egg-laying period, particularly in the early hours of egg development, and also increase before pupal eclosion in late-stage pupae. Hemocytes, which are known for their involvement in the immune response. Ongoing molecular dynamics simulations aim to elucidate the structural basis of Prip selectivity towards water and H_2O_2, while *in vivo* RNAi-mediated knockdown of Prip in hemocytes is being used to evaluate its role during ROS-dependent immune responses. Current experiments involve lifespan analysis in the knockdown group compared to the control group, and assessing fly survival following injury to the thoracic muscle using a tungsten needle.
Together, these approaches will establish whether Prip-mediated ROS transport influences immune activation and organismal resilience to injury. The findings are expected to provide new insights into the role of aquaporins in oxidative signaling and innate immunity, with implications extending to ROS-associated pathologies in higher organisms.

P108

Silent Side Effects: How Chronic ACEI Usage Shapes Blood and Immunity

Suman Kumar Singh[1], Devki Devi[1], Lolitika Mandal[1]

Developmental Genetics Laboratory, Department of Biological Sciences, Indian Institute of Science Education and Research Mohali (IISER Mohali), Knowledge City, Sector 81, Manauli PO 140306, INDIA

Hypertension, or high blood pressure, is one of the most common health issues worldwide and can lead to diseases affecting the heart, kidneys, leading to physiological complications. Managing hypertension typically requires long-term medication, with one of the most commonly prescribed options being angiotensin-converting enzyme inhibitors (ACEi). However, some studies suggest that these medications may adversely affect blood cell homeostasis.
My research utilizes the fat body and blood cells of Drosophila, along with human stem and progenitors cells (HSPCs), to explore the underlying mechanisms of this adverse effect. We discovered that prolonged use of ACE inhibitors accelerates blood cell differentiation and heightens the immune response in Drosophila. Interestingly, this same phenomenon is observed in hematopoietic stem and progenitor cells (HSPCs) cultured in the presence of ACE inhibitors. Both model systems indicate that this sustained hyperactivity in the immune response can be detrimental to physiological functioning of blood cells affecting both pathogen clearance and the production of antimicrobial peptides.

Overall, our findings suggest that long-term use of ACE inhibitors may unintentionally compromise the immune system, which could be harmful to patients whose blood pressure is otherwise well-controlled with these medications.

P109

Understanding the role of developmental diet in shaping metabolic outcomes and reproductive fitness of *Drosophila melanogaster*

Sunil Choudhary[1], Himanshu Bhatt[1], N.G. Prasad[1]

Evolutionary biology Laboratory, Indian Institute of Science Education and Research, Mohali (IISER Mohali), Sector 81, SAS Nagar, Manauli, PO 140306, Punjab. India

Diet has been a major evolutionary force shaping human metabolism and adaptation to environmental conditions. The relationship between early-life nutrition and adult physiology provides crucial insights into the origins of modern metabolic diseases, particularly obesity. Nutritional status during developmental stages can program long-term changes in metabolism, organ function, and energy regulation, thereby influencing susceptibility to obesity and related disorders. *Drosophila melanogaster*, with its well-characterized genetics and conserved metabolic pathways, serves as an excellent model to investigate how developmental diet influences adult physiology and obesity-related traits. In this study, we examined the impact of dietary fat during development on the life-history traits of *Drosophila melanogaster*. Interestingly, even after switching from a high-fat developmental diet to a control diet during adulthood, flies exhibited increased body weight compared to those reared entirely on a control diet. Moreover, triacylglycerol (TAG) levels remained elevated in adults following this dietary switch, indicating that early-life nutritional exposure induces metabolic alterations. We also assessed the effects of developmental nutrition on reproductive fitness. our goal is to elucidate how developmental diet shapes physiological and reproductive traits across the lifespan, thereby providing insights into the biological basis of health and disease.

