From cell to organism

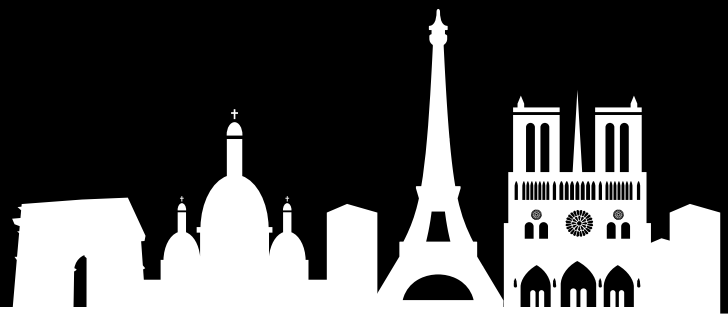
When cell biology meets development

KEYNOTE SPEAKERS

Eileen E. FURLONG • Caren NORDEN

INVITED SPEAKERS

Anna AKHMANOVA
Ivan BEDZHOV
Lionel CHRISTIAEN
Marie DELATTRE
Spencer FREEMAN
Pierre GÖNCZY
Aissam IKMI
Wolfgang KEIL
Kinneret KEREN
Mounia LAGHA
Pierre LEOPOLD
Chema MARTIN-DURAN
Nicolas MINC
Patrick H. O'FARRELL
Ewa PALUCH
Nicoletta PETRIDOU
Eugenia PIDDINI
Matthieu PIEL
Rashmi PRIYA
Emma RAWLINS
Klemens ROTTNER
Peter RUGG-GUNN
Sara SIGISMUND
Sebastian STREICHAN
Maria-Elena TORRES-PADILLA
Miltos TSIANTIS



OCTOBER 16-19, 2024

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BOOK OF ABSTRACTS

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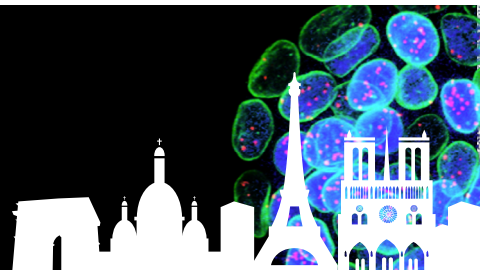

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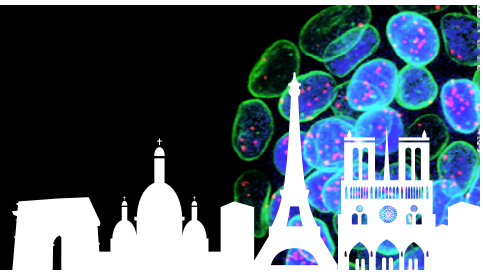

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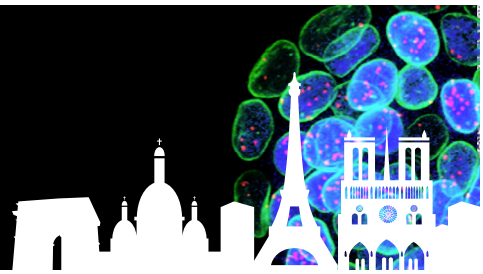


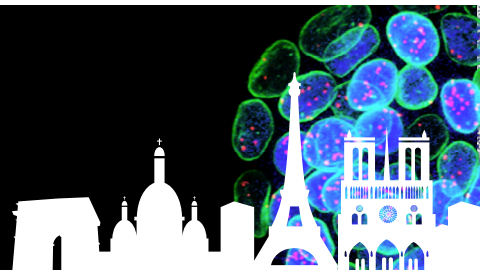
SCHEDULE

TUESDAY, OCTOBER 15TH | ALL DAY	
Outreach activities - Off-site: Espace Robespierre	

WEDNESDAY, OCTOBER 16TH | 8:30AM - 6:40PM	
8:30am	**Welcoming participants**
9:45am	**Conference Opening**
10:00am	**The EMBO Keynote Lecture** **The many ways to make a retina: Studies from cells to tissue** *Caren NORDEN*
11:00am	**SESSION 1 - NUCLEAR ARCHITECTURE & GENE REGULATION**
2:00pm	**SESSION 2 - MOTILITY AND POLARITY**
4:20pm	**SESSION 3** *(Part. 1)* **- SIGNALING AND PATTERNING**
5:05pm	**SBCF and SFBD awards**
6:00pm	**Outreach: General Public Seminar** **Les Cellules - Une histoire de la vie** *Christian SARDET*

THURSDAY, OCTOBER 17TH | 8:30AM - 6:00PM	
9:00am	**SESSION 3** *(Part. 2)* **- SIGNALING AND PATTERNING**
10:15am	**SESSION 4 - CELL CYCLE, CELL GROWTH & MORPHOGENESIS**
12:55pm	**7 Flash Talks**
2:10pm	**Poster Session 1**
4:00pm	**SESSION 5 - MECHANOBIOLOGY ACROSS SCALES**

During each session:
Speakers communications
& Selected talks from oral communications



SCHEDULE

FRIDAY, OCTOBER 18TH | 8:30AM - 6:40PM	
9:00am	SESSION 6 - SYNTHETIC BIOLOGY FROM MOLECULES TO ORGANS
11:20am	SESSION 7 - PHYSIOLOGY METABOLISM & DISEASES
12:50pm	7 Flash Talks
2:00pm	Poster Session 2
4:00pm	SESSION 8 - EVOLUTION & CO-EVOLUTION
8:00pm	CONGRESS DINNER

SATURDAY, OCTOBER 19TH | 8:30AM - 12:35PM	
9:00am	SESSION 9 STEM CELLS, CELL FATE AND REGENERATION
11:15am	Session Tribute M. Bornens
11:45am	Keynote Lecture **Genome regulation:** **Properties and function during embryonic development** *Eileen E. FURLONG*
12:25pm	Closing remarks

During each session:
Speakers communications
& Selected talks from oral communications

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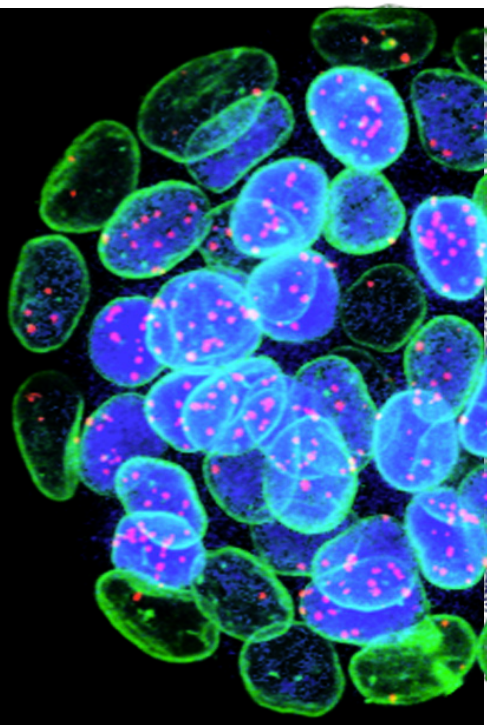
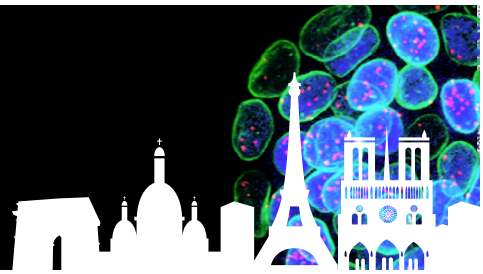


SCIENTIFIC PROGRAM



WEDNESDAY, OCTOBER 16TH

8:30 - 9:45am **Welcoming participants**

9:45 - 10:00am **Conference Opening**

10:00 - 10:40am **The EMBO Keynote Lecture**

Chair: Yohanns Bellaiche

The many ways to make a retina: Studies from cells to tissue

Caren NORDEN

10:40 - 11:00am **Coffee and break around partners**

11:00am - 1:00pm
SESSION 1
NUCLEAR ARCHITECTURE & GENE REGULATION

Chairs: Véronique Azuara & Claire Chazaud

11:00 - 11:30am **Establishing the epigenome in human development and pluripotency**

Peter RUGG-GUNN

11:30 - 12:00pm **The EMBO Young Investigator Lecture : Gene expression dynamics during embryonic patterning**

Mounia LAGHA

12:00 - 12:30pm **Consequences of cellular confinement on the physical state and integrity of the nucleus**

Matthieu PIEL

12:30 - 12:45pm **RNA and genome regionalization in giant single cells: implications for cellular patterning**

Ashley ALBRIGHT

12:45 - 1:00pm **A scaffolding element rewires local 3D chromatin architecture during differentiation**

Ivana JERKOVIC

1:00 - 2:00pm **Lunch around partners**

WEDNESDAY, OCTOBER 16TH

2:00pm - 4:00pm
SESSION 2
MOTILITY AND POLARITY

Chairs: Renaud Poincloux & René-Marc Mège

2:00 - 2:30pm **Design principles of early animals: Insights from Cnidaria**
Aissam IKMI

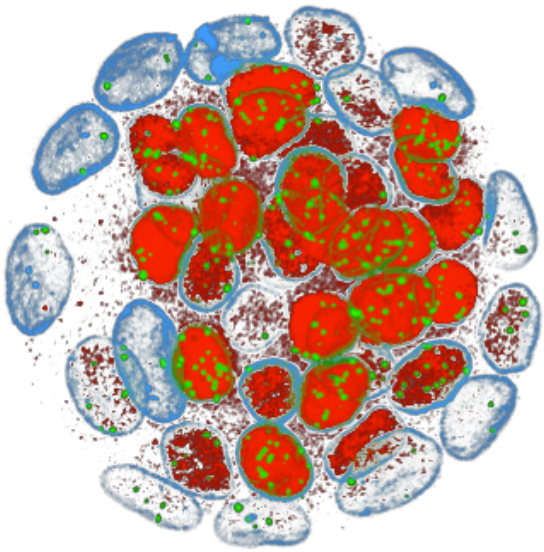
2:30 - 3:00pm **The ins and outs of the microtubule tip control**
Anna AKHMANOVA

3:00 - 3:30pm **Molecular dissection of actin-based cell edge protrusion using advanced imaging and genetics**
Klemens ROTTNER

3:30 - 3:45pm **Membrane flows, membrane tension propagation, and membrane trafficking**
Erdem KARATEKIN

3:45 - 4:00pm **Actin dynamics at tricellular junction and cell intercalation resolution**
Vincent MIROUSE

4:00 - 4:20pm **Coffee and break around partners**



WEDNESDAY, OCTOBER 16TH

4:20 - 5:05pm
SESSION 3 *(Part. 1)*
SIGNALING AND PATTERNING

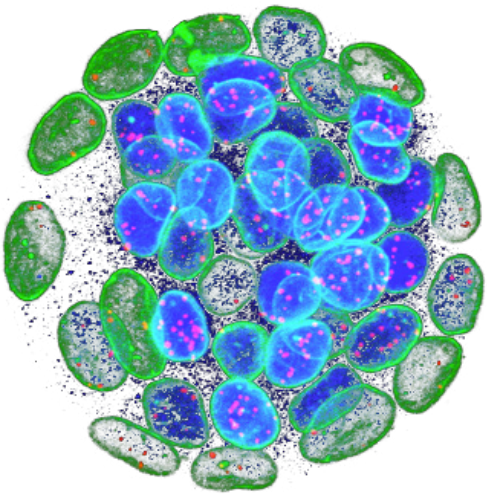
Chairs: Xavier Morin & Delphine Duprez

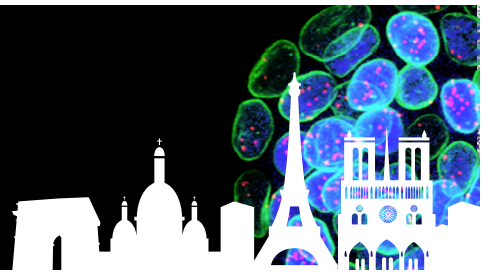
4:20 - 4:50pm **Timekeeping C. elegans post-embryogenesis with pulsatile miRNA transcription**
Wolfgang KEIL

4:50 - 5:05pm **A novel function of an unconventional type 1 myosin in zebrafish left-right asymmetry**
Maximilian FÜRTHAUER

5:05 - 5:55pm **SBCF and SFBD awards**
(session open to the general public)

6:00 - 6:40pm **Outreach: General Public Seminar**
Chair: Isabelle Tardieux
Les Cellules - Une histoire de la vie
Christian SARDET
Chercheur émérite, CNRS / Univ. Sorbonne, IMEV Villefranche sur Mer





THURSDAY, OCTOBER 17TH

8:30 - 9:00am **Welcoming participants**

9:00 - 10:15am
SESSION 3 *(Part. 2)*
SIGNALING AND PATTERNING
Chairs: Xavier Morin & Antoine Zalc

9:00 - 9:30am **P53-mediated stem cell competition: insights into mechanisms of clonal dominance**
Eugenia PIDDINI

9:30 - 10:00am **Interorganelle communication regulates growth factor signaling**
Sara SIGISMUND

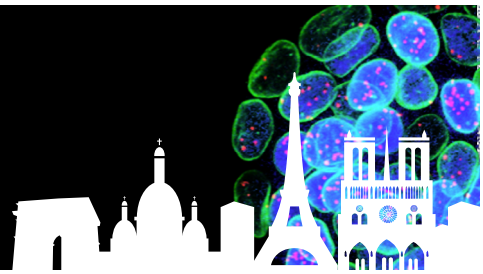
10:00 - 10:15am **Deciphering early neural crest patterning at a single cell resolution**
Anne-Hélène MONSORO-BURQ

10:15 - 1:00pm
SESSION 4 *(Part. 1)*
CELL CYCLE, CELL GROWTH & MORPHOGENESIS
Chairs: Arnaud Echard & Bénédicte Delaval

10:15 - 10:45am **Clearing an awesome organelle: mechanisms of centriole elimination**
Pierre GÖNCZY

10:45 - 11:00am **Modulating division orientation reveals robust intrinsic and extrinsic mechanisms governing epithelial cell number regulation**
Floris BOSVLED

11:00 - 11:30am **Coffee and break around partners**



THURSDAY, OCTOBER 17TH

10:15 - 1:00pm
SESSION 4 *(Part. 2)*
CELL CYCLE, CELL GROWTH & MORPHOGENESIS

Chairs: Arnaud Echard & Bénédicte Delaval

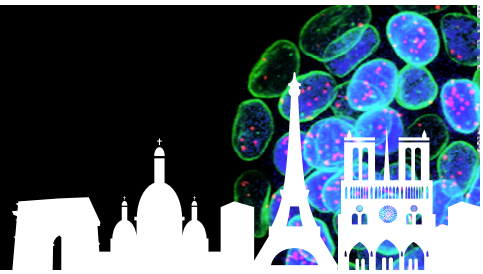
11:30 - 12:00pm **Collective regulation of cell fate decisions**
Nicoletta PETRIDOU

12:00 - 12:30pm **ISDB-C&D Lecture**
Traffic control on the DNA template
Patrick H. O'FARRELL

12:30 - 12:45pm **Shaping the lumen and connecting the tubes: the role of ERM-1 and actomyosin contractility in valve morphogenesis within the C. elegans reproductive system**
Ronen ZAIDEL-BAR

12:45 - 1:00pm **7 Flash Talks**

- **Modulation of mammalian embryonic growth by intracellular glycosylation**
  Sara FORMICHETTI
- **Dynamics and contribution of actin cytoskeleton in 3D cell intercalation**
  Sandra CARVALHO
- **A non-cell autonomous role of Myosin-II in guiding collective migration**
  Nicolas DAVID
- **Combining spatial transcriptomics and biophysical measurements unravel the genetic control of tissue morphogenesis**
  Adrien LEROY
- **A BMP mediated PAX3/7 transcriptional activity switch creates cell fates patterns in the developing spinal cord**
  Robin RONDON



THURSDAY, OCTOBER 17TH

12:45 - 1:00pm **7 Flash Talks** *(continuation)*

- **A place and time to die - Selective cell death and morphogenesis of the mammalian foregut pocket**
  Jenny KRETZSCHMAR

- **Investigating growth control in the Drosophila melanogaster abdomen using transcriptomics**
  Anastasia MORAITI

1:00 - 2:10pm **Lunch** *in Hall 102*

2:10 - 3:50pm **Poster Session 1** *(Rooms 106 & 108)*

3:50 - 4:00pm **Coffee and break around partners**

4:00 - 6:00pm
SESSION 5
MECHANOBIOLOGY ACROSS SCALES

Chairs: Romain Levayer & Yohanns Bellaiche

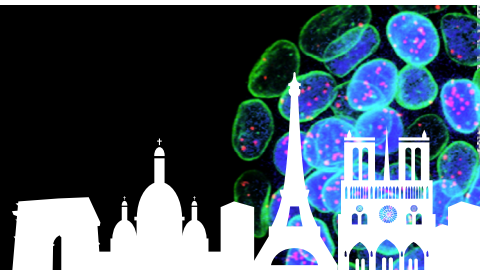
4:00 - 4:30pm **Organ geometry constrains extracellular matrix fractures to pattern cell fate**
Rashmi PRIYA

4:30 - 5:00pm **Mechanical strain focusing at topological defect sites in regenerating Hydra**
Kinneret KEREN

5:00 - 5:30pm **Cross-talk between cell mechanics, cell shape and cell fate**
Ewa PALUCH

5:30 - 5:45pm **Cellular scale cytoskeleton guides migration of extra-embryonic tissue during early avian development**
Lakshmi BALASUBRAMANIAM

5:45 - 6:00pm **Force transmission is a master regulator of mechanical cell competition**
Andreas SCHONIT



FRIDAY, OCTOBER 18TH

8:30 - 9:00am **Welcoming participants**

9:00 - 11:00am
SESSION 6
SYNTHETIC BIOLOGY FROM MOLECULES TO ORGANS

Chairs: Nathalie Sauvonnet & Stéphanie Lebreton

9:00 - 9:30am **Tissue morphogenesis and cell fate dynamics in the early mouse embryo**
Ivan BEDZHOV

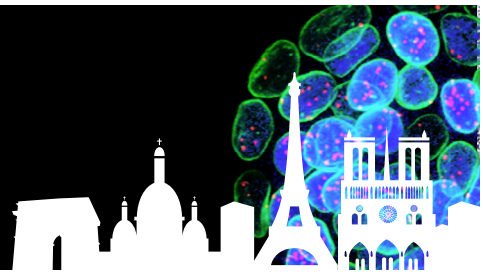
9:30 - 10:00am **Physics of living matter: from molecule to embryo**
Sebastian STREICHAN

10:00 - 10:30am **How large cells do it? : Division positioning in early embryos**
Nicolas MINC

10:30 - 10:45am **Establishment of an in vitro morphogenetic process of non-embedded endothelial self-organization towards a lumenized capillary**
Mathieu HAUTEFEUILLE

10:45 - 11:00am **Functional regulation of the mitotic kinesin HSET by Intraflagellar Transport proteins**
Benjamin VITRE

11:00 - 11:20am **Coffee and break around partners**



FRIDAY, OCTOBER 18TH

11:20 - 1:05pm
SESSION 7
PHYSIOLOGY METABOLISM & DISEASES

Chairs: Raphaël Gaudin & Florence Niedergang

11:20 - 11:50am **Adjusting organ size during Drosophila development**
Pierre LEOPOLD

11:50 - 12:20pm **Pressure sensing and responses of lysosomes**
Spencer FREEMAN

12:20 - 12:35pm **Illuminating the live cell dynamics of the early neutrophil- Encephalitozoon cuniculi interplay as a "Trojan horse" strategy**
Eugénie CARRIÈRE

12:35 - 12:50pm **The intracellular citrate/acetyl-CoA flux is mechanistically linked to developmental defects and intellectual disability**
Luigi PUGLIELLI

12:50 - 1:05pm **7 Flash Talks**

- **Development of a synthetic hydrogel to study the invasion of glioblastoma cells**
  Matthieu GÉLIN
- **Symmetry breaking and self-organization of bi-layered epithelia are orchestrated by conserved signals during development and regeneration**
  Robin JOURNOT
- **Polyploidy in Xenopus lowers metabolic rate by increasing cell size**
  Clotilde CADART
- **Mechanical stimulation reverses oncogenic properties in ECM-enriched vocal fold cancer**
  Jasmin KAIVOLA

FRIDAY, OCTOBER 18TH

12:50 - 1:05pm **7 Flash Talks** *(continuation)*

- **Exploring cellular origins and differentiation during non-embryonic development with the single cell RNAseq atlas of B. schlosseri budding**
  Marie LEBEL

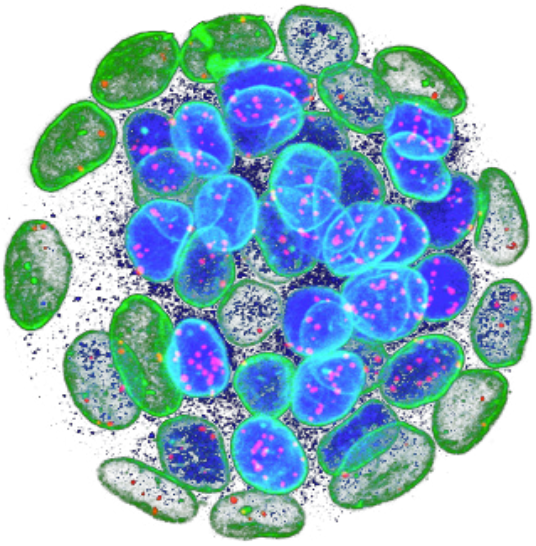
- **How developing tissues compensate for unwanted cell death: Lessons from the zebrafish retina**
  Catarina FIGUEIREDO

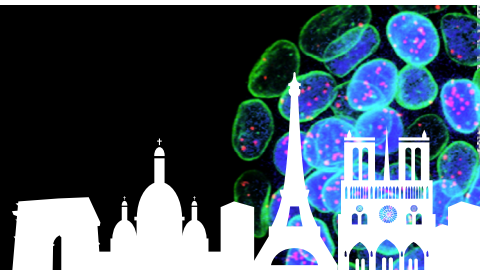
- **From pluripotent stem cells to intervertebral disc progenitor cells: a reconstruction based on single-cell transcriptomics**
  Julie WARIN

1:05 - 2:00pm **Lunch** *in Hall 102*

2:00 - 3:45pm **Poster Session 2** *(Rooms 106 & 108)*

3:45 - 4:00pm **Coffee break around partners**





FRIDAY, OCTOBER 18TH

4:00 - 6:00pm
SESSION 8
Evolution & Co-evolution

Chairs: Agathe Chaigne & Delphine Duprez

4:00 - 4:30pm **From genes to shape in leaf development and evolution**
Miltos TSIANTIS

4:30 - 5:00pm **The evolution of cell fate specification modes in spiral cleavage**
Chema MARTIN-DURAN

5:00 - 5:30pm **Mechanisms and evolution of programmed-DNA elimination in nematode embryos**
Marie DELATTRE

5:30 - 5:45pm **Molecular and cellular mechanisms underlying embryo colonization by pluripotent stem cells in primates**
Irène AKSOY

5:45 - 6:00pm **Variations in cell plasticity and proliferation underlie distinct modes of regeneration along the antero-posterior axis in the annelid Platynereis**
Eve GAZAVE

8:00pm **CONGRESS DINNER**

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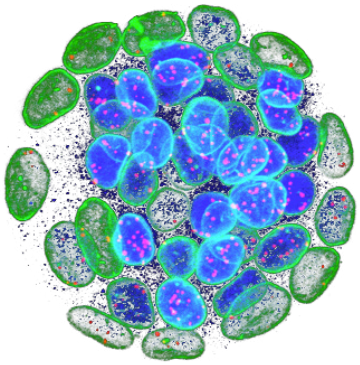
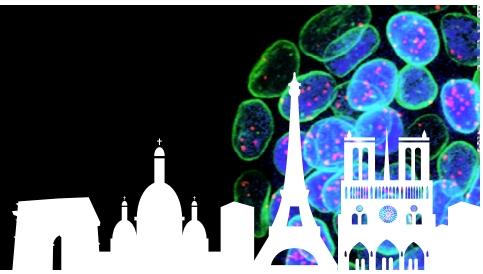
RIVE GAUCHE

36, Quai d'Austerlitz - 75013 Paris





SATURDAY, OCTOBER 19TH

8:30 - 9:00am **Welcoming participants**

9:00 - 11:00am
SESSION 9
STEM CELLS, CELL FATE AND REGENERATION

Chairs: Hitoyoshi Yasuo & Claire Chazaud

9:00 - 9:30am **Multipotency, fate choices and cellular behaviors in the cardiopharyngeal lineage**
Lionel CHRISTIAEN

9:30 - 10:00am **Building the human lungs: Lessons from organoids and gene editing**
Emma RAWLINS

10:00 - 10:30am **Epigenetic mechanisms of cellular plasticity**
Maria-Elena TORRES-PADILLA

10:30 - 10:45am **Uncovering molecular mechanisms driving asymmetric cell division with synthetic biology**
Lara KRÜGER

10:45 - 11:00am **Adhesion-controlled forces in the glial niche regulate stem cell proliferation in the developing Drosophila brain**
Pauline SPÉDER

11:00 - 11:15am **Coffee Break around partners**

11:15 - 11:45pm **Session Tribute M. Bornens**
Coordinated Control of Chromosomal Pairing and Centrosome Regulation by the bouquet-MTOC machinery in Meiosis and Oocyte Polarity
Karine LEVY

11:45 - 12:25pm **Keynote Lecture**
Chair: René-Marc Mège
Genome regulation: Properties and function during embryonic development
Eileen E. FURLONG

12:25 - 12:35pm **Closing remarks**

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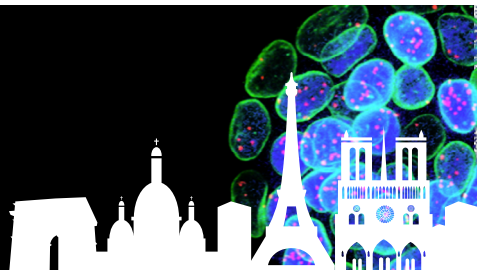

