

ABSTRACT BOOK

Interfacing biophysical and molecular mechanisms of animal homeostasis and repair

6 – 10 April 2026 | Haining, China

General Information



Conference Venue

The Multifunction Hall, No. 7, International Campus, Zhejiang University
No.718 Haizhou East Road, Haining, Jiaxing, Zhejiang.

Dining Information

Meals are served in the campus cafeteria with a meal coupon.

Poster Exchange

For better exchange and communication, posters are welcome.

Please PRINT and BRING Poster to the venue by yourself, then post them according to the corresponding poster abstract numbers.

The size of the Poster is 120cm(high)*90cm(wide).

Accommodation

Zheda Yuanzheng International Hotel

(near West Gate of Zhejiang University)

Address: No.718 Haizhou East Road, Haining, Jiaxing, Zhejiang.

Price: 340 RMB/night

Tel: 0573-87375666 (Hotel Reception)

13095609911(Same number as Wechat)

Email: 542177057@qq.com

The room is limited, please call the hotel's reception to book accommodation.

Transportation to Registration Hotel

1. Self-driving:

Hotel ground or underground parking lot, free.

2. Public transportation:

1.4 kms from the International Campus Station of the Intercity Railway to the hotel, walking for about 20 mins; about 4.5 kms from Haining Station to the hotel, 12 mins by car, and a taxi cost of about 13 RMB; Haining West Station to the hotel is about 36 kms, 56 mins by car, the taxi cost is about 85 RMB.

Contact Us

Conference:

HU yue, 021-64221776, meeting@cscb.org.cn

Payment and Invoice:

WU xialin, 021-64220196, treasure@cscb.org.cn

CAMPUS MAP

校园地图



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|--|-------------------------------------|--|--|
| 1C ZJU-UIUC Institute
浙江大学伊利诺伊大学
厄巴纳香槟校区联合学院 | 6 Lecture Theatre East
东讲堂 | 15 Weixue College
惟学书院 | 22 Hospital
校医院 |
| 2A ZJU-UoE Institute
浙江大学爱丁堡大学联合学院 | 7 Multifunctional Hall
多功能厅 | 16 Student Center
学生中心 | 23 Gymnasium
体育馆 |
| 2E Laboratory Building
教学实验楼 | 8 No.8 Building
8号楼 | 17 Bell Tower
钟楼 | 24 Faculty Club
教工俱乐部 |
| 3A ZJU International
Business School
浙江大学国际联合商学院 | 9 Auditorium
学术大讲堂 | 18 Library
图书馆 | 25 Serviced Apartment
教师公寓 |
| 3B Administration Building
行政楼 | 10 No.4 Residential College
4号书院 | 19 Learning and Teaching
Building North B
北教学楼B楼 | 26 Academic Exchange
Center
学术交流中心 |
| 4 Learning and Teaching
Building South
南教学楼 | 11 Guantong College
观通书院 | 20 Learning and Teaching
Building North A
北教学楼A楼 | |
| 5 Lecture Theatre West
西讲堂 | 12 Laitong College
来同书院 | 21 Arts and Science
Building
文理楼 | |

Agenda

Day 1 | 6 April 2026

09:00–11:00 **Registration**

11:00–11:15 **Welcome and Introduction**
Yanlan Mao

Opening Keynote

Chair: Yanlan Mao

11:15–12:00 **Pattern formation and regeneration in a single cell**
Wallace Marshall

12:00–13:30 **Lunch**

Session 1: Genome Homeostasis and Repair

Chair: Suhong Xu

13:30–14:00 **Replication stress response as a molecular safeguard of cellular homeostasis**
Ting Liu

14:00–14:15 **The Mechanoresponsive Chromosomal Passenger Complex Sustains Furrow Ingression Under Confinement**
Chew Ting Gang

14:15–14:45 **Nuclear mechanobiology during DNA damage and repair**
Chris Toseland

14:45–15:00 **ZFP42 Maintains Stemness and Rhythmic Gene Expression in Human Epidermal Stem and Progenitor Cells Via CRY1**
Jingting Li

15:00–15:30 **Break & Poster Viewing**

Session 2: Membrane /Organelle Homeostasis and Repair

Chair: Ting liu

15:30–16:00 **Molecular physiology of lysosomes**
Haoxing Xu

16:00–16:15 **Synchronizations of Epithelial Cells by Mechanosensitive Tmc Channels During Tissue Morphogenesis**
Deqing Kong

16:15–16:45 **Basement membrane dynamics in skin morphogenesis**
Hiro Fujiwara

16:45–17:00 **Edge-vertex Flow Enables Rapid Adhesion Reinforcement Under Tension**
Huapeng Yu

17:00–18:30 **Poster Presentation (Odd Number Posters)**

18:30–20:30 **Opening Dinner**

21:00 **Meeting Speakers in Yulin Space**

Day 2 | 7 April 2026

Keynote 2

Chair: XueBiao Yao

09:00–09:45 Cell volume regulation of epidermal stem cells
Fiona Watt

Session 3: Cell Homeostasis and Repair

Chair: Yi Arial Zeng

09:45–10:15 How Cells Heal Themselves: An Interdisciplinary View of Membrane Repair
Jesper Nylandsted

10:15–10:30 Moving Sensors: Dynamic Protrusions Drive Enteroendocrine Cell Motility
Xuan Zheng

10:30–11:00 **Break & Poster Viewing**

Session 4: Neuronal Homeostasis and Repair

Chair: Lin Lin

11:00–11:30 Homeostasis and regeneration of peripheral nerves
Alison Lloyd

11:30–11:45 How Stiffness Controls Stem Cell Fate and Maintenance in the Avian Body Axis
Ana Hernandez Rodriguez

11:45–12:15 How morphodynamics shape development: from embryos to organoids
Akanksha Jain

12:15–12:30 Peripheral Glia Constitute a Pro-reparative Niche Triggering Skin Wound Healing
Salome Stierli

12:30–14:00 **Lunch**

Session 5: Immune Homeostasis and Repair

Chair: Filipa Simoes

14:00–14:30 Mechanical shaping of T-cell receptor specificity for treating solid tumors
Jack Wei Chen

14:30–14:45 Proximity Labeling for Investigating and Manipulating Cellular Interactions
Shuo Han

14:45–15:15 Mechanical regulation of B cell activation at the immune synapse
Katelyn Spillane

15:15–15:30 One Protein, Divergent Cell Fates: Matricellular Protein Mindin Orchestrates Fibroblast Heterogeneity in Tissue Repair and Fibrogenesis
Gaurav Kansagar

15:30–16:00 **Break & Poster Viewing**

Session 6: Organ Homeostasis and Repair I

Chair: Shuo Han

16:00–16:30 Systems learning of biophysical and molecular mechanisms from single-cell omics data
Qing Nie

16:30–16:45 Mechanics of Cell Extrusion in Intestinal Organoids
Marija Matejic

16:45–17:00 Dual Hepatocyte Programs Sustain Endothelial WNT Signaling During Liver Homeostasis and Repair
Yinhua Jin

Agenda

Keynote 3

Chair: Suhong Xu

17:00-17:45	Talk Title: TBA Hongkui Deng
17:45-19:00	Dinner
19:00-20:30	Poster Presentation (Even Number Posters)
21:00	Meeting Speakers in Yulin Space

Day 3 | 8 April 2026

Keynote 4

Chair: Yanlan Mao

09:00-09:45	Coordination of morphogenesis and cell states by mechanical forces Sara Wickstrom
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Session 7: Organ Homeostasis and Repair II

Chair: Elif Eroglu

09:45-10:15	Maintaining cell and tissue shape through molecular turnover Andela Saric
10:15-10:30	Multiscale Patterning of Extracellular Matrix in Skin Homeostasis and Repair Andrew Chisholm
10:30-11:00	Break & Poster Viewing

Session 8: Organ Homeostasis and Repair III

Chair: Yinhua Jin

11:00-11:30	Cell identity conversion: Liver regeneration and cell therapy Lijian Hui
11:30-11:45	Mechanical Principles in Tissue Morphogenesis Shi-Lei Xue
11:45-12:15	Modular hydrogels for organoid-based disease modelling Eileen Gentleman
12:15-12:30	Cellular Responses to Tissue Wounding upon Altered Tissue Mechanics Samantha Jane Warrington
12:30-13:30	Lunch
13:30-18:30	Free Academic Exchange
19:00-20:30	Dinner
21:00	Meeting Speakers in Yulin Space

Day 4 | 9 April 2026

Closing Keynote

Chair: Yi Arial Zeng

09:30–10:15 Skin Stem Cells in Homeostasis, Wound Repair and Cancer
Elaine Fuchs

10:15–10:30 Poster Prize Presentation

10:30–11:00 **Break**

Session 9: Organ Homeostasis and Repair IV

Chair: Hiro Fujiwara

11:00–11:30 Modulating adult stem cells and their niche to stimulate tissue regeneration
Yi Arial Zeng

11:30–11:45 Mechanobiology in Organoid Formation
Qiutan Yang

11:45–12:15 Soft But Tough! Engineered Cell-Instructive Microdroplets for Stem Cell Technologies
Julien Gautrot

12:15–12:30 Biophysical Remodeling of Epithelial Polarity During Intestinal Renewal and Repair
Lin Lin

12:30–14:00 **Lunch**

Session 10: Organ Homeostasis and Repair V

Chair: Akanksha Jain

14:00–14:30 Deciphering immune–cardiac niche interactions in development and regeneration
Filipa Simoes

14:30–14:45 Deciphering Injury-Induced Signals that Trigger Regeneration in the Mammalian Heart
An Zeng

14:45–15:15 More than a barrier? The role of tight junctions in the salamander heart regeneration
Elif Eroglu

15:15–15:30 How an Electrophysiological Signal Is Integrated into Scaling the Fins During Regeneration and Development
Christopher Antos

15:30–16:00 **Break**

Session 11: Organism Homeostasis and Repair

Chair: Yanlan Mao

16:00–16:30 Cellular Coordination of Appendage Regeneration in Axolotls
Jifeng Fei

16:30–16:45 ‘Active Neutral Buoyancy’: a Goal-directed Multiscale Homeostatic Organisation for Balancing Gravity
Nicholas Wilkinson

16:45–17:15 Modelling regeneration of tissues in the axolotl and beyond
Osvaldo Chara

17:15–17:45 Regulation of neuronal morphology: genetic insights from *C. elegans*
Yishi Jin

17:45–18:00 Closing remarks
Yanlan Mao

18:30–21:00 **Closing Dinner**

Day 5 | 10 April 2026

08:00–10:00 **Breakfast and Departure**

Organizers



Yanlan Mao
University College London, UK



Suhong Xu
Zhejiang University, CN



Yi Arial Zeng
*Shanghai Institute of Biochemistry
& Cell Biology, CN*



Xuebiao Yao
*University of Science and
Technology of China, CN*

Invited Speakers



Pattern formation and regeneration in a single cell
Wallace Marshall *University of California San Francisco, USA*