P110

Impact of enteric Tau on the development and structural integrity of sensory and non-sensory organs in *Drosophila melanogaster*

Surajita Sahu[1], Subashchandrabose Chinnathambi[2], Monalisa mishra[1]

[1]*Neural Developmental Biology Lab, Department of Life Science, National Institute of Technology Rourkela, Rourkela - 769008, Odisha, India.*
[2]*Department of Neurochemistry, National Institute of Mental Health and Neuro Sciences (NIMHANS), Institute of National Importance, Hosur Road, Bangalore - 560029, Karnataka, India.*

Tau (Tubulin Associated Unit) is a widely recognized microtubule-associated protein that play crucial role in Alzheimer's diseases (AD). Under pathological conditions, hyperphosphorylated Tau detaches from microtubules, contributing to neurodegeneration through inflammation, neuronal dysfunction, and cell death. Aggregated Tau is present in the brain and gut of AD patients. Although, the role of Tau in the brain has been extensively investigated; its significance within the gut remains comparatively unexplored. Similarly, less information is available for the toxic effect of monomeric and oligomeric Tau. In this study, we have investigated the effect of monomeric, oligomeric, and aggregated Tau within the gut of *Drosophila melanogaster*. To evaluate the toxic effect of three different forms of Tau different cytotoxic and genotoxic parameters were taken into account. Third-instar larvae were fed to 10 µM concentrations of different Tau protein and guts were analyzed using Dichloro-dihydro-fluorescein diacetate, DAPI and TUNEL assay. Reactive oxygen species levels were measured from hemolymph extracts using the NBT assay. Developmental defects after exposure of Tau proteins were analyzed across larva, pupa, and adult stages. Histological examinations revealed cytoskeletal alterations within the sensory and non-sensory organs of adult flies. These results reveal Tau's effects beyond the nervous system, emphasizing the need to study its role in peripheral tissues to understand the AD pathology.

P111

Evolution of metabolic strategies under resource constraint in *Drosophila* males selected for divergent traits

Surbhi Yadav[1], Abhishek Kumar Farand[1], Neha Rauhila[1], Abhishek Yadav[1], Mallikarjun Shakarad[1,*]

[1]*Evolutionary Biology Laboratory, Department of Zoology, University of Delhi, New Delhi-110007*

Organisms allocate energy amongst competing life history traits to maximize their overall fitness. Under resource limitations, such allocation often entails tradeoffs and shape evolution of key fitness traits such as growth, reproduction and survival. The classic prediction of a negative relationship between metabolism and longevity remains a central question in the field of evolutionary biology. We investigated this trade-off using *Drosophila melanogaster* male's population that are under conscious laboratory selection for faster pre-adult development and longer lifespan. Selected flies are small in size, have reduced energy reserves at the time of eclosion and live longer lifespan. According to the theory and published literature, the selected flies are expected to have slower metabolic rate compared to their ancestral control population. Contrary to the expectation, selected flies showed significantly increased metabolic rate at late ages, challenging the conventional metabolism-longevity tradeoff.

P112

A micro-screen to identify the role of amino acid and glucose transporters in the fruit fly trachea.

Sohela Sarkar[1], **Swaroop Kumar Rishi**[1] and Jishy Varghese[1].

[1.] *IISER-TVM*

Diet has a crucial role to play in maintaining the growth and development of living organisms, such as the fruit fly, *Drosophila melanogaster*. The fruit fly trachea is a system of complex networks of tubes made up of tracheal epithelial cells that supply oxygen to all parts of the body. The trachea thus acts as a potent human lung equivalent and is useful in advancing research on respiratory physiology and disease. The impact of nutrition directly on the respiratory tissue is an underexplored area in pulmonary research.
In our research, we investigate how variations in dietary macronutrient content impact tracheal development in *Drosophila melanogaster*. We investigate the impact of different amounts of dietary protein: carbohydrate (P:C) ratios on tracheal branching morphology, as well as their resultant impacts on developmental timing and body size. In a complementary strategy, we conducted a micro-screen, where we genetically

downregulated specific amino acid and glucose transporters in tracheal cells and evaluated its impact on the growth, development, survival and the behaviour of flies.
The study aims to expand our understanding of the importance of different classes of amino acid and glucose, on tracheal cell growth and physiology.