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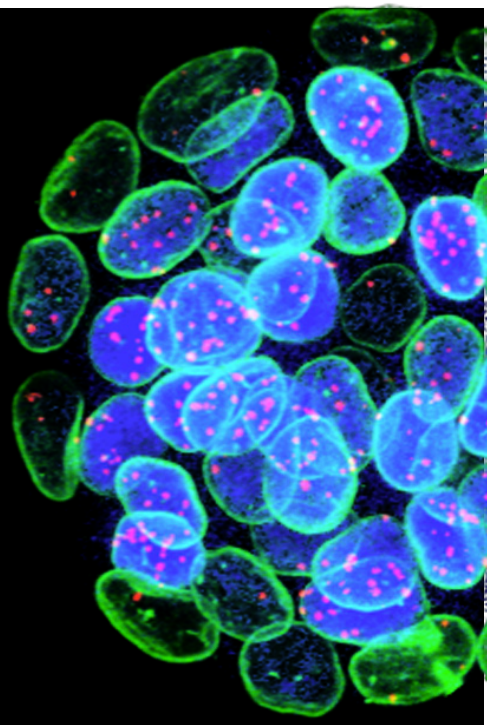
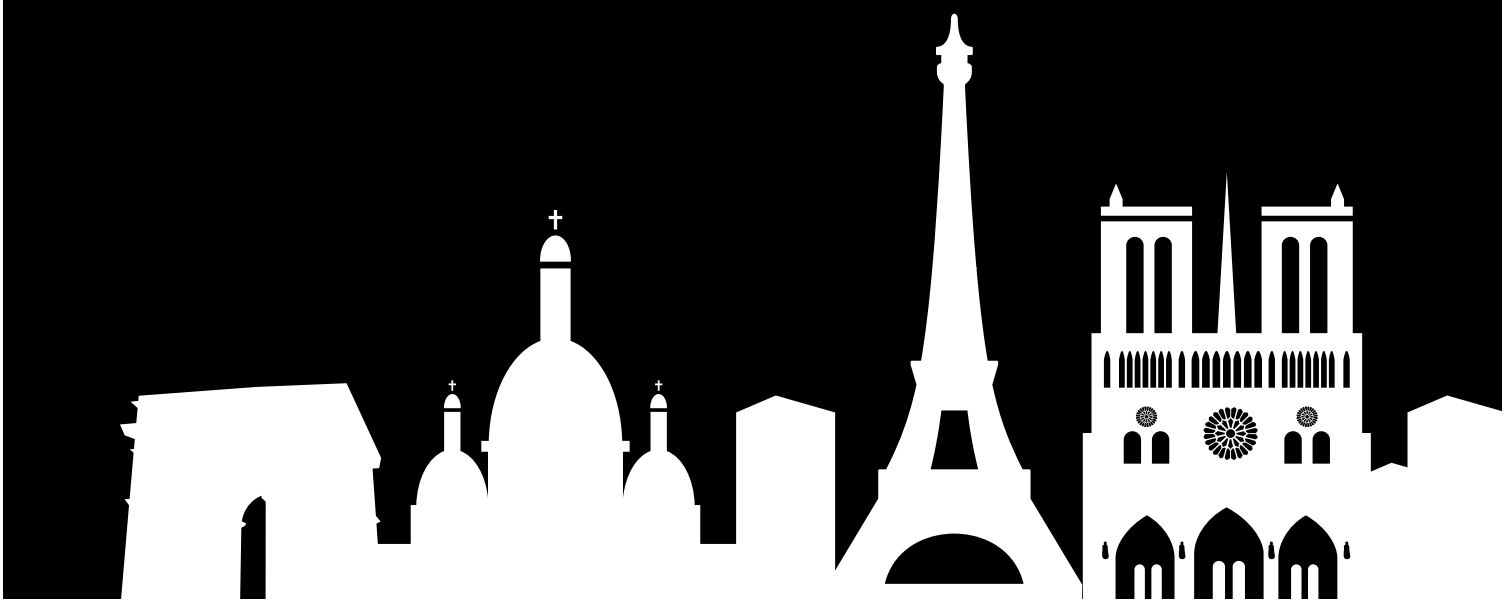
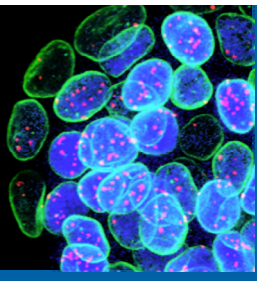
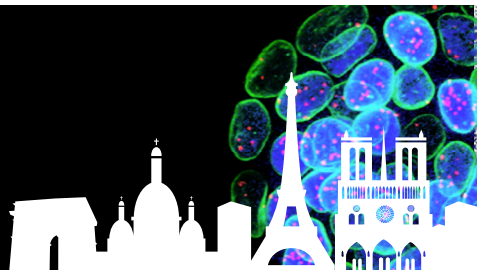


ORAL COMMUNIATIONS





11:00AM - 1:00PM
SESSION 1
NUCLEAR ARCHITECTURE & GENE REGULATION



NUCLEAR ARCHITECTURE & GENE REGULATION

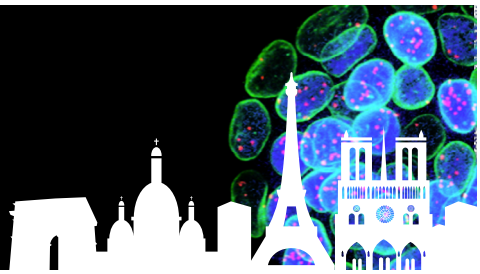
Ashley ALBRIGHT

Jamarc Allen-Henderson, Connie Yan, David Angeles-Albores, Wallace Marshall

UCSF, San Francisco, California, USA

RNA and genome regionalization in giant single cells: implications for cellular patterning

Ciliates possess striking features and patterns that allow them to perform complex behaviors, such as directed swimming and learning. Stentor coeruleus can extend to 1 mm in length, maintain a clear anterior-posterior (A-P) axis, heal wounds, and regenerate from physical damage. These properties make Stentor an ideal system for studying subcellular patterning or regionalization, defined by the separation of different molecules or organelles within specific regions of the cell. Little is known regarding how regionalization is established, or re-established following cellular injury, thus we investigate the relationship between cellular pattern and regionalization in Stentor from two perspectives: (1) RNA and (2) genome regionalization. The surface of Stentor is covered in parallel bundles of stacked microtubules that run in one direction along the length of the cell and provide the cell with structure. We targeted structural and motor components of the cytoskeleton with RNAi and performed RNA-sequencing in bisected cell halves. We observed morphological defects in beta-tubulin and dynein knockdown cells as well as global disruptions in RNA regionalization, and shifts in A-P skew for many individual transcripts. This suggests the microtubule cytoskeleton may play a role in patterning the cell beyond its structure by serving as tracks for the delivery of transcripts. In the Stentor macronucleus (MAC), which resembles beads-on-a-string extending along the length of the cell, we also observe that several aspects of genome structure and function occur non-uniformly in the MAC, including histone modification and DNA replication. Overall, we show that RNAs and the genome are regionalized in Stentor. Ultimately, we aim to understand how RNA and genome regionalization contribute to cellular patterning and re-establishing patterning following regeneration.



NUCLEAR ARCHITECTURE & GENE REGULATION

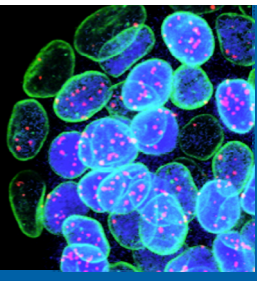
Ivana JERKOVIC

Marco Di Stefano, Hadrien Reboul, Flora Paldi, Michael F Szalay, Davide Normanno, Giorgio L Papadopoulos, Frederic Bantignies and Giacomo Cavalli

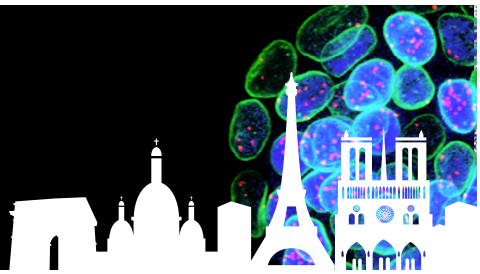
CIRB, College de France and Institute of Human Genetics, CNRS-UM, UMR9002

A scaffolding element rewires local 3D chromatin architecture during differentiation

Upon differentiation, chromatin rewires to reflect its new cellular identity and function. While it is widely known that this process involves cooperative changes in transcription, chromatin composition, and 3D conformation, it is unclear what exactly drives these changes and how they influence one another. Here, we used ESC-to-NPC differentiation to study rewiring at a 3 Mb large neuronal Zfp608 locus. During this process, this large chromatin domain splits in half right at the Zfp608 promoter, local chromatin gets littered with activating marks, compacts in 3D space and Zfp608 abounds in transcription. We investigated the cis and trans elements using capture Hi-C (cHi-C), extensive biophysical modelling, and 3-colour 3D-FISH with technical and analytical breakthroughs and found that transcription abundance modulates the contacts in the region as well as the insulation at the domain split. Furthermore, we found a genetic element we named the scaffolding element, with a dual enhancer and architectural function that is essential for chromatin rewiring and loop formation at the NPC stage. The loss of this element disrupts the formation of all local NPC loops irrespective if they are anchored in this element or not, highlighting the hierarchical relationship between elements that act as loop anchors. Furthermore, we uncovered that the scaffolding function, although driven by multiple mechanisms, can form loops independent of loop extrusion and that other molecular attractions were necessary to form NPC-specific contacts in the region. Together, these results demonstrate that a hierarchy of genetic elements in cis allows successful rewiring during differentiation and that multiple trans-acting elements contribute to making this rewiring efficient.



2:00PM - 4:00PM
SESSION 2
MOTILITY AND POLARITY



MOTILITY AND POLARITY

Erdem KARATEKIN

Carolina Gomis Perez*, Aleah Roberts, Justin Taraska, David Zenisek

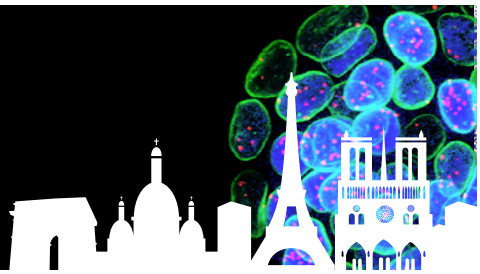
Cellular & Molecular Physiology, Yale University
**First Author*

Membrane flows, membrane tension propagation, and membrane trafficking

Many cellular activities, such as cell migration, cell division, phagocytosis, and exo-endocytosis, generate and are regulated by membrane tension gradients. Membrane tension gradients drive membrane flows, but there is controversy over how rapidly plasma membrane flow can relax tension gradients. We show that resistance to membrane flow spans orders of magnitude, depending on the cell type, and regulates exo-endocytosis coupling. For two cell types both specialized for calcium-triggered secretion, we find that membrane flow and tension equilibration is very rapid in one case, and unmeasurably slow in the other. In both cell types, stimulated exocytosis adds membrane to the cell surface through fusion of cargo-laden vesicles with the plasma membrane. The extra membrane is then retrieved more slowly through compensatory endocytosis. How exo- and endocytosis are coupled is not well understood in either case.

In a neuronal terminal, we find that rapid membrane flow equilibrates membrane tension gradients within seconds. The rapid flow allows membrane added at the active zone via exocytosis to be endocytosed at a distant site. By contrast, in neuroendocrine adrenal chromaffin cells, membrane flow is too slow to relax membrane tension gradients for minutes. In these cells, membrane added to the plasma membrane via exocytosis is retrieved locally. Thus, the differences in membrane flow and tension equilibration can explain the very different exo-endocytosis coupling in these two cell types and likely represent adaptations to distinct membrane recycling requirements.

In addition, we find that membrane tension propagation slows dramatically in B-cells upon activation of the B-cell receptor clustering and signaling.



MOTILITY AND POLARITY

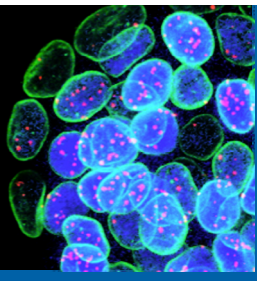
Vincent MIROUSE

Lisa Calvary*, Hervé Alégot, Pierre Pouchin, Graziella Richard, Caroline Vachias

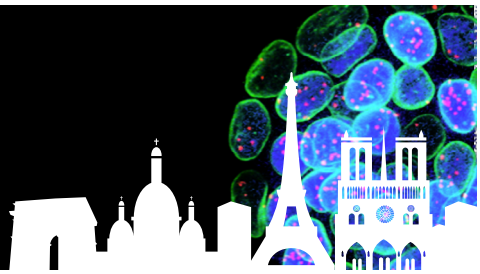
Institute of Genetics, Reproduction and Development CNRS, INSERM, UCA
**First Author*

Actin dynamics at tricellular junction and cell intercalation resolution

Cell intercalation, a fundamental morphogenetic process characterized by the exchange of neighboring cells, plays a pivotal role in epithelial tissue development. While the initiation of new junctions remains poorly understood, recent research indicates the involvement of tricellular junction actors. In this study, we explore the contribution of the WAVE regulatory complex (WRC), a critical regulator of branched F-Actin generation, in tissue elongation and cell intercalation within the Drosophila ovarian follicular epithelium. WRC localized at tricellular junctions, where it orchestrates the generation of highly dynamic protrusions emanating from one cell and extending between the bicellular junctions of neighboring cells. This protrusive activity is essential for the initiation of new junctions in cells located at the extremities of these junctions. Furthermore, our findings indicate that WRC recruitment at tricellular junctions is a redundant process, involving the cooperative action of the two transmembrane proteins Sidekick and Lar. Disruption of this recruitment impairs protrusive activity, cell intercalation resolution, and tissue elongation thereby mechanistically bridging molecular, cellular and tissular scales. Consequently, this elucidates a critical mechanism underlying epithelial morphogenesis through actin polymerization at tricellular junctions.



4:20 - 5:05PM
SESSION 3
SIGNALING AND PATTERNING



SIGNALING AND PATTERNING

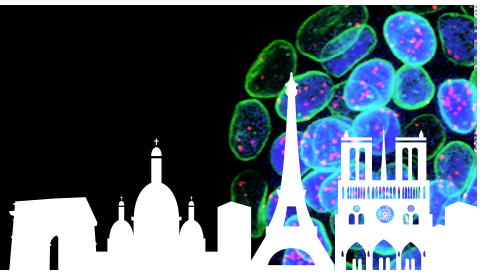
Maximilian FÜRTHAUER

Akshai Janardhana Kurup*, Florian Bailet

Institut de Biologie Valrose CNRS UMR7277 - INSERM1091 - Université Côte d'Azur
**First Author*

A novel function of an unconventional type 1 Myosin in zebrafish Left-Right Asymmetry

While evolutionarily conserved mechanisms controlling animal antero-posterior and dorso-ventral polarity have been known for decades, the establishment of Left-Right (LR) asymmetry has long been thought to rely on strikingly different species-specific mechanisms that range from cilia-driven fluid flows to chiral cell rearrangements. In spite of this apparent diversity, we previously identified the unconventional Myosin Myo1D as a conserved regulator of LR asymmetry. While Drosophila Myo1D acts locally and in the absence of cilia to control the chirality of individual organs, zebrafish Myo1D controls motile cilia orientation and the establishment of a symmetry-breaking fluid flow in the central fish Left-Right Organizer. In addition to Myo1D, the zebrafish genome encodes the closely related protein Myo1G. Although myo1g mutations impair laterality and enhance the defects of myo1d mutants, we show that myo1g and myo1d exert entirely distinct functions. In contrast to the flow-dependent control of LR asymmetry exerted by Myo1D, Myo1G regulates LR asymmetry by promoting the Nodal-mediated transfer of laterality information from the central LR Organizer to different target tissues. At the cellular level, Myo1G is associated with endosomes positive for the TGFbeta signaling adapter SARA. myo1g mutants present a lower number of SARA/Activin receptor endosomes and a reduced responsiveness to Nodal ligands that impairs the capacity of Nodal ligands to propagate by inducing their own expression. As a consequence, myo1g mutants present a delay in left-sided Nodal propagation that causes tissue-specific laterality defects in organs most distant from the LR Organizer. Beyond LR asymmetry, our work identifies Myo1G as a novel Nodal pathway regulator that promotes signalling by different Nodal ligands in specific biological contexts.



SIGNALING AND PATTERNING

Anne-Hélène MONSORO-BURQ

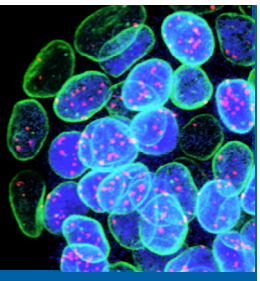
Alexandr Kotov, Subham Seal*, Mansour Alkobtawi, Vincent Kappès, Sofia Medina Ruiz, Hugo Arbès, Richard Harland, Leonid Peshkin

Université Paris-Saclay / Institut Curie, France
**Firsts Authors*

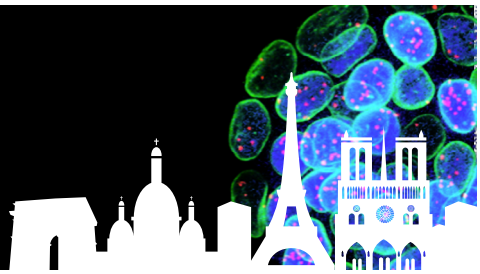
Deciphering early neural crest patterning at a single cell resolution

Neural crest cells exemplify cellular diversification from a multipotent progenitor population. However, the full sequence of early molecular choices orchestrating the emergence of neural crest heterogeneity from the embryonic ectoderm remains elusive. Gene-regulatory-networks (GRN) govern early development and cell specification towards definitive neural crest. Here, we combine ultra-dense single cell transcriptomes with machine-learning and large-scale transcriptomic and epigenomic experimental validation of selected trajectories, to provide the general principles and highlight specific features of the GRN underlying neural crest fate diversification from induction to early migration stages using Xenopus frog embryos as a model. Our main results include that during gastrulation, a transient neural border zone state precedes the choice between neural crest and placodes which includes multiple converging gene programs; and that during neurulation, transcription factor connectome and bifurcation analyses demonstrate the early emergence of neural crest fates at the neural plate stage, alongside an unbiased multipotent-like lineage persisting until epithelial-mesenchymal transition stage. We also decipher circuits driving cranial and vagal neural crest formation and provide a broadly applicable, high-throughput, in vivo, experimental validation strategy for investigating single cell transcriptomes in vertebrate GRNs in development, evolution, and disease.

Reference: Kotov, Seal et al., PNAS 2024, PMID: 38683994



10:15 - 1:10PM
SESSION 4
CELL CYCLE, CELL GROWTH & MORPHOGENESIS



CELL CYCLE, CELL GROWTH & MORPHOGENESIS

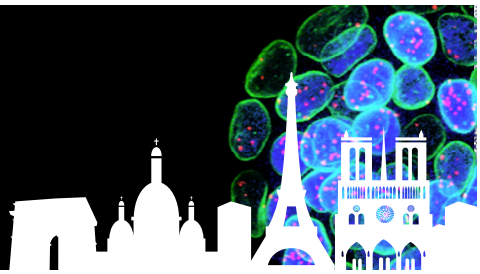
Floris BOSVLED

Sam Amirebrahimi, Raphael Thinat, Eric van Leen, Yohanns Bellaïche

Institut Curie, PSL Research University, Sorbonne University, Paris, France

Modulating division orientation reveals robust intrinsic and extrinsic mechanisms governing epithelial cell number regulation

Tissue cell number is a fundamental attribute of any epithelium. Despite extensive characterization of the mechanisms underlying cell growth, cell cycle progression, and apoptosis, the control of final tissue cell number remains poorly understood. To address this question, we need to manipulate cell numbers and determine whether and how compensatory mechanisms adapt to such changes. In our study, we modified cell number by affecting division orientation in Drosophila epithelial tissue. The absence of spindle pulling forces, centrosomes, or mitotic rounding leads to spindle mis-orientation, resulting in the mispositioning of epithelial cells within the tissue or their displacement outside the tissue, inducing substantial epithelial cell loss.
First, we identified that acentrosomal microtubule dynamics and cell contractility prevent excessive epithelial cell loss by enabling mispositioned cells to reintegrate back into the epithelium. However, this mechanism is insufficient to fully control the total epithelial cell number. Consequently, we found that the epithelium compensates for cell loss primarily by reducing physiological apoptosis. We show that mechanochemical feedback between global tissue tension and local cell apex area sensing through Hippo/YAP signaling accounts for this compensatory change in apoptosis. Finally, we discovered that systemic TNF signaling safeguards the animal against potentially harmful non-reintegrating cells by eliminating basally misplaced cells incapable of reintegration, ensuring that the total number of cells outside the tissue remains unaffected. Overall, our results delineate the complementary roles of tissue mechanics and systemic signaling in regulating epithelial tissue cell number during development.



CELL CYCLE, CELL GROWTH & MORPHOGENESIS

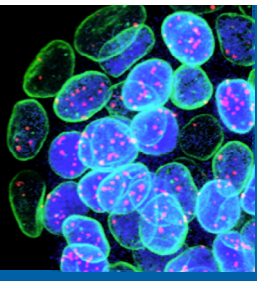
Ronen ZAIDEL-BAR

Meghna Suhag*

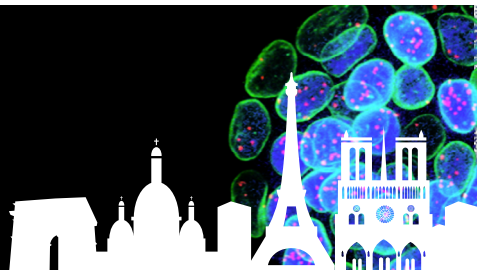
Faculty of Medical & Health Sciences, Tel Aviv University
**First Author*

Shaping the lumen and connecting the tubes: the role of ERM-1 and actomyosin contractility in valve morphogenesis within the C. elegans reproductive system

The reproductive tract in C. elegans consists of several tubular tissues connected in series. The sperm-storing spermatheca and the egg-collecting uterus are separated by a sphincter called the spermatheca-uterine (sp-ut) valve, which regulates the passage of fertilized eggs. These tissues are derived from cells of the spermatheca and uterine lineages, each forming a separate lumen, which must be eventually aligned to allow the passage of embryos. However, the mechanism responsible for aligning their lumens is currently unknown. We used high-resolution long-term imaging and RNAi to follow sp-ut valve morphogenesis, and discovered an unconventional mechanism of lumen formation that ensures connection of the three tissues. It begins with a donut-shaped syncytial sujn cell, of uterine lineage, wrapping around a binucleate sujc core cell, of spermatheca lineage. After wrapping over the sujc core cell, sujn forms novel cell-cell junctions with the spermatheca. Next, circumferential actomyosin cables assemble along the apical membrane of sujn and it proceeds to squeeze the core cell. ERM-1 is required for the correct positioning of the actomyosin cables and NMY-1 is essential for their contraction. Concomitant with sujc compression, its two nuclei are actively transported along microtubules from the spermathecal to the uterine side, and the sujc cell adopts a dumbbell shape, connecting the three lumens. The sujc cell functions as a temporary scaffold that is pushed out during the first embryo transit. Our findings identify a novel mechanism for coordinating lumens of neighbouring tissues.



4:00 - 6:00PM
SESSION 5
MECHANOBIOLOGY ACROSS SCALES



MECHANOBIOLOGY ACROSS SCALES

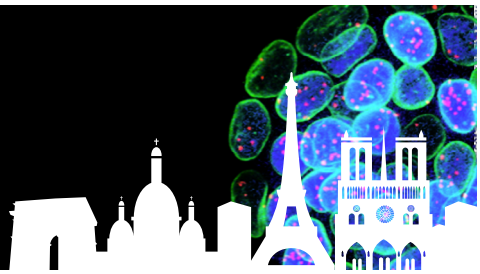
Lakshmi BALASUBRAMANIAM

Fengzhu Xiong

1. Wellcome Trust / CRUK Gurdon Institute, University of Cambridge, Cambridge, UK
2. Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK

Cellular mechanisms of blastoderm expansion during early avian development

Large scale tissue expansion of the blastoderm (epiboly) drives the morphological transition of early embryos of many vertebrates. In avian embryos, the extraembryonic tissue area opaca (AO) expands drastically in the first several days of development to cover the surface of the yolk, laying foundations of key structures (e.g., vasculature) that support embryo development. The driving mechanisms and regulation of this expansion are poorly understood. In this work, using a combination of live imaging, surgery, electron microscopy and drug-based inhibitions, we show that the cells at the blastoderm edge (edge cells) adhere onto the vitelline membrane via microtubule and actin-rich protrusions. The outward motion of the AO requires these protrusions which only form on the edge cells with a flattened shape. These edge cells, are followed by acto-myosin cables that are associated with the frequency and size of protrusions, potentially allowing circumferential tension mediated coordination of the expansion process along the blastoderm edge. Interestingly, ablating edge cells did you abrogate expansion, while AO and epiblast cells from behind the original edge quickly recapitulate edge cell phenotype and outward migration. These results suggest that the edge cell phenotype arises not from genetically specialized cells but rather in the local mechanical context of the AO rim where cells' affinity to others and the vitelline membrane promote protrusive and migratory behaviour. The radial and circumferential tensions generated drive a steady and even expansion of the entire blastoderm.



MECHANOBIOLOGY ACROSS SCALES

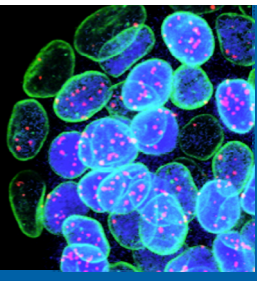
Andreas SCHOENIT

Lucas Anger, Siavash Monfared, Carine Rosse, Rene-Marc Mege, Amin Doostmohammadi, Benoit Ladoux

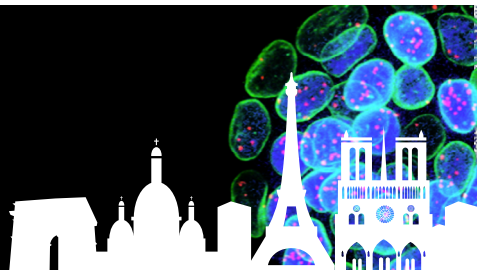
Institut Jacques Monod, CNRS, Paris, France

Force transmission is a master regulator of mechanical cell competition

Cell competition is a tissue surveillance mechanism for eliminating unwanted cells and as such is indispensable in development, infection and tumorigenesis. Although different biochemical mechanisms are proposed, due to the dearth of direct force measurements, how mechanical forces determine the competition outcome remains unclear. Here, using ex vivo tissues and different cell lines, we have discovered an unknown form of cell competition that is regulated by differences in force transmission capabilities, favoring cell types with stronger intercellular adhesion. Direct force measurements reveal increased mechanical activity at the interface of the two competing cell types in the form of large stress fluctuations which can lead to upward forces and cell elimination. We show how a winning cell type endowed with a stronger intercellular adhesion exhibits a higher resistance to elimination while benefiting from efficient force transmission to neighboring cells. This cell elimination mechanism could have broad implications of keeping strong force transmission ability for maintaining tissue boundaries and cell invasion pathology.



9:00 - 11:00AM
SESSION 6
SYNTHETIC BIOLOGY
FROM MOLECULES TO ORGANS



SYNTHETIC BIOLOGY FROM MOLECULES TO ORGANS

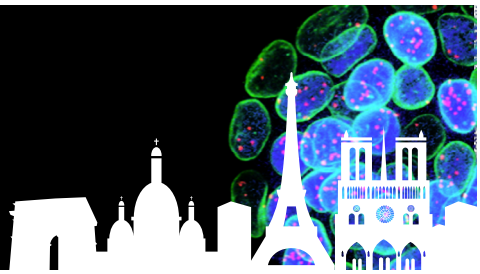
Mathieu HAUTEFEUILLE

Ana Ximena Monroy-Romero*, Brenda Nieto-Rivera, Wenjin Xiao

Laboratoire De Biologie Du Développement UMR 7622, Sorbonne Université, Paris, France

Establishment of an in vitro morphogenetic process of non-embedded endothelial self-organization towards a lumenized capillary

Microvascular engineering seeks to exploit known cell-cell and cell-matrix interactions in the context of vasculogenesis to restore reliable capillary models in vitro. However, current systems generally focus on recapitulating microvessels embedded in extracellular matrix hydrogels, overlooking the significance of discontinuous capillaries, albeit their role in tissue-blood exchanges, particularly in the liver. Here, we introduce a novel method to stimulate self-organization of endothelial cells into non-embedded microvessels. By creating an anisotropic micropattern at the edge of a GelTrex dome using Marangoni-flow, we achieved a long, non-random orientation of endothelial cells, forming stable lumenized microvessels. Our findings revealed a distinctive morphogenetic process leading to mature lumenized capillaries,for murine and human immortalized liver-sinusoidal-endothelial-cell lines (LSEC). Cell migration, proliferation and polarization were guided by the micropattern, initiating a multicellular cord that caused a piecewise circumferential deformation. This generated a wave-like gel folding gel, hinged at a laminin depleted zone, enveloping the cord with laminin. This event marked the onset of lumenogenesis, regulated by the gradual apico-basal polarization of the wrapped cells and to the maturation of tight junctions and matrix remodeling—recapitulating the development of vessels in vivo. We believe our facile engineering method holds promise for future integration into microphysiological systems of non-embedded capillaries.



SYNTHETIC BIOLOGY FROM MOLECULES TO ORGANS

Benjamin VITRE

Audrey Guesdon*, Valérie Simon, Juliette van Dijk, Bénédicte Delaval

CRBM CNRS - Université de Montpellier
**First Author*

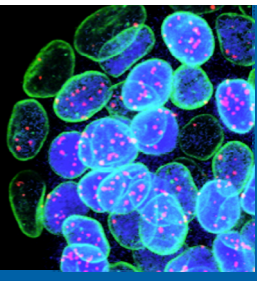
Functional regulation of the mitotic kinesin HSET by Intraflagellar transport proteins

Intraflagellar Transport (IFT) machinery proteins are well characterized for their role in cilia, where they act as adaptors between motors and cargos to allow for proper assembly and function of cilia. Recent evidences also introduce new perspectives on cellular processes involving IFT proteins beyond their role in cilia. These include immune synapse polarization, cell migration, regulation of cytoplasmic microtubule dynamics and cell division. We recently showed that proteins from IFT subcomplex B interact with the mitotic kinesin HSET in cellulo and we showed that this interaction is necessary for efficient centrosome clustering in cells harbouring supernumerary centrosomes. However, whether and how IFT proteins directly interact with and potentially regulate HSET at the molecular level remains unknown.