Replication stress response as a molecular safeguard of cellular homeostasis
Ting Liu *Zhejiang University, CN*



Nuclear mechanobiology during DNA damage and repair
Chris Toseland *Sheffield University, UK*

Invited Speakers



Molecular physiology of lysosomes

Haoxing Xu *Zhejiang University, CN*



Basement membrane dynamics in skin morphogenesis

Hiro Fujiwara *Riken BDR, JP*



Cell volume regulation of epidermal stem cells

Fiona Watt *EMBL, Heidelberg, DE*



How Cells Heal Themselves: An Interdisciplinary View of Membrane Repair

Jesper Nylandsted *University of Southern Denmark, DK*



Homeostasis and regeneration of peripheral nerves

Alison Lloyd *University College London, UK*



How morphodynamics shape development: from embryos to organoids

Akanksha Jain *University of Zurich, CH*



Mechanical shaping of T-cell receptor specificity for treating solid tumors

Jack Wei Chen *Zhejiang University, CN*

Invited Speakers



Mechanical regulation of B cell activation at the immune synapse

Katelyn Spillane *Imperial College London, UK*



Systems learning of biophysical and molecular mechanisms from single-cell omics data

Qing Nie *University of California Irvine, USA*



Talk Title: TBA

Hongkui Deng *Peking University, CN*



Coordination of morphogenesis and cell states by mechanical forces

Sara Wickstrom *Max Planck Institute for Molecular Biomedicine, DE*



Maintaining cell and tissue shape through molecular turnover

Andela Saric *Institute of Science and Technology Austria (IST Austria), AT*



Cell identity conversion: Liver regeneration and cell therapy

Lijian Hui *Shanghai Institute of Biochemistry and Cell Biology, CN*



Modular hydrogels for organoid-based disease modelling

Eileen Gentleman *University of Lausanne, CH*

Invited Speakers



Skin Stem Cells in Homeostasis, Wound Repair and Cancer

Elaine Fuchs *The Rockefeller University, USA*



Modulating adult stem cells and their niche to stimulate tissue regeneration

Yi Ariel Zeng *Shanghai Institute of Biochemistry & Cell Biology, CN*



Soft But Tough! Engineered Cell-Instructive Microdroplets for Stem Cell Technologies

Julien Gautrot *Queen Mary University of London, UK*



Deciphering immune-cardiac niche interactions in development and regeneration

Filipa Simoes *Oxford University, UK*



More than a barrier? The role of tight junctions in the salamander heart regeneration

Elif Eroglu *Karolinska Institute, SE*



Cellular Coordination of Appendage Regeneration in Axolotls

Jifeng Fei *Southern Medical University, CN*



Modelling regeneration of tissues in the axolotl and beyond

Osvaldo Chara *Nottingham University, UK*

 Selected Speaker Abstracts

The Mechanoresponsive Chromosomal Passenger Complex Sustains Furrow Ingression Under Confinement

Ting Gang Chew

The Zhejiang University-University of Edinburgh Institute,
Zhejiang University School of Medicine, Zhejiang University, Haining 314400, China.

Cells sense and respond to forces from neighbouring cells and the extracellular matrix during growth and division. When cells undergo mitosis in a confined environment like in the tumour environment, high compressive stress causes unstable cell cortex and prolonged mitosis. Confined mitotic cells frequently experience chromosome loss and multipolar division. How the cortical instability affects cytokinesis under confinement is unclear. Here, we show that confined mitotic cells undergo furrow ingression comparable to unconfined mitotic cells but are strongly reliant on Aurora B kinase, a catalytic subunit of the chromosomal passenger complex (CPC) for its completion. Mechanistically, the cortical pool of CPC via the scaffolding protein INCENP sustains Aurora B at the equatorial cortex to drive furrow ingression under confinement. We identified mechanoresponsive elements within the single alpha-helix domain of INCENP that maintain the cortical CPC at the equatorial cortex to promote furrow ingression in response to high compressive stress. Thus, the cortical INCENP not only binds to actin filaments but also mechanically responds to forces at the equatorial cortex to regulate the CPC during confined cytokinesis.

 Selected Speaker Abstracts

ZFP42 Maintains Stemness and Rhythmic Gene Expression in Human Epidermal Stem and Progenitor Cells Via CRY1

Jingting Li

Institute of Precision Medicine, The First Affiliated Hospital of Sun Yat-sen University

The role of circadian rhythm in regulating stemness in adult stem cells remains unclear. We investigated this in human epidermal stem and progenitor cells (EPSCs), finding that ~10% of genes exhibit rhythmic expression, with overlaps between fetal and adult EPSCs involved in critical biological processes, including the cell cycle, senescence, and apoptosis. Promoter motifs analysis revealed ZFP42, a pluripotent stem cell marker, enriched in fetal rhythmic genes. ZFP42 knockdown led to the loss of stemness in human EPSCs and reduced CRY1 expression, which in turn decreased cell proliferation and increased differentiation gene expression. These results highlight the critical role of ZFP42 in the circadian regulation of epidermal homeostasis, linking stemness maintenance to circadian mechanisms. Our findings deepen the understanding of how circadian rhythms govern epidermal stem cell functions.

 Selected Speaker Abstracts

Synchronizations of Epithelial Cells by Mechanosensitive Tmc Channels During Tissue Morphogenesis

Deqing Kong

Institute of Evolution & Marine Biodiversity, Ocean University of China

Coordination of cell behaviors is central to morphogenesis, when arrays of cells simultaneously undergo shape changes or dynamic rearrangements. In epithelia, changes in cell shape invariably exert mechanical forces that adjacent cells can sense to trigger an active response. However, molecular mechanisms underlying such mechanotransduction, and especially their role in tissue-wide coordination during morphogenesis, have remained ambiguous. Here, we investigate the function of Tmc, a key component of cellular mechanotransduction in vertebrate hearing, in coordinating cell dynamics in the epithelial amnioserosa of *Drosophila* embryos. We directly probed cell-cell mechanotransduction in vivo by opto-chemically inducing single-cell contractions and discovered a Tmc-dependent contraction response in neighboring cell groups. At the tissue scale, we uncover synchronization of oscillations in neighboring cell areas, which is impaired in Tmc mutants. A data-driven model of Tmc-dependent cell-cell interactions predicts that synchronization leads to an isotropic force map and effectively shields the tissue from external mechanical pulling. By microdissection, we detect equal junction tension along the axial and lateral axes in wild type, but increased lateral tension in Tmc mutants. Thus, Tmc transduces forces into an intracellular response that coordinates mechanical cell behaviors in epithelial tissue.

 Selected Speaker Abstracts

Edge-vertex Flow Enables Rapid Adhesion Reinforcement Under Tension

Huapeng Yu

Southern University of Science and Technology

A general mechanism to maintain epithelial integrity during tissue movements is to couple adhesion strength with mechanical force. Mechanosensitive proteins are recruited to cell-cell contacts to reinforce membrane- cortex linkage in response to elevated tension. However, subcellular mechanisms for such rapid and precise protein transport remain elusive. Here we identify a direct “edge-to-vertex” transport mechanism that couples the flow of the adhesion protein Canoe/Afadin to pulsatile actomyosin dynamics, ensuring that adhesion is reinforced precisely where and when force is applied. Genetically, this mechanosensitive transport is gated by kinase-independent activities of Mbt/PAK. In its absence, Canoe/Afadin forms aberrant elliptical condensates at cell edges, becoming unresponsive to mechanical cues. Remarkably, these condensates are dissolved by a simple, physiological increase in temperature, which restores directional protein flow and rescues adhesion—bypassing the genetic requirement of Mbt/PAK. Lastly, we demonstrate that transport efficiency is governed by cortical mobility, fine-tuned through Canoe/Afadin condensation. These results identify a force-coupled transport strategy to ensure adhesion-tension coupling with spatial and temporal precision in living tissues.

Selected Speaker Abstracts

Moving Sensors: Dynamic Protrusions Drive Enteroendocrine Cell Motility

Xuan Zheng^{1,2}, Johan van ES^{1,2}, Hans Clevers^{1,2}

¹Hubrecht Institute, Royal Netherlands Academy of Arts and Sciences (KNAW)
and University Medical Centre Utrecht (UMC), Utrecht, the Netherlands.

²Oncode Institute, Utrecht, the Netherlands

Enteroendocrine cells (EECs) are rare intestinal epithelial cells that sense luminal nutrients and microbial products. They secrete hormones, including serotonin (5-HT) and glucagon-like peptide-1 (GLP-1), to regulate physiological processes such as appetite. EECs are solitary cells with migratory behaviors distinct from the collective “conveyor-belt” migration of enterocytes (1). They extend specialized cytoplasmic neuropods that may form rapid synapses with neurons, bypassing slower hormonal signaling (2). Despite their physiological importance, the physical dynamics and motility of EECs remain poorly understood. This is largely due to limited access for live-cell imaging in mice. To address this, we used human colon organoids with fluorescent live reporters for EECs, nuclei, and actin. Live-cell imaging combined with quantitative tracking allowed us to visualize individual EECs in real time and capture both their motility and actin cytoskeleton dynamics. Our observations revealed that EECs extend highly dynamic, actin-dependent protrusions, such as lamellipodia and filopodia, and display migration behaviors distinct from neighboring epithelial cells. Pharmacological inhibition of cytoskeletal regulators disrupted both protrusions and motility and unexpectedly altered hormone secretion profiles. Together, these results highlight cytoskeletal remodeling as a key driver of EEC spatial organization and endocrine function. The molecular mechanisms driving EEC protrusions and motility are largely unknown. To investigate this, we are generating knockouts of genes involved in cell adhesion and cell-cell interactions. These genes likely control how EECs navigate the epithelium, maintain spatial positioning, and communicate with neighboring cells and neurons. Understanding their role will reveal how cytoskeletal and adhesion pathways coordinate EEC morphology, motility, and endocrine function. Together, our findings establish EECs as morphologically and mechanically active components of the intestinal epithelium and identify cytoskeletal remodeling as a central regulator of their spatial organization and hormone secretion. 1. H. Gehart et al., Identification of Enteroendocrine Regulators by Real-Time Single-Cell Differentiation Mapping. *Cell* 176, 1158–1173.e1116 (2019). 2. M. M. Kaelberer et al., A gut-brain neural circuit for nutrient sensory transduction. *Science* 361, eaat5236 (2018).

Selected Speaker Abstracts

How Stiffness Controls Stem Cell Fate and Maintenance in the Avian Body Axis.