P113

Modulating Mitochondrial Priming in Drosophila Stem Cells: Dietary Supplement Strategies for Promoting Healthy Aging

Swati Agarwala and Kasturi Mitra

Department of Biology, Trivedi School of Biological Sciences, Ashoka University, New Delhi (NCR), India

Aging is hallmarked by a decline in mitochondrial functionality and adult stem cell activity, limiting tissue homeostasis and regenerative capacity. Our previous studies demonstrate that Drp1-dependent mitochondrial fission establishes a mitochondrial-primed stem cell state in Drosophila ovaries characterized by heightened self-renewal and proliferative potential. Extending this work, we investigated amino acid–based dietary supplement strategies, guided by metabolomic analyses of mouse fibroblasts, to identify metabolic pathways preserving mitochondrial priming during aging. Nutrient formulations informed by these findings were tested in Drosophila, resulting in maintenance of ovarian stem cell function, enhanced fecundity, and improved neurocognitive outcomes with age. Genetic perturbation of mitochondrial dynamics regulators validated their key roles in controlling mitochondrial morphology, stem cell maintenance, and lifespan extension. This integrated cross-species approach leverages the genetic tractability of Drosophila along with metabolomics-guided nutritional interventions to elucidate mechanisms sustaining stem cell function through mitochondrial metabolism. Our results highlight promising strategies for geronutrition to delay age-dependent decline across tissues by targeting the mitochondrial-stem cell axis. These findings hold translational potential for developing dietary supplements to enhance adult stem cell resilience and promote healthy aging with relevance to human healthspan.

P114

A *Drosophila* Wolfram Syndrome 1 (WFS1) homolog synergizes with the intracellular Ca^{2+} release channel, IP_3R to affect mitochondrial function

Rose Sebastian Kunnappallil, **Syed Kavish Nizami**, Gaiti Hasan

National Centre for Biological Sciences and The University of Trans-Disciplinary Health Sciences and Technology (TDU)

Wolfram syndrome (WFS) is a rare autosomal recessive neurodegenerative disorder that affects approximately one in every 770000 individuals. In 90% of the cases, it is caused by the endoplasmic reticular membrane protein Wolframin, also known as WFS 1. In humans, Wolfram syndrome causes Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness (DIDMOAD). In mammalian cells, WFS1 interacts with the ER-localised intracellular Ca^{2+} release channel, Inositol Trisphosphate Receptor 1 (IP3R1), required for IP3-mediated Ca^{2+} release from the endoplasmic reticulum. We examined the functional links between IP3R and WFS1 protein in the context of flight behaviour and neuronal mitochondrial physiology in a subset of central dopaminergic neurons in *Drosophila melanogaster*. By assessing flight deficits, we observed strong genetic interactions between trans-heterozygotes of *wfs1* and *itpr* mutants. Further, we rescued flight deficits in the heteroallelic mutant by overexpressing $WFS1^{+}$ and $ITPR^{+}$ respectively. We have also examined the effect of *loss of function* of WFS1 on mitochondrial biogenesis and mitochondrial morphology. In conclusion, our findings show that *Drosophila* can be used as a model system to study the cellular and molecular basis of Wolfram syndrome, its impact on systemic physiology, and its possible applications in testing potential pharmaceutical interventions.

P115

Deciphering the development of *Drosophila melanogaster* flight mechanics

Syed Zeeshan Ali[1], Krishan Badrinath[1], Sunil Prabhakar[1], K.VijayRaghavan[1]

[1]*National Centre for Biological Sciences Bangalore*

In Drosophila the patterning of muscles occurs twice; during embryogenesis, leading to the formation of larval muscles and during pupation, giving rise to the adult muscles. The adult muscles arise from Adult Muscle Precursors (AMPs) which are set aside during embryogenesis. These AMPs differentiate during pupal stages and give rise to flight muscles in the adult. The flight muscles involve a set of small direct flight muscles (DFMs) required for steering the wing position, and the indirect flight muscles (IFMs) that generate the power for flight. Although extensive research has identified genes which specify muscle properties in the larva and the indirect flight muscles in the adult, however many such genes remain uncovered in case of direct flight muscles of an adult.

Studies have shown that IFM and DFM AMPs differ in their expression of Cut (Ct) and Vestigial (Vg) (Sudarshan et al., 2001). Additionally, the Lateral muscle scarcer (Lms) gene has been identified to be expressed in DFM myoblasts within the wing disc (Muller et al., 2010. Building on this data, we aim to examine the expression patterns of genes potentially involved in DFM differentiation.
Using single-cell transcriptomics data, (Everetts et al., 2021) identified a list of candidate genes potentially involved in DFM differentiation. Based on this data, we examined the expression of Lms and Nrt in the wing disc and tracked their expression patterns throughout pupation.
Furthermore, the direct flight muscles (DFMs) and their attachment sites are mapped using MicroCT; however, traditional iodine staining does not clearly delineate the membrane boundaries. To improve this, we refined the staining protocol by reduced osmium followed by staining with Lead Aspartate. This enhanced membrane boundaries, allowing for more precise mapping of the DFMs and the connective tissue.