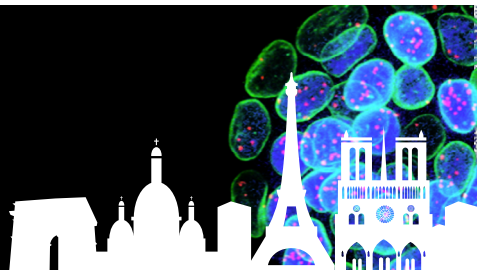
Due to the complexity of the IFT machinery and its numerous potential molecular interactions in cells, a precise understanding of IFT functions at the molecular level remains a challenge. To circumvent these difficulties, we developed a reconstituted in vitro system using purified HSET and IFT proteins and we study it using biochemistry and TIRF microscopy approaches.

We identified a minimal subcomplex made of IFT52/IFT70 capable of a direct binding to HSET dimer. We show that this binding stimulates HSET motor activity and its capacity to achieve long processive runs. We also show that HSET activation by IFTs accounts for an increased ability to slide microtubules and to organize complex contractile microtubule networks.

Overall, this in vitro work reveals for the first time that IFT proteins can directly activate a mitotic kinesin motor and explains mechanistically the in cellulo phenotypes of HSET or IFTs perturbations.



11:20 - 1:05PM
SESSION 7
PHYSIOLOGY METABOLISM & DISEASES



PHYSIOLOGY METABOLISM & DISEASES

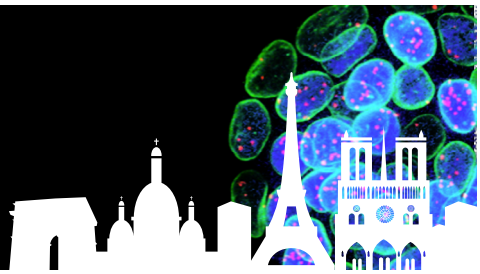
Eugénie CARRIÈRE

Juliette Gilbert, Caroline Vachias, Frédéric Delbac and Pascale Gueirard

Clermont Auvergne University/LMGE/UMR CNRS 6023/Interactions Host-Parasite (IHP)

Illuminating the live cell dynamics of the early neutrophil-Encephalitozoon cuniculi interplay as a «Trojan horse» strategy

Encephalitozoon cuniculi is a eukaryote, unicellular, spore-forming microorganism that belongs to the phylum Microsporidia. It is an obligate intracellular parasite of mammals, including human. In response to infection, innate immune system serves as the first line of defense and allows only a partial clearance of the parasite. Indeed, microsporidia can also modulate macrophages and dendritic cells effector functions to avoid killing. We postulate that they can also manipulate neutrophils (PMN) antimicrobial mechanisms, including phagocytosis, degranulation, ROS production and Neutrophil Extracellular Traps (NETs) formation to promote survival. However, to which extend PMN contribute to the infection outcome remains elusive. Therefore, to gain insights in the PMN and E. cuniculi interplay, we used live and static cell imaging and explored the dynamics of the interactions between murine PMN and E. cuniculi in vitro. To this end, we prepared fluorescent spores of E. cuniculi and exposed them to fluorescent PMN purified from the bone marrow of LysM-EGFP transgenic mice and monitored cells' behaviours over 48 h of interaction with videomicroscopy, high resolution confocal imaging, FISH and MET. We first observed that some parasites rapidly adhered to PMN or extruded their polar tube without establishing a direct contact. We bring also evidence of specific changes in the structural and functional properties of PMN that support immune activation (emission of pseudopodia, parasite lysis inside phagolysosomes, modified motility and shape parameters), but only when a "direct" contact is established. Importantly, we could also detect a small proportion of remaining viable parasites that initiated a development intracellularly. Meronts early stages of parasite development were indeed detected inside PMN 48h after contact. In summary, our current data argue that apoptotic PMNs could be hijacked as a "Trojan horse" by E. Cuniculi to disseminate in tissues of the host (lungs, liver, central nervous system).



PHYSIOLOGY METABOLISM & DISEASES

Luigi PUGLIELLI

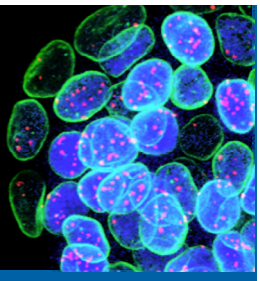
University of Wisconsin-Madison, Department of Medicine

The intracellular citrate/acetyl-CoA flux is mechanistically linked to developmental defects and intellectual disability

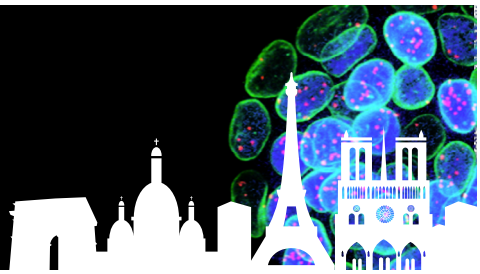
Nϵ-lysine acetylation within the endoplasmic reticulum (ER) has emerged as a novel mechanism that regulates proteostasis and dynamics of the secretory pathway. Loss-of-function mutations or gene duplication events that affect ER acetylation are linked to developmental delay and premature death, peripheral neuropathy, and autism spectrum disorder (ASD) with intellectual disability and progeria. Mouse models of dysfunctional ER acetylation (PMCID:PMC4019794; PMCID:PMC4925020; PMCID:PMC6156544) mimic associated human phenotypes. The ER acetylation machinery depends on the synergistic activity of the citrate transporters, SLC25A1 and SLC13A5 (PMCID:PMC6718414). Together, they regulate intracellular metabolic crosstalk and the proteostatic functions of the secretory pathway. Gene duplication events affecting SLC25A1 and SLC13A5 are also associated with developmental defects and intellectual disability. Mice with neuron-specific overexpression of either SLC25A1 or SLC13A5 display ASD-like behavior (PMCID:PMC9014753; PMCID:PMC8823335). In both cases, the ASD-like phenotype appears to depend on dysfunctional ER acetylation and alterations in dynamics of the secretory pathway, which cause changes in neuronal morphology.

To expand our studies, we have generated mice with neuron-specific (nTg) and systemic (sTg) overexpression of the two ER-based acetyltransferases, ATase1 and ATase2. The nTg animals exhibit cognitive impairments, autistic-like social behavior, synaptic plasticity abnormalities and widespread alterations in their proteomic profile. The sTg animals display developmental arrest when the ATases are overexpressed at conception, and a segmental form of progeria when the ATases are overexpressed at birth. Mechanistically, the phenotype is linked to defective engagement of the secretory pathway with a block in the induction of ER-autophagy.

Overall, our findings establish the intracellular citrate/acetyl-CoA pathway, with the ATases acting as the last output, as a fundamental branch of the general nutrient-signaling pathway, which enables rapid modulation and reprogramming of different intracellular activities upon fluctuation of metabolites/nutrients. They also highlight a fundamental role for developmental biology.



4:00 - 6:00PM
SESSION 8
EVOLUTION & CO-EVOLUTION



EVOLUTION AND CO-EVOLUTION

Irène AKSOY

Anaïs Amzal, Yannicke Pijoff, Cloé Rognard, Charlotte Bréhier, Guillaume Marcy, Véronique Cortay, Angèle Bellemin-Ménard, Thierry Joly, Marielle Afanassieff, Pierre Savatier

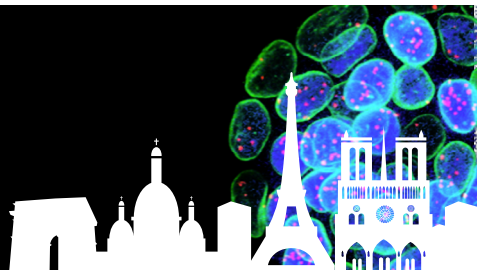
Stem Cell and Brain Research Institute INSERM, Bron

Molecular and cellular mechanisms underlying embryo colonization by pluripotent stem cells in primates

In rodents, naïve pluripotent stem cell (PSC)-based germline chimeras, associated with gene knockout technology, have been instrumental in elucidating developmental processes in healthy and diseased animals. Mice-rat blastocyst complementation has provided proof-of-concept for interspecies chimerism, paving the way for clinical applications in human organ transplantation. Unlike rodents, generating chimeras in primates remains challenging. We recently established that, mainly due to a defective cell cycle, human and non-human primate PSCs survive and proliferate poorly after injection into pre-implantation embryos.

The pre-implantation embryo is a challenging environment for foreign cells, likely eliminated by active cell-death mechanisms. Cell competition serves as a quality-control mechanism, ensuring genetic/phenotypic integrity of the stem cell pool before gastrulation. We reprogrammed human, chimpanzee, marmoset and rhesus macaque PSCs to a naïve state of pluripotency using a novel culture regime, ALGöX. Investigating their behavior in an in vitro cell competition assay, we found that human, rhesus, and marmoset PSCs were rapidly outcompeted by chimpanzee PSCs. We therefore qualified the chimpanzee PSCs as "winners", in contrast to the other primate PSCs, which acted as "losers". Additionally, we performed embryo colonization experiments: while human and rhesus monkey PSCs did not survive after injection into rabbit and monkey morulae, chimpanzee and marmoset PSCs colonized host blastocysts with high efficiency. We investigated the signaling pathways involved in cell competition and embryo colonization. MEK-ERK was found to inhibit apoptosis through BIM:MCL1interaction. PI3K-AKT accelerated the cell cycle through a mechanism yet to be identified. Finally, by modulating the activity of these pathways, we were able to convert embryo colonization-deficient "loser" human PSCs into embryo colonization-competent "winner" cells.

This study describes for the first time molecular and cellular mechanisms by which primate PSCs can colonize pre-implantation embryos to generate intra- and interspecies chimeras.



EVOLUTION AND CO-EVOLUTION

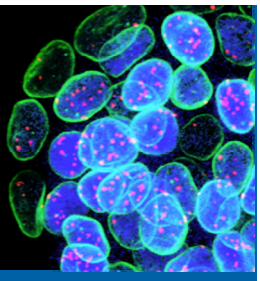
Eve GAZAVE

Loïc Bideau*, Zoé Velasquillo-Ramirez, Loeiza Baduel, Marianne Basso, Pascale Gilardi-Hebenstreit, Vanessa Ribes, Michel Vervoort

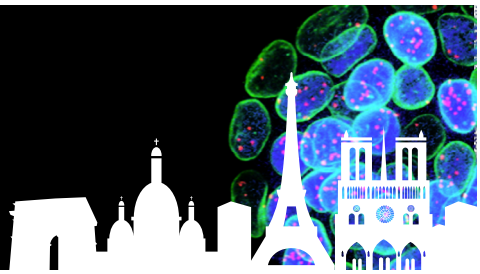
Institut Jacques Monod, CNRS
**First Author*

Variations in cell plasticity and proliferation underlie distinct modes of regeneration along the antero-posterior axis in the annelid Platynereis

The capacity to regenerate lost tissues varies significantly among animals. Some phyla, such as the annelids, display substantial regenerating abilities, though little is known about the cellular mechanisms underlying the process. To precisely determine the origin, plasticity and fate of the cells participating in blastema formation and posterior end regeneration following amputation in the annelid Platynereis dumerilii, we developed specific tools to track different cell populations. Using these tools, we find that regeneration is partly promoted by a population of proliferative gut cells whose regenerative potential varies as a function of their position along the worm's antero-posterior axis. Gut progenitors from anterior differentiated tissues are lineage-restricted, whereas gut progenitors from the less differentiated and more proliferative posterior tissues are much more plastic. However, they are unable to regenerate the stem cells responsible for the growth of the worms. Those stem cells are of local origin, deriving from the cells present in the segment abutting the amputation plane, as are most of the blastema cells. Our results favour a hybrid and flexible cellular model for posterior regeneration in Platynereis relying on different degrees of cell plasticity (Bideau et al., 2024, Development, in press).



9:00 - 11:00AM
SESSION 9
STEM CELLS, CELL FATE AND REGENERATION



STEM CELLS, CELL FATE AND REGENERATION

Lara KRÜGER

Joseph Watson, Kashish Singh, Vicente Jose Planelles-Herrero, David Baker, Emmanuel Derivery

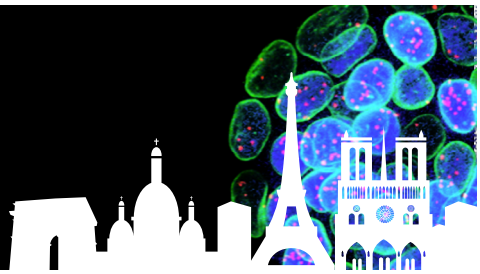
Laboratory of Molecular Biology (LMB) MRC, Cambridge, United Kingdom

Uncovering molecular mechanisms driving asymmetric cell division with synthetic biology

Asymmetric cell division promotes the generation of two daughter cells with different fates, as they inherit distinct fate determinants, and is, thus, crucial for organism development and tissue homeostasis. The process critically relies on a polarized cell cortex, which controls the profound polarization of the cell cytoskeleton. In particular, polarized microtubule networks promote the asymmetric partitioning of fate determinants to eventually generate two different daughter cells. Yet, the mechanisms underlying the formation of asymmetric microtubule networks, in particular, during mammalian asymmetric cell division remain largely elusive.

We recently developed a synthetic biology approach to artificially polarize normally unpolarized mammalian cells in culture, allowing an in-depth study of mammalian asymmetric cell division. Capitalizing on designed 2D protein arrays allowed us to ectopically induce cortical polarity of virtually any protein of interest during mitosis in various cell types. Strikingly, cortical clustering of the conserved polarity cue, the Par complex (Par3/Par6/aPKC), is sufficient to polarize the microtubule cytoskeleton and induce key processes of asymmetric cell division: spindle orientation (via Par3) and central spindle asymmetry (via aPKC).

We further establish that molecularly, the formation of an asymmetric central spindle, where on side contains a higher microtubule density as opposed to the other, requires an asymmetric kinase activity of aPKC at the cortex. Unlike the metaphase spindle, the central spindle at late mitosis, is not directly linked to the cortex via astral microtubules. Hence, how does aPKC at the cortex regulate central spindle microtubules in the cytosol? Our recent results indicate that this communication depends on Lis1, a conserved dynein-adaptor. In unpolarized cells Lis1 mainly localizes to the cell cortex, yet, when an asymmetric aPKC cap is formed, Lis1 localizes to central spindle microtubules at late mitosis in an aPKC kinase-activity-dependent and dynein-independent manner. At the central spindle, Lis1 is involved in central spindle symmetry breaking.



STEM CELLS, CELL FATE AND REGENERATION

Pauline SPÉDER

Anna Segú-Cristina*, David Briand, Stéphane Rigaud, Emeline Perthame, Agata Banach-Latapy, Aman Kukde, Léo Valon, Yohanns Bellaïche

Institut Pasteur/CNRS UMR3738/ Sorbonne Université/ Université Paris Cité, Paris, France
**First Author*

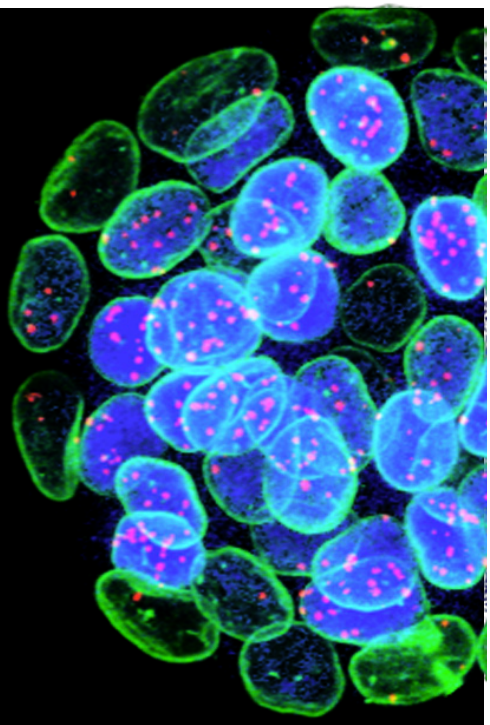
Adhesion-controlled forces in the glial niche regulate stem cell proliferation in the developing Drosophila brain

Neural Stem/progenitor Cells (NSCs) exist in a niche, a complex and dynamic cellular microenvironment supporting their functions. The niche must respond to NSC needs while mediating the impact of local and systemic inputs to support neurogenesis. In particular, the intricate structure of the niche, rich in direct cell-cell contacts and adhesions, has the potential to be a critical regulator of NSPC behaviour. However, how structural interactions between the NSCs and their niche control neurogenesis remains poorly explored.
The Drosophila developing, larval brain harbours genuine NSC niches that contain common players and recapitulate core features of the vertebrate microenvironment. Here, a specific subpopulation of glial cells, the cortex glia, are known to be essential for neurogenesis and intimately enclose each NSC and its neuronal progeny within a membrane chamber. The precise encasing of each individual NSC chamber pinpoints the existence of tightly controlled interactions between CG and NSCs lineages.
We first performed transcriptional analysis of cortex glia along chamber morphogenesis, which identified an enrichment in surface immunoglobulins. We choose to focus on a specific immunoglobulin whose partner is expressed in NSCs. We discovered that these binding partners act as adhesion complexes bringing together NSC and cortex glia membranes. Further, the independent knockdown of these immunoglobulins in either cortex glia or NSCs resulted in a remarkable phenotype in NSCs, which displayed altered nuclear shape and slower cell cycle progression. Strikingly, we found that such immunoglobulin-mediated adhesion impinges on NSC proliferation by regulating the cortical tension in the cortex glia. Altogether, these findings highlight a mechanism by which tension cues in the niche are relayed to the stem cells and regulate neurogenesis. This work demonstrates that the niche exerts mechanical constraints directing NSC behaviour at an individual level.

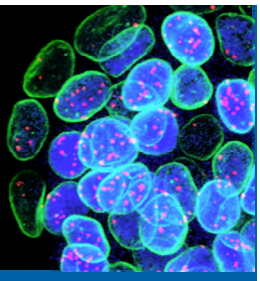
From cell to organism

When cell biology meets development

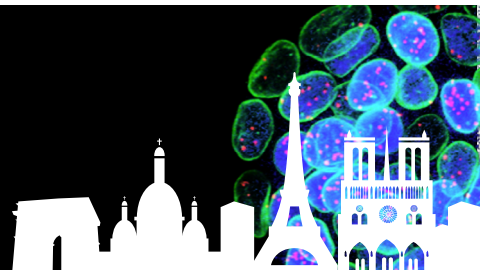
OCTOBER 16-19, 2024 | CICSU, SORBONNE UNIVERSITÉ - PARIS



POSTERS

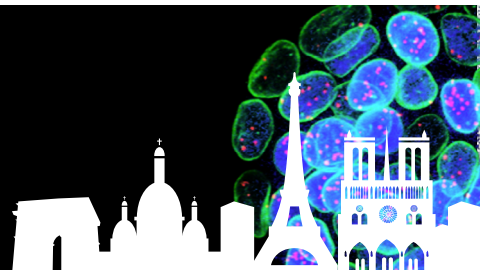


THURSDAY, OCTOBER 17TH
2:10 - 3:50PM
POSTER SESSION 1



LIST OF POSTERS

#	LAST NAME	FIRST NAME	TITLE
1	AGSU	Gökçe	Microtubule-Driven Nuclear Deformations Trigger Histone Remodeling in Human Hematopoietic Stem Cell Differentiation
2	ALMONACID	Maria	Deciphering nuclear mechano-transduction in mouse oocytes
3	ANGER	Lucas	Intercellular stress anisotropy as a regulator of proliferation in epithelia
4	ARKOWITZ	Gregory	Intracellular mechanics of migrating epithelial tissues
5	ARNALDOS PÉREZ	Irene	Mesenchymal stem cells properties and early differentiation in the context of leukemia: response to matrix bound growth factors
6	BARROS-CARVALHO	André	Identification of conserved mechanisms that regulate cortex remodelling during epithelial cell division
7	BERNARD	Fred	Nucleus positioning by membrane-associated microtubules in Drosophila oocyte
8	BOISMOREAU	Franck	Exploring the development of the gut-brain axis through the nodose ganglion projections
9	CAETANO	Ana	Development and plasticity of oral neuroglia
10	CAIROLI	Andrea	Model of colliding active tissues recapitulates the Drosophila abdominal morphogenesis during metamorphosis
11	CALDERARI	Sophie	Integration of transcriptome and chromatin accessibility in embryos developed in vivo or in vitro
12	CARVALHO	Sandra	Dynamics and contribution of Actin cytoskeleton in 3D cell intercalation
13	CERQUEIRA CAMPOS	Fabiana	Investigating Drosophila embryonic muscle diversification by Muscle-Specific-Single Nuclei-RNA-Sequencing
14	CHENEVERT	Janet	Cell cycle control of spindle positioning forces in the ascidian embryo



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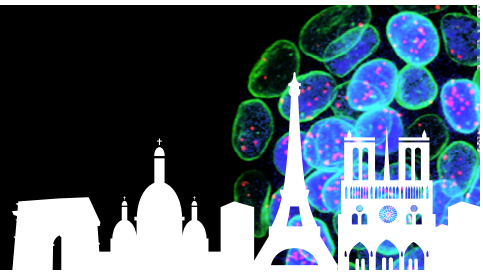
15	CIK	Klara	New Extracellular Mode of B-Cell Activation Through Release of Native Antigen by Dendritic cells
16	CRUZ	Margarida	How neurons reach their place: a Bipolar Cell perspective
17	DALDELLO	Enrico Maria	Understanding how changes in protein homeostasis regulate meiotic cell divisions.
18	DAVID	Nicolas	A non-cell autonomous role of Myosin-II in guiding collective migration
19	DAVILMA	Marlène	3D imaging-based analysis of the germline in teleost
20	DEDUYER	Irène	Polar cortex contractility provides adaptability of cytokinesis to distinct tissue specificities
21	DESGRANGE	Audrey	Plasticity of ventricle position after heart looping in heterotaxy
22	DHARMADHIKARI	Shivani	Plasma membrane mechanics during mammalian preimplantaion development
23	DI PIETRO	Florencia	Mitotic cell reshaping in epithelial tissue
24	DOHADWALA	Lamiya	Morphodynamic characterisation of the proneural neighbourhood during the specification of embryonic neuroblasts in Drosophila
25	EIVERS	Sarah	Predicting the Translational Fingerprint of M-phase Using Machine Learning: An Attribute Network-Based Ranking Model.
26	FORBES BEADLE	Lauren	A simple MiMIC based approach for tagging endogenous genes to visualize live transcription in vivo
27	FORMICHETTI	Sara	Modulation of mammalian embryonic growth by intracellular glycosylation
28	FORTUNATO	Saverio	Investigating cranial neural crest patterning and its influence on cell plasticity
29	GRACIA	Mélanie	Epithelial apoptotic pattern emerges from global and local regulation by cell apical area



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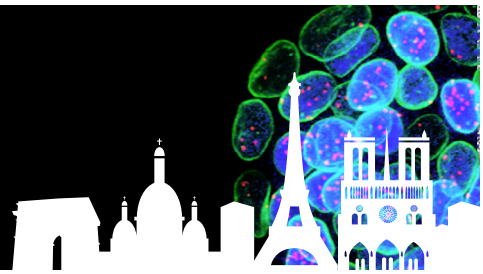
30	GUPTA	Kirti	Notch signalling patterns the myocardial wall during vertebrate heart development
31	GUTTIERES	Lucas	The function of β-catenin during development in the ctenophore Mnemiopsis leidyi
32	HEUZÉ	Mélina	Connection between the endoplasmic reticulum and focal adhesions during cell migration: membrane contact sites join the dance
33	INOUE	Megumi	Branching Morphogenesis in Human Lung Development
34	JI	Fengtong	Probing mesenchymal tissue viscosity in vivo with magnetic nanorobots
35	JUGE	François	Discovery and functional characterization of α-tubulin detyrosinase in Drosophila
36	KHALILIAN	Parisa	MACF1 regulate apical sorting of GPI-APs in polarized epithelial cells
37	KICKUTH	Alison	A mechanical ratchet drives unilateral cell division
38	KINTEROVÁ	Veronika	Effect of inhibition of protein neddylation on bovine oocyte maturation
39	KÖHLER	Melina	sox1a:eGFP transgenic line and single-cell transcriptomics reveal the origin of zebrafish intraspinal serotonergic neurons
40	KRETZSCHMAR	Jenny	A place and time to die – Selective cell death and morphogenesis of the mammalian foregut pocket
41	LANGE	Merlin	Building a Multimodal Atlas of Vertebrate Development
42	LERIA	Marvin	Fast coordinated reorientation of basal body polarity in Trichoplax
43	LEROY	Adrien	Combining spatial transcriptomics and biophysical measurements unravel the genetic control of tissue morphogenesis



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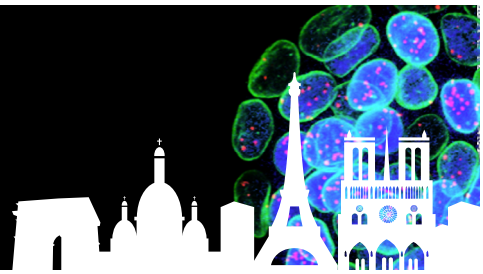
44	LOBJOIS	Valérie	Control of the progression in the G1 phase of the cell cycle during neurogenesis: a new function for the protein phosphatase CDC25B
45	LOVE	Jennifer	Spatially regulated mRNA degradation defines the expression pattern of even-skipped in early Drosophila development
46	LUYAN	Cao	Arpc5 isoforms differentially impact the ability of Arp2/3 complexes to generate linear filaments to regulate lamellipodia protrusion
47	MAILLARD	Louise	Quantifying how cis regulatory sequences affect gene expression heterogeneity
48	MANCINI	Laure	Control of the spiral phyllotaxis from a single stem cell in the moss Physcomitrium patens
49	MEDJKANE	Souhila	METHYLATION REGULATES THE TIMING OF CYTOKINETIC ABSCISSION
50	MEDYOUF	Amina	Regulation of lumen remodelling in the zebrafish developing spinal cord by cilia-dependent Hh signaling
51	MIRVIS	Mary	Harnessing whole-cell morphometrics to probe organelle interdependencies and cell anatomy: a two-pronged approach
52	MIZIA	Paulina	The influence of busulfan on gonad development in the zebra finch (Taeniopygia guttata)
53	MORAITI	Anastasia	Investigating growth control in the Drosophila melanogaster abdomen using transcriptomics
54	MOYANO RODRIGUEZ	Yolanda	Mechanistical investigation of X-chromosome reactivation in the germline
55	OSTEIL	Pierre	Primitive Endoderm Patterning Provides a Head Start for Axis Positioning
56	PÉZERON	Guillaume	A function for Uts2 signaling in intervertebral disc formation and homeostasis.