Ana Hernandez Rodriguez^{1,2}, Kristian Franze²,
Fengzhu Xiong^{1,2}, et al.

¹Gurdon Institute, University of Cambridge, Cambridge, UK

²Department of Physiology, Development and Neuroscience,
University of Cambridge, Cambridge, UK

Embryonic development is characterized by rapid growth and differentiation, but homeostasis plays a crucial role in this process, as the maintenance of pools of progenitor cells is essential for the formation and expansion of diverse tissue types. This is the case during body axis elongation, where tissues such as the neural tube, the notochord and the somites are formed by proportioning cells from a pool of progenitors at the posterior of the embryo (PD). Whilst the biochemical signals that regulate homeostasis and differentiation are well described, the role of mechanics in the PD is less understood. It has been shown that a positive feedback loop mechanically drives elongation; with the notochord pushing on the PD and driving cell migration, in turn constricting the notochord and generating the pushing force. We explore how the PD responds to this mechanical strain, and what role mechanics plays in stem cell maintenance and differentiation. Our custom-built microscope, the TiFM, enables us to mechanically manipulate a variety of tissues, including the PD of embryos. Using this unique tool, we can bend the body axis, locally stretch and compress specific tissues and compare material properties within the embryo. In conjunction with atomic force microscopy, we reveal that not only are different tissues in the progenitor region mechanically distinct, but that within the PD there is an anterior to posterior gradient of decreasing stiffness. We propose this gradient acts as a mechanical transducer, enabling posterior PD cells to respond to notochord generated forces and exit into the axial tissues, ensuring the correct proportion of progenitor cells into each tissue. We show that this gradient of stiffness is abolished with a matrix metalloprotease inhibitor, and that, unexpectedly, increasing ECM organization leads to a softer, more deformable tissue. In addition, we observe decrease in length, a reduction in somite size and a decrease of cell movement out of the PD. Our results show that in vivo, in situ mechanical measurements of the PD reveal the importance of mechanical environment for the maintenance of stem cell nature of the PD and the correct contribution of cells to axis elongation.

 Selected Speaker Abstracts

Peripheral Glia Constitute a Pro-reparative Niche Triggering Skin Wound Healing

Salome Stierli¹, Adrian Salas-Bastos¹, Sofia Micheli¹, Isabel Ballwein¹,
Andrea Kelemen¹, Julia Lehmann¹, Benjamin Loos¹,
Whitney Shannon Jordan¹, Sebastian A. Stifter², Myriam Gwerder¹,
Ravidu Nakandalage¹, Janine Stadler¹, Melanie Greter², Lukas Sommer¹

¹Institute of Anatomy, University of Zurich; 8057 Zurich, Switzerland.

²Institute of Experimental Immunology, University of Zurich; 8057 Zurich, Switzerland.

Skin repair is a complex, dynamic process involving multiple cell types. Using multiplex imaging, spatial transcriptomics, and single-cell RNA sequencing, we show that peripheral nerves —containing repair glia— form a pro-reparative niche closely interacting with macrophages and proliferating fibroblasts in acute skin wounds. Repair glia function as critical early-stage regulators of wound healing by initiating the inflammatory response through secretion of monocyte chemoattractant proteins, such as CCL2, which recruit monocyte-derived macrophages. Accordingly, depletion of repair glia as well as glia-specific deletion of CCL2 reduces the number of macrophages, leading to impaired fibroblast proliferation and diminished fibroblast to myofibroblast transition. These findings position repair glia as a central component of the pro-reparative niche, coordinating the early immune response and orchestrating the temporal progression of wound healing.

Selected Speaker Abstracts

Proximity Labeling for Investigating and Manipulating Cellular Interactions

Shuo Han

Center for Excellence in Molecular Cell Science, CAS

The application of proximity labeling, a chemical strategy that uses enzyme-catalyzed, promiscuously-reactive intermediates for nanometer scale biotinylation of neighboring proteins, as a discovery tool has yielded tremendous insights into molecular and cellular interactions over the past decade. However, proximity labeling is by no means restricted to biotin-containing substrates for detection purposes and whether the chemical features of proximity labeling reactions can be harnessed for other applications has thus far not been explored. In this talk, I will present our recent work on using cell surface proximity labeling both as a research tool for studying intercellular communication during tissue regeneration, and more importantly, as a potential therapeutic strategy for cell surface engineering to manipulate immune-organ crosstalk, which we hope would lay the groundwork for future translation of this unique and diverse class of chemistry to treat cancer, fibrosis, and tissue aging.

Selected Speaker Abstracts

One Protein, Divergent Cell Fates: Matricellular Protein Mindin Orchestrates Fibroblast Heterogeneity in Tissue Repair and Fibrogenesis

Gaurav Kansagara^{1,2,3}, Sunny Kataria^{4,7}, Isha Rana⁷,
Arnab Mukherjee³, Tuan Lin Tan^{5,6}, Colin Jamora^{2,7}, et al.

¹IFOM-inStem Joint Research Laboratory, Centre for Inflammation and Tissue Homeostasis,
Institute for Stem Cell Science & Regenerative Medicine, Bangalore, KA, India

²Department of Life Sciences, Shiv Nadar Institution of Eminence, Gautam Buddha Nagar, UP, India

³Manipal Academy of Higher Education, Manipal, KA, India

⁴Department of Internal Medicine, Division of Rheumatology,
University of Michigan Medical School, Ann Arbor, MI, USA

⁵School of Chemical & Life Sciences, Singapore Polytechnic, Singapore, Singapore.

⁶Previously at: Department of Bioengineering, Jacobs School of Engineering,
University of California San Diego, San Diego, California, USA

⁷Previously at Centre for Inflammation and Tissue Homeostasis,
Institute for Stem Cell Science and Regenerative Medicine, Bengaluru, KA, India

Fibroblast activation is essential for wound healing and tissue repair, but when it is deregulated can lead to tissue fibrosis and drives the formation of the tumour stroma. “Activation,” however, is an overarching term encompassing diverse fibroblast functions, including proliferation, migration, contraction, cytokine production, and secretion of extracellular matrix (ECM) proteins, raising these questions: whether specialized subpopulations uniquely contribute to tissue repair and fibrogenesis? What are the molecular cues that regulate fibroblast heterogeneity and its functions in homeostasis, repair, and pathology? Furthermore, organ fibrosis results from persistent myofibroblast activation; however, the mechanisms sustaining fibroblast activation post-repair are poorly understood. Using a novel mouse model of skin fibrotic disease, scleroderma (or systemic sclerosis) (Rana et al., JID, 2023) as a discovery platform, we revealed functional heterogeneity of dermal fibroblasts and their key molecular regulator during tissue repair, which drives fibrosis when dysregulated. We identified a critical role for the protein Mindin (Spondin-2) during organ repair and fibrosis. We find that this matricellular protein is elevated in multiple mouse models of organ fibrosis and in human fibrotic tissues, and its knockout ameliorates fibrotic hallmarks. We show that Mindin selectively activates distinct fibroblast subpopulations, enhancing inflammatory cytokine release and migration in reticular fibroblasts, while promoting contractility and ECM secretion in papillary fibroblasts. In vitro, Mindin treatment induces primary reticular fibroblasts to resemble inflammatory cancer-associated fibroblasts (iCAFs) and papillary fibroblasts to mimic myofibroblastic CAFs (myCAFs) (Kataria, Kansagara, et al., JCI Insight, 2025).

Selected Speaker Abstracts

We employed a combined biochemical, biophysical and computational approach to define Mindin's minimal functional domain, identify its putative receptors, and elucidate the downstream signaling components in dermal fibroblast subpopulations. We find that Mindin signals through innate immune receptors on fibroblasts, resulting in downstream activation of specific Src-family kinases (Src & Fyn), Rho-family GTPases (Rac1 & ROCK), and the MyD88-dependent NF- κ B pathway to drive distinct functional responses in these subpopulations. (Kansagara et al., manuscript in preparation). In summary, our findings provide mechanistic insights into the role of fibroblast heterogeneity in tissue repair and fibrosis. By delineating the signaling pathways regulating fibrogenesis, we have also uncovered novel routes for therapeutic intervention in fibrotic diseases.

Mechanics of Cell Extrusion in Intestinal Organoids

Marija Matejic

Institute for Bioengineering of Catalonia

Every day, the mammalian intestinal epithelium extrudes millions of cells to sustain tissue self-renewal. Despite its fundamental role in intestinal homeostasis, the mechanisms that trigger, compartmentalize, and execute intestinal cell extrusion remain largely unknown. Here, using intestinal organoids, we map the three-dimensional forces and cytoskeletal dynamics that drive intestinal cell extrusion. We show that, unlike in other epithelia, extrusion is initiated by the sudden dissolution of a contractile myosin 2A meshwork triggered by a calcium influx. Following meshwork dissolution, the extruding cell and its neighbors generate an upwards traction force that requires myosin contractility but is generated by lamellipodial protrusions in neighboring cells. Importantly, these lamellipodia not only act as force generators but also determine whether extrusion occurs apically or basally, serving as symmetry breakers of the process. Finally, we show that compartmentalization of cell extrusion to the outside of the intestinal crypt does not require curvature and instead depends on myosin 2A. Our findings reveal that the intestinal epithelium exhibits a distinctive mode of extrusion, in which tension differentials—rather than compressive stresses from crowding—trigger and compartmentalize cell removal.

 Selected Speaker Abstracts

Dual Hepatocyte Programs Sustain Endothelial WNT Signaling During Liver Homeostasis and Repair

Yinhua Jin

Zhejiang University (International Campus)

Tissue homeostasis requires robust mechanisms that preserve essential signaling outputs under stress. In the liver, endothelial WNT signaling is critical for metabolic zonation and regeneration, yet how hepatocytes instruct endothelial cells to maintain WNT signaling during stress remains unclear. Here, we show that hepatocytes engage two compensatory feedback programs to sustain endothelial WNT production during signaling failure. Using inducible hepatocyte-specific β -catenin loss and sub-hepatotoxic acetaminophen injury models, we identify VEGFa-ETS1 and estrogen-ESR1 as parallel hepatocyte-to-endothelial pathways that preserve endothelial Wnt2 and Wnt9b expression. In response to hepatocyte stress, VEGFa activates endothelial ETS1 to induce WNT output in both sexes. In parallel, altered hepatocyte metabolism elevates intrahepatic estrogen levels, selectively engaging endothelial ESR1 to enhance WNT signaling in a sex-dependent manner. Genetic disruption of either endothelial ETS1 or ESR1 reduces endothelial WNT production, disrupts metabolic zonation, and impairs hepatocyte proliferation. Importantly, acute acetaminophen injury reactivates these compensatory circuits, restoring endothelial WNT signaling and promoting tissue repair. Together, our findings reveal that hepatocytes actively instruct endothelial niche signaling through metabolic and vascular feedback loops, ensuring liver homeostasis and regeneration under stress.