P116

Impact of Developmental Nutrition on Sex- and Mating-Specific Resource Allocation and Starvation Resistance in *Drosophila melanogaster*

Tanisha Kohli[1], Chandrakanth M[1], Devashish Kumar[1], Chetan S[1], Chand Sura[1], Nishant Kumar[1], Sudipta Tung[1]

[1] *Ashoka University*

Nutritional conditions during early development can profoundly influence adult physiology by modulating metabolic and stress-related pathways. In this single-generational study, we examine how variations in larval diet composition, specifically differing protein-to-carbohydrate (P: C) ratios, affect starvation resistance in adult *Drosophila melanogaster*. Larvae were reared on defined isocaloric diets with distinct macronutrient (protein and carbohydrate) ratios, and adult survival under starvation was assessed in both virgin and mated individuals. Our findings reveal a significant interaction between sex, mating status, and larval diet in determining starvation resistance. Virgin males reared on protein-rich diets exhibited higher starvation resistance compared to those from carbohydrate-rich diets, whereas virgin females showed no significant dietary effect. Mating substantially reduced survival in both sexes, consistent with the energetic costs of reproduction. Interestingly, mated males raised on carbohydrate-rich diets survived longer than those reared on protein-rich diets, while mated females exhibited the lowest starvation resistance overall, with the steepest decline observed in those from protein-rich conditions. These results highlight the crucial role of developmental nutrition in shaping adult stress physiology and energy allocation. Further work is needed to pinpoint the specific metabolic pathways and nutrient utilisation strategies driving these trade-offs, enhancing our understanding of how early-life diet influences adult fitness and survival.

P117

Studying effects of light on sleep-wake cycle of *Drosophila melanogaster* by simulating natural light in laboratory

Tejas Kulkarni[1]; Zephyr Chak[1]; BéatriceMartin[1]; Dr. Francois Rouyer[1]

[1]*Paris-Saclay Institute of Neuroscience, Université Paris-Saclay, CNRS, Saclay, France*

The daily pattern of animal behaviour and physiology are governed by the circadian clock. The circadian clock has evolved to get entrained to a 24-hour geophysical cycle of Earth. Light and temperature are known to be the most important cues for this entrainment. Numerous laboratory studies have shown the bimodal activity-rest rhythm of *Drosophila melanogaster* under standard lightdark cycles with anticipation of morning and evening. However, in natural conditions, the spectral composition and intensity of light change throughout the day. Our study focuses on studying the effects of these properties on Drosophila activity-rest rhythm by using a novel intensity-controlled light system with a more natural-like spectrum along with temperature in the laboratory. Several mutants of the clock and visual system were studied under these conditions. Strong and persistent bimodal activity has been observed in clockless mutants under these cycling light conditions. This was also observed before in flies studied in semi-natural conditions outside and we show here that natural-like light is sufficient to drive this clock-independent rhythmic behaviour. We also show the consistent temperature-dependent phase advancement of the evening peak in control and mutant genotypes. Such controlled study of Drosophila activity-rest rhythm focusing on light provides new insights on circadian clock and entrainment in conditions very similar to natural ones.

P118

Comprehensive meta-analysis of gene expression reveals conserved and distinct patterns in the regulation of immune responses in *Drosophila melanogaster*

Triveni Shelke[1], Vanika Gupta[2]*, Ishaan Gupta[1]*

[1]*Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology, New Delhi, India-110016;* [2]*Department of Zoology, University of Delhi, India-110007*