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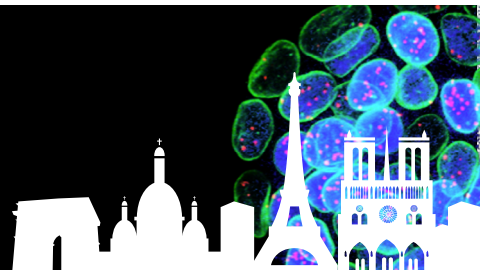
57	PIGACHE	Rémi	Regulation of epithelial folding downstream of homeotic gene
58	PIMMETT	Virginia	Dissecting the dynamics of coordinated active transcriptional repression in the Drosophila mesoderm
59	PIROZHKOVA	Iryna	DiPRO1/ZNF555 distinctly reprograms muscle and mesenchymal cancer cells
60	POMPILI	Chiara	Phagocytosis via mannose receptors analysed using chemically functionalised lipid particles
61	PUTTI	Elena	Lrrn2 and Lrrn3a cell adhesion molecules govern precise retino-tectal circuit formation in the zebrafish visual system
62	RONDON	Robin	A BMP mediated PAX3/7 transcriptional activity switch creates cell fates patterns in the developing spinal cord
63	RUSTARAZO-CALVO	Laura	The emergence and function of different types of tissue material phase transitions during embryo development
64	SANCHEZ GARRIDO	Frida	Pleiotropic role for Dlx5/6 transcription factors in the formation of the mammalian acoustic system
65	SANTONI	Martina	Exploring the multi-branched pathway connecting PKA inhibition and Cdk1 activation
66	SARKANY	Tasmin	Modelling the mechanical effect of out of plane division on tissue bending in insect gastrulation
67	SEAL	Subham	The epigenetic factor Prdm12 regulates neural crest EMT: a link between epigenetics, signaling and cell migration
68	SHIHABI	Anastasia	Consequences of excessive cortical tension on oocyte development
69	SOLER	Cédric	Exploring Tendon Cell Diversity and Its Contribution to Muscle Development
70	SOUCAT	Eglantine	Identification of asexual and sexual germarial cell identity markers during Pea aphid embryogenesis



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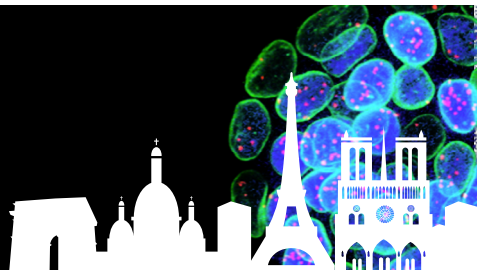
71	THIANT	Clemence	Transmission of front-back polarity in trains of cells
72	TORALOVÁ	Tereza	The timing of maternal protein degradation is species-specific in mammals
73	TOUQUET	Bastien	Deciphering the dynamics interplay between the Toxoplasma invasive nanodevice and the host cell cortical cytoskeleton
74	WAPPNER	Marcos	The role of Delta-Notch in the synchronization of the zebrafish segmentation clock
75	WOELK	Michaela	A gene regulatory network that supports organism-wide oscillatory gene expression to time development
76	WURMSER	Maud	Compartmentalized cAMP signaling modulates HUVEC migration in response to repulsive cues
77	YANAKIEVA	Iskra	Role of cell shape fluctuations in cell spreading during epithelial-to-mesenchymal transition
78	YASUO	Hitoyoshi	Cell geometry, signal dampening, and a bimodal transcriptional response underlie the spatial precision of an ERK-mediated embryonic induction
79	YOSHIDA	Mari	Deciphering the temporal control of mechanosensing during development
80	ZHOU	Chenxi	The glycolysis regulators PFKFB3 and PFKFB4 regulate cell migration in melanoma



POSTER 1

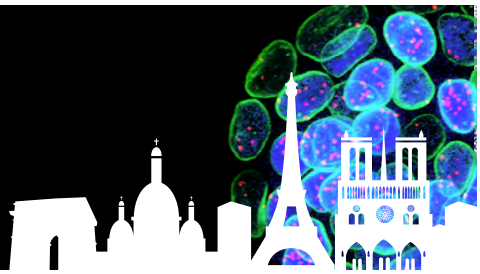
Gökçe AGSU

Mathilde Dura, Laurent Blanchoin, Déborah Bourc'his, Stéphane Brunet, Manuel Théry, Camille Lobry

1. Cambridge Stem Cell Institute, University of Cambridge, Cambridge, CB2 0AW, UK
2. INSERM, CEA, U976 - HIPI, Institut de Recherche Saint Louis, Université de Paris, Paris, France

Microtubule-driven nuclear deformations trigger histone remodeling in human hematopoietic stem cell differentiation

The cell nucleus, known as the most rigid organelle, undergoes significant deformation during morphogenesis. These deformations often result from cytoskeletal forces transmitted from the cytoplasm to the nucleus. Despite the prevalence of this process in development, our understanding remains limited. We recently discovered a novel nuclear mechanotransduction event during human myelopoiesis, where hematopoietic stem cells (HSCs) differentiate into myeloid progenitors. During myelopoiesis, the microtubule network forms bundles along the nuclear envelope through dynein tethering, actively deforming the ovoid HSC nucleus. We found these deformations to be microtubule-dependent and irreversible. Image analysis revealed nuclear envelope and chromatin remodeling at the deformed regions, characterized by the loss of Lamin B and both facultative and constitutive heterochromatin marks. Our CUT&RUN-based epigenome analysis showed that microtubule-dependent nuclear deformation specifically triggers histone remodeling associated with key myeloid genes, leading to their transcriptional activation. Furthermore, pharmacological disruption of microtubule forces in HSCs resulted in the retention of repressive histone markers on key myeloid genes, impeding myeloid identity acquisition during ex vivo expansion, even in myelopoiesis-enhancing culture media. These findings reveal a novel regulatory role of microtubule dynamics in hematopoiesis. HSCs maintain lifetime blood homeostasis through balanced self-renewal and differentiation; a failure in differentiation can lead to severe consequences, including leukemia and fatality. Therefore, understanding the functional significance of microtubule-dependent nuclear deformations in myelopoiesis is crucial. Our study advances the understanding of nuclear mechanotransduction in HSC differentiation and blood maintenance.



POSTER 2

Maria ALMONACID

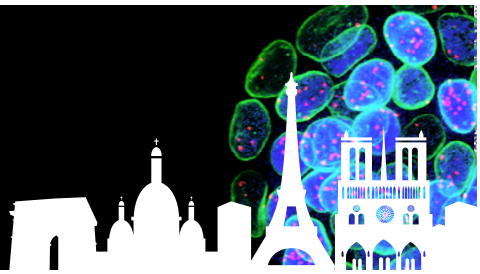
Christelle Da Silva, Sophie Lemoine, Marie-Christine Birling and Marie-Hélène Verlhac

CIRB, Collège de France, Université PSL, CNRS, INSERM, 75005 Paris, France

Deciphering nuclear mechano-transduction in mouse oocytes

Understanding the mechanism of nucleus positioning and its subsequent significance are important research axes in Developmental and Reproductive Biology. In most species, the position of the oocyte nucleus predefines the axes of the future embryo. In the mouse oocyte, the nucleus is centered by a cytoplasmic actin meshwork (1) yet does not instruct any axis in the embryo. The discovery of this centering mechanism provides further insight into its role. Centering the nucleus in mouse oocytes involves a novel mechano-transduction process which shapes and shakes the nucleus and its content, including chromatin and nuclear bodies, thereby modulating gene expression. This explains why nucleus centering is predictive of the quality of the female gamete and of its developmental potential after fertilization (2,3). To identify this mechano-transduction cascade, we previously performed rescue experiments in mouse oocytes knock-out for Formin 2, a nucleator of the cytoplasmic meshwork. We now want to revisit our model of mechano-transduction using a double conditional knock-out of Spire 1 and Spire 2, two actin nucleators that both cooperate with Formin 2 to nucleate the cytoplasmic actin meshwork (4,5). Our data show that, unlike Spire 1 and Spire 2 single knock-outs, Spire 1 & 2 double knock-outs recapitulate the phenotype of Formin 2 knock-out oocytes (off-centered, and misshapen nuclei). By comparing the genes deregulated in both Formin 2 and Spire 1 & 2 knock out oocytes, we aim at identifying a list of genes responsive to mechano-transduction in mouse oocytes, significant for oocyte and embryo development.

References:
1. Almonacid et al, Nat Cell Biol 17, 470–479 (2015)
2. Almonacid et al, Dev Cell 51, 145-157 (2019)
3. Al Jord et al, Nat Comm 13 (2022)
4. Pfender et al, Curr Biol 21, 955–960 (2011)
5. Montaville et al, Plos Biol 12 (2014)



POSTER 3

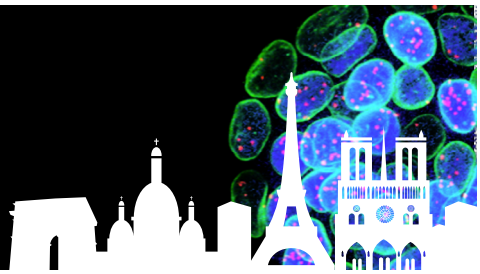
Lucas ANGER

Sameer Kumar, Amin Doostmohammadi, René-Marc Mège, Benoit Ladoux

Institut Jacques Monod, CNRS UMR7592 / Université Paris Cité, Paris, France

Intercellular stress anisotropy as a regulator of proliferation in epithelia

Cell division is one of the most basic process involved in building a complex living organism, and dysfunction of cell division usually leads to severe tissue pathology, during both development and homeostasis. Although the biochemical regulation of the cell cycle has been extensively studied, various works in the field of mechanobiology have also shown how tissue mechanics can affect the spatio-temporal organization of cell division. Due to the lack of direct intercellular mechanical stress measurements, how intercellular deformations impact cell division fate remains unclear, but the widely accepted process is that local tension can induce cell division. Here, building on the framework of continuum mechanics, we show that the mechanical stress within epithelial monolayers exhibits a principal stress direction, revealing the highly anisotropic nature of epithelia as a soft material, regardless of the cell density. Using traction force microscopy and stress inference technique, we demonstrate that increased anisotropic stress causes cells to divide along the principal stress direction, and that cell division allows anisotropic stress within the tissue to decrease. We show that the anisotropic stress is a mechanical predictor of cell division, covering the usual view (tension-induced division) as well as non-trivial cases (division happening under compression or no clear mechanical state). Our findings indicate a mechanical feedback loop between tissue homeostasis and intercellular stress anisotropy in epithelia, and suggest broad implications in development and in pathology involving unregulated division.



POSTER 4

Gregory ARKOWITZ

Jean François Berret, Olivier Destrian

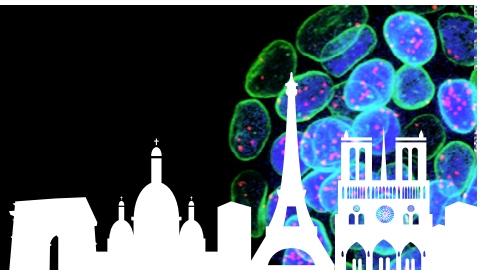
Ladoux/Mege lab, Institut Jacques Monod, Université Paris Cité, Paris, France

Intracellular mechanics of migrating epithelial tissues

An ongoing objective of mechanobiology is to establish the fundamental relationship between the mechanical properties of cells and the regulation of their morphology and dynamics which are crucial to maintaining homeostasis across scales, from a single cell to a tissue. Therefore, several recent studies have successfully highlighted the interplay existing between the geometric and mechanical properties of single cells by using standardized methods, such as AFM or optical tweezers. While single cell studies have shown promising results, there is currently very little knowledge on how internal cell mechanical properties impact collective cell movements occurring in tissue scale dynamics.

We investigate the interaction between the intracellular viscoelastic properties of MDCK cells with their cell morphology and collective motion in an epithelial monolayer tissue. The rheology of the cytoplasm is characterized by performing live measurements of its static viscosity and elastic modulus through the use of a method based on rotational magnetic spectroscopy (Berret, J.-F. Local Viscoelasticity of Living Cells Measured by Rotational Magnetic Spectroscopy, Nat. Commun, 7, 2016). This active microrheology method consists in measuring the inner rheology of cells by tracking the motion of internalized magnetic nanowires subjected to an external rotating magnetic field. This process allows for simultaneous measurements of the internal viscosity and elasticity of cells in a monolayer, by probing low frequencies in time scales relevant to tissue dynamics (i.e mHz).

We apply this method to decipher the correlation between the inner cell viscoelasticity, the cell volume and area as well as the monolayer velocity. The morphological and dynamical properties of cells in a monolayer are modulated by varying several physiologically relevant parameters such as the external osmotic pressure, the cell confluency, and the substrate stiffness. These conditions allow us to quantify the effect of molecular crowding on the intracellular rheological properties of cells within a monolayer.



POSTER 5

Irene ARNALDOS PÉREZ

Paul Machillot, Kevin Geistlich, Agnès Desroches-Castan, Véronique Maguer Satta, Sabine Bailly, Corinne Albiges-Rizo , Laurent Guyon, Sylvain Lefort, Catherine Picart

Université Grenoble Alpes UMR U1292 Biosanté, Grenoble, France

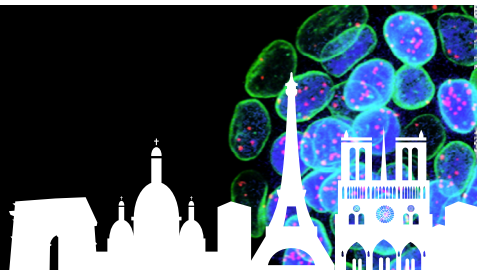
Mesenchymal stem cells properties and early differentiation in the context of leukemia: response to matrix bound growth factors

Background and purpose: Acute myeloid leukemia is originated in the bone marrow, where the hematopoietic stem cells proliferate in an uncontrolled manner. However, how leukemia affects bone tissue, especially mesenchymal stem cells (MSCs) from bone marrow, is unclear.
BMP levels of the bone microenvironment are deregulated in leukemia. We have developed a thin biomimetic film made of hyaluronic acid that can physically bind growth factors like BMP proteins, and present them to cells in a matrix-bound manner. We showed that matrix-bound BMP2 triggers stem cell adhesion, which is due to an interplay between BMP receptors and integrin receptors. Thus, cell adhesion is coupled to cell differentiation.
Here, we aim to investigate how matrix-bound BMPs influence early differentiation and the adhesive properties of MSCs in leukemic versus healthy context. To this end, we used a recently developed high-content fluorescence microscopy to study cell adhesion and differentiation.

Methods: Human MSC response to matrix-bound growth factors was studied at different time points up to 24h. Cell adhesion was quantified by counting adherent cells and measuring their spreading area. The differentiation potential was assessed by quantifying SMAD signaling at high-content. Next, we studied quantitative gene expression of growth factor receptors and adhesion receptors in MSCs. Bioinformatics tools were used for data analysis and correlations.

Conclusions:An increased and sustained pSmad signal was observed in leukemic MSC, suggesting that other pathways might activate the pSmad pathway in leukemic MSC. Both healthy and leukemic MSC adhered to the matrix-bound BMP, but the spreading of leukemic MSC was strongly impaired and delayed. The receptor repertoire was similar between the two populations, but 33% of leukemic MSC exhibited an increased gene expression of their receptors. A striking correlation between them was observed in the case of leukemia.

Keywords: Mesenchymal stem cells, biomimetism, leukemia, BMP/TGFbeta signaling



POSTER 6

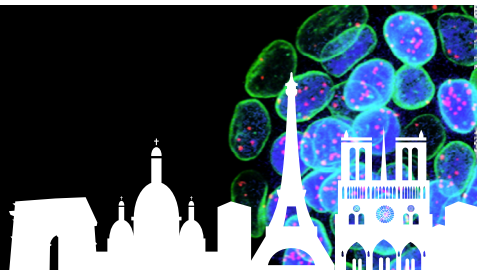
André BARROS-CARVALHO

Oliver Rocks, Eurico Morais-de-Sá

i3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, ICBAS - Instituto de Ciências Biomédicas Abel Salazar

Identification of conserved mechanisms that regulate cortex remodelling during epithelial cell division

Epithelia act as vital barriers to the external environment of animal organs, relying on intracellular complexes distributed along an apical-basal axis to correctly position adherens junctions and maintain tissue architecture. During cell division, epithelial cells must coordinate the remodeling of their apical-basal organization with the cytoskeleton to orient the mitotic spindle and form a contractile cortex that exerts outward forces on neighbouring cells. This is crucial to maintain mitotic fidelity whilst preserving tissue integrity within a proliferative epithelium. However, the molecular interplay between apical-basal polarity proteins and cytoskeletal regulators remains poorly understood. Following a localisation screen that characterized RhoGTPase regulators (RhoGAPs and RhoGEFs) with potential roles during epithelial cell division, we are identifying conserved pathways that remodel the mitotic epithelial cell cortex by testing whether their mammalian orthologs recapitulate their mitotic redistribution in polarized MDCK cells. Among these, we discovered that both Drosophila RhoGAP19D and mammalian ARHGAP21/ARHGAP23 are released from cell-cell junctions and lateral cortex at mitotic entry. Live imaging revealed that RhoGAP19D mitotic redistribution coincides with mitotic rounding, while quantitative imaging analysis indicates that cortical retention of RhoGAP19D during mitosis interferes with cell rounding and mitotic progression. We are currently investigating how the cell cycle triggers RhoGAP19D (ARHGAP21/23) cortical and junctional release and how this mechanism coordinates apical-basal organization with a contractile cytoskeleton for proper cell division in animal tissues.



POSTER 7

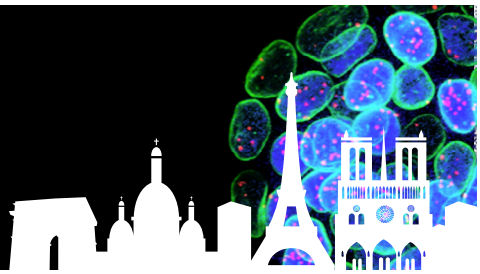
Fred BERNARD

Fanny Roland-Gosselin*, Antoine Guichet

Univ. Paris Cité, Institut Jacques Monod, UMR7592
**First Author*

Nucleus positioning by membrane-associated microtubules in Drosophila oocyte

During Drosophila oogenesis, the asymmetric positioning of nucleus is essential for dorso-ventral polarity acquisition. This polarity induces the future back of the embryo and eventually of the adult fly. The migration of the oocyte nucleus migration is dependent on microtubules. Recently, we identified a network originating from the plasma membrane. We're currently investigating how this membrane associated network is generated and how it integrates with the other sources of microtubules in order to participate to the robustness of nucleus positioning within Drosophila oocyte.



POSTER 8

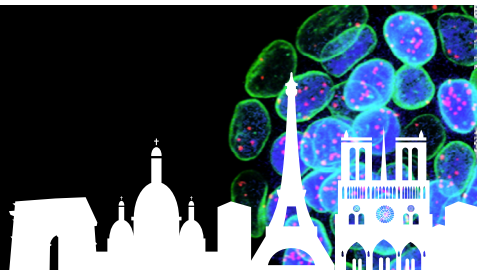
Franck BOISMOREAU

Maëlys André, Muriel Bozon, Guillaume Marcy, Maxime Le Petit, Jérémy Ganofsky, Jingyun Yi, Carola Meyer, Thomas Worzfeld, Julien Falk, Valérie Castellani*

MeLiS, UCBL
**Co-First Author*

Exploring the development of the gut-brain axis through the nodose ganglion projections

The enteric nervous system plays a crucial role in regulating various aspects of gastrointestinal function, including motility, nutrient absorption, among others. Notably, a fascinating discovery has revealed a direct connection between sensory neurons of nodose ganglia located at the brainstem level and physically attached to the vagus nerve, and specialized epithelial cells called enteroendocrine cells that sense gut stimuli. Nodose neurons, which originate from the branchial arches, are pseudo-unipolar. Their central axon branch connects to the nucleus of the solitary tract in the hindbrain, while their peripheral branch projects to various target organs, with a significant presence in the heart and gut but their development isn't known yet. To address this gap in knowledge, we conducted a study on the development of nodose peripheral projections using the chicken embryo model. We employed unilateral electroporation of placodes with an integrative vector containing GFP to trace the axon projections. Embryos were collected at different time points and labeled with Tuj1 antibody to track the two nodose tracts. Surprisingly, our observations revealed that nodose axon projections exhibit an ipsilateral and commissural organization. The left and right axon tracts merge to form a single bundle that traverses the thoracic-abdominal subdivision and subsequently diverges into two tracts, each possessing both ipsilateral and contralateral components and then invade the gut by migrating on the tube and extending radial projection toward the epithelium. To gain further insights into the mechanisms that govern the pathfinding of nodose axons to the gut, we conducted single nucleus RNA sequencing of the nodose ganglia. Our focus was on two specific developmental stages that correlate with the early nodose axon chiasm formation and the subsequent navigation towards the targets within the gut. We anticipate that our study will provide novel insights into the developmental processes and molecular pathways that underlie the establishment of the intricate gut-brain connection.



POSTER 9

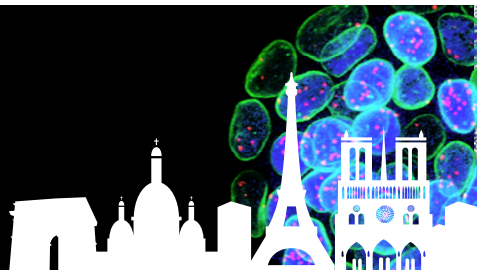
Ana CAETANO

Paul Sharpe, Elysia James

Barts and the London School of Medicine and Dentistry, Queen Mary University of London , London, UK

Development and plasticity of oral neuroglia

Oral and craniofacial tissues are uniquely adapted for life-sustaining functions, including breathing, feeding and communication. Peripheral glia, the non-neuronal cells of the peripheral nervous system are now considered important regulators of tissue homeostasis and immunity; however, their functional relevance in oral mucosa physiology and disease is unknown. Neuroglia networks are found in close association with oral epithelial stem cells, and express important drivers of epithelial turnover. Using single-cell and spatial transcriptome profiling, we also demonstrate that glial cells switch to distinct molecular profiles in inflamed and tumour patient samples with upregulation of immune and neurogenic gene signatures, suggestive of functional heterogeneity. We hypothesise that neuroglia is central to the structural, functional and defence roles of the oral barrier. To understand the molecular and mechanistic drivers underpinning glia plasticity, we use single-cell multiome profiling across mouse and human development. We identify conserved and species-specific gene regulatory temporal programs and investigate how mature glial cell lineages acquire immunoregulatory and neurogenic functions. Together, our work reveals an unappreciated role of neuroglia in oral barrier tissue homeostasis and provides insight into the regulatory landscape shaping the development of oral neural circuits.



POSTER 10

Andrea CAIROLI

John R. Davis, Ana Ferreira, John J. Williamson, Anna P. Ainslie, Matthew B. Smith, Marcus Michel, Christian Dahmann, Nicolas Tapon, Guillaume Salbreux

The Francis Crick Institute, London, UK

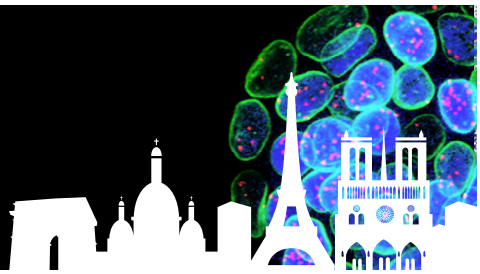
Model of colliding active tissues recapitulates the Drosophila abdominal morphogenesis during metamorphosis

Cellular tissues form through self-organized, controlled programs of development relying on feedback between cellular processes, tissue-wide properties, and external cues. This complex interplay is exemplified by the metamorphic program the Drosophila abdominal epidermis undergoes during pupal development.

Before metamorphosis, histoblasts, the progenitor cells of the adult epithelium, sit quiescent in nests, confined regions in the abdomen located symmetrically to the dorsal midline and surrounded by the larval epidermal epithelium. During metamorphosis, histoblasts proliferate and replace the larval epidermis by coordinating the extrusion of larval cells through apoptosis. Histoblasts from the left and right abdominal half-segments flow towards the dorsal midline and eventually collide. This collision leads to the closure of the adult epidermis.

The mechanics of abdominal histoblasts collision, as well as the underlying cellular processes, have yet to be characterized. How the histoblasts regulate their proliferation, divisions and kinetics, and interact with the larval cells, is especially relevant to understand how the correct adult abdomen size is achieved consistently throughout development.

Here, we investigate the morphogenetic process during metamorphosis of the abdomen of Drosophila. We characterize the mechanics of histoblasts collision, by reconstructing the spatiotemporal evolution of cell elongation, area and velocity of both the histoblasts and larval cells. We measure these parameters using confocal microscopy movies of the abdominal epithelium in vivo. We formulate a continuum, mechanistic model on these parameters that can recapitulate our experimental observations. We employ the model to elucidate on the physical mechanisms driving morphogenesis in this system. We show nematic behaviour of epithelial cells elongation, extra-cellular matrix degradation modelled as a coarse-grained friction coefficient, and differences in material properties of larval cells and histoblasts are key drivers of the histoblasts collision process.



POSTER 11

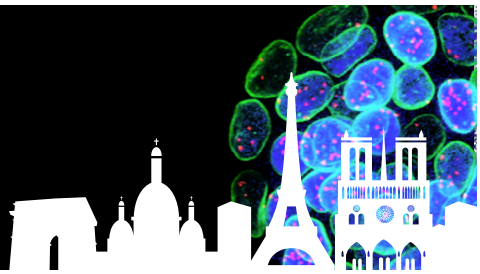
Sophie CALDERARI

Emilie Trautmann*, Catherine Archilla, Luc Jouneau, Anne Frambourg, Romina Via y Rada, Nathalie Daniel, Veronique Duranthon, Alice Jouneau and Sophie Calderari

INRAE
**First Author*

Integration of transcriptome and chromatin accessibility in embryos developed in vivo or in vitro

Embryonic preimplantation development is a highly dynamic process, involving the embryonic genome activation and the differentiation of the first cells. This process, which is tightly regulated epigenetically, ensures the development of the fetus and the extraembryonic tissues. With the increasing use of assisted reproductive technologies, safety concerns, especially during in vitro culture, have become a major public health issue. To identify the impact of in vitro culture on the first embryonic lineages, we analysed gene expression and chromatin accessibility in rabbit embryos developed either in vivo or in vitro. The rabbit was chosen as a model because its characteristics are close to those of the human embryo (i.e. timing of EGA, metabolism).
Embryos developed in vivo were harvested at 86 hours post-coitum (hpc) (early blastocyst) and at 96 hpc (mid blastocyst). Embryos developed in vitro were produced by culture from the zygote. The inner cell mass (ICM) and the trophectoderm (TE) were separated by immunosurgery. Genome wide transcriptome and chromatin accessibility were profiled by RNA-seq and ATAC-seq, respectively.
Genes involved in metabolic pathways such as oxidative phosphorylation, Krebs cycle, mTORC1 and fatty acid metabolism were less expressed in ICM and TE from in vitro than in vivo developed embryos. Genes involved in gene expression regulation and chromatin organization were more highly expressed in ICM and TE from in vitro than in vivo developed embryos. Vitro-TE exhibited more similarities with vivo-TE from early embryos and inversely, vitro-ICM exhibited more similarities with vivo-ICM from mid embryos.
We observed major differences in transcriptome and chromatin accessibility in both ICM and TE between embryos developed in vivo and in vitro. These dissimilarities may be involved in long-term effects.



POSTER 12 & FLASH TALK

Sandra CARVALHO

Antoine Guichet, Véronique Brodu

Institut Jacques Monod, CNRS - UMR7592, Paris, France

Dynamics and contribution of Actin cytoskeleton in 3D cell intercalation

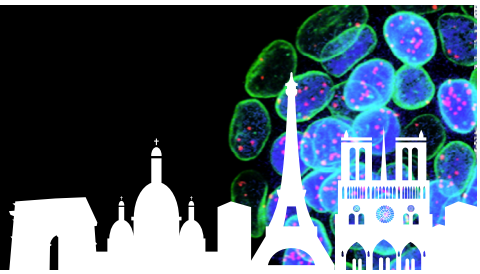
Cell intercalation allows a coordinated change of cell position in a developing tissue. This process contributes to the organ shaping, which is necessary to ensure properly its physiological function. To change position, cells undergo important reorganisations of their cell-cell contacts, formed in part by the Adherens Junction (AJ) complex. The mechanical forces required to reorganise the AJs depend on their association with the subcortical actin network. Indeed, 2D intercalation has been extensively studied and relies largely on forces generated by the contraction of the subcortical actin network associated with MyosinII (MyoII).

However, 3D cell intercalation, which supports most organ structures, has been less examined. To investigate this process, we study the morphogenesis of the tracheal system of Drosophila melanogaster embryo. Contrary to known mechanisms, it offers an original intercalation process that does not require MyoII. Thus, we investigated if actin contribute or not to 3D cell intercalation.

Using an innovative in vivo tool to depolymerise actin at a precise cell resolution, we show that actin alone can support and transmit mechanical forces in the intercalating cells. By following the in vivo actin dynamics during 3D intercalation, we find a gradual redistribution of actin from the cytoplasm to the AJs. Our study shows that this actin enrichment at AJs is tightly controlled by the actin-binding protein Girdin specifically in tracheal cells.

During cell intercalation, bicellular and tricellular AJ (tAJ) are completely remodeled. Interestingly, we characterise an actin pulsatile behaviour restricted at tAJs, that is associated with Sidekick, a key component of tAJs. We find that actin regulators, such as the actin polymerase Enabled and the Arp2/3 branched actin nucleator complex, are localised at tAJ and vary with actin pulses.

These findings highlight how actin dynamics alone can generate forces sufficient to reorganise cell-cell contacts and allow intercalation without MyoII.