 Selected Speaker Abstracts

Multiscale Patterning of Extracellular Matrix in Skin Homeostasis and Repair

Andrew Chisholm
UC San Diego

The skin is a structurally complex organ that functions as permeability barrier and mechanical support. Skin layers are homeostatically maintained throughout life and repair themselves after acute damage (wound healing). Skin layers are made up of epithelia that generate a multilayered apical extracellular matrix (aECM) composed of proteins, glycans and lipids. We focus on the simple skin of the nematode *C. elegans* as a tractable model for aECM patterning, homeostasis and repair in vivo. The skin's apical ECM or cuticle is composed of dozens of collagens and non-collagenous proteins. Three collagens collaborate to form intricately patterned columns that hold the cortical and basal matrix layers apart in the adult, and which function in damage sensation (Adams, Pooranachithra et al 2023 Nat. Comms). The cortical layer of the aECM contains many non-collagenous proteins, including epicuticlins defined by perfect or near-perfect low-complexity tandem repeats that regulate the lipid layers of the matrix (Pooranachithra et al 2024 Development). The aECM contains many other substructures whose molecular organization and biogenesis remain little-understood, including chirally patterned layers of fibres that control organismal shape. To better understand such multiscale aECM patterning we have developed a toolkit of over 100 strains expressing endogenously labeled aECM components (in collaboration with Jordan Ward, UC Santa Cruz). Localization of such tagged aECM proteins reveal multiple intricately patterned matrix compartments that mature and are maintained in adult life. Understanding this model aECM should help understand patterning and repair of more complex aECMs such as the vertebrate skin.

Mechanical Principles in Tissue Morphogenesis

Shi-Lei Xue

Westlake University

The morphogenesis of embryos is governed by diverse physical forces, such as active cytoskeletal tensions and compressive stresses arising from external constraints or differential growth. This talk introduces three examples on the role of mechanics in tissue morphogenesis. (1) Morphological self-similarity of the notochord: during axial elongation, the notochord's cross-sectional area is conserved in the trunk yet increases markedly at the tip, a process mediated by active cell migration and mechanical feedback controlling proliferation. (2) Morphological differentiation of the neural tube: mechanical and geometrical pre-patterning dictates the disparate inflation of the hindbrain and spinal cord in response to elevated luminal fluid pressure. (3) Crypt budding in intestinal organoids: the coordination of apical-basal tension in stem cells and luminal pressure drives crypt budding, theoretically predicted and experimentally validated to confer self-locking and bi-stability. These examples illustrate that embryonic development and organoid self-organization arise from the interplay between biochemical factors and mechanical/geometric cues, coordinated by physical forces across multiple spatiotemporal scales. Future interdisciplinary research, combined with advanced organoid techniques, will be key to deciphering these complex mechano-chemo-biological coupling mechanisms.

 Selected Speaker Abstracts

Cellular Responses to Tissue Wounding upon Altered Tissue Mechanics

James Van Hear¹, Samantha Jane Warrington¹, Chris Tape², Yanlan Mao¹

¹Laboratory for Molecular Cell Biology, University College London, UK

²Department of Oncology, University College London Cancer Institute, London, UK

The mechanical properties of a tissue impact its growth, development and response to injury. Changes to the status quo can lead to a variety of diseases including cancer. The stiffness of the cells is one aspect of tissue mechanics that can be affected through genetic mutations, or external toxins, often leading to altered cellular responses to injury and changes to the extracellular matrix. Wounds sustained by a tissue present a challenging situation for the cells damaged but also for wider tissue integrity. During wound closure wound edge cells must remodel their cell shape in 3D and may undergo exchange of cell neighbours to close the wound. All this requires communication with their surrounding neighbour cells, with underlying tissues and with the extracellular matrix. The challenge increases if the cellular mechanics have been altered, for example by genetic mutations, as cells may have to adapt even more by remodelling their cell shape as well as changing adhesion to or moving past underlying substrates. Here we address the question of: How do cells respond to tissue wounding when the tissue mechanics have been altered? We used mechanobiological approaches to investigate tissue repair in mouse colon organoids that are either wild-type or contain common human colorectal cancer mutations, which in vivo stiffen the tumour microenvironment. Our results show that organoids expressing colorectal cancer mutations achieve a slower wound closure than control organoids, correlating with a reduced ability to rapidly alter cellular morphology and remodel the wound area through cellular intercalations. Understanding the mechanics of a tissue in concert with tissue repair is essential to elucidate how cells can survive and repair upon altered tissue mechanics.

 Selected Speaker Abstracts

Mechanobiology in Organoid Formation

Qiutan Yang, Yanmei Wu

Institute of Zoology, Chinese Academy of Sciences

Organoids are three-dimensional in vitro tissue cultures whose chemical and mechanical properties can be quantitatively measured across multiple spatial and temporal scales. This makes them powerful models for dissecting tissue mechanics and mechanosensation, and for uncovering the physical principles governing mammalian tissue development, homeostasis and regeneration. By integrating live imaging, force measurements, perturbations, and modeling, we previously showed how coordinated mechanical and osmotic forces drive crypt morphogenesis in intestinal organoids (Nat. Cell Biol. 2021; Nat. Phys. 2025). More recently, using intestinal-organoid-derived cells, we developed a self-organizing multicellular system that recapitulates the complex cell-cell and cell-ECM interactions underlying intestinal epithelial regeneration. Within six hours, single cells assemble into regularly patterned clusters that consistently give rise to mature, budding organoids. Live imaging combined with finite-element modeling showed that this initial clustering is orchestrated by a rare subpopulation of highly motile “active” cells, which mechanically pull and aggregate less-motile “passive” neighbors. By integrating lineage tracing, live imaging, pharmacological perturbations, targeted fate induction, single-cell RNA sequencing across finely resolved time windows and in vivo validation, we identified this rare active cell type and elucidated the signaling pathways driving its autonomous migration and pro-regenerative function. Remarkably, the same active-cell population and molecular mechanism are responsible for tissue phenotypes in both mouse cancerous and human regenerative epithelia, underscoring their broad physiological and pathological relevance.

 Selected Speaker Abstracts

Biophysical Remodeling of Epithelial Polarity During Intestinal Renewal and Repair

Lin Lin

Shanghai Institute of Biochemistry and Cell Biology, Center for Excellence
in Molecular Cell Science, Chinese Academy of Sciences

The intestinal epithelium functions as a dynamic interface between the internal milieu and the external environment, coordinating nutrient absorption, barrier integrity, immune surveillance, and signaling transduction. These diverse functions depend on the generation and maintenance of a highly organized epithelial architecture, characterized by precise cell-type composition and apical–basal polarity. To maintain homeostasis and enable rapid repair in response to environmental perturbations, intestinal epithelial cells undergo continuous self-renewal and differentiation. This process is accompanied by extensive remodeling of epithelial polarity, which involves coordinated changes in cell geometry, cytoskeletal tension, and organelle positioning. Such biophysical reorganization constrains intracellular transport, establishes directional signaling, and couples mechanical states of cells to fate decisions. While epithelial polarity is recognized as essential for intestinal function, how biophysical cues and molecular programs are integrated to establish, remodel, and stabilize polarity remains poorly understood. Intestinal organoids provide an experimentally tractable system that recapitulates epithelial geometry, cellular heterogeneity and force-dependent polarity in three dimensions. By combining organoid models with targeted gene perturbations and live imaging approaches, we aim to dissect how biophysical constraints and molecular regulatory networks jointly govern epithelial polarity, cell fate determination, and tissue-level homeostasis in the intestine.

 Selected Speaker Abstracts

Deciphering Injury-Induced Signals that Trigger Regeneration in the Mammalian Heart

An Zeng

Shanghai Institute of Biochemistry and Cell Biology, CAS

Adult mammalian hearts fibrose after injury, whereas neonatal hearts regenerate. The mechanisms underlying this divergence remain poorly understood. Using comparative spatiotemporal single-cell analyses combined with dual recombinase-mediated lineage tracing, we identify an injury-induced population of Clusterin-expressing cardiomyocytes (Clu⁺ CMs) that orchestrate a pro-regenerative cardio-immune response. After injury, Clu⁺ CMs appear prominently in the border zone of regenerative hearts but remain sparse in non-regenerative settings. Clu⁺ CMs secrete CLU, which engages macrophage Toll-like receptor 4 (TLR4) to dampen inflammation and promote reparative polarization via Cpt1a-dependent fatty acid oxidation. These macrophages subsequently release BMP2, activating BMPRII signaling in cardiomyocytes to drive proliferation. In myocardial infarction patients, reduced CLU levels are associated with worsened cardiac function. Conversely, Clu overexpression or transplantation of engineered CLU⁺ human cardiac organoids enhances repair and improves cardiac outcomes in adult mice. Together, these findings uncover a pivotal injury-induced cardio-immune axis in which Clu⁺ CMs reprogram macrophages to resolve inflammation and stimulate cardiomyocyte proliferation, offering new avenues for regenerative cardiac therapies.

 Selected Speaker Abstracts

How an Electrophysiological Signal Is Integrated into Scaling the Fins During Regeneration and Development

Christopher Antos et al.
Shanghaitech University

Tissue homeostasis and regeneration require the controlled growth of stem and progenitor cells to scale the structure to the correct size. Findings from several labs showed that the electrophysiological activities of K⁺ channels scale adult zebrafish fins, but it remained unknown how their electrophysiological activities are controlled and how these channels regulate proportional growth. We uncovered how intracellular K⁺ levels are regulated and how this K⁺-mediated electrophysiological mechanism scales entire anatomical structures. Using 3D in vivo Fluorescence Lifetime Microscopy (FLIM), we observed that the rate and proportions of outgrowth are inversely proportional to coordinated in vivo decreases in intracellular K⁺. We not only observed that overexpression of the different K⁺-leak channels is sufficient to increase the proportions of regenerating adult fins, we also discovered that they control the size of embryonic pectoral fin buds by enhancing the coordinated transcription of several morphogens that control tissue development. This finding is important, because the developmental program of the fin bud is very similar to the developmental program that controls the development of all early vertebrate limbs. In vivo and in vitro experiments show that Kcnk5b-regulated scaling requires IP3R-mediated Ca²⁺ release from the endoplasmic reticulum and that the Ca²⁺-dependent kinase CaMKK mediates Kcnk5b's control the transcription of shh, a morphogen that is required and sufficient to regulate proportional growth. The electrophysiological activity of Kcnk5b controls resting membrane potential of cells, and contrary to expected hyperpolarizing effect of this K⁺-leak channel, we observed that Kcnk5b leads to depolarization. This depolarization is required for Kcnk5b-mediated scaling and requires voltage-gated Na⁺ channels. In vivo FLIM measurements show that Retinoic Acid (RA) leads to decrease intracellular K⁺ levels and that these K⁺ levels are controlled by RA regulation of Kcnk5b-activity. Our findings identify how that the hormone RA, which is known to regulate positional identity and growth, decreases intracellular K⁺ via Calcineurin's regulation of Kcnk5b and how the Kcnk5b-mediated depolarization controls IP3-mediated Ca²⁺ release to promote shh transcription via CaMKK. Thus, we show how a bioelectrical mechanism can control regenerative/developmental programs and how this bioelectrical mechanism is regulated to scale the size of entire anatomical structures.