Insects thrive in highly diverse environmental niches, exposing them to a wide range of pathogens. This complex interaction has led to the development of a variety of defence mechanisms collectively termed as innate immunity. Although the prospect of infection has been extensively studied in insects, the broader understanding of its regulation is limited. *Drosophila melanogaster* serves as a powerful model for understanding the genetic regulation of immune responses. Despite extensive research on insect immunity,

existing transcriptomic studies are limited to specific pathogens or experimental conditions, making it challenging to identify overarching patterns that distinguish between conserved and context-specific gene regulation. To address this, we present a comprehensive meta-analysis integrating transcriptomic datasets from diverse infection models to identify specific signatures related to the regulation of innate immunity. By aggregating and re-analysing 8 publicly available RNA-seq datasets spanning Gram-positive, negative, and fungal challenges, we explore the relevance of gene expression, differential transcript usage, and alternative splicing in host defences. The study reveals conservation of core transcriptional signatures shared across pathogen types, including consistent upregulation of cellular and humoral response genes. Interestingly, varying genes showed differential transcript usage specific to each infection type, hence asserting transcriptional divergence in immune regulation. We also analysed alternative splicing events, unravelling the contribution of exon usage to the diversity of immune responses, especially intron retention events dominating in immunity genes. The study hints at mosaic patterns in the functional implication of innate immunity in *Drosophila*. The candidate genes identified could facilitate monitoring pest control and disease management.

P119

Dissecting the molecular and cellular mechanisms of volatile anesthetic action using *Drosophila melanogaster*

Venkatesh Pal Mahadevan[1] and Richard Benton[1]

[1]*Center for Integrative Genomics, Faculty of Biology and Medicine, University of Lausanne, CH-1015 Lausanne, Switzerland.*

Volatile anesthetics (VAs) are indispensable tools of clinical medicine, yet their precise modes of action remain incompletely understood. We have initiated a project to investigate the molecular and cellular mechanisms underlying VA action using *Drosophila melanogaster* (*Dmel*) as a model. We first developed a novel high-throughput, quantitative behavioral bioassay sensitive enough to measure variation in anesthetic sensitivity across VAs. Optimization of this assay using CO_2 as a natural anesthetic revealed that its effects are robust and independent of multiple biotic (sex, satiation state, age) and abiotic (light, humidity) factors. In addition, the anesthetic effect of CO_2 does not depend on vision or CO_2 sensing itself. To identify genetic determinants underlying VA sensitivity, we next performed a screen using the *Drosophila* Genetic Reference Panel (DGRP), uncovering significant intraspecific variation in CO_2 responses. These phenotypic data provide the foundation for genome-wide association studies (GWAS) aimed at mapping genetic loci linked to differential anesthetic sensitivity. Lastly, we plan to further characterize the fine-scale temporal dynamics of VA-induced micro-behaviors using high-resolution tracking and analysis. Taken together, this combined approach will provide new insights into the fundamental biology of anesthesia, reveal novel neuronal (and possibly non-neuronal) molecular targets and enhance our understanding of the behavioral effects of VAs.

P120

Constant exposure to light causes early and exaggerated severity in the *Drosophila* models of human tauopathies

Virender[1], Prerna Aggarwal[1], and Surajit Sarkar*

Department of Genetics, University of Delhi South Campus, Benito Juarez Road, New Delhi - 110 021, India
**Correspondence: sarkar@south.du.ac.in*

Tauopathies like Alzheimer's disease, Parkinson's disease, Pick's disease, etc., represent a class of neurodegenerative disorders that are signified by the pathological accumulation of hyperphosphorylated tau protein aggregates in the form of neurofibrillary tangles (NFTs). The gradual, age-associated accumulation of these neurotoxic NFTs within brain neurons disrupts neuronal function and eventually leads to cell death. Although overall sleep/wake pattern disturbance is an inherent clinical feature of tauopathies but the impact of uninterrupted light exposure-mediated sleep disturbance on disease progression and severity is poorly investigated. We utilized *Drosophila* models of human tauopathies to investigate the effects of constant light exposure on tau-induced phenotypic markers during early stages of aging. Our results demonstrate that flies subjected to continuous light show accelerated progression and amplified features of tau pathology, including increased neurofibrillary tangles (NFTs), brain vacuolization, and impaired locomotor activity. Future studies are expected to provide valuable insights into the specific contributions of light-induced stress and disrupted sleep patterns in exacerbating the age-dependent severity of human tauopathies.