POSTER 13

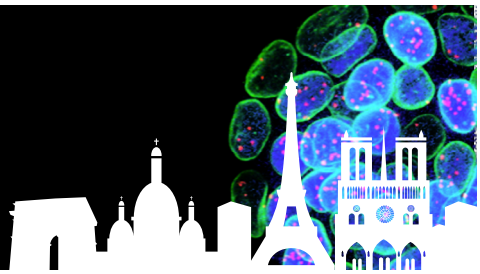
Fabiana CERQUEIRA CAMPOS

Elia Ragot, Sandy Al-Hayek, Stéphanie Maupetit-Méhouas, Nicolas Allegre, Léa Bellenger, Guillaume Junion

iGReD, CNRS UMR6293, INSERM U1103, Université Clermont Auvergne

Investigating Drosophila embryonic muscle diversification by Muscle-Specific-Single Nuclei-RNA-Sequencing

In Drosophila melanogaster, larval somatic muscles are progressively established during embryonic development according to a specific pattern. This muscle organization is consistently repeated in each embryonic segment, with each muscle acquiring unique physical propertie (such as orientation, attachment, innervation, length, and number of nuclei) thanks to different combinations of various muscle identity transcription factors (mITFs) expression. The process of muscle identity acquisition is progressive and varies among different muscles, but its description remains incomplete. Moreover, notable muscle architecture differences in the thoracic and the posterior regions suggest a muscle specification regulation along the antero-posterior axis, potentially controlled by the highly conserved Hox transcription factors.
We carried out single-nucleus RNA-sequencing specific to the entire somatic musculature at different embryonic stages to identify new regulators and follow their dynamics through the successive steps of myogenesis. We also aim to integrate these regulators into the miTFs and Hox transcriptional networks. This will provide a more complete description of muscle diversification throughout myogenesis which could lead to a better understanding of the differential sensitivity of muscle types to diseases.



POSTER 14

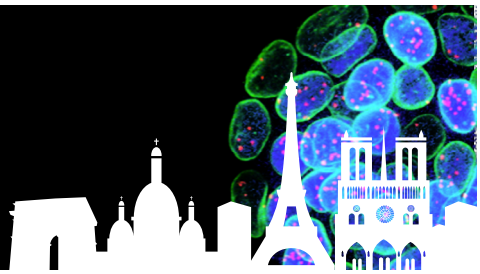
Janet CHENEVERT

Anne Rosfelter, Ghislain de Labbey, Benjamin Lacroix, Vlad Costache, Herve Turlier, Remi Dumollard, Alex McDougall

LBDV_UMR7009, Villefranche-sur-mer, France

Cell cycle control of spindle positioning forces in the ascidian embryo

We are examining the mechanisms of spindle position in the ascidian embryo, which displays an invariant cleavage pattern. Spindle poles are positioned by motors anchored in the cortex or in the cytoplasm pulling on astral microtubules (MTs). Using visual assays to evaluate cortical pulling and cytoplasmic pulling and treatments with cell cycle inhibitors, we found that cortical pulling is strong in interphase and switched off upon entry to mitosis. This temporal regulation allows centration forces (cytoplasmic pulling and pushing) to move the sperm aster to the egg center (Rosfelter et al J Cell Science 2024). During embryonic cleavages (2-16 cell stages), we observe that cortical pulling initiates at anaphase at membrane sites close to each of the spindle poles. In the two germ line cells, a localized patch of LGN and NuMA (which together activate cortical Dynein) causes enhanced cortical pulling and unequal cleavage. Disruption of LGN or NuMA with dominant negative constructs randomizes spindle position.
We developed a computational model which varies MT dynamics to simulate mitosis vs interphase and recapitulates centration of single asters or of a spindle. If the two spindle poles are non-identical, application of centration forces causes spindles to shift off-center. The direction of spindle shift depends on the origin of aster asymmetry, whether from a depolymerizing gradient or from the centrosome itself. Predictions of the model are borne out in vivo : in the germ line blastomeres the two asters display unequal sizes and MT dynamics and the spindle shifts off-center even prior to the onset of cortical pulling. Overall, our studies indicate two phases of mitotic spindle positioning: during metaphase centration forces dominate then at anaphase MTs lengthen and are captured by cortical pullers which lock the spindle in place to specify the site of cytokinesis.



POSTER 15

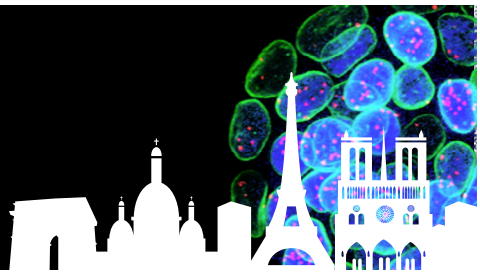
Klara CIK

L. Vasselin, M. Thépaut, A. Robert, P. Courrieu, H. El-Barbry, F. Niedergang and F. Ouaaz

INSERM U1016, Institut Cochin, Paris, France; CNRS, UMR8104, Institut Cochin, Paris, France; Université Paris Cité, France

New extracellular mode of B-cell Activation through release of native antigen by dendritic cells

Dendritic cells (DCs) are antigen-presenting cells (APCs), which sample antigen (Ag) in the periphery and migrate to the lymph node (LN) where they activate T cells. Previously, we showed that DCs were able to store Ag and to release it not degraded into the extracellular medium. Alternative modes of B-cell activation beyond cell-to-cell contact, such as release of Ag by DCs remain however not investigated. Using subcutaneous delivery of Ag-loaded DCs in vivo, and co-culture in vitro, we aimed to visualize Ag trafficking by DCs to the LN; to investigate the modalities of Ag transfer and B-cell activation by the distinct DC subsets; and to probe the role of exosomes (Exo) in Ag release and its regulation by glucocorticoids. Peripheral DCs are transporters of Ag to the LN-B cell zone and potent B-cell activators in vivo and in vitro. We highlight a novel extracellular mode of B-cell activation by DCs by showing that Ag release by DCs is sufficient to efficiently induce early B-cell activation through the transcription factor NF-κB/cRel. Strikingly, this mechanism consists of an Exo-free release of native Ag, contrasting with the Exo-dependent extracellular T-cell activation by DCs. Interestingly, glucocorticoids inhibit Ag release. Furthermore, LN-resident DC subsets including cDCs and pDCs are also able to release native Ag with an observed superiority for pDCs. Thus, our study provides new mechanistic insights into the modes of Ag delivery for B-cell activation by DCs and a promising approach of drug modulation of the DC-elicited Ag-dependent B-cell responses.



POSTER 16

Margarida CRUZ

Caren Norden

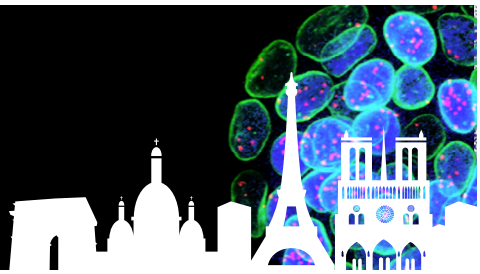
Instituto Gulbenkian de Ciência, Oeiras, Portugal

How neurons reach their place: a Bipolar Cell perspective

The organization of neurons into layers is crucial for neuronal connectivity and organ function. During retinal development, neurons need to relocate from their birthplace to the layer at which they later function. While neuronal translocation and lamination has been studied for most retinal neurons, how Bipolar Cells (BCs) achieve correct positioning is still unclear. This is particularly surprising, as correct BC lamination is crucial for the flow of information since these cells connect the Photoreceptors, which receive the visual information, to the Retinal Ganglion Cells, which transmit information to the brain. Previous studies revealed that BCs are born at both apical and subapical positions. However, whether their birthplace influences BC movement in the developing retina is unknown.

Here, we investigate the kinetics and mechanisms of BC positioning in the vertebrate retina by taking advantage of the live imaging potential of zebrafish. We show that BC translocation has distinct phases that occur with different kinetics: an initial fast and directed basal movement, and a subsequent more saltatory movement towards the final, more apical position. Interestigly, the kinetics of BC translocation depend on their birthplace. In particular, the basal movement of subapically-born cells is less efficient than that of apically-born cells, suggesting that the mechanism driving this movement is also different based on birthplace. Additionally, our preliminary results indicate that the microtubule cytoskeleton is involved in the basal movement of apically-born BCs, but might not be necessary for the translocation of subapically-born BCs. This hints at a common initial basal movement driven by the microtubule cytoskeleton that is shared by apically-born neurons.

Overall, this work will contribute to a better understanding of the events and mechanisms involved in retinal lamination during development, which could provide a platform for a comprehensive understanding of neuronal translocation and lamination in other areas of the brain.



POSTER 17

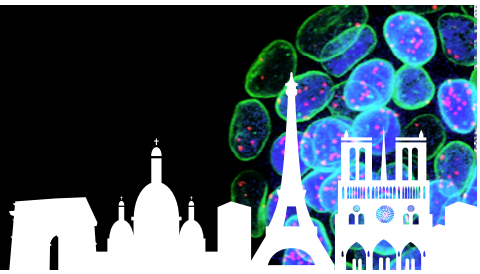
Enrico Maria DALDELLO

M. Santoni*, M. Santoni, S. Eivers, M. Kirschner, L. Peshkin, C. Jessus

IBPS-LBD, CNRS, Paris, France
**First Author*

Understanding how changes in protein homeostasis regulate meiotic cell divisions

Protein translation and degradation rates are crucial in determining cellular fates, such as the decision to undergo cell division. Previous studies on how changes in protein homeostasis affect the G2-M transition in mitotic cell lines have faced challenges due to the complex interactions between transcription, translation, and post-translational regulations, and the need for artificial synchronization of cell populations. To address these challenges, we are using the meiotic division of Xenopus laevis oocytes as a model system. These oocytes are naturally arrested in the G2-phase, and their entry into the M-phase occurs without transcription, relying instead on translation reprogramming. Both meiotic and mitotic M-phases are governed by the same highly conserved molecular machinery, coordinated by the kinase Cdk1, the universal trigger of eukaryotic cell division. In vertebrates, G2-arrest in oocytes is maintained by the cAMP-dependent kinase PKA. Downregulation of PKA in response to progesterone is necessary and sufficient to trigger M-phase entry by initiating a signaling pathway involving protein accumulation and culminating in Cdk1 activation. To characterize the events connecting PKA downregulation to Cdk1 activation, we are using two experimental approaches. First, we block Cdk1 activation using a specific inhibitor, Cip1. Second, we study small oocytes that have not completed their growth and are unable to activate Cdk1 upon hormonal stimulation. These two frameworks allow to identify molecular events downstream of PKA inhibition and independent of Cdk1 activation. By combining unbiased genome-wide methodologies with functional studies, we have identified proteins accumulating both upstream and downstream of Cdk1 activation, pinpointing important new regulators of the G2/M transition. Additionally, we are exploring the molecular mechanisms linking PKA downregulation to the regulation of protein translation and degradation. This research aims to elucidate how cellular decisions are encoded into translation switches, revealing specific proteins whose translation and accumulation control entry into the M-phase.



POSTER 18 & FLASH TALK

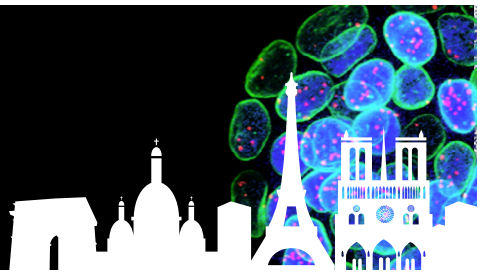
Nicolas DAVID

Amélie Elouin*, Arthur Boutillon

Laboratory for Optics and Biosciences, CNRS UMR 7645, Inserm U1182, Institut Polytechnique de Paris, 91128 Palaiseau, France

A non-cell autonomous role of Myosin-II in guiding collective migration

Collective cell migration is crucial in embryonic development and tumor dissemination. How cell-cell interactions guide collective cell migration is partially understood but there is a growing body of evidence pointing to a role for mechanical signals and mechanoperception. During zebrafish gastrulation, a group of cells called the polster migrates collectively from the embryonic margin to the animal pole. We have shown that each cell is guided by its immediate followers and that this guidance relies on mechanotransduction by ??catenin, adopting an open conformation upon tension application. Here we investigate the role of non-muscular myosin II (NMII) which is known to generate tension and opening of ??catenin in epithelial cells. Embryos were injected with dominant-negative forms of MLCK or ROCK, or treated with drug inhibitors of NMII. Analysis of cell trajectories showed that NMII is required for polster migration speed and orientation; however, using cell transplants to inhibit NMII autonomously revealed that NMII is required in neighbouring cells for cell orientation. Within cells, NMII is enriched at the cortex with a posterior bias and in protrusions. Laser ablation at the basis of protrusions showed that NMII is required cell-autonomously for protrusion contractility. Together, these results reveal a non-cell-autonomous role for NMII in orienting collective migration and strongly support the idea that follower cells orient forward cells by pulling on them via their protrusions.



POSTER 19

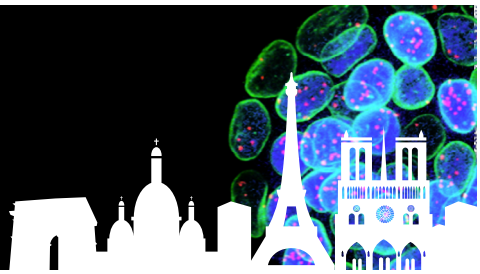
Marlène DAVILMA

Stéphanie Gay, Manon Thomas, Laurence Dubreil, Frédérique Clément, Violette Thermes

SOCS Team, LPGP, INRAE, Campus de Beaulieu, 35042 Rennes

3D imaging-based analysis of the germline in teleost

In teleost fish, female fecundity depends essentially on the oocyte reserve, which determines the number of eggs laid in each reproductive cycle. Unlike mammals, which have a limited and predefined stock of oocytes at birth, this reserve can be renewed throughout female's life. In adult teleost, this reserve is, on the one hand, used to generate mature oocytes ready to be laid and, on the other hand, replenished from germline stem cells present in specialized structures called germinal cradles. A main issue is to understand the contribution of these germline stem cells in the renewal of the oocyte reserve in both juveniles and adults, as well as the involved regulatory mechanisms.
To this end, we have implemented a 3D whole ovary imaging strategy in Medaka to provide quantitative data and study the cellular dynamics of the germinal cradle. We have refined ovary clearing protocols combined with immunolabelings (e.g., anti-vasa, anti-pH3, anti-GFP), and imaged the ovaries using light sheet microscopy. In addition, we have set up 3D image analysis pipelines that integrates pre-trained open-source neural networks suitable for precise segmentation. These deep-learning based pipelines have greatly improved our ability to manage complex 3D analysis of the germinal cradle and allow us to access quantitative data at the level of the entire ovary. We are now analyzing the number, the distribution and the composition of germinal cradles in wild-type females, as well as in two KO lines (miR-202 -/- and miR-187 -/-) showing a drastic decrease in female fecundity, to uncover the miRNA-mediated regulatory mechanisms. In the future, this approach should also provide us with the means to explore in depth the interactions between the somatic and germ cells within germinal cradles, including their spatial organisation.



POSTER 20

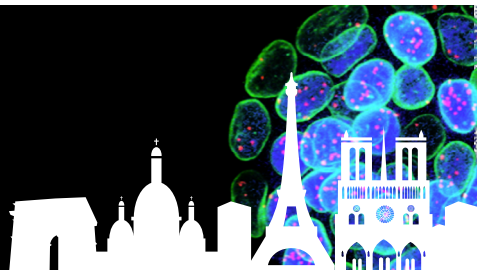
Irène DEDUYER

Anne Royou

IBGC, CNRS, Bordeaux, France

Polar cortex contractility provides adaptability of cytokinesis to distinct tissue specificities

Animal cell shape changes are driven by the contractile properties of the cell cortex, a network of actin and myosin II filaments beneath the plasma membrane. One dramatic example of actomyosin-dependent shape change occurs during cytokinesis, when one cell forms two distinct daughter cells. After chromosome segregation, the actomyosin network forms a ring at the cell equator, and myosin motors slide along actin filaments to create the contractile force needed for the cleavage furrow ingression. While the role of the actomyosin ring at the cell equator is well known, the involvement of actomyosin contractility at the polar cortex is less understood, a question particularly relevant in multicellular organisms where cytokinesis must adapt to various cell types while preserving tissue organization. Using Drosophila as a model, we previously discovered that polar cortex contractility increases globally during cytokinesis and that the level of this polar cortex contractility can be genetically manipulated. Examining cytokinesis upon elevated or reduced levels of polar cortex contractility in various cell types revealed tissue-specific requirements for polar cortex contractility. A reduced polar cortex contractility caused cytokinesis failure in spermatocytes and abnormally small daughter cells in neural stem cells, while excessive contractility in thoracic epithelial cells led to loss of adhesion and basal extrusion of the nascent daughter cells, disrupting tissue organization. These results highlight how the contractility of the polar cortex provides adaptability of cytokinesis to tissue specificities.



POSTER 21

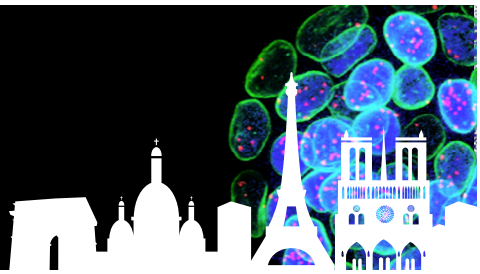
Audrey DESGRANGE

Emeline Perthame, Carmen Marchiol, Daphné Madec, Mohamed El Beheiry, Jean-Baptiste Masson, Olivier Raisky, Ségolène Bernheim, Lucile Houyel, Sigolène M. Meilhac

Université Paris Cité, 2Imagine - Institut Pasteur Unit of Heart Morphogenesis, INSERM U1163, Paris, France,

Plasticity of ventricle position after heart looping in heterotaxy

The heart functions in two parallel but asymmetric circuits, in which the right and left ventricles drive the pulmonary and systemic circulations, respectively. In the heterotaxy syndrome, abnormal left-right embryo patterning leads to a spectrum of severe congenital heart defects, including ventricle malposition. A postulate anchored in the clinical nomenclature, assumes that the looping direction of the embryonic heart tube determines ventricle position at birth. However, this has not been demonstrated experimentally. Here, we performed a unique longitudinal analysis of heterotaxy with right isomerism, using multi-modality imaging of Nodal mouse mutants. Based on direct correlations and advanced statistics, we dissected the contribution of heart looping variations to specific structural heart malformations. We uncovered unexpected plasticity of ventricle position after heart looping, in 30% of revertant samples. Hearts of revertants are enriched in ventricular anomalies, a phenotype also observed in human patients with heterotaxy and right isomerism. Genetic tracing and topological associations do not support molecular reprogramming of ventricles but rather point to a novel step of heart remodelling after heart looping. Our work reveals distinct asymmetric events shaping the heart, beyond initial symmetry breaking in the node.



POSTER 22

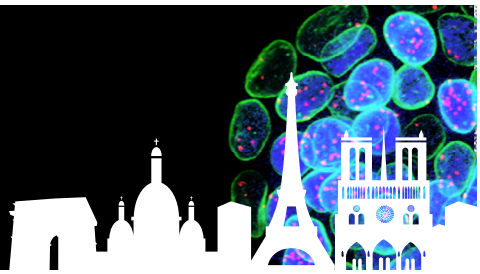
Shivani DHARMADHIKARI

Hugo Lachuer, Nicolas Borghi, Jean-Leon Maitre

Institut Curie UMR 3215/U934, Paris, France

Plasma membrane mechanics during mammalian preimplantaion development

During epithelial stretching, cells must increase their surface area by unfolding plasma membrane reservoirs which remain poorly characterised in vivo. During mouse preimplantation development the trophectoderm (TE) constitutes a thin, epithelial monolayer that stretches and quadruples is surface area to accommodate an inflating lumen. My research focuses on understanding the mechanics of plasma membrane reservoirs during lumen formation. Using optical tweezers to pull membrane tubes, we probed plasma membrane mechanics throughout preimplantation development. We found that membrane tension decreases from the zygote to 4-cell stage, before increasing again at the 8-cell stage when apico-basal polarity is established. Importantly, this result was further confirmed using fluorescence lifetime imaging microscopy (FLIM) of a membrane tension probe. The apical surface of 8 cell embryo is characterized by a tuft of microvilli and thus we hypothesise that these microstructures could act as membrane reservoirs. Future measurements will target localised regions of the plasma membrane, anticipated to exhibit unique properties and behaviours due to membrane reservoirs during epithelial stretching in preimplantation morphogenesis.



POSTER 23

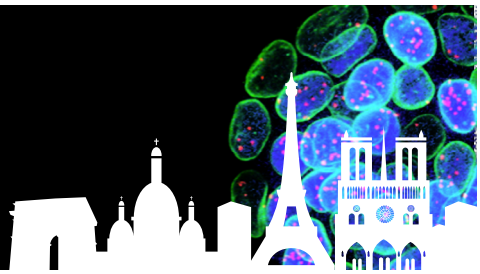
Florencia DI PIETRO

Priscillia Pierre-Elies & Yohanns Bellaïche

Institut Curie, InsermU934, CNRS UMR3215, Paris, France

Mitotic cell reshaping in epithelial tissue

Cell division is key to organism development and homeostasis. In animal cells, cell division entails drastic cell shape changes which ensure faithful chromosome segregation. Extensive studies in single cells had led to a broad understanding of the biochemical and physical mechanisms allowing cell reshaping during mitosis. In epithelia, the mitotic cell remains connected to the surrounding cells by adherens junctions, raising the fundamental questions of how mitotic cell shape changes impact on the neighbouring cells and vice versa. To address these questions, we set out to investigate mitotic cell reshaping in epithelia in vivo, by combining time-lapse microscopy with genetics and optogenetics in Drosophila tissues. We first characterized the cell geometrical changes associated to mitosis in epithelia. Second, we described how major cytoskeletal components and their regulators relocalize during epithelial mitosis, to delineate the mechanisms ensuring the coordinated reshaping of the mitotic cell and its neighbours.



POSTER 24

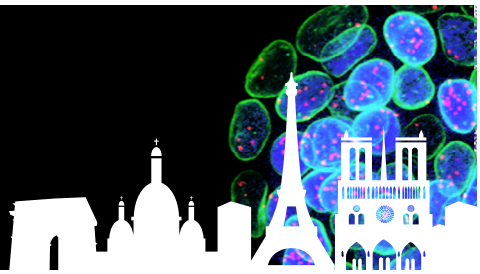
Lamiya DOHADWALA

Anupriya Garg, Maithreyi Narasimha

Tata Institute of Fundamental Research, Mumbai, India

Morphodynamic characterisation of the proneural neighbourhood during the specification of embryonic neuroblasts in Drosophila

Tissue sculpting relies on gene regulatory networks that confer cell fates, and on intracellular force generation mechanisms that influence cell morphodynamics. We investigate the interplay between fate determination and morphodynamics during the sculpting of the Drosophila embryonic nervous system. Embryonic neuroblasts singled out from each ectodermal proneural cluster through the process of lateral inhibition exit the surface and become basally positioned through the process of delamination. Here we characterise the morphodynamic properties of the proneural cluster and the prospective neuroblast within it through real time confocal microscopy and in fixed preparations. We uncover morphodynamic differences between neuroblast delamination and delamination in other contexts. Our current work is aimed at understanding the requirement of morphodynamics for neuroblast specification and differentiation, and the force generation mechanisms that underlie the morphodynamics.



POSTER 25

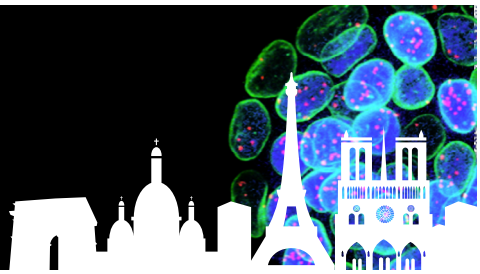
Sarah B. EIVERS

Gabriel Dominico, Catherine Jessus, Juliana Silva Bernardes, Enrico Maria Daldello

Laboratoire de Biologie du Développement,Institut de Biologie Paris Seine, Sorbonne Université, Paris, France

Predicting the translational fingerprint of M-phase using machine learning: an attribute network-based ranking model

Meiotic maturation is governed by the sophisticated relationship between post-translational modification of proteins and translation of mRNAs. Activation of Cdk1 is a key meiotic event and regulates the downstream activities of kinases and phosphatases involved in protein phosphorylation, necessary for meiotic maturation. Protein translation is required for Cdk1 activation in most vertebrates. However, the identities of the proteins required for Cdk1 activation remain largely unknown with only a few determined by biochemical methods, such as Mos and Cyclin B1. The advancement of the 'omics' era has allowed not only high-throughput analysis of translation on a global scale, but also access to considerable amounts of protein translation-related datasets. Nonetheless, as these datasets are produced in different model systems, using different experimental methods, this poses difficulties in extracting information that may enable us to create a fingerprint of the M-phase transition. Herein, using combined computational and experimental approaches, we aimed to gain a greater understanding of the landscape of protein translation during meiosis resumption by identifying novel players controlled at the protein translation level. This may allow us to identify new proteins interacting with and/or activating Cdk1. Furthermore, using Xenopus laevis oocytes as a model system, we sought to first generate a new benchmark dataset of protein translation in M-phase, and second, experimentally validate predicted candidates using translational reporters. Employing an Attribute Network-based Ranking model that uses machine learning, and previous protein translation datasets mined from the literature from human, mouse and Xenopus laevis, we developed a program to predict candidates that are translated following the transition from prophase to M-phase. Combined with experimental validation by translational reporters, these results may give us a greater understanding of protein translation during M-phase. In addition, the Attribute Network-based Ranking model can be exploited in the future to predict other factors beyond the current study.



POSTER 26

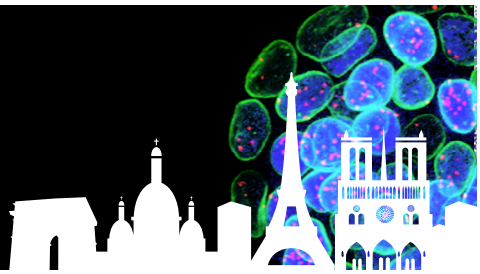
Lauren FORBES BEADLE

Catherine Sutcliffe, Hilary L. Ashe

Faculty of Biology, Medicine and Health, University of Manchester, United Kingdom

A simple MiMIC based approach for tagging endogenous genes to visualize live transcription in vivo

Recent technological advancements allow transcription to be visualised and quantitated in living cells using the MS2 or PP7 systems. The Drosophila embryo is the premier model for studying transcription in real-time during development, with studies in this model revealing new concepts relating to transcriptional regulation. However, insertion of the MS2/PP7 stem loops into endogenous genes in Drosophila requires laborious CRISPR genome editing. Here we build upon the previously described Minos-mediated integration cassette (MiMIC) transposon system, to tag genes with MS2/PP7 stem-loops to visualise transcription. With an easy crossing scheme, recombination mediated cassette exchange allows the insertion of stem-loop sequences into any MiMIC locus. We have generated a variety of loop donor and complementary fluorescently tagged coat protein fly stocks, which can be used with the existing MiMIC insertions to target thousands of genes. We show the utility of this gene tagging system for studying transcription live during development in the early embryo, wing disc and ovary. Overall, this first high throughput method for tagging mRNAs in Drosophila will facilitate the study of transcription dynamics of thousands of endogenous genes in different Drosophila tissues.