Selected Speaker Abstracts

‘Active Neutral Buoyancy’: a Goal-directed Multiscale Homeostatic Organisation for Balancing Gravity

Nicholas Wilkinson

Independent researcher/University of Leeds (until 31/12/2025)

Organisms are necessarily inhomogeneous collections of matter, challenging multiscale mechano-regulation under gravity. A jar of oil and water in air will stratify by density, and drop to the floor and smash. Biological systems must resist this disintegrative tendency to maintain multiscale organisation. Gravity management (‘balance’) is a multiscale task currently characterised differently at different scales. Crucially, neutral buoyancy enables passive balance. Hence deviation from neutral buoyancy demands active balance. My recent work¹ reformulates whole-body balance from a subsidiary sensorimotor control task (the current formulation) to a biophysically fundamental mechano-regulation task; compensating the density gradient at the body-medium interface. This approach formulates buoyancy B_{Body} (a property of matter distinct from buoyant force) as a multiplicative gain term on gravitational acceleration according to; $B_{\text{Body}} = 1 - \rho_{\text{Medium}} / \rho_{\text{Body}}$ Here I will share ongoing work generalising this approach to multiscale ‘balance’ homeostasis. Importantly, the framework specifies how animal phenotypes are developmentally calibrated to apprehend and physiologically embed the vital goal state (‘active neutral buoyancy’) as a far-from-equilibrium attractor. The organism is developmentally calibrated to necessarily embody and hence homeostatically conserve this vital goal by formative suspension in approximately equidense amniotic fluid (i.e. ~neutral buoyancy), across scales from the cellular to the organismic. This developmental calibration defines a distributed homeostatic ‘objective function’ and associated error signal when the goal state is perturbed by load. A well-calibrated multiscale error signal enables efficient search in the space of nested, co-dependent balance solutions by error gradient descent over multiple spatial and temporal scales. One solution class is nested containment/compartmentalisation e.g. cell walls or skin. At container level heterogeneous contents project their mean density to the surface, transforming contained density gradients from vertical liabilities to more manageable rotational liabilities. Within, containment establishes a local frame of equilibrium stratification (as in oil-water in a jar). A second class is mechanical compensation/eradication of density gradients, crucial to maintaining physiological organisation far from nested equilibrium stratifications. Overall, the ‘active neutral buoyancy’ framework elaborates a goal-directed multiscale organisation for balancing gravity, implying testable predictions from cellular to organism scales. Wilkinson, N.M. (2025) “What is balance? A vital mechano-regulation paradigm” MIT Open Mind <https://doi.org/10.1162/OPMI.a.257>

 Selected Speaker Abstracts

Regulation of Neuronal Morphology: Genetic Insights from *C. Elegans*

Yishi Jin

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Neuronal morphology underlies functional connection. Neurons employ a variety of mechanisms to maintain morphology throughout adult life. In studies of *C. elegans* mutants displaying aberrant neuronal morphology, we uncovered a genetic network that regulate phospholipid asymmetry. Loss of function in two conserved genes, *dip-2*, a member of the Dip2 family of lipid metabolic regulators, and *sax-2*, a member of the Furry/Fry scaffold proteins, causes minor to moderate neurite abnormality. Combined loss of *dip-2* and *sax-2* results in dramatic disruption of neuronal morphology and severe behavioral deficits. From screens for suppressor mutations of *dip-2 sax-2* double mutant phenotypes we identified gain-of-function (gf) mutations that promote the activity of the membrane phospholipid flippase TAT-5/ATP9A. TAT-5 is known to flip phosphatidylethanolamine (PE) and inhibit extracellular vesicle release. I will discuss our on-going work to understand the regulation of phospholipid asymmetry in neuronal architecture.

Poster Abstracts

01

Epidermal Regeneration Dynamics in Axolotl Limb and Wound Healing: Image-based Quantification and Mathematical Modelling.

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The axolotl (*Ambystoma mexicanum*) is an ideal animal model to study tissue repair as it is capable of complete limb regeneration. In this work, we study the spatiotemporal tissue dynamics underlying epidermal regeneration in the limb. In other axolotl's tissues, such as the spinal cord, the regeneration process is heavily driven by an increase in cell proliferation as a response to the damage in the tissue. However, the regeneration of the epidermis in the limb seems to be mostly driven by cell migration from other tissues. Using time-lapse imaging, we investigated both limb regeneration following amputation and wound healing in non-amputated limbs. We followed cell movements over time by performing image analysis of the limb and tracking its cells. We proposed a mathematical diffusion model to describe cell movement during regeneration. From experimental cell trajectories, we computed velocity fields which we used to parameterize the mathematical model. Our approach provides a quantitative framework linking experimental data, image analysis and modelling to better understand limb regeneration.

Poster Abstracts

02

A Spatially Explicit Model of Notch-mediated Coordination in Adult Neural Stem Cell Populations

Marcos Wappner, Nicolas Dray, Laure Bally-CUIF

Institut Pasteur, Université Paris Cité, CNRS UMR3738,
Zebrafish Neurogenetics Unit, F-75015 Paris, France

Over a lifetime, adult neural stem cell (NSC) populations in vertebrates produce new neurons, sustaining growth, learning and memory. In the zebrafish adult telencephalon, the NSC population maintains long-term spatiotemporal homeostasis, although individual NSCs activate, divide and eventually exhaust. This implies that NSCs do not behave independently: they must exchange signals that coordinate their lineage decisions in space and time. Among these signals, components of the Notch pathway show spatial patterns of expression and activity, closely linked to NSC state and fate. However, how these signalling patterns translate into population-level equilibrium, and how they contribute to the system's robustness, remains an open question. Notch-mediated interactions are therefore strong candidates for the local communication mechanisms underlying NSC coordination, but we currently lack a mechanistic framework that connects these interactions to the spatiotemporal dynamics of the population. Such a framework must integrate tissue geometry, multi-ligand signalling dynamics, and the stochastic nature of NSC activation and progression. To address this, in this work we combine a biophysically grounded mechanical simulation of the adult telencephalic tissue with a quantitative description of Notch pathway dynamics. This approach allows for systematic exploration of how spatially structured signalling landscapes influence activation frequencies, local correlations, and the system's capacity to recover from global perturbations. I will present current progress toward this integrative description, including the construction and validation of a vertex model that reproduces the geometry and neighbourhood relationships of zebrafish adult telencephalic NSCs, and preliminary simulations in which Notch-mediated communication rules are coupled to NSC state transitions. These developments provide a platform for interpreting existing *in vivo* observations and for generating testable predictions about the signalling feedbacks that stabilise NSC populations. By linking molecular interactions to emergent tissue-level behaviour, this work aims to clarify how coordinated decisions among adult NSCs support long-term brain homeostasis.

Photo-Responsive Inorganic Hydrogel Interfaces for Modulating Retinal Homeostasis and Neurodegeneration

Sharadrao Vhanalkar

Laboratory of Bio-Interface Materials (LBiM), K. H. College, Shivaji University, Kolhapur, India

Dyshomeostasis; a root cause of retinal degenerative disorders includes metabolic imbalance, blood-retinal barrier, oxidative stress-driven neuronal loss, auto- and mitophagy, homeostatic plasticity and reduced synaptic transmission ultimately leading to photoreceptor loss. The compact integrated microenvironment of the visual system triggers and accelerates immune, vascular, and metabolic signaling disease progression and limit repair. The conventional lifestyle and adjunctive measures, pharmacological interventions, as well as novel treatments like as gene and stem cell therapy, offer hope for slowing disease progression and recovery. The majority of treatments can effectively improve the retinal microenvironment and preserve homeostasis, restoring and delaying RPE and photoreceptor cell function; however, conventional methods are unable to replace lost RPE and photoreceptor cells. In order to interface with retinal tissue and modify neuronal function through regulated photo-stimulation, we have presented a polymer-inorganic semiconductor hydrogel platform. This prosthetic rehabilitation generates spatially confined electrical and ionic signals under illumination, which regulates redox imbalance, neuronal activation, and reduction in ROS-related dyshomeostasis. The hydrogel matrix offers mechanical flexibility along with water-mediated proton/electron transport and on the other hand, the embedded semiconductor phase permits photon-to-charge transduction under low-intensity light. This non-genetic, free standing, light-induced form of neuronal functional restoration causes membrane depolarization and affect redox pathways. Despite being in its early stages, this platform uses both electrophysiological and redox regulatory mechanisms to propose a biophysical paradigm for retinal neuron stimulation, activation and repair.

Mechanism and Intervention of Neural Tube Defects

Chengji Zhou

ADA Forsyth Institute

Neural tube closure is a key process of neurulation during embryonic brain and spinal cord formation, and the underlying cellular, molecular, and biophysical mechanisms remain largely unclear. We have demonstrated that canonical Wnt/beta-catenin signaling is required for caudal neural tube closure by regulating crucial downstream transcription factors in the dorsal neural folds of mice. Maternal intervention with small molecules of Wnt signaling activators can significantly reduce the rate and severity of neural tube defects. We have further revealed that the non-neural surface ectodermal cells at the boarder region of the dorsal neural epithelia form multicellular rosette structures with convergent cellular protrusions and an F-actin cable network encircling the pending closure site of the posterior neuropore. These unique arrangements are disrupted in the surface ectodermal mutants with neural tube defects. We propose a “rolling rosette” model of mammalian neural tube closure driven by F-actin-based biomechanical force of the boarder surface ectodermal cells. We have generated novel mutants with neural tube defects by conditional gene-targeting of representative signaling regulatory genes in the non-neural surface ectodermal cells. Our preliminary results demonstrate that canonical Wnt signaling is essential for activating the surface ectodermal transcription factors and modulating multicellular rosette formation and polarized cellular protrusions to generate the biomechanical force to close the neural tube, and that maternal intervention with Wnt signaling activators can effectively prevent neural tube defects. Currently we are working on spatial transcriptomics to determine the single-cell transcriptomic properties and gene-regulatory networks of the rosette-forming surface ectodermal cells during neural tube closure, which may also provide a clue for tissue homeostasis and repair.