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To investigate the role of the Gut-Hemocyte axis during wound healing in *Drosophila melanogaster.*

Yash Suresh Sheregare[1],and Sveta Chakrabarti[1]

[1]*Manipal Institute of Regenerative Medicine, Bengaluru, Manipal Academy of Higher Education, Manipal, Karnataka, India*

The Drosophila intestine is a vital organ not only for digestion but also for nutrient absorption, toxin excretion, and defense against pathogens (Miguel-Aliaga et al., 2018). In flies, hemocytes serve as key immune sentinels, producing antimicrobial peptides, phagocytosing pathogens, and contributing to wound healing (Pablo et al., 2019; Ayyaz, 2015; Chakrabarti, 2016). Both in Drosophila and mammals, injury triggers local and systemic responses, with hemocytes playing a critical role (Miura, 2014). Previous studies have shown that upon injury or infection, hemocytes release Upd3, which activates the

JAK-STAT pathway in distant organs such as the fat body and gut (Chakrabarti, 2016). However, the specific intestinal effects and gene regulatory events following this systemic STAT activation remain largely unexplored.
Our preliminary findings reveal that upon a distant, clean thoracic injury, hemocyte localize to the intestine seen around at 3 days post injury using *Hml >UASnls* red stinger reporter line. We also detect chronic JAK-STAT activation in the gut as early as six hours post-injury, particularly in the posterior midgut. Using the 10X-STAT-GFP reporter line, we see sustained STAT activity in the gut's visceral muscles and enterocytes up to five days post-injury. Prospero-positive enteroendocrine (EE) cells showed mild STAT activation until three days post-injury, after which the response diminished. These findings suggest the possibility that hemocytes may be dynamically recruited to the gut following injury and could contribute to prolonged STAT activation through signaling interactions.
Our central aim is to elucidate the significance of chronic STAT activation in the midgut after distant injury. Specifically, we seek to identify which genes are transcriptionally regulated in response to this sustained signaling. To achieve this, we plan to perform ChIP sequencing on intestinal tissue to profile STAT-bound genomic targets. This approach will allow us to uncover STAT-responsive genes involved in maintaining intestinal homeostasis following systemic injury. Identifying these targets will provide crucial insights into how JAK-STAT signaling orchestrates cellular responses, fate decisions, and tissue regeneration in the Drosophila gut during systemic wound-induced stress.

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Drp1-regulated priming of *Drosophila melanogaster* Ovarian Stem cells involves Light and Diet cues through Cry.

Yoshita Sriramkumar[1], Rhea Wali[1] and Kasturi Mitra[1*]

[1]*Department of Biology, Trivedi School of Biological Sciences, Ashoka University, New Delhi (NCR), India *Corresponding author: Kasturi Mitra*

Circadian rhythms and metabolism form an interconnected feedback loop, with the brain's central clock synchronizing peripheral oscillators through entraining cues like light and diet. Mitochondria, beyond their role in ATP production, respond to these environmental stimuli by altering their structure, which modulates their functionality. Mitochondrial dynamics, fission and fusion, are regulated by key proteins like Drp1, major fission regulator, whose activity is influenced by the circadian clock. Our lab has shown that Drp1-mediated mitochondrial fission regulates stem cell priming and follicle stem cell differentiation in Drosophila, and that mitochondrial compartments in mouse cardiomyocytes exhibit distinct diurnal responses to nutrient availability. Cryptochrome, beyond its photoreceptor role, regulates metabolism and stem cell function through pathways like AMPK and glucocorticoid signaling, linking metabolic and mitochondrial functions for cellular adaptability. The Drosophila ovarian stem cells serve as an excellent model system to study circadian impact on stem cell mitochondria since it has a well-

established rhythmicity and are responsive to nutritional changes. Although mammalian studies have revealed links between mitochondrial dynamics and the circadian clock, this connection remains largely unexplored in Drosophila stem cells. Our preliminary findings reveal that Drp1-dependent mitochondrial priming in ovarian stem cells occurs under protein-rich diets only with a diurnal light–dark cycle and persists even under high-sugar conditions when this cycle is maintained. This study is the first of its kind to examine how light and diet, integrated by Cryptochrome, regulate Drp1-mediated mitochondrial dynamics to control stem cell proliferation and differentiation in Drosophila ovaries. Overall, this study reveals how peripheral oscillators integrate light and diet cues through mitochondrial modulation to sustain cellular and physiological balance.

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