POSTER 27 & FLASH TALK

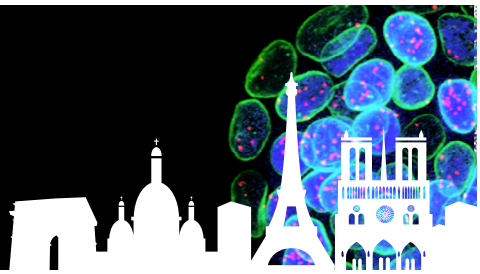
Sara FORMICHETTI

Agnieszka Sadowska, Urvashi Chitnavis, Na Liu, Michela Ascolani, Neil Humphreys, Ana Boskovic and Matthieu Boulard

EMBL, Rome, Italy

Modulation of mammalian embryonic growth by intracellular glycosylation

The main form of intracellular glycosylation in animals is O-GlcNAcylation, the reversible linkage of a monosaccharide (O-GlcNAc) to serine and threonine protein residues. The donor substrate for O-GlcNAc, UDP-GlcNAc, is the end product of a metabolic pathway that is responsive to nutrient levels. O-GlcNAc is present on thousands of mammalian proteins in all cellular compartments, especially the nucleus, and an ever-increasing number of in vitro studies report the regulation by O-GlcNAc of essential cellular functions such as the cell cycle, translation, glycolysis and transcription. In spite of its pleiotropy, only one enzyme is responsible for O-GlcNAcylation, called O-GlcNAc transferase (OGT). The mammalian Ogt gene is essential for both cellular proliferation and embryonic development. Specifically, a functional maternal Ogt copy is required for the mouse embryo to pass the blastocyst stage. Because of this huge obstacle for genetics studies, the molecular function of O-GlcNAc in early mammalian development remains poorly understood and certainly never addressed in vivo. This is however a burning question, considering the presence of O-GlcNAc on RNA Polymerase II and master regulators of pluripotency such as OCT4. We addressed O-GlcNAc's role in the early mouse embryo through two parallel routes both overcoming cellular and embryonic lethality: i. We depleted the O-GlcNAc modification itself from the embryonic nuclei, by overexpressing in the zygote the enzyme catalyzing O-GlcNAc removal; ii. We created four mouse models bearing single-amino acid substitutions reducing the catalytic activity of OGT to a range of degrees. By analyzing the transcriptome of single embryos at key pre- and postimplantation stages upon different level of disruption of O-GlcNAc homeostasis, we discovered that nuclear O-GlcNAc is dispensable for embryonic genome activation and blastocyst differentiation, but that reducing O-GlcNAc slows down embryonic growth. Therefore, we establish a novel link between intracellular protein glycosylation and the pace of developmental progression.



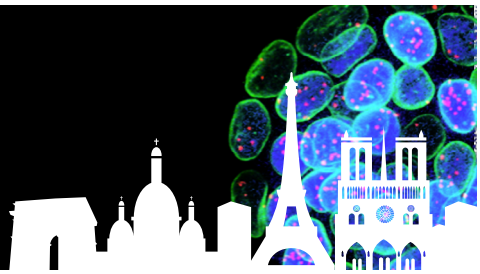
POSTER 28

Saverio FORTUNATO

Institut Cochin, INSERM/CNRS, Paris, France

Investigating cranial neural crest patterning and its influence on cell plasticity

During embryonic development, cranial neural crest cells (CNCC) form within the anteriormost part of the dorsal neuroepithelium. Initially this cell population is heterogeneous and carries positional information reflective of their spatial origin along the anteroposterior axis. However, this positional identity is erased when CNCC delaminate from the neuroepithelium and start migrating ventrally to contribute to craniofacial structures. The significance of CNCC initial positional patterning and whether it affects future cell plasticity remains unknown. In addition, distal regulatory elements in loci associated with CNCC mesenchymal derivatives are accessible in pre-migratory CNCC almost 24 hours before gene expression can be detected. Whether this epigenetic priming is heterogeneous along the anterior-posterior axis and whether it carries positional information through the erasure of the transcriptional program remains undetermined. Through a combination of in vivo and in vitro approaches, we seek to decipher the transcriptional programs and epigenetic regulations controlling CNCC positional identity remodeling and understand how these affect CNCC proliferative, migratory and differentiative capabilities. To this end, we are characterizing CNCC transcriptomes dynamics during their development in vivo using single-cell omics methods. In parallel, we developed and characterized a 3D in vitro differentiation protocol that recapitulates CNCC anterior-posterior positional identity remodeling. We are now generating double fluorescent reporter cell line to study changes in chromatin accessibility during the establishment and erasure of CNCC positional identity. Altogether these experiments will allow us to better understand the significance of CNCC positional identity remodeling and how it influences CNCC plasticity.



POSTER 29

Mélanie GRACIA

Victoire M.L. Cachoux*, Maria Balakireva, Floris Bosveld, Jesús M. López-Gay, Aude Maugarny-Calès, Isabelle Gaugue, Florencia di Pietro, Stéphane U. Rigaud, Lorette Noiret, Boris Guirao and Yohanns Bellaïche

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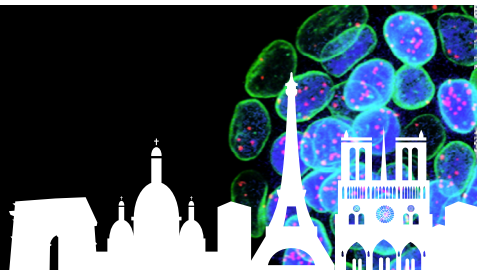
**First Author*

Epithelial apoptotic pattern emerges from global and local regulation by cell apical area

Geometry is a fundamental attribute of biological systems, and it underlies cell and tissue dynamics. Cell geometry controls cell-cycle progression and mitosis and thus modulates tissue development and homeostasis. In sharp contrast and despite the extensive characterization of the genetic mechanisms of caspase activation, we know little about whether and how cell geometry controls apoptosis commitment in developing tissues. Here, we combined multiscale time-lapse microscopy of developing Drosophila epithelium, quantitative characterization of cell behaviors, and genetic and mechanical perturbations to determine how apoptosis is controlled during epithelial tissue development. We found that early in cell lives and well before extrusion, apoptosis commitment is linked to two distinct geometric features: a small apical area compared with other cells within the tissue and a small relative apical area with respect to the immediate neighboring cells. We showed that these global and local geometric characteristics are sufficient to recapitulate the tissue-scale apoptotic pattern. Furthermore, we established that the coupling between these two geometric features and apoptotic cells is dependent on the Hippo/YAP and Notch pathways. Overall, by exploring the links between cell geometry and apoptosis commitment, our work provides important insights into the spatial regulation of cell death in tissues and improves our understanding of the mechanisms that control cell number and tissue size.



POSTER 30

Kirti GUPTA

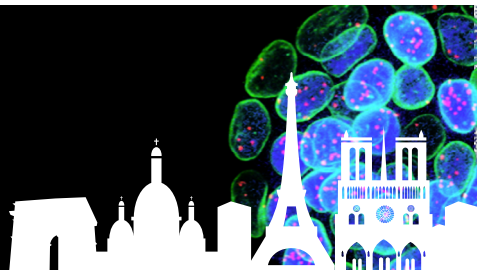
Héctor Sánchez-Iranzo, Rashmi Priya

The Francis Crick Institute, London, United Kingdom

Notch signalling patterns the myocardial wall during vertebrate heart development

Trabeculation is a critical step in vertebrate cardiac development, which is crucial for heart function. During trabeculation in zebrafish, the myocardial wall transforms from a single-layered epithelium into a complex 3D architecture consisting of two distinct cell types: outer compact layer and inner trabecular layer cardiomyocytes. We have shown that mechanical heterogeneity triggers stochastic single cell delamination to seed the inner trabecular layer, which is sufficient to induce differential Notch signalling. Yet how Notch signalling gets activated and whether it plays a role in patterning these ridges remain elusive.

Using live imaging, genetic and pharmacological manipulations, we find that Notch signalling is essential for trabecular ridge morphogenesis. Notch activity relies on the expression of ligand Jag2b expression in the delaminated cells. Using a genetic loss of function approach, we find that in the absence of Jag2b, trabecular ridge morphology is affected. Instead of projecting into the lumen to form a spongy meshwork, they appear flat and form a multilayered disorganized structure. This multilayered phenotype does not result from defects in cell proliferation, as cell numbers are similar in wild-type and Jag2b mutant hearts. Also, internalised trabecular cells in the mutants exhibit canonical markers of trabecular layer such as loss of polarity and BMP activation. Interestingly, constitutively activating Notch through NICD expression rescues ridge pattern suggesting that Notch is required to spatially pattern trabecular cells. Additionally, the Jag2b mutant hearts with multilayered trabecular layer exhibit reduced fractional shortening, stroke volume and reduced cardiac output, suggesting that these cells have to organise into a spongy meshwork architecture to support optimal heart function. Further, we have performed scRNA-seq to identify Notch targets and are currently investigating mechanisms of how Notch guides ridge patterning during heart development. Considering the ubiquitous role of Notch during development, these findings have broad implications for Notch-mediated tissue patterning during embryonic morphogenesis.



POSTER 31

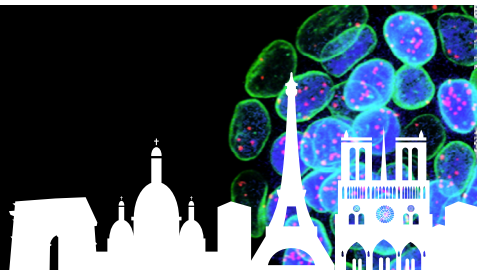
Lucas GUTTIERES

Mark Q. Martindale, Brian M Walters, Athula H Wikramanayake

University of Florida, Whitney Laboratory for Marine Bioscience, Floride, USA

The function of β-catenin during development in the ctenophore Mnemiopsis leidyi

β-catenin is a structurally and functionally highly conserved metazoan protein. In its role as a key nuclear signal transducer in the canonical Wnt (cWnt) pathway, β-catenin regulates many developmental processes such as embryonic axis determination, and mesendodermal germ layer specification in many metazoans. Additionally, it is a critical regulator of cell-to-cell adhesion within the cadherin-catenin-complex in adherens junctions. The cytoplasmic availability of β-catenin is tightly regulated by both the β-catenin degradation complex (itself regulated by the cWnt pathway), and cadherins at the plasma membrane. Despite the importance of β-catenin in all studied metazoans, no investigations have been done in the earliest lineage, the ctenophores. Genome sequencing in ctenophore species revealed that many components of both the Wnt signaling pathway and the cadherin-catenin-complex are conserved. Nevertheless, a previous bioinformatic study showed that Mnemiopsis leidyi cadherins don't possess a β-catenin binding site, casting doubt on the conservation of the β-catenin function in cell-to-cell adhesion in ctenophores. However, using a polyclonal antibody raised against M. leidyi β-catenin (Ml-βcat), we show that Ml-βcat is localized at the cell-cell junctions during M. leidyi embryonic development, which suggests that the role of Ml-βcat in cell-to-cell adhesion is conserved. Moreover, initial analyses indicate nuclear translocation of Ml-βcat, but no relationship to any particular cell lineages have been determined yet. Further experiments are necessary to fully understand the ancestral β-catenin functions in the ctenophore M. leidyi.



POSTER 32

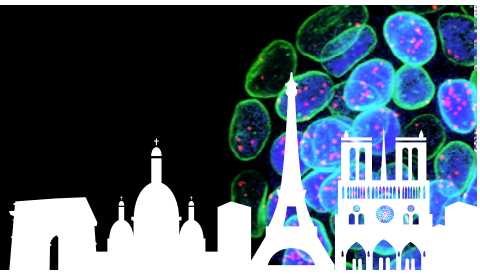
Mélina L. HEUZÉ

Hugo Siegfried*, Georges Farkouh, Julie Beaucousin, Rémi Le Borgne, Catherine Durieu, Thaïs De Azevedo Laplace, Agathe Verraes, Lucien Daunas, Jean-Marc Verbavatz

Institut Jacques Monod Université Paris Cité, CNRS UMR7592
**First Author*

Connection between the endoplasmic reticulum and focal adhesions during cell migration: membrane contact sites join the dance

Cell motility processes highly depend on the membrane distribution of lipids, in particular Phosphoinositides, giving rise to cytoskeleton reshaping and membrane trafficking events. Membrane contact sites between the ER and other membrane compartments play a crucial role in lipid composition and dynamics, as they serve as platforms for lipid exchange between the two membranes. Here, we show that during cell motility, ventral ER-plasma membrane contact sites anchor close to focal adhesions (FA), at the time of FA disassembly. Our results reveal that VAPA, an ER membrane-resident contact site tether, is essential to stabilize ventral ER-PM contact sites and to maintain their spatial connection to FA. Caco2 adenocarcinoma epithelial cells depleted for VAPA fail to properly disassemble FA during migration and exhibit several collective and individual motility defects, disorganized actin cytoskeleton and altered protrusive activity. Despite the involvement of VAPA in various ER-membrane contact sites throughout the cell, our results suggest that in Caco2 migrating cells, the role of VAPA in Phosphoinositide homeostasis stands mainly at the plasma membrane where it is required for the maintenance of PI(4,5)P2 and PI(4)P levels, which is not the case in the Golgi or in early endosomal compartments. To conclude, our results reveal unprecedented functions for VAPA-mediated membrane contact sites during cell motility and provides a dynamic picture of ER-plasma membrane contact sites connection with FA mediated by VAPA.



POSTER 33

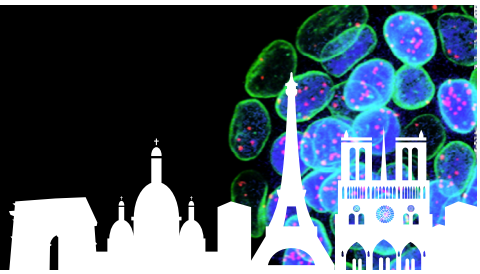
Megumi INOUE

Ivan Lobaskin, Ignacio Bordeu, Adrien Hallou, Cadisha Saint-Hilaire, Yorick Gitton, Edwin Hernandez-Garzon, Benjamin Simons, Alain Chedotal

Institut de la Vision, INSERM, Sorbonne University, Paris, France

Branching morphogenesis in human lung development

Organs such as the lung, kidney, and salivary glands are built by a process of branching morphogenesis to construct an intricate network of epithelial trees. In the human lung, this process takes place between 5-17 post-conceptional weeks, but technical limitations in resolution and access to fetal tissues have prevented large scale studies of this process. Here, we utilize the French Human Developmental Cell Atlas (HuDeCA) fetal tissue biobank to study branching morphogenesis during PCW5-12. We combine whole-mount immunostaining, tissue clearing, light-sheet microscopy and computational image analysis to reconstruct the developing airway epithelial tree and provide the first quantitative reference of human lung development in 3D. We quantified 30 individual left upper lobes and find total branch numbers increased from 18 branches at PCW5 to around 60,000 branches at PCW12. Human lung development has been known to be built primarily via rounds of tip bifurcations. While primarily built by bifurcations, our data suggests the presence of lateral branching early in development, and even trifurcations in PCW12+ lungs. Our systematic quantifications show exponential branching with a doubling rate of approximately half a week in the early weeks of branching. These results provide an important benchmark for embryonic and fetal human lung development.



POSTER 34

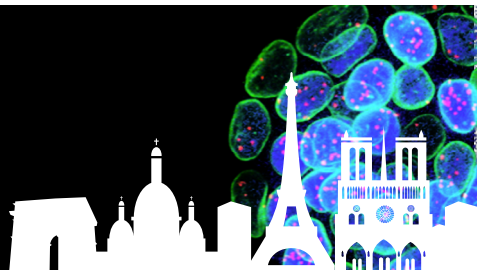
Fengtong JI

Yisha Lan, Vivian Wang, Fengzhu Xiong

Wellcome Trust / Cancer Research UK Gurdon Institute, University of Cambridge, Cambridge, UK.
Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK.

Probing mesenchymal tissue viscosity in vivo with magnetic nanorobots

The morphology of tissues and organs, whether normal or diseased, is shaped by cell phenotype changes that drive tissue mechanics. Central to this process is the epithelial-to-mesenchymal transition (EMT), a crucial mechanism for cell reorganisation and tissue formation. Unravelling the interplay between EMT and tissue mechanics could enable the regulation of tissue shapes and cell fates. During development, reversible cell-type transitions alter tissue mechanical properties, with tissue viscosity indicating the ease of cell rearrangement. Compared to currently used tools, magnetic nanorobots, engineered nanoparticles with precise motion control in programmable magnetic fields, offer a novel approach for fine measurements of viscosity in vivo. The self-assembly of these nanorobots from nanoparticles makes them particularly effective for probing dynamic and heterogeneous tissue microenvironments. Using early-stage chick embryos as a model, we employed magnetic nanorobots to detect local tissue viscosity in the developing presomitic mesoderm. These remotely controlled nanorobots synchronise to a rotating field and exhibit distinct dynamics in epithelial and mesenchymal tissues. Correspondingly, we developed a model to map nanorobot rotation to tissue viscosity in situ. Our findings reveal that local tissue viscosity varies as cells transition, potentially guiding the body axis elongation in the tail bud of chick embryos. This nanorobotic sensing technique holds promise as a versatile tool for studying developmental mechanics. Furthermore, understanding the mechanical property changes during cell transitions may inspire new treatments for EMT-related conditions, such as developmental defects and cancer invasion.



POSTER 35

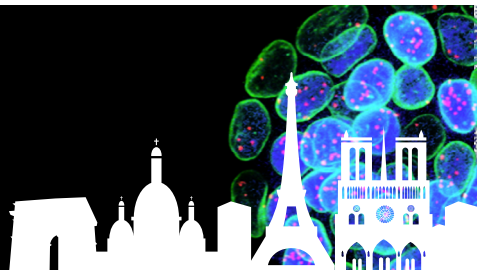
François JUGE

Ghislain Gillard, Clémence Gaufichon, Simon Nicot and Krzysztof Rogowski

Institut de Génétique Humaine, CNRS UMR9002, Montpellier, France

Discovery and functional characterization of α-tubulin detyrosinase in Drosophila

Detyrosination is a post-translational modification specific to α-tubulin, which consists in the removal of the C-terminal tyrosine residue encoded by most α-tubulin isotypes. In mammals, this modification is associated with stable microtubules (MTs) and is particularly important for neuronal and cardiac function. Detyrosination is also enriched on the axonemes of cilia and flagella where its function remains unknown. Two families of detyrosinases have been identified so far in mammals: VASH1/2 and MATCAP. Strikingly, neither VASHs nor MATCAP have homolog in Drosophila despite the presence of detyrosination. This suggests the existence of additional class of enzymes catalyzing this modification.
In Drosophila, α-tubulin detyrosination is found almost exclusively in testes where it is present on the meiotic spindles and is highly abundant on sperm axonemes. To identify the enzyme responsible for this modification in Drosophila, we performed a RNAi-based genetic screen combined with immunoblot analysis in fly males. This led to the identification of an uncharacterized protein, that we named Tubulin Carboxy-Peptidase (TCP), which upon depletion reduced detyrosination on sperm axonemes. Expression of TCP in mammalian cells increases detyrosination, whereas active site mutant did not. Furthermore, purified TCP modifies α-tubulin in in vitro assays demonstrating that TCP is a bona fide detyrosinase. CRISPR mediated deletion of the TCP gene in Drosophila (TCP[KO]) completely abolishes α-tubulin detyrosination. Absence of detyrosination on sperm axonemes does not affect their polyglycylation, which appears at later stages of spermatogenesis. TCP[KO] males show almost normal fertility but produce gender-biased progeny with a deficit of males. As a complementary approach to analyze the role of tubulin detyrosination in vivo, we engineered Drosophila carrying a point mutation in the major α-tubulin gene αTub84B to generate fully detyrosinated (Δ1) and "non-detyrosinatable" tubulin mutants. Strikingly, whereas absence of detyrosination is rather well tolerated, excess of detyrosination results in complete male sterility. Our results reveal the existence of a new class of α-tubulin detyrosinase and show that a balanced level of detyrosination is necessary for proper Drosophila spermatogenesis.



POSTER 36

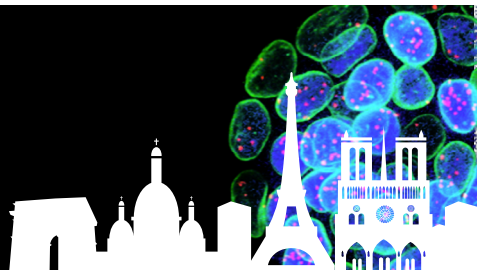
Parisa KHALILIAN

Thibault Lagache, Maël Rabottin, Gaëlle Boncompain, Franck Perez, Chiara Zurzolo & Stéphanie LebretonChiara Zurzolo

Institut Pasteur - Sorbonne Université, Paris, France

MACF1 regulate apical sorting of GPI-APs in polarized epithelial cells

Despite extensive research, the mechanisms underlying the apical sorting of epithelial membrane proteins in epithelial cells remain incompletely understood. We investigated how microtubules (MTs) enable intracellular trafficking of post-Golgi carriers using the RUSH assay in polarized MDCK cells. Our data reveal that apical carriers of GPI-anchored proteins exit the Golgi apparatus in MT-aligned tubular structures. Disruption of MTs with Nocodazole leads to unpolarized sorting and Golgi apparatus morphological disruption, resulting in ministacks formation. Moreover, tubular carriers of GPI-anchored and transmembrane proteins become vesicular post-Nocodazole treatment, highlighting MTs' role in maintaining their tubular structure. Additionally, our findings identify the microtubule-associated protein MACF1 as crucial for MT-dependent post-Golgi trafficking of apical carriers, essential for Golgi integrity and proper apical sorting. Knockdown of MACF1 disrupts the Golgi complex and leads to basolateral missorting.



POSTER 37

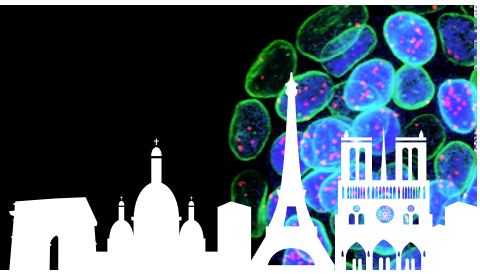
Alison KICKUTH

Ursa Ursic, Michael F. Staddon, Jan Brugues

Physics of Life Cluster of Excellence, TU Dresden, Germany

A mechanical ratchet drives unilateral cell division

The canonical mechanism driving cell division comprises the formation and constriction of a contractile actin ring. However, this model is not compatible with the initial developmental stages of many vertebrates. Since a complete ring typically does not form in yolk-anchored embryos, it is unclear how a partial circular arc with loose ends can divide the cell. Here, by combining laser ablation of the cytokinetic band with rheological measurements in vivo, we show that gelation of the bulk cytoplasm, facilitated by the interphase microtubule network, stabilises the contractile band by anchoring it along its length during growth. Conversely, as the cell cycle progresses, the cytoplasm fluidises, diminishing band-cytoplasmic anchoring and facilitating band ingression. This dynamic interplay between stability and growth versus instability and ingression repeats for several cell cycles until division is complete, resulting in a mechanical ratchet that drives cell division. Our study underscores the role of temporal control over cytoplasmic rheology as a key feature driving unilateral cytokinesis in the absence of a closed actin ring.



POSTER 38

Veronika KINTEROVÁ

Jiri Kanka, Shanjida Afrin, Tereza Toralova

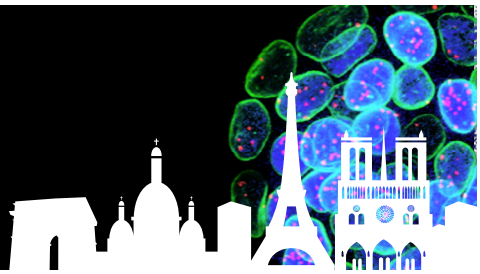
Institute of Animal Physiology and Genetics, Czech Academy of Sciences, Libechov, Czech Republic

Effect of inhibition of protein neddylation on bovine oocyte maturation

During mammalian oogenesis, oocytes undergo several important processes to be fully matured and able to be fertilized. Obtaining the meiotic competence requires precise regulation of metabolism and chromosome segregation. Post-translational modifications, including ubiquitination and neddylation, are critical steps for meiotic competence acquisition. Neddylation is a process of binding of a small protein NEDD8 to Cullin family proteins to activate SCF ligases that mediate protein degradation via ubiquitin-proteasome system. In recent years, more and more studies have dealt with the role of SCF ligases in oocyte maturation and early preimplantation development. When cumulus - oocyte complexes were treated with MLN4924, a specific inhibitor of neddylation, no expansion of cumulus cells was found and after in vitro fertilization, higher polyspermy rate and deteriorated embryonic development were detected. We detected significantly decreased maturation rate, delayed polar body extrusion and different cortical granules distribution in MLN4924-treated oocytes. Cortical granules were distributed to clusters around the membrane, which indicate that higher polyspermy can be due to the impaired cortical granules-dependent anti-polyspermy block. To clarify the effect of neddylation inhibition on cumulus cells, important proteins expression from signalling pathway of cumulus cells expansion were observed. We have found out that expression of hyaluronan synthase 2 protein in MLN4924-treated cells did not differ in comparison to control. That indicate that synthesis of extracellular matrix between cumulus cells is not affected, but the ability of these cells to bind hyaluronan to create the extracellular mass may be influenced.

Using mass spectrometry of MLN4924-treated and control oocytes 107 differently expressed proteins were found. 42 of them were detected only in MLN4924-treated oocytes, suggesting that they are substrates of SCF ligases. The GO analysis has shown that these proteins play role especially in controlling microtubule organization, protein modification, cell division and mitochondrial fission.

This work was supported by GACR 23-05108S.



POSTER 39

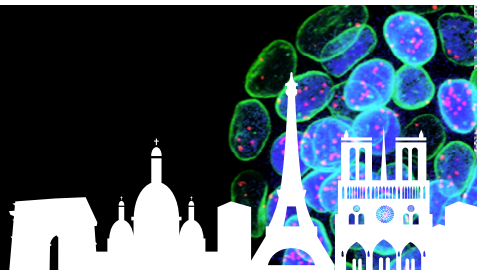
Melina KÖHLER

Fushun Chen*, Gokhan Cucun, Masanari Takamiya, Caghan Kizil, Mehmet Ilyas Cosacak, Sepand Rastegar

Karlsruhe Institute of Technology, IBCS-BIP, Eggenstein-Leopoldshafen, Germany
**First Author*

sox1a:eGFP transgenic line and single-cell transcriptomics reveal the origin of zebrafish intraspinal serotonergic neurons

The vertebrate spinal cord comprises an enormous diversity of functionally distinct cell types which arise from a variety of different progenitor domains. However, the progenitor populations and the mechanisms underlying the differentiation process of specific neurons often remain elusive. Transcription factors of the Sox family play a critical role in vertebrate central nervous system development and are expressed in neural progenitor cells and their derived neurons of the ventral spinal cord in zebrafish. In this study, the transcriptome of sox1a lineage progenitors and neurons from the transgenic zebrafish Tg(sox1a:eGFP) line was obtained, sequenced, and analyzed at four different time points. Using scRNA-seq, we have found that sox1a is also expressed in late-born intraspinal serotonergic neurons (ISNs) in addition to the previously characterized sox1a-positive neurons. Developmental trajectory analysis and ablation of the lateral floor plate (LFP) by morpholino knockdown indicate that the LFP progenitor population is the origin of ISNs. Furthermore, inhibition of Notch signaling revealed the involvement of this pathway in timely ISN differentiation. These results suggest that the zebrafish LFP is not only a source of earlier developing KA'' and V3 interneurons but also of ISNs.



POSTER 40 & FLASH TALK

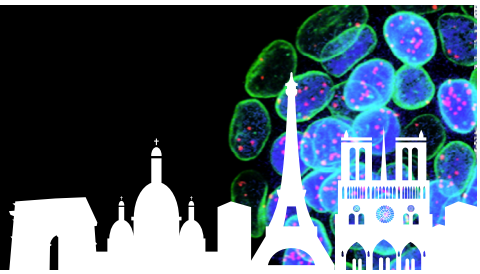
Jenny KRETZSCHMAR

Kate McDole

MRC Laboratory of Molecular Biology, University of Cambridge, United Kingdom

A place and time to die - Selective cell death and morphogenesis of the mammalian foregut pocket

One of the largest tissue-shaping events of early post-implantation mouse development is the sudden and dramatic involution of the anterior endoderm, resulting in the formation of the foregut pocket. This pocket extends to form the foregut tube - the precursor of vital organs like the lung and liver – and its formation is crucial for the proper anterior positioning of the heart and the early brain. Despite the importance of the precise formation of the foregut in time and space, the mechanisms underlying this major tissue-shaping event remain poorly understood. Combining advanced, long-term live imaging, genetic and chemical perturbations, as well as RNA sequencing, we have quantitatively and comprehensively characterised the formation of the foregut in post-implantation mouse embryos. We discovered a small population of cells undergoing selective cell death, and show that this cell death event is not only spatiotemporally confined but is also restricted to cells of a specific identity – the extra-embryonic visceral endoderm. These cells die via apoptosis but fail to extrude apically. Blocking apoptosis specifically in visceral endoderm cells allowed us to study the role of cell death in the involution of the anterior endoderm. We generated an extensive RNA sequencing dataset of the endoderm spanning all stages of the foregut formation. This has provided us with insights into the molecular mechanisms involved in restricting cell death to anterior visceral endoderm cells and the potential drivers of this major tissue-shaping event. Our findings offer valuable insights into how cell death is controlled in crowded tissues and its influence on mammalian tissue morphogenesis in vivo.