Mechanical Regulation of Basement Membrane Turnover Dynamics During Hair Follicle Morphogenesis

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Basement membranes (BMs) are sheet-like extracellular matrices that underlie epithelia, endothelia, and many other tissues. Our previous study revealed that collagen IV turnover and expansion were spatially regulated in developing mouse hair follicles in a matrix metalloproteinase-dependent manner. However, it remains unclear how spatiotemporal BM degradation and turnover are regulated. As developing tissues grow and experience spatially heterogeneous strains, precise cell-instructed BM remodeling becomes challenging. Thus, we hypothesize that BMs possess an intrinsic mechanoregulatory mechanism that interprets tissue expansion-associated mechanical inputs to spatially control BM turnover and expansion. To investigate this possibility, we combined live imaging-based quantification of BM dynamics with mechanical perturbation of the BM zone. Using a second-generation collagen IV visualization mouse model with enhanced fluorescence, we found that the BM zone at the hair follicle tip showed larger ablation-induced recoil, consistent with elevated tension. Relieving BM-zone tension by laser ablation reduced collagen IV incorporation into the BM, whereas ablation of surrounding epidermal and dermal cells had no effect, suggesting that mechanical stretching increases BM susceptibility to degradation. Furthermore, inhibition of actomyosin contractility with Y-27632 reduced BM recoil/tension and disrupted bell-shaped tip morphogenesis. Together, these findings suggest that actomyosin-generated forces provide mechanical inputs that are converted into in-plane tension within the BM, enabling its intrinsic mechanoregulatory mechanism to spatially control BM turnover and shape tissue architecture.

Poster Abstracts

06

Stem Cell Niche Protein C Levels Are Sustained by Progesterone to Inhibit Mammary Gland Inflammation

Yishu Xu, Chunye Liu, Yi Zeng

Shanghai Institute of Biochemistry and Cell Biology, CAS.

Aging is associated with chronic inflammation and stem cell dysfunction, but the mechanistic linking these processes are poorly understood. Protein C (PC), traditionally recognized as a liver-derived anticoagulant circulating in serum, has recently been implicated in stem cell biology via its receptor, Procr. However, the cellular source of protein C required for tissue stem cell function remains unknown. Here, we demonstrated that HR⁺ luminal cells locally produce Protein C (PC) to mediate stem cell-dependent anti-inflammatory functions. Local PC conditional deletion increases inflammation and macrophage infiltration. Age-related chronic inflammation in mammary glands with dysregulated chemokine expression in MaSCs is associated with PC reduction in aged luminal cells. Mechanistically, age-related progesterone decline reduces PC expression, elevating STAT3 signaling and pro-inflammatory characters in MaSCs. We defined the progesterone-PC axis as a critical immune niche modulator, uncovering a novel link between hormonal changes, stem cell aging, and inflammaging. This study reveals that stem cell aging is not only about senescence but also a decline in anti-inflammatory ability, which mediates systemic hormonal decline and chronic inflammation, offering new therapeutic targets for age-related inflammatory diseases.

Poster Abstracts

07

Nodal-regulated Mechanochemical Programs Linking Molecular Signalling to Tissue Homeostasis

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Tissue homeostasis and repair require the coordinated integration of molecular signalling, collective cell behaviours, and mechanical forces to restore stable tissue architecture after perturbation. Although many signalling pathways involved in tissue repair have been identified, how molecular cues interface with biophysical mechanisms to generate robust, self-organized tissue states remains incompletely understood. My research addresses this question by investigating how the morphogen Nodal couples molecular regulation to tissue mechanics in vertebrate gastrulation. I use zebrafish and chick embryos to study how localized Nodal signalling reorganizes cell behaviours and tissue mechanics. Combining live confocal imaging with AI-based 3D single-cell reconstruction, I quantitatively analyse cell shape, volume, polarity, and migration during Nodal-induced tissue remodelling. These approaches are integrated with direct biomechanical measurements, including Fluorescence Lifetime Imaging (FLIM) to assess membrane tension and Tissue Force Microscopy (TiFM) to quantify tissue rigidity. In zebrafish, ectopic Nodal signalling at the animal pole induces a stable blastoderm thickening that subsequently internalizes to form a circular, blastopore-like structure. This structure closely mimics the formation of the embryonic shield and germ ring during normal gastrulation, but arises in a simpler, spatially isolated context, largely independent of other patterning cues. This system provides a powerful framework to dissect how a single signalling input drives collective cell migration, tissue folding, and mechanical stabilization. Our results show that blastopore-like formation is governed by a spatially patterned mechanical programme: local reduction of envelope-layer tension permits deformation, while changes in cell adhesion, cell geometry, and collective migration lead to cell jamming and pressure accumulation that mechanically stabilise the newly formed tissue.

At the cellular level, Nodal establishes leader-follower dynamics in collective migration. We recently found that Nodal regulates Rnd1b signalling, linking morphogen input to cytoskeletal control of cell movement while coordinating cell fate decisions. Extending these studies to chick embryos reveals conserved Nodal-induced cell clustering and mesodermal fate acquisition, suggesting evolutionary conservation of Nodal-controlled mechanochemical programs. Together, these findings demonstrate how molecular signalling actively regulates tissue-scale mechanical homeostasis, providing insights to tissue repair, regeneration, and pathological remodelling.



A Mesenchymal-derived Hepatocyte Lineage Parallels Endodermal Development in the Fetal Liver

Zhiyao Xie, Lanyue Bai, et al.

Center for excellence in molecular cell sciences, CAS

Hepatocytes in the fetal liver are classically derived from endodermal hepatoblasts. While a mesenchymal gene-expressing hepatoblast subset has been observed, its lineage potential and developmental role remain undefined. Here, we identify a Procr +/Pdgfra + mesenchymal-like progenitor that emerges during a restricted developmental window (E10.5–E11.5) and establishes a parallel hepatocyte lineage, contributing ~30% of the hepatocyte pool. Fate-mapped hepatocytes derived from this progenitor retain a transient mesenchymal-like transcriptome and exhibit enhanced proliferative capacity relative to endoderm-derived hepatoblasts at E13.5. These cells subsequently mature, losing their mesenchymal signature to become conventional hepatocytes by E16.5. Targeted ablation of these progenitors using a Pdgfra-Cre;Procr-lsl-rtTA;TetO-DTA;R26-mTmG model impairs liver development. Our findings establish a bona fide mesenchymal-origin hepatocyte lineage, revealing a complementary developmental pathway that operates alongside the canonical endodermal route to build the fetal liver.

Mechanical Response of Phospholipids at the Plasma Membrane

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Cells are subjected to compressive stress when growing and dividing in a confined environment. Excessive cell growth and infiltration such as during tumor growth crowd the environment and result in high compressive stress that distorts cellular health. Plasma membrane (PM) as the outermost layer of cells senses and responds to compression. How the glycerophospholipids, which are the major lipid species of the PM, are regulated mechanically remains largely unclear. We found that in the breast epithelial MCF10A cells, there was an increase of two negatively charged phospholipid species, phosphatidic acid (PA) and phosphatidylserine (PS), in response to compressive stress during cell division. Increased PA synthesis at the PM under compression was driven by Phospholipase D2 (PLD2), which was activated by the Ca^{2+} influx into the cytosol. Mechanical activation of PLD2 by Ca^{2+} appeared direct as PLD2 mutants defective in binding to Ca^{2+} did not support mechanoaccumulation of PA under compression. Increase of PS at the PM was likely to derive from the endoplasmic reticulum (ER) as the inhibition of the ER-localized PS synthesis enzymes prevented mechanoaccumulation of PS. We speculated that there is an increased transfer of PS from the ER to the PM in response to compression as the ER–PM membrane contact sites increased when cells were compressed. When mechanoaccumulation of PA and PS was inhibited in cells entering mitosis under compression, cells were arrested at the mitotic phase for prolonged periods of time without going through chromosome segregation and cytokinesis. Depletion of PA and PS affected mitochondria activity as both are involved in the mitochondria lipid homeostasis, which in turn preventing mitotic progression. Our study provides mechanistic insight into how phospholipid dynamics integrate physical forces to support cell division under mechanical stress.

10

Cell Behaviors Under Confinement

Yan-Jun Liu

Institutes of Biomedical Sciences, Fudan University, Shanghai, China.

The cellular microenvironment plays a critical role in regulating cell behavior through a combination of biochemical and biomechanical signals derived from neighboring cells, the extracellular matrix (ECM), and soluble factors. However, conventional 2D cell culture systems fail to replicate the complexity of in vivo microenvironments. While collagen gels are commonly employed as simplified models to study 3D cell environments, they remain inherently complex. Multiple physical parameters—including geometric confinement, matrix constrictions, gel heterogeneity, and elasticity—often act simultaneously, making it difficult to dissect their individual contributions to cell behavior. To overcome these challenges, we have developed innovative tools based on micro- and nanofabrication techniques to precisely reconstitute cell microenvironments. By independently modulating the physical and chemical properties of these environments, we are able to systematically investigate cellular dynamics and behavior under confinement. Using this approach, we discovered that confinement and low adhesion can induce mesenchymal cells switch to fast amoeboid migration (MAT). This suggests that tumor cells may adopt diverse migratory strategies to escape primary tumors and invade surrounding tissues, without requiring specific genetic alterations. Despite these insights, the molecular mechanisms governing such phenotypic plasticity have remained elusive. In this study, we uncover a previously underappreciated role of H3K9me3-heterochromatin as an epigenetic barrier and nuclear mechano-responder that regulates cell fate decisions during A2 amoeboid transition in response to mechanical forces. Our findings highlight the potential of targeting H3K9me3 dynamics as a therapeutic strategy to control pathological cell migration in immune-related disorders and cancer metastasis.