POSTER 41

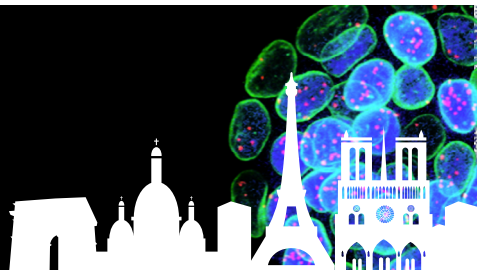
Merlin LANGE

Alejandro Granados, Shruthi VijayKumar, Jordão Bragantini, Sarah Ancheta, Yang-Joon Kim, Michael Borja, Bin Yang, Xiang Zhao, Hirofumi Kobayashi, Norma Neff, Angela Oliveira Pisco, Loïc A. Royer

Chan Zuckerberg Biohub, San Francisco, USA

Building a multimodal atlas of vertebrate development

Elucidating the developmental processes of organisms requires a comprehensive understanding of cell lineages across spatial, temporal, and molecular dimensions. Advances in imaging and omics technologies allow us to generate technically challenging multidimensional datasets that capture developmental dynamics at unprecedented resolution and across scales (from molecule to organism). We integrate large-scale light-sheet microscopy with scRNAseq, yielding a comprehensive time-resolved multimodal atlas of zebrafish development named Zebrahub (zebrahub.org). We showcase its application in elucidating the differentiation of complex late (post-gastrulation) pluripotent progenitors. We developed computational tools leveraging our Multiomic assays (scRNAseq, ATACseq, spatial transcriptomic) and tracking data to perform in silico experiments and gain mechanistic insights into development and differentiation. Using our multimodal resource and the in-silico experiment, we shed new light on the pluripotency of Neuro-Mesodermal Progenitors (NMPs) and reveal a transition fate dynamic at both transcriptional and morphodynamic levels. Our work provides a general framework for multimodal cell lineage reconstruction incorporating spatial, temporal, and transcriptomics information at single-cell resolution.



POSTER 42

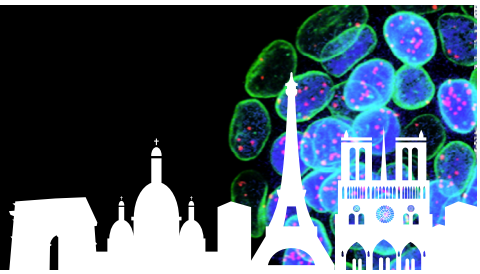
Marvin LERIA

Magali Requin, André Le Bivic, Raphaël Clément, Andrea Pasini

Aix-Marseille University, CNRS, Institute of Developmental Biology of Marseille, Turing Centre for Living Systems

Fast coordinated reorientation of basal body polarity in Trichoplax

Trichoplax, a flat benthic simple marine animal, does not display any body symmetry axis and does not have any organs. Moreover, it shows coordinated behaviours that are essential to seek food and escape physical threats, while it has no neurons or muscles. Its lower epithelium, facing the substrate, is covered by locomotor cilia that propel the animal for ciliary gliding locomotion. However, the cellular mechanisms of coordinated ciliary locomotion in such animal remain enigmatic. In this study, we have developed labelling of Trichoplax subcellular ciliary structures (basal bodies and rootlets) to characterise ciliary polarity orientation, allowing us to determine, from the cell-level to the whole-animal-level, the polarity patterns in different conditions. We have discovered that basal body polarity is planar polarised and correlated not only with the direction of movement but also with body shape plasticity. Then, we investigated the effect of mechanical stimuli on basal body polarity. We showed for the first time that basal body polarity can quickly reorient within few seconds in a coordinated manner following mechanical stimuli, a novel phenomenon until now among animals. Our multiscale approach offers new perspectives to understand how an animal lacking a network based neural system can interact with and quickly adapt to its surrounding environment.



POSTER 43 & FLASH TALK

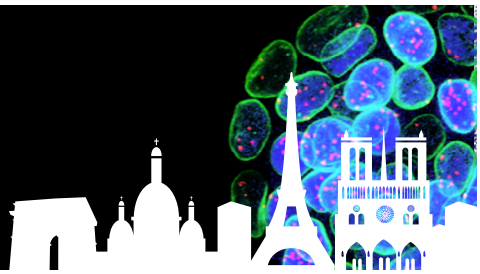
Adrien LEROY

Lorette Noiret, Eric Van Leen, Lale Elif Alpar, Maria Balakireva, Floris Bosveld, Yohanns Bellaïche

Institut Curie, Paris Sciences et Lettre Université Psl, Paris, France

Combining spatial transcriptomics and biophysical measurements unravel the genetic control of tissue morphogenesis

During development, tissue morphogenesis is modulated by genetic expression profiles controlling tissue mechanical properties and forces. However, tools allowing a systematic exploration of genetic factors controlling morphogenesis and their mechanical function are lacking. To identify the regulators of morphogenesis, we present a framework that integrates two approaches: (i) Multiscale biophysical measurements of tissue morphogenesis; (ii) Spatial transcriptome inference from single-cell RNA sequencing. We apply this framework to the development of the Drosophila dorsal thorax to identify several «morphogenetic domains» within the developing notum, characterized by distinct properties at the cell and tissue scales (e.g. cell area, rate of cellular proliferation, tissue deformation). Using our spatial transcriptome, we then identify a set of domain-specific transcription factors and reconstruct their gene regulatory networks, leading to the identification of several putative modulators of morphogenesis. Lastly, we validate the function of these modulators through loss of function experiments, quantitative measurements of tissue properties and the spatial organization of mechanical regulators of tissue morphogenesis. Our framework provides a powerful tool to unravel the genetic control of tissue morphogenesis, bridging the gap between gene expression and tissue mechanics. It can be applied to various developmental processes, paving the way for a better understanding of the fundamental principles governing tissue development.



POSTER 44

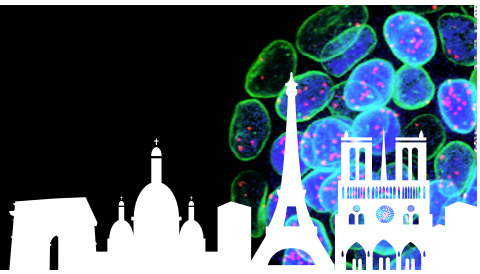
Valérie LOBJOIS

Julie Pignolet*, Angie Molina, Eric Agius , Odile Mondésert, Sophie Bel-Vialar, Fabienne Pituello

Unité de Biologie Moléculaire, Cellulaire et du Développement (MCD), Centre de Biologie Intégrative (CBI), Université de Toulouse, CNRS, Université Toulouse III
**First Author*

Control of the progression in the G1 phase of the cell cycle during neurogenesis: a new function for the protein phosphatase CDC25B

Building a functional nervous system involves regulation of the proliferation/differentiation balance of neural progenitors. A major mechanism to control proliferation is the cell cycle. Lengthening of the G1 phase of the cell cycle is associated to the maturation of neuronal progenitors and although this lengthening is a generic feature of tissue maturation during development, the underlying mechanism remains poorly understood.
The progression through the G1 phase of the cell cycle is regulated by the restriction point which depends on phosphorylation of the retinoblastoma protein Rb. It has been shown on asynchronous cell cultures that the timing of R point crossing during G1 is variable and regulated by molecular events occurring during the G2 phase of the mother cell.
We have recently demonstrated, in vivo in the vertebrate embryo, the involvement of a G2 phase regulator, CDC25B phosphatase, in controlling the progression of neural progenitors in G1 phase. By using a time-lapse imaging strategy, we measured the four cell cycle phases in single chick neural progenitors. We have shown that neural progenitors are widely heterogeneous with respect to length of the G1 phase and CDC25B induces an increase in the duration and variability of the G1 phase in neuronal progenitors. The analysis of the phosphorylated retinoblastoma protein reveals that CDC25B increases the proportion of proliferative neural progenitors negative for this marker, suggesting that it could partly delay passage through the restriction point. We thus propose that CDC25B increases the variability of G1 phase length through the regulation of the restriction point, revealing a previously undescribed mechanism of G1 lengthening that is associated with tissue development. We will present our latest results on deciphering the dynamics of the restriction point crossing in neural progenitors and the mechanism involved in this regulation.



POSTER 45

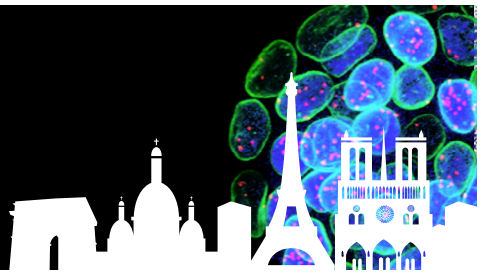
Jennifer LOVE

Lauren Forbes Beadle, Catherine Sutcliffe, Magnus Rattray, Hilary L. Ashe

Faculty of Biology, Medicine and Health, University of Manchester, United Kingdom

Spatially regulated mRNA degradation defines the expression pattern of even-skipped in early Drosophila development

The processes of transcription, splicing, translation and mRNA degradation together shape the mature mRNA abundance in cells; the regulation of mRNA decay is widespread and important for numerous cellular and developmental processes. Here, we investigate the post-transcriptional regulation of the patterning gene even-skipped in the early Drosophila embryo. Through P-body colocalisation analysis and mathematical modelling of live and fixed imaging data, we present evidence that eve mRNA stability is regulated across stripe 2, with enhanced mRNA decay at the edges of the stripe. To test whether eve mRNA instability helps define the mature expression pattern, we perturbed mRNA decay by optogenetic degradation of the 5′ to 3′ exoribonuclease Pcm. Depleting Pcm results in altered patterns of eve expression, suggesting that mRNA decay is important for anterior-posterior patterning of the Drosophila embryo. Overall, this work indicates that mRNA decay is important for correct body plan specification in early development and that, like other parameters of gene expression, mRNA decay can be spatially regulated across gene expression domains in the embryo.



POSTER 46

Cao LUYAN

Angika Basant, Miroslav Mladenov, Antoine Jegou, Guillaume Romet-Lemonne, Michael Way

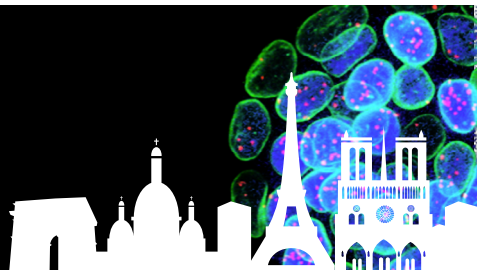
The Francis Crick Institute, London, United Kingdom

Arpc5 isoforms differentially impact the ability of Arp2/3 complexes to generate linear filaments to regulate lamellipodia protrusion

When activated by nucleating-promoting factors, such as WAVE and N-WASP, the Arp2/3 complex binds to the side of a pre-existing actin filament to initiate the formation of a new daughter actin branch. Alternatively, activation of Arp2/3 by SPIN90 generates a linear actin filament. Finely coordinating between these two activities, the Arp2/3 complex regulates both the architecture and dynamics of actin networks that are required for many cell processes, including cell migration, phagocytosis, and DNA repair. It is important to gain a deeper understanding of how Arp2/3 regulate its transition between nucleating branched and linear actin filaments.

The Arp2/3 complex, consisting of seven evolutionarily conserved subunits (Arp2, Arp3, and ARPC1-5), has been regarded as a single entity in most research. However, in mammals, Arp3, ARPC1, and ARPC5 exist as two different isoforms (Arp3/Arp3B, ARPC1A/ARPC1B, and ARPC5/ARPC5L) that are 91%, 67%, and 67% identical, respectively. This means that the Arp2/3 complex in humans is not a single entity but a group of eight iso-complexes with different properties.

All the Arp2/3 iso-complexes can generate actin branches, however, we found that only a subset of complexes can be activated by SPIN90 to generate linear actin filaments. This is due to the varying affinity between SPIN90 and different Arp2/3 iso-complexes. Live cell imaging of CRISPR edited B16 cells reveals that SPIN90 is recruited to the leading edge of lamellipodia where it locally regulates the level of different Arp2/3 iso-complexes to control the speed of lamellipodia protrusion.



POSTER 47

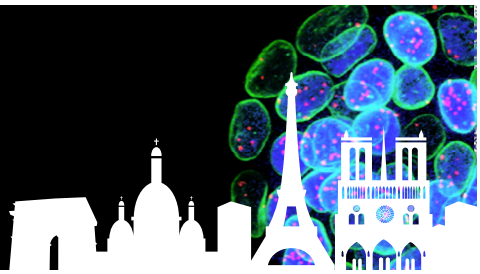
Louise MAILLARD

Maria Douaihy, Virginia Pimmett, Pablo Garcia, Amélie Brun, Antonio Trullo, Ovidiu Radulescu and Mounia Lagha

Institut de Génétique Moléculaire de Montpellier, CNRS, Montpellier, France

Quantifying how cis-regulatory sequences affect gene expression heterogeneity

Monitoring mRNA synthesis in living cells revealed that in most eukaryotic cells, transcription is discontinuous, whereby active periods (bursts) are separated by one or several types of inactive periods of distinct lifetimes. Transcription bursting has the potential to modulate gene expression significantly and can lead to cell-to-cell heterogeneity (noise). While such variability can be profitable for phenotypic plasticity, it should be buffered during critical periods of embryogenesis to drive the deployment of accurate and reproducible cell fate specification programs. How the cis-regulatory code dictating gene expression, affects the kinetics of transcription bursts and impacts transcriptional noise, remains largely unexplored. In this study, we decoded the effect of promoter motifs (TATA box, INR, DPE) and redundant enhancers, on transcriptional heterogeneity. We used the stereotypical patterning of the early Drosophila embryo and two model loci as a paradigm, snail and sog. During early embryogenesis, these developmental genes are each regulated by two enhancers, a proximal and a distal one. Using genetic manipulations and live imaging of transcription, we quantified the effect of individual versus multiple enhancers, as well as promoter motifs, on bursting kinetics and the resulting spatio-temporal cell-to-cell heterogeneity.



POSTER 48

Laure MANCINI

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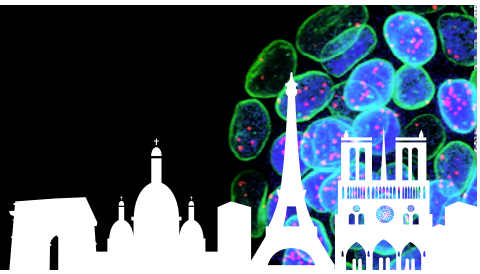
**Co-First Author*

Control of the spiral phyllotaxis from a single stem cell in the moss Physcomitrium patens

The architectural plan of an organism determines its main axes of symmetry and is key to position each organ relative to each other with precision and robustness. In plants, botanical elements such as leaves are arranged following a periodic and geometric pattern called “phyllotaxis”, which can be spiral, whorled or opposite. This pattern emerges at the cellular level from the shoot tips where stem cells are located. So far, phyllotaxis has mainly been studied in flowering plants with shoot tips composed of hundreds of cells. Unlike flowering plants, the shoot tip of the model moss Physcomitrium patens is composed of a single stem cell, known as the apical cell. As a result, the position of each new leaf strongly depends on the division pattern of the apical cell. However, the mechanisms that control the positioning of the apical cell division plane to pattern moss phyllotaxis remain to be discovered.
Within this framework, my project aims to decipher the molecular and biophysical mechanisms that control spiral phyllotaxis in P. patens. Using a combination of quantitative time-lapse imaging, cellular shape analysis and modeling in various transgenic lines, I have been able to provide a quantitative description of the division dynamics at the moss shoot apex with a cellular resolution. These results bring the first insights into how a single stem cell directs its division plan to generate a complex and robust biological pattern.



POSTER 49

Souhila MEDJKANE*

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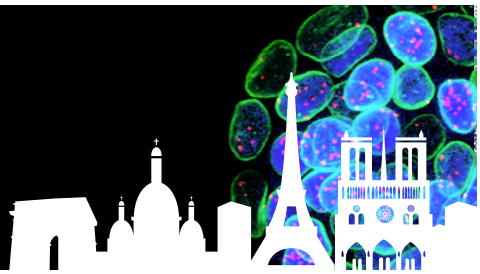
Methylation regulates the timing of cytokinetic abscission

Abscission is the final stage of cytokinesis, which cleaves the intercellular bridge (ICB) connecting two daughter cells. Abscission requires tight control of the recruitment and polymerization of the Endosomal Protein Complex Required for Transport-III (ESCRT-III) components. We explored the role of post-translational modifications in regulating ESCRT dynamics and cell division.
We discovered that SMYD2 methylates human CHMP2B, a key ESCRT-III component at the ICB. We showed the functional importance of CHMP2B methylation in actively promoting abscission by facilitating the repositioning of ESCRT-III proteins at the scission point. We demonstrated that methylation acts as a positive regulator of abscission, and that abnormal methylation leads to disrupted cell division and multinucleation, a hallmark of cancer. Importantly, our findings extend beyond cytokinesis, as CHMP2B methylation also facilitates HIV-1 viral budding, suggesting its broader involvement in ESCRT-dependent cellular processes.



POSTER 50

Amina MEDYOUF

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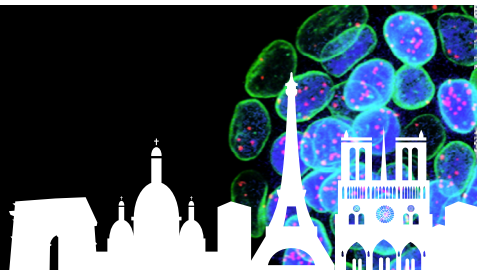
Regulation of lumen remodelling in the zebrafish developing spinal cord by cilia-dependent Hh signaling

The developing spinal cord has been instrumental in understanding the coordinated control of the proliferation, patterning and differentiation of embryonic neural progenitors and stem cells. These early works have led to a detailed characterisation of the role of Hedgehog activity in neural patterning. However, the role of tissue remodelling in this process has not been fully explored.

At the end of spinal neurogenesis, the lumen of the spinal cord, which allows cerebrospinal fluid circulation, remodels drastically. The lumen height reduces to form a smaller ventral central canal surrounded by quiescent stem cells, a process conserved in all vertebrates. Neural tube remodelling involves the coordination of lumen reduction with the elongation of a glia population, the dorsal roof plate. We are currently studying how this remodelling is controlled and its significance for spinal cord development and regeneration. We are using the dzip1 zebrafish mutant that fails to fully reduce the lumen size and is known to present Hedgehog signaling defects due to an absence of cilia. We are characterising the behaviour of progenitor cells associated with this inaccurate lumen reduction in the dzip1 mutant. We are currently assessing how Hedgehog signalling is impaired, and how it impacts lumen remodeling. We are also studying the consequence of increasing the speed of lumen remodelling through quantitative live timelapse imaging of the dorsal roof plate elongation.This project aims to refineour understanding of neural tube development, by including morphogenetic rearrangements into the current models.



POSTER 51

Mary MIRVIS

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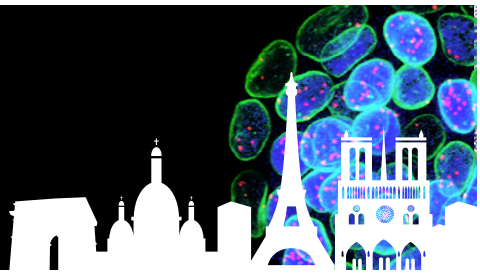
University of California, San Francisco, USA

Harnessing whole-cell morphometrics to probe organelle interdependencies and cell anatomy: a two-pronged approach

The bridge between the cellular meso- and whole-cell scales is an under-appreciated level of biological organization. The past decade has seen massive progress in unraveling the complex interconnectivity of organelles through contact sites and functional crosstalk. However, how the entire organelle network spatially arranges within the cytoplasm is only beginning to be explored. How do structural interdependencies influence organelle morphology and overall cell anatomy, and how do these interdependencies shift in dysfunctional states? We approached these questions through two complementary strategies. First, we used single-cell soft X-ray tomography in Saccharomyces cerevisiae to examine three aspects of the vacuole-nucleus interaction: size scaling, morphology, and interface geometry. Custom automated segmentation enabled us to reconstruct hundreds of whole cells, including several organelles, at 30-35nm isotropic resolution. 3D morphometric analysis and statistical integrated modeling showed that vacuole enlargement (vac14) progressively breaks the linear scaling of the nucleus and drives nuclear displacement and flattening. Our working model is that physical packing of organelles within the cytoplasm plays a significant role in establishing organelle morphology and global cell patterning. Second, we comprehensively curated the whole-cell imaging literature to facilitate meta-analysis and reanalysis of these information-rich data. Characterization of bibliometrics, study design, reporting practices, and language revealed accelerated technological and research output, but a lack of common reporting standards and a standardized conceptual framework for questions at the whole-cell scale. We argue for "cell anatomy" as a potential unifying term to describe the cumulative pattern of organelles in a whole-cell context. We used our curated dataset to compare the volumetric organelle composition, variations in inter-organelle relationships, and general anatomical motifs across cell types and contexts. We hope that both datasets will serve as valuable resources for deepening understanding of cell anatomy, and that our work will promote the establishment of the novel field of 'cell anatomy' research.



POSTER 52

Paulina C. MIZIA

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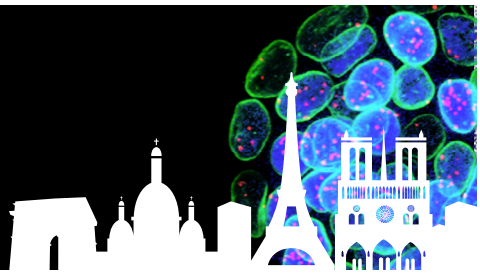
The influence of busulfan on gonad development in the zebra finch (Taeniopygia guttata)

Zebra finches have emerged as a widely used avian species in research. Nevertheless, the gonadal development of these birds has remained unexplored. The objective of this study was to elucidate the influence of busulfan on the formation of gonads in zebra finches (Taeniopygia guttata). Eggs were collected on the day they were laid and incubated at 37.5 °C with 70% humidity. On day 2.5 of embryonic development (E 2.5), busulfan (chemotherapeutic agent) was injected into the yolk. Embryos dissected from the eggs were staged according to the Hamburger-Hamilton stages. We employed histological staining according to Dubreuill's modifications and compared it with immunohistochemistry. The histological staining provided comprehensive insights into the morphological features, distinguishing germ cells from somatic cells. Immunohistochemistry enabled the identification of collagen and laminin in the gonadal structure.

Our results indicated that busulfan effectively removed germ cells from the gonads, resulting in a lack or significant reduction of germ cells in the gonads. Moreover, the germ cells that were not removed by busulfan were predominantly present in the left gonad rather than the right. Additionally, the absence of germ cells disrupted the formation of sex cords, making it difficult to distinguish between the cortex and medulla of the gonads.

In summary, our study highlights the significant impact of busulfan on gonadal development in zebra finches. disruption in sex cord formation and the subsequent incomprehensibility in identifying the cortex and medulla further underscore the crucial role of germ cells in gonadal development. These findings contribute to a better understanding of gonadal differentiation and may have broader implications for reproductive biology and toxicology studies in avian species. This research is particularly significant in light of the serious issue of fertility disorders resulting from chemotherapy, emphasizing the need for further studies on the reproductive impact of chemotherapeutic agents.



POSTER 53 & FLASH TALK

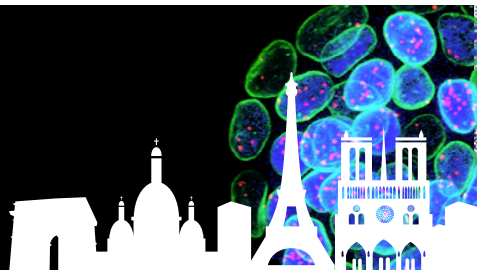
Anastasia MORAITI

Ana De Almeida Ferreira, Andrea Cairoli, Miriam Llorian Sopena, Guillaume Salbreux, Nic Tapon

The Francis Crick Institute, London, United Kingdom

Investigating growth control in the Drosophila melanogaster abdomen using transcriptomics

Growth and pattern formation during development are regulated by a complex network of signals that act together to ensure robust and reproducible growth. The coordinated effect of these inputs is captured in gene expression changes that instruct the morphogenetic behaviours of individual cells. Here, we utilise single-cell transcriptomics to explore the signals that regulate developmental growth in the Drosophila melanogaster abdominal histoblast model system. We examined five stages of histoblast development, to reveal the transient cell states and the mechanisms that drive progression through development, and, eventually, to growth arrest.
Growth arrest in the histoblast model system has previously been shown to occur through an abrupt transition to cell cycle exit. Our transcriptomics analysis indicated changes in the expression of gap junctions components, which form intercellular channels that allow sharing of solutes between neighbouring cells. This led us to investigate how growth arrest is affected after knocking down innexins, the channel-forming components of gap junctions. We observe a less steep transition to growth arrest and a loss of cell cycle coordination during histoblast development. These findings indicate that coordinated cell cycle exit in this system is mediated by cell-cell communication between neighbouring cells.



POSTER 54

Yolanda MOYANO RODRIGUEZ

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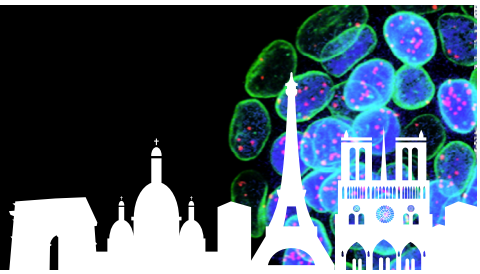
CNRS, Université de Montpellier - France
IGMM (UMR5535), CNRS - France

Mechanistical investigation of X-chromosome reactivation in the germline

During mammalian embryogenesis, specific chromatin epigenetic marks, such as histone modifications and DNA methylation, are acquired. These determine gene expression and maintain cell identity of the different lineages. Among these epigenetic changes, transcriptional inactivation of one of the two X chromosomes occurs in females by a process called X-chromosome inactivation (XCI). This is established and clonally propagated in female somatic cells to ensure gene dosage balance compared to males.
Exceptionally, gamete precursors, the primordial germ cells (PGCs), undergo profound global epigenetic remodeling to ultimately acquire competency to form the germline and express germline-specific genes. Reprogramming includes genome-wide DNA demethylation, redistribution of histone marks, erasure of genomic imprints, and, in females, X-chromosome reactivation (XCR). XCR involves the loss of coating of the long non-coding RNA Xist, DNA demethylation at promoters and re-expression of X-linked genes from the Xi.
Although XCI –in vivo and in vitro– has been well studied, how XCR is regulated in PGCs and its biological impact –i.e. in X pairing and/or synapsis during meiosis– remains largely unknown. In our lab, we have recently contributed to the understanding of how XCR is established during PGCs specification in vivo (Roidor, Syx et al 2023).
Now, we aim to dissect the regulatory mechanisms underlying XCR. To achieve this, we have generated a unique culture-based PGC-like cell (PGCLCs) system, carrying a fluorescent reporter for XCR, an inducible XCI system, and allele-specific information. To unveil the major contributors to XCR during in vitro PGCLCs specification, we combined our system with: 1. Genome-wide CRISPR-gene screening, and 2. candidate-based approaches. This novel model allows us to study sex-specific reprogramming during germline differentiation, advancing our understanding of the epigenetic mechanisms behind this process, as well as the influence of XCR on gametes formation.



POSTER 55

Pierre OSTEIL

Laura Nivet, Léa Rogue, Nicolas Allègre, Ronan Quenec'hdu, Claire Chazaud

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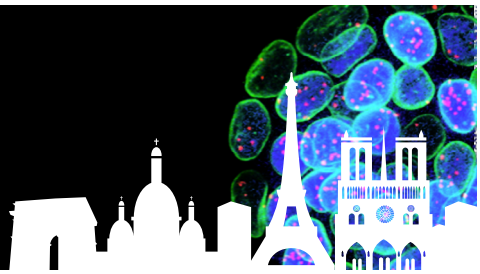
Primitive endoderm patterning provides a head start for axis positioning

During embryo development, synchronized morphogenetic events shape the adult body. A crucial step is the establishment of the anteroposterior axis, noticeable in the mouse embryo from 6.5 days post coitum (E6.5) by the distinctive aspect of the primitive streak (PS). The site of gastrulation is directed by Wnt anf TGFβ signalling pathways that are particularly active in this region. On the opposite side, cells of the visceral endoderm (VE) express antagonists like Dkk1, Sfrp1 which inhibit Wnt signalling and Lefty1 and Cer1 counteracting TGFβ/Nodal. This gradient establishes the body's first axis, from the anterior visceral endoderm (AVE) to the posterior primitive streak (PPS).
Studies from 2006 found that the AVE cells could be traced back to the exact moment of implantation, in the late blastocyst at E4.5. At this stage the embryo is composed from only three cell types: the epiblast at the origin of the individual; the trophectoderm which will lead to the placenta; and the primitive endoderm (PrE) which give rise to the yolk sac, an intermittent structure supporting the embryo development until the placenta becomes functional.
The PrE is more than a simple epithelial layer of cells between the blastocoel and the epiblast. It shows a complex expression pattern of Leftys, with one to three cells exhibiting a unique profile, that is co-expressing Lefty1 and Lefty2. Single cell data mining revealed that these cells have a distinctive molecular signature from the other cells of the PrE. Due to limited embryonic material, we used embryoid bodies to mimic the epiblast and PrE establishment and manipulated molecular pathways to explore the origin of the Lefty expression pattern in the PrE.
Our findings provide new insights into the establishment of the anteroposterior axis in the embryo.



POSTER 56

Guillaume PÉZERON

Anne-Laure Gaillard*, Elsie Rousteau, Hervé Tostivint

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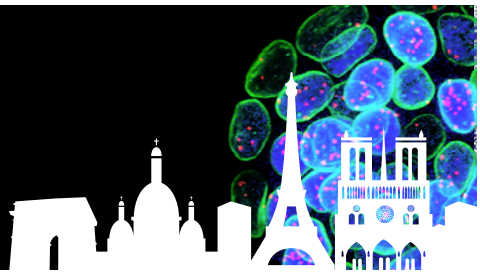
**First Author*

A function for Uts2 signaling in intervertebral disc formation and homeostasis

In vertebrates, the spine provides postural stability and protects the spinal cord. It comprises a segmented series of ossified vertebral bodies, separated by intervertebral discs (IVD). These discs are fibrocartilaginous joints that connect adjacent vertebrae, absorb mechanical compression, and facilitate vertebral flexibility. IVD originate from the notochord, a transient embryonic structure. During spine morphogenesis, the notochord segments and contributes to the formation of the nucleus pulposus (NP) in mature IVDs. Urotensin 2 (Uts2) and Urotensin 2-related peptides (Urp, Urp1, and Urp2) constitute a family of neuropeptides conserved across all vertebrates, characterized by a high degree of sequence identity. These peptides interact with a family of GPCR receptors known as Uts2r. Research, including our own, has demonstrated that in zebrafish, two members of this neuropeptide family, Urp1 and Urp2 (collectively referred to as Urp1/2), are essential for body axis and spine formation most likely through the regulation of muscle tone.
More recently, we have discovered evidence for a novel and independent function of Uts2/Urp signaling in spine development and maintenance. Specifically, in zebrafish, we have identified that two Uts2 receptors (uts2r1 and r4) are expressed in the notochord of embryos and in the intervertebral discs (IVDs) of adult zebrafish. We will present our latest findings on the role of Uts2r signaling in spine formation and homeostasis in zebrafish.



POSTER 57

Rémi PIGACHE

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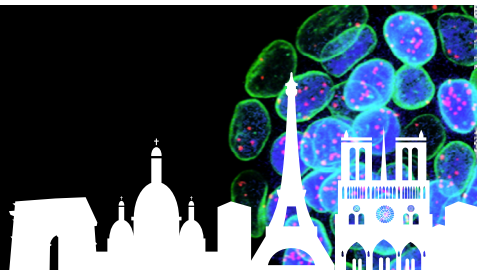
Institut Curie, PSL Research University, CNRS UMR3215, INSERM U934, Paris, France

Regulation of epithelial folding downstream of homeotic gene

Epithelial folding is a key morphogenetic event transforming a two-dimensional flat tissue into a three-dimensional complex structure. During Drosophila melanogaster metamorphosis, the Hox gene Deformed (Dfd) defines the identity of the neck segment, which undergoes invagination at the pupal stage. This process is regulated by Dfd-induced Myosin II (MyoII) enrichment, which increases in-plane tension that drives invagination downstream of the apical Tollo and the basal Dystroglycan receptor. The Toll-like receptor Tollo mediates this MyoII apical localization. Here, we explore the mechanisms of Tollo-dependent invagination and of 3D cell shape regulation during tissue invagination. We first describe the dynamics of Rho activation and its regulatory mechanisms during neck invagination by performing an exhaustive screen for RhoGEF/GAP enriched in the neck. We then develop novel tools to characterize 3D cell shape geometry and orientation. By systematically studying 3D cell shape orientation, we delineate how 3D cell shape is modulated during tissue invagination and test whether the Dg receptor regulates cell shape. Collectively, these results highlight the complex interplay between homeotic gene expression, cell adhesion, contractility, and 3D tissue architecture. This study provides insights into the mechanisms underlying tissue morphogenesis and development, furthering the understanding of how epithelial folding shapes organisms.



POSTER 58

Virginia PIMMETT

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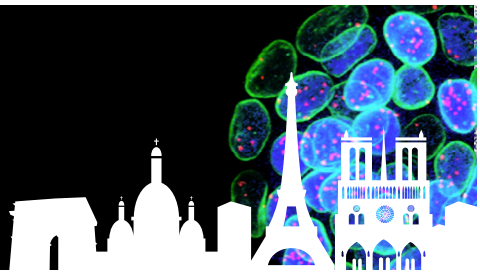
Dissecting the dynamics of coordinated active transcriptional repression in the Drosophila mesoderm

The ability to refine transcriptional levels via active repression in an euchromatic context repre-sents a critical regulatory process. While the molecular players of active repression are well de-scribed, their dynamics remain obscure. In this study, we used snail expression dynamics as a para-digm to uncover how active repression, mediated by the Sna repressor, can be imposed within a developing tissue. By combining live imaging of transcription to theoretical approaches, we uncov-ered and quantified the timescale of the kinetic bottlenecks tuning transcription during repression. Repression is associated with the transition of the promoter from two states to a three-state re-gime, comprising two temporally distinct inactive periods. Surprisingly, repression occurs without abrupt changes in Pol II initiation rates. By monitoring nuclear Sna protein levels, we show that Sna-mediated repression operates with high cooperativity. We further reveal that cooperativity dictates the degree of cell-cell coordination in the imposition of repression. Our approach offers quantitative insights into the dynamics of repression mediated by short-range repressors and how their cooperativity may coordinate cell fate decisions within a tissue.



POSTER 59

Iryna PIROZHKOVA

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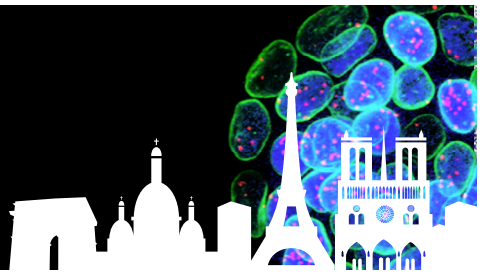
DiPRO1/ZNF555 distinctly reprograms muscle and mesenchymal cancer cells

We have recently identified the uncharacterized ZNF555 protein as a component of a productive complex involved in the morbid function of the 4qA locus in facioscapulohumeral dystrophy. Subsequently named DiPRO1 (Death, Differentiation, and PROliferation related PROtein 1), our study provides substantial evidence of its role in the differentiation and proliferation of human myoblasts. DiPRO1 operates through the regulatory binding regions of SIX1, a master regulator of myogenesis. Its relevance extends to mesenchymal tumors, such as rhabdomyosarcoma (RMS) and Ewing sarcoma, where DiPRO1 acts as a repressor via the epigenetic regulators TIF1B and UHRF1, maintaining methylation of cis-regulatory elements and gene promoters. Loss of DiPRO1 mimics the host defense response to virus, awakening retrotransposable repeats and the ZNP/KZFP gene family. This enables the eradication of cancer cells, reprogramming the cellular decision balance towards inflammation and/or apoptosis by controlling TNF-α via NF-kappaB signaling. Finally, our results highlight the vulnerability of mesenchymal cancer tumors to si/shDiPRO1-based nanomedicines, positioning DiPRO1 as a potential therapeutic target.



POSTER 60

Chiara POMPILI

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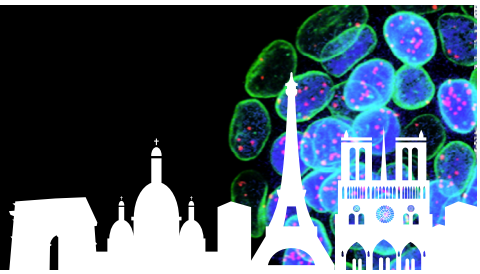
Phagocytosis via mannose receptors analysed using chemically functionalised lipid particles

Phagocytosis is a cellular process that enables uptake and digestion of particles larger than 0.5 µm, playing a fundamental role in innate immune responses to pathogens and in tissue homeostasis. Phagocytic cells, such as macrophages, display a high variety of surface receptors that allow target recognition and internalisation. Engaged receptors induce signals triggering actin remodelling and phagosome formation. The orchestration of this process has been widely studied using opsonic receptors (i.e. Fc Receptor and Complement Receptor) as models. However, there are receptors, such as C-type lectin receptors, whose phagocytic function is not fully characterised. Here we focus on mannose receptors, known to recognise glycoconjugates with terminal mannose, fucose or N-Acetylglucosamine, expressed on microbial surfaces. Indeed, the mannose receptor signalling remains a mystery as the receptor lacks any intracellular signalling motif. A likely explanation is that it depends on receptor lateral organisation in the plasma membrane during engagement of microbes and soluble molecules.
To model the uptake of pathogens by mannose receptor, we use a novel approach based on lipid droplets functionalised with fluorescent glycolipids coupled to mannose. We showed that these coated particles are specifically recognised by human primary macrophages. We are currently monitoring the interaction of the functionalised droplets with living macrophages to identify phagocytic receptor clustering. Besides, with two glycolipids conjugated to newly synthetised fluorophores used as FRET pairs, we showed that it is possible to study ligand clustering at the interface of the droplets. Therefore, FRET will be an additional readout for receptor clustering in macrophages. Moreover, we have set out to decipher downstream signalling activation and actin dynamics that are important to coordinate membrane remodelling and engulfment upon mannose receptors engagement. In conclusion, here we present our unique methodology with some recent findings regarding mannose-mediated phagocytosis, from receptor clustering to intracellular signalling and actin polymerisation.



POSTER 61

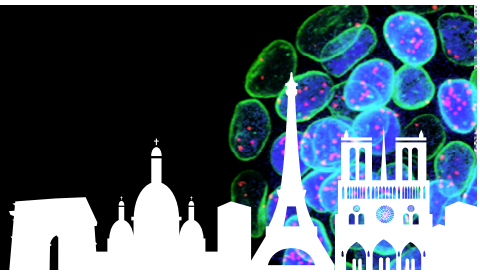
Elena PUTTI

Fanny Eggeler, Jonathan Boulanger-Weill, Giulia Faini, Julie Dang, Karine Duroure, Shahad Albadri and Filippo Del Bene

Institut de la Vision, Paris, France

Lrrn2 and Lrrn3a cell adhesion molecules govern precise retino-tectal circuit formation in the zebrafish visual system

The formation of neuronal circuits involves an intricate interplay of molecular signals that ensure axons navigate accurately to their designated synaptic targets, enabling the development of complex and interconnected cellular networks. The zebrafish visual system, characterized by diverse retinal ganglion cells (RGCs) projecting to the optic tectum (OT), serves as an exemplary model of this complexity. Transcription factors, axon guidance proteins, and cell adhesion molecules are some of the fundamental cues orchestrating the accurate targeting of RGC axons. In Drosophila, Capricious is a cell adhesion molecule vital for the proper targeting of a subset of photoreceptors to the fly visual processing centers in the brain. In zebrafish, the orthologue of Capricious belongs to the leucine-rich repeat neuronal proteins (Lrrns). The leucine-rich repeat (LRR) proteins have recently been shown to be key players in various aspects of neuronal circuit development, from axonal guidance to synapse formation and stabilization. Within the LRR protein family, the Lrrn subfamily comprises distinct adhesion molecules, including Lrrn2 and Lrrn3a. Remarkably, their expression patterns are conserved across species, ranging from Drosophila to humans, particularly in the developing retina. However, the functional significance of Lrrn2 and Lrrn3a in the context of visual system formation and axonal targeting in vertebrates remains elusive. Using CRISPR/Cas9-mediated loss-of-function approaches, we investigated the roles of Lrrn2 and Lrrn3a in RGC axon targeting within the zebrafish OT. Disruption of these adhesion molecules impaired proper synaptic wiring and visual function, revealing a novel role for SAC-projecting RGCs and their synaptic targets, confirmed through EM-segmentation. Together, our findings suggest that Lrrn2 and Lrrn3a are crucial for the specification and function of precise retino-tectal circuits in the vertebrate visual system. This study presents a comprehensive analysis of a neuronal circuit, offering insights into its genetic profile, development, structure, and function.



POSTER 62 & FLASH TALK

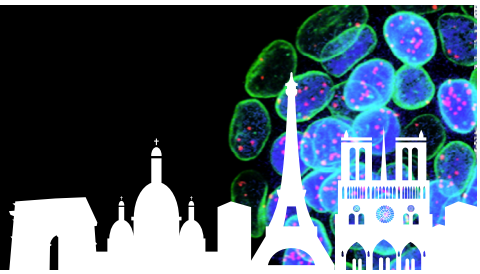
Robin RONDON

Richard-Albert Julien, Dugast Claire, Gilardi-Hebenstreit Pascale, Ribes Vanessa

Université Paris Cité, CNRS, Institut Jacques Monod (UMR7592), Paris, France

A BMP mediated PAX3/7 transcriptional activity switch creates cell fates patterns in the developing spinal cord

The emergence of cellular diversity in the developing central nervous system is controlled by the combined activity of secreted signals and transcription factors. The mechanisms by which neural progenitors integrate these two signals have yet to be deciphered. For this, we investigate the interplay between BMPs and the transcription factors PAX3 and PAX7 during the specification of dorsal spinal relay and associating neurons. Our data show that PAX activity prevents ventralisation of relay and associating progenitors by two distinct molecular mechanisms depending on BMPs exposure. In absence of BMPs, PAX mediated associating neurons specification relies on a repressive PAX transcriptional activity. Accordingly, PAX bind cis-regulatory genomic regions nearby key ventral specifier genes and their activity is required for the deposition of the repressive H3K27me3 mark on these regions. In presence of BMPs, this PAX repressive activity is maintained onto some ventral gene loci. In addition, at the same time, part of PAX is relocated to other cis-regulatory regions, some of which are nearby relay neurons specifier genes and are opened and activated by the PAX. This transactivating activity of the PAX is necessary for relay neurons generation. Altogether, our data demonstrate that BMP signalling acts as a switch for PAX transcriptional activity, increasing their specification potential tenfold. Evidence of cooperativity between PAX and other transcription factors, as well as the recruitment of specific units from major chromatin remodelling complexes that play a role in the switch of PAX transcriptional activity in response to BMP signalling, will be discussed.



POSTER 63

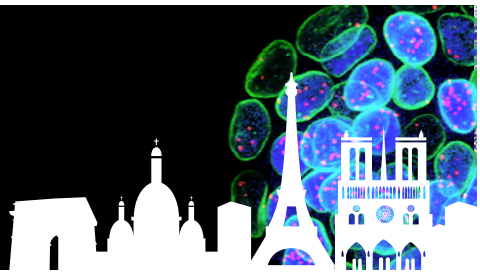
Laura RUSTARAZO-CALVO

Cristina Pallares-Cartes, Maximilian Hingerl, Adrián Aguirre Tamaral, Elisa Floris, Bernat Corominas-Murtra, Nicoletta Petridou

EMBL Heidelberg, Heidelberg University, Germany

The emergence and function of different types of tissue material phase transitions during embryo development

Multiple morphogenetic processes occurring during development and disease depend on material phase transitions (MPTs), during which tissues abruptly switch between non-deformable (solid-like) and deformable (fluid-like) states. Theoretical work identified that several cellular parameters can trigger MPTs, such as density, connectivity, cell shape, and cell contact fluctuations. However, whether the different cellular parameters trigger different types of MPTs and whether the different types of MPTs have distinct biological functions is yet unknown.
Our work uncovers that density-dependent MPTs (passive) versus adhesion strength-dependent MPTs (active) can be uncoupled in embryonic tissues and that they can elicit differential signalling events. To explore the material phase space and MPTs, we combine quantitative live imaging, optogenetics, and pharmacological perturbations in early zebrafish embryos with theoretical frameworks of rigidity percolation, jamming and membrane surface tension. We propose that embryonic tissues exist in a phase space with four distinct material regimes determined by critical points in cell density and cell adhesion strength. Morphological and molecular analyses pinpoint differences between tissues in the different regimes, depending on the type of MPT they undergo: while active rigidity transitions initiate epithelial polarity signalling pathways, passive rigidity transitions do not. To explore the molecular mechanisms by which the different MPTs instruct differential signalling pathways, we set up transplantation experiments where cells from a donor embryo expressing a marker of interest are transplanted into host embryos of different material regimes. To explore cell responses to active versus passive rigidity transitions we monitor effects at short timescales, e.g. cellular dynamics, and at long timescales, e.g. gene expression changes.
Altogether, by developing methodology to modify tissue rigidity, we show that passive versus active MPTs instruct different morphogenetic trajectories, and we are currently investigating the underlying molecular mechanisms.



POSTER 64

Frida SANCHEZ GARRIDO

Benjamin Bouzerand, Anastasia Fontaine, Marketa Tesarova, Tomás Zikmund, Jozef Kaiser & Églantine Heude

Muséum National d'histoire Naturelle, CNRS, Paris, France

Pleiotropic role for Dlx5/6 transcription factors in the formation of the mammalian acoustic system

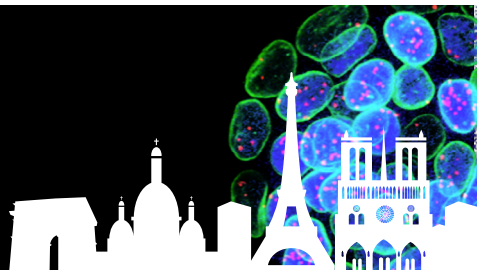
In mammals, acoustic communication is essential for social interaction. It involves both effector and receptor organs, the vocal and the auditory systems, in order to produce and hear sounds. Vocalization and hearing are assured by the simultaneous control of a set of cranio-cervical organs such as the ossicles, the jaws, the pharynx and the larynx skeletal components that originate from cephalic neural crest cells (CNCC). Dlx5 and Dlx6 are homeotic genes that encode for transcription factors essential for the establishment of the mandibular identity. During development, these genes are expressed by CNCC in the otic vesicle and in the pharyngeal arches that house the musculoskeletal precursors of the vocal apparatus.

Here we seek to characterize the functions of Dlx5/6 in the morphogenesis of the vocal and hearing systems by targeted CNCC invalidation in the mouse.

We first studied the phenotype of our mutant mice perinatally using classical histological and µCT scan and 3D reconstruction approaches. We observed musculoskeletal malformations all along the vocal tract and major defects of the inner, middle, and external ear components.

We are now investigating the cellular and molecular origins of the phenotype at earlier development stages. We first performed a genetic tracing of CNCC in control and mutant conditions and we observed a defective pattern of CNCC organization in both pharyngeal arches and otic vesicle, without affecting CNCC fate and differentiation. Dlx5/6 inactivation also affects the development of some cranial and cervical muscle groups and of the facial, tongue and inner ear nervous system.

Our data demonstrate that Dlx5/6 in CNCC orchestrate the morphogenesis of both vocal and auditory apparatus, thus revealing the pleiotropic role of the genes in the formation of the mammalian acoustic system.



POSTER 65

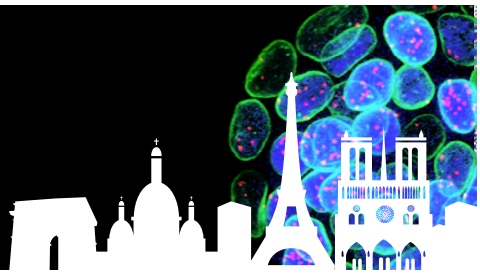
Martina SANTONI

Catherine Jessus, Enrico Maria Daldello

IBPS - Sorbonne Université, LBD - UMR7622, Paris, France

Exploring the multi-branched pathway connecting PKA inhibition and Cdk1 activation

The oocyte meiosis is arrested in prophase of the first division. At the time of ovulation, a hormonal stimulation triggers meiosis resumption: the oocytes undergo two consecutive meiotic divisions becoming haploid and competent for fertilization. In vertebrates, the prophase arrest is ensured by the activity of the cAMP-dependent protein kinase (PKA), which indirectly inhibits the universal inducer of M-phase, the cyclin-dependent kinase 1 (Cdk1). Upon the hormonal stimulation, progesterone in Xenopus laevis, PKA is inhibited, allowing the activation of Cdk1 and entry into M-phase.
In a recent publication (Santoni et al, 2024 – Cell Report), we took advantage of a Cdk1 inhibitor, Cip1, to investigate the events occurring downstream of PKA inhibition and upstream of Cdk1 activation. Three Cdk1 upstream events were identified: the accumulation of Cyclin B1, a global wave of de novo protein translation and the translation of Mos, the activator of MAPK pathway in the oocyte. We demonstrated that Arpp19, which is the only known upstream substrate of PKA, is not involved in controlling any of these events. These findings highlight the presence of multiple pathways connecting PKA inhibition to Cdk1 activation, thus pointing to the existence of other PKA substrates than Arpp19 controlling these events.
Currently, we are identifying novel PKA substrates using the BIO-ID combined to Mass Spectrometry. This approach allows to identify in vivo transient protein interactions, as between a kinase and its substrates. Further studies will aim at understanding the function of these substrates in the multi-branched pathway connecting PKA inhibition to Cdk1 activation.



POSTER 66

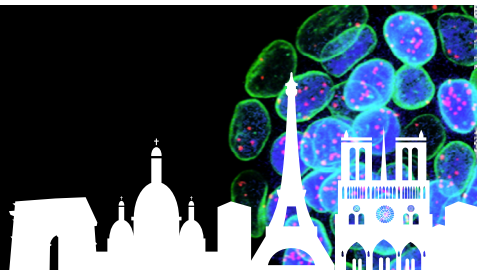
Tasmin SARKANY

Margherita Battistara, Quentin Vagne, Matthew Benton, Wolfram Pönisch, Guillaume Salbreux, Ewa Paluch

Department of Physiology, Development and Neuroscience, University of Cambridge, United Kingdom

Modelling the mechanical effect of out of plane division on tissue bending in insect gastrulation

Epithelial mechanics has been modelled extensively in 2D, however in 3D it is much less well understood. In gastrulation for example, complex cell movements in 3D lead to tissue ingression and the formation of a second layer of cells. This process has been extensively studied in Drosophila where cells internalise through the folding of an epithelial monolayer. However, the cellular processes underlying gastrulation are not conserved between species. For instance, in the Tribolium beetle, mesoderm invagination is preceded by a wave of out-of-plane cell divisions. The functional importance of these out-of-plane divisions is not understood. This raises the question: what is the mechanical role of out-of-plane divisions in Tribolium gastrulation? Answering this question using experimental techniques in vivo is challenging, as the tissue is often inaccessible to mechanical measurements and perturbations, and perturbing one factor influences many others. Here we use mathematical models, which allow us to fine-tune contributions from cell surface tensions and patterning and observe the behaviour of the tissue as the cells form layers from out-of-plane division. We use a 3D Voronoi model to investigate the effect of individual cell surface tensions and morphology on tissue shape and a continuum active surface model where we coarse grain these effects to pinpoint the importance of compressive stress and torque on the tissue mechanics of the embryo. By using these models we are able to link between the cellular and tissue scales and gain physical insight into tissue mechanics during Tribolium gastrulation.



POSTER 67

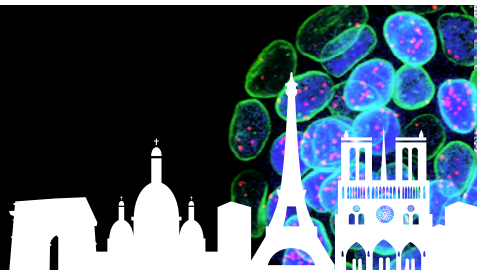
Subham SEAL

Cécile Milet, Anne-Hélène Monsoro-Burq

U1021/UMR3347, Institut Curie, Orsay, France

The epigenetic factor Prdm12 regulates neural crest EMT: a link between epigenetics, signaling and cell migration

After its induction in the dorsal ectoderm, the neural crest cells undergoes epithelial-to-mesenchymal transition and travels to various positions of the embryo, where they give rise to many different derivatives. In the recent past, although several studies have uncovered epigenetic factors that regulate neural crest development, the exact mechanisms of control are not well understood. Here, we show that Prdm12, an H3K4 methyl transferase, regulates neural crest EMT and cell migration in Xenopus laevis. Prdm12 is a PR-domain containing protein which is highly expressed in parts of the CNS and in the lateral preplacodal ectoderm, the precursor of the cranial placodes. Interestingly, using both in vivo and spatial transcriptomics approaches, we observed that Prdm12 is also expressed at low levels in the neural crest progenitors. Morpholino-mediated depletion leads to severe defects in neural crest migration in a cell-autonomous manner, and strongly affects the expression of neural crest specifiers such as Sox10. Introduction of an inducible version of Sox10 partially rescues the migration defects, which establishes an epistasis relationship. In vitro, we observed that loss of Prdm12 leads to neural crest cells being unable to detach from clusters and form single cells. When we probed further into the mechanism, we found that Prdm12 regulates the levels of N-cadherin, which is necessary for cell detachment. We also observe that Prdm12 regulates multiple components of the Wnt signaling pathway, which subsequently seem to affect N-cadherin expression. Currently, we are probing the possible relationships between Sox10, N-cadherin and Wnt signalling, and the mechanism of how Prdm12 may regulate them in order to control neural crest migration. Together, this project will help establishing novel epistasis relationships in the NC-GRN and provide a link between epigenetics, signaling and cell migration.



POSTER 68

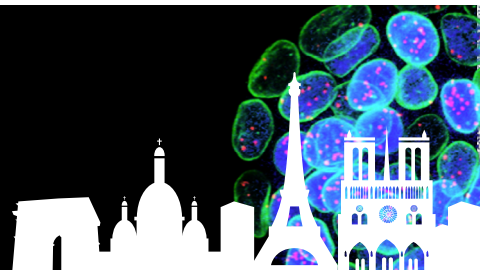
Anastasia SHIHABI

Rose Bulteau, Gaëlle Letort, Marie-Hélène Verlhac, Marie-Emilie Terret

Center for Interdisciplinary Research in Biology (CIRB), Collège de France, Université PSL, CNRS, INSERM, 75005 Paris, France

Consequences of excessive cortical tension on oocyte development

Female meiosis produces oocytes. In mammals, this process ends with two successive asymmetric divisions in size (meiosis I and II), resulting in a large haploid oocyte containing all the maternal stores required for early embryonic development after fertilization. The geometry of these divisions is controlled by cortical tension, a mechanical property dependent on the actomyosin network, affecting how soft or stiff a cell is. We previously showed that cortical tension decreases in a spatiotemporal manner after meiosis I entry, allowing the spindle to migrate along its long axis towards the closest cortex via a Myosin-II dependent pulling mechanism, resulting in an asymmetric division in size. Strikingly, mechanical defects are rather frequent in mammalian oocytes. In particular, too stiff mouse and human oocytes produce embryos that stop developing after fertilization for unknown reasons. This project aims to elucidate the consequences of excessive cortical tension on oocyte development. In order to answer this question, we engineered extra stiff oocytes by manipulating the actomyosin cortex, forcing active Myosin-II to the cortex. Our results show that too stiff mouse oocytes progress through meiosis I as successfully as control oocytes, with comparable timing and