Epicardial Softening and Mechanical Heterogeneity Define the Regenerative Niche in Newt Heart Regeneration

Tuba Majid, Sofia Kagioglou, Elif Eroglu

Department of Cell and Molecular Biology, Karolinska Institutet, Stockholm, Sweden

Cardiac function relies on a dynamic equilibrium between ventricular geometry, myocardial mechanics, and hemodynamics. In mammals, myocardial infarction triggers progressive fibrosis, and while this stiffening initially stabilizes the injury, it eventually leads to heart failure. Conversely, regenerating species such as the Iberian ribbed newt (*Pleurodeles waltl*) successfully restore lost myocardium. We previously reported that the newt epicardium has an intrinsic capacity to differentiate into cardiomyocytes. Following cryo-injury, the epicardium gets activated and gives rise to epicardium-derived cells (EPDCs), which at the injury site undergo lineage reprogramming. However, how tissue stiffness changes in response to cryoinjury and subsequently returns toward baseline during regeneration has not been characterized. We hypothesized that dynamic modulation of the injury site establishes a specific mechanical niches that facilitate EPDC recruitment and regeneration. To test this, we probed tissue-scale mechanical properties in relation to EPDC infiltration. Using nanoindentation, we mapped tissue stiffness (Young's modulus) at micron-scale resolution. Furthermore, we employed dynamic mechanical analysis to quantify the frequency-dependent viscoelastic properties: storage modulus (E') and loss modulus (E'') of the epicardium across multiple time points post-cryoinjury. Our results reveal that the epicardium progressively softens from 7 to 14 days post-cryoinjury (dpci). Both E' and E'' decrease during this window, indicating a reduction in both elastic and viscous resistance. Notably, peak epicardial softening at 14 dpci coincides with maximal EPDC infiltration into the injury site. We also observed that the injury site is mechanically heterogeneous, encompassing a wide range of stiffness values. While these data do not yet establish causality, they demonstrate that the regenerative niche is mechanically fluid rather than static. Ongoing work seeks to investigate the reciprocal relationship between EPDCs and their environment: do these cells actively remodel the regenerative niche, or is their behavior primarily dictated by it? By perturbing the physical state of EPDCs through the disruption of tight junction formation, we aim to determine whether cell-intrinsic mechanical properties are required for injury-site infiltration.

Poster Abstracts

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Retinoic Acid-*rcan2* Regulates Bioelectrical Control of Chromatin Remodeling Factors to Regulate Scaling of Appendages During Regeneration and Development

Yi Sun, Sen Wang, Xiaowen Jiang, Yuxin Zhu, Christopher Antos

Yi Sun, Sen Wang, Xiaowen Jiang, Yuxin Zhu, Christopher Antos

The proportions of all anatomical structures are controlled during regeneration, development and tissue homeostasis to achieve proper proportions with the body. However, how bioelectrical signals are involved in coordinated growth control remains unclear. We show how an electrophysiological mechanism involving K⁺-leak channels is integrated into molecular mechanisms to regulate the proportions of entire anatomical structures; specifically, the regeneration adult fins and developing embryonic fin buds. We observed that the K⁺-leak channel *Kcnk5b* is expressed in the mesenchyme during outgrowth of the regenerating fin blastema and developing fin bud. Overexpression of *Kcnk5b* was sufficient to increase the size of the entire anatomical structure by enhancing the transcription of several morphogens. Retinoic acid (RA) is a hormone morphogen that can increase limb proportions, and we found that it decreased intracellular K⁺ in all bud tissues. We also found that RA up-regulated the transcription of regulator of calcineurin (*rcan2*) in adult fins and embryonic fin buds and that *rcan2* overexpression was sufficient to decrease intracellular K⁺ as well as to enhance growth of the regenerating fins and developing fin buds. Conversely, knockout of *rcan2* increased intracellular K⁺ and decreased the growth proportions. We also found that *Rcan2*'s ability to scale was dependent on *Kcnk5b*, since the knockout of *Kcnk5b* prevented *Rcan2*-induced decreases in intracellular K⁺ and *Rcan2*-enhanced proportional growth. To define how *Kcnk5b* activity leads to the coordinated control of all morphogens during regeneration and development, we performed RNA-seq experiments and looked for factors that could regulate chromatin structures. We observed that chromatin remodeling factors *smarcd3a* and *arid3c* were up-regulated soon after *Kcnk5b* overexpression. We determined that overexpression of these genes was sufficient to induce specific developmental genes' activity such as *shha*, *lef1*, and increase the growth proportions of fin buds. We also observed that knockout of *smarcd3a* impaired the *Kcnk5b*'s ability to enhance proportional growth. Our findings identify how a bioelectrical signal that controls proportional growth of anatomical growth during regeneration and development is regulated by RA via *Rcan2* and how the bioelectrical signal regulates chromatin remodelers to coordinately scale the growth proportions of regenerating fins and embryonic fin buds.

A Probiotic-Based Oral Subunit Vaccine Approach to Address Multidrug-Resistant *Shigella* Infections

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Shigella is a major contributor to child mortality in developing countries of Asia and Africa. Four species and multiple serotypes make it challenging to develop a vaccine against *Shigella*, as immune responses are primarily serotype-specific. Although past efforts have focused on live attenuated and subunit vaccines, no licensed *Shigella* vaccine currently exists, and treatment relies entirely on hydration and antibiotics. *Shigella* strains are emerging to be resistant to antibiotics such as Tetracycline, Ampicillin, Chloramphenicol, Azithromycin, Ciprofloxacin, and Ceftriaxone, heightening the urgency for a preventive approach. Given that *Shigella* establishes infection at the gastrointestinal epithelium, leveraging mucosal immune responses offers a rational and effective strategy to counter *Shigella* infection. In the presented work, we aim to develop an oral subunit vaccine using *Lactococcus lactis* expressing OmpA (Outer Membrane Protein A, a highly conserved and highly expressed membrane protein) from *Shigella dysenteriae* type 1 as an antigen to be expressed in the host cells. As *Lactococcus lactis* is non-pathogenic, it doesn't generate a robust immune response on its own. To elicit an effective immune response, the *Lactococcus* need to be recognised by M-cells in the small intestine. To achieve this, we employ dual recombinant *Lactococcus* strains, with one plasmid encoding the OmpA antigen and the other encoding an M-cell-targeting ligand to promote uptake in the intestinal mucosa. We are currently evaluating the antigen delivery system utilising an in vitro and in vivo *Shigella* infection mouse model. If successful, this platform could provide a scalable, non-pathogenic, and probiotic-based oral vaccine to induce protective mucosal immunity against *Shigella*.

Mechanical Contributions of Intestinal Cell Populations to Organoid Regeneration

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Regeneration of the intestinal epithelium following injury requires rapid resealing of the luminal barrier and subsequent restoration of tissue homeostasis. Despite its physiological importance, the mechanobiology underlying this process remains incompletely understood, and different cell populations—such as villus cells[1] and transit-amplifying cells [2]—have been proposed as key drivers of regeneration. Here, we introduce a hydrogel-based 2D intestinal organoid model that enables direct, spatiotemporal monitoring of cell dynamics and mechanical forces in both crypt and villus regions following the induction of a localized gap within the villus domain. Using this system, we identify differentiated enterocytes as the primary cell population responsible for covering and resealing the injured area through active migration. Gap closure emerges as a strongly mechanically regulated process, characterized by elevated traction forces at the wound edge. Following gap closure, migratory enterocytes upregulate regenerative markers and re-enter the cell cycle, thereby repopulating the wounded region and preventing mechanical failure of the epithelial monolayer under sustained contractile stress. Together, these results reveal a central mechanical role for differentiated enterocytes in intestinal wound healing and regeneration. More broadly, this experimental platform provides a powerful framework to dissect how cell-type-specific mechanical behaviors govern regeneration and homeostasis in highly dynamic epithelial tissues. References 1. Grzegorz M., et al. Stem Cell Reports, 2024, 19(8): 1172–1188. 2. Takahiro E. O., et al. Developmental Cell, 2022, 57(2): 166–179.e6.

Identification and Characterization of Sdl Genes in the Maintenance of Lysosomal Membrane Integrity in *C. Elegans*

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Lysosomes degrade macromolecules, damaged organelles, and recycle catabolites to maintain cell and tissue homeostasis. Lysosomes also function as a signaling hub that integrates nutrient, energy, and growth signaling and coordinates cellular responses. Lysosome dysfunction is associated with various human diseases such as metabolic disorders, neurodegenerative diseases, and cancer. Lysosomes are membrane-bound acidic organelles that contain >60 soluble hydrolases and >100 membrane-associated proteins. Defects in lysosome membrane integrity cause leakage of luminal hydrolases that may degrade cellular components and lead to cell death. We utilize the multicellular organism *C. elegans* to investigate how lysosome membrane integrity is maintained and how this contributes to animal development and longevity. To do this, we perform forward genetic screenings to isolate *lid* (lysosome integrity defective) and *sdl* (suppressor of damaged lysosomes) mutants, clone affected genes and investigate their roles in the maintenance of lysosome integrity or in the repair or clearance of damaged lysosomes. We isolated *sdl-2* mutations which effectively suppresses lysosomal damage caused by multiple *lid* mutants. *sdl-2* encodes a conserved mitochondrial protein and its mutation may impair electron transport chain (ETC) function. *sdl-2* mutants affect mitochondria morphology and function, while they contain increased number of vesicular lysosomes that are smaller in size. Moreover, both acidity and degradation activity of lysosomes are affected in *sdl-2* mutants. TEM analyses indicate that cargo-containing lysosomes reduce significantly in *sdl-2* mutants. In line with this, lysosomal fusion with endosomes and autolysosomes is impaired in *sdl-2* mutants. *sdl-2* mutants cause elevated cytosolic ROS level, which impairs lysosomal fusion and suppresses lysosomal damage. These data suggest that loss of *sdl-2* may affect lysosomal fusion, causing defects in lysosomal biogenesis and cargo delivery. We are currently investigating the role of *sdl-2* in lysosomal fusion and its relevance to the mitochondrial function of *sdl-2*.

Key words: lysosome integrity; *sdl*; mitochondria; membrane fusion

Leader Cell Emerged from the Epithelial Single-cell Population Guides the Formation of Patterned Cell Clusters

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Conventional injury repair models in vitro often differ significantly from authentic processes in vivo. To address this, we developed a specialized intestinal injury-repair model that faithfully recapitulates the multicellular scenario during regeneration in vivo. In this system, epithelial single cells could form regular clusters within the extracellular matrix in migration guided and self-organized manner. Each cluster can develop into organoid-like tissue containing stem-cell niches and differentiated tissue regions. A specific type of active cells consistently emerges from the epithelial single-cell population and guides collective cell migration, which eventually leads to the formation of well-patterned cell clusters. Furthermore, we demonstrated that such active cells are present in healthy epithelial tissues but absent in cancerous tissues. We developed a biophysical model that accurately predicts the migratory and clustering behavior of intestinal epithelial cells within the extracellular matrix. Combining chemical and genetic cell labeling and single-cell RNA sequencing, we identified the fate of the active cells and confirmed their essential function in migration and regeneration. Importantly, we confirmed the existence and function of these active cells in both mouse and human gut, which promote post-damage repair of gut.

Identification and Characterization of Genes in the Regulation of Lysosome Membrane Fission

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Lysosomes are degradation and signaling centers crucial for homeostasis, development and ageing. To meet diverse cellular demands, lysosomes remodel their morphology and function through constant fusion and fission. We have recently identified *C. elegans* HPO-27 and human MROH1 as lysosomal fission factors. HPO-27 and MROH1 are Heat-Repeat proteins that are recruited to lysosomes by Rab7, where they self-assemble to mediate lysosome membrane fission. Interestingly, HPO-27 and MROH1 sever supported membrane tubes in vitro without the direct use of energy, suggesting that they are a new type of fission factor. To understand how HPO-27/MROH1-mediated membrane scission is regulated and achieved, we perform large-scale genetic screens to identify genes involved in HPO-27-mediated lysosome fission. To achieve this, we utilise a tripartite split-GFP reporter that detects the self-interaction of HPO-27. From the screens, we isolated 18 enhancer mutants that exhibit stronger split-GFP signals, accompanied by diverse lysosomal morphologies. Moreover, 12 suppressor mutants were identified, which either lose or have significantly reduced split-GFP signals, while showing varying lysosome morphologies. We are currently characterising the mutant phenotypes and identifying the affected genes through whole-genome sequencing. In the meantime, we performed proximity labeling coupled with LC-MS to identify MROH1-interacting proteins in mammalian cells. The candidate proteins are being analyzed in both mammalian cells and worms. These studies will help us to understand the mechanisms underlying HPO-27/MROH1-mediated lysosome fission.

Poster Abstracts

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Perturbing Transepithelial Electric Potential Influences Epithelial Cell Events

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Abstract: Epithelial tissues create transepithelial electric potential, due to basal-apical polarity, tight junctions and active ion pumping. This potential (few to few tens of millivolts) is important in regulating transport across epithelium but its role in regulating cell behaviors is poorly understood. Here using two distinct methods to perturb the endogenous Transepithelial Electric Potential, we investigate how this endogenous biophysical parameter regulates important cell events. The two methods are A) a microfluidic device to apply a tunable and physiologically relevant electric field perpendicular to the epithelial tissue plane, and B) a laser-ablation gap creation assay to prevent ionic difference build-up across the monolayer. We find that cell division and extrusion rates in Madin Darby Canine kidney (MDCK) cells depend on electric field direction and the monolayer gap that theoretically weakens the Transepithelial Electric Potential. These results demonstrate the importance of bioelectric parameters at the tissue level and necessitate further mechanistic studies and investigations in other model systems.

Key words: Transepithelial Electric Potential (TEP); Cell extrusion and division; Microfluidics; Laser ablation

3D Interfacial and Spatiotemporal Regulation of Human Neuroepithelial Organoids

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Neuroepithelial (NE) organoids with dorsal–ventral patterning provide a useful three-dimensional (3D) in vitro model to interrogate neural tube formation during early development of the central nervous system. Understanding the fundamental processes behind the cellular self-organization in NE organoids holds the key to the engineering of organoids with higher, more in vivo-like complexity. However, little is known about the cellular regulation driving the NE development, especially in the presence of interfacial cues from the microenvironment. Here a simple 3D culture system that allows generation and manipulation of NE organoids from human-induced pluripotent stem cells (hiPSCs), displaying developmental phases of hiPSC differentiation and self-aggregation, first into NE cysts with lumen structure and then toward NE organoids with floor–plate patterning, is established. Longitudinal inhibition reveals distinct and dynamic roles of actomyosin contractility and yes-associated protein (YAP) signaling in governing these phases. By growing NE organoids on culture chips containing anisotropic surfaces or confining microniches, it is further demonstrated that interfacial cues can sensitively exert dimension-dependent influence on luminal cyst and organoid morphology, successful floor–plate patterning, as well as cytoskeletal regulation and YAP activity. This study therefore sheds new light on how organoid and tissue architecture can be steered through intracellular and extracellular means.

Poster Abstracts

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To Kill or Not to Kill: Mechanical and Spatial Control of NK Cell Cytotoxic Decision Making at the Immunological Synapse

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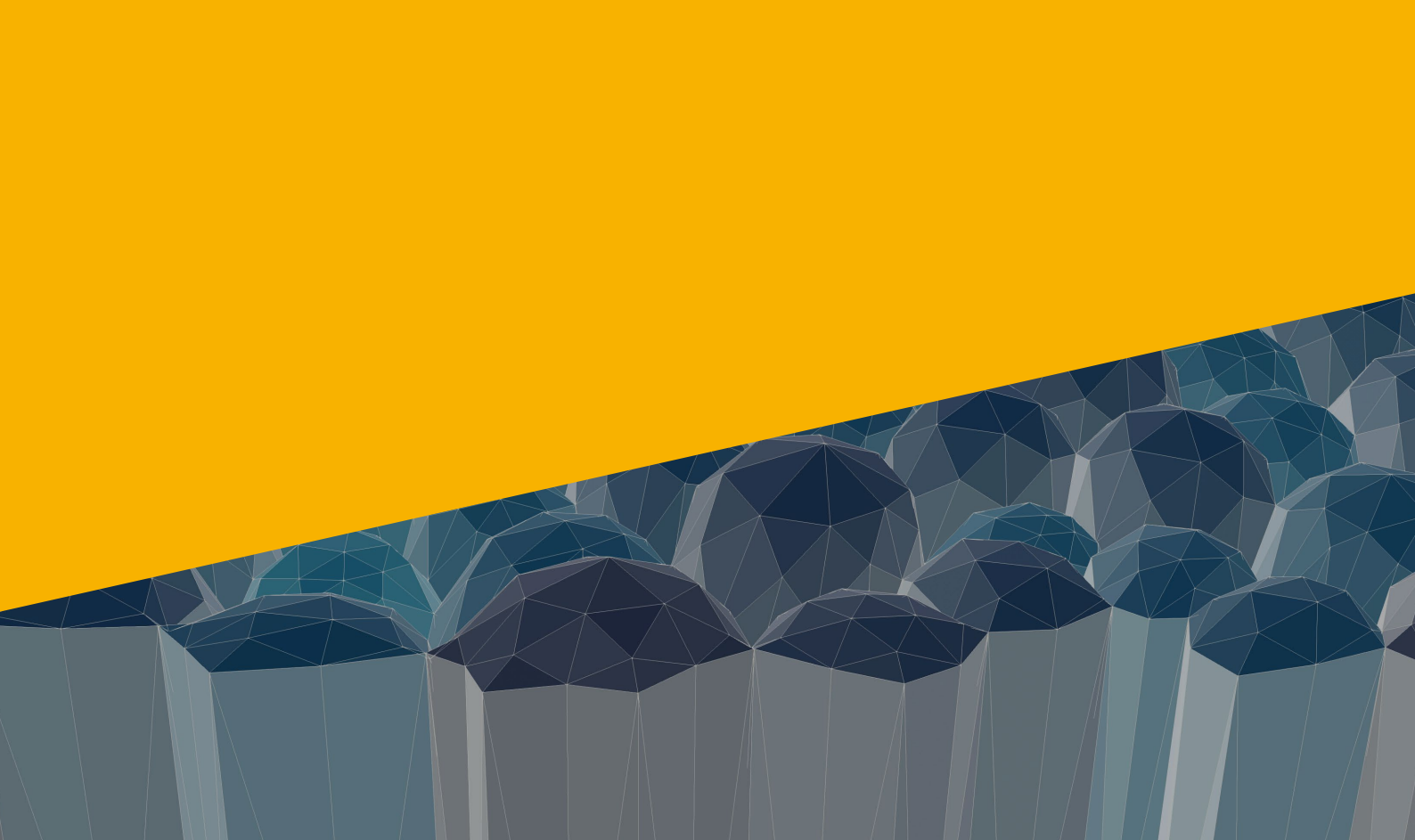
Natural killer cells preserve immune homeostasis by eliminating infected or transformed cells through formation of the immunological synapse, a mechanically organised and spatially structured signalling interface. At this contact zone, activating and inhibitory receptors do not act in isolation but are dynamically arranged into microdomains whose nanoscale segregation, clustering, and force dependent interactions shape downstream signalling. Experimental studies show that ligand spacing, receptor co clustering, and mechanical engagement modulate cytotoxicity, yet it remains unclear how spatial receptor architecture collectively determines whether an NK cell commits to killing or maintains tolerance. In particular, how do local receptor interactions generate robust discrimination between healthy and abnormal targets, and can spatial organisation alone produce switch like cytotoxic decisions? To address these questions, we develop a general theoretical framework for NK signal integration at the synapse. Individual receptors are represented as three state continuous time Markov cycles corresponding to inactive, intermediate, and signalling competent configurations. Completion of the signalling cycle depends on local cofactor availability, which is released upon receptor activation and diffuses away with rate λ , creating short range positive feedback. Neighbour dependent coupling, modulated by strength β , alters transition rates between receptor states and captures spatial communication between adjacent receptors within the synaptic lattice. Mean field analysis reveals that this feedback architecture produces a sigmoidal dependence of signalling probability on cofactor availability, allowing multiple fixed points and bistability in receptor activity. Lattice simulations confirm stochastic switching between inactive and active basins, with switching and dwell times consistent with barrier crossing dynamics. Parameter sweeps identify regimes where bistability emerges on biologically relevant timescales, demonstrating that spatial coupling and local feedback are sufficient to generate decision thresholds without invoking detailed pathway specific tuning. These results suggest that mechanical and spatial organisation at the immunological synapse can generate emergent, collective decision states that support immune discrimination and stable homeostasis. By linking nanoscale receptor distribution to synapse level signalling dynamics, this framework provides a mechanistic foundation for understanding how physical organisation governs cytotoxic commitment during immune surveillance and tissue repair.

Lipid-Laden Hematopoietic Lineage Macrophages in Liver Regeneration and Fibrosis

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Liver fibrosis arises from dysregulated tissue repair and can progress to irreversible organ dysfunction. Macrophages are central regulators of regeneration and fibrosis, yet the mechanisms governing their functional heterogeneity remain incompletely understood. Utilizing a multi-omics approach—integrating lineage tracing, single-cell RNA sequencing, and spatial transcriptomics, we identify a novel subset of hematopoietic-lineage macrophages in both rodent and human livers recruited upon injury. Termed lipid-enriched inflammatory macrophages (LIMMs), these cells exhibit concurrently heightened lipid metabolic and inflammatory programs, and are essential for coordinating reparative immune responses during liver regeneration. LIMMs are robustly recruited during early stages of toxin- or diet-induced liver fibrosis, where they localize adjacent to proliferating hepatocytes, promote hepatocyte regeneration to restore tissue homeostasis. Pharmacologic or genetic activation of lipid metabolism enhances LImm function and attenuates liver fibrosis. Collectively, our findings establish LIMMs as essential orchestrators of hepatic repair and identify them as a previously unrecognized link between lipid metabolism and anti-fibrotic immunity. Targeting LImm function through metabolic modulation or cell therapy offers a promising precision strategy for treating chronic liver disease.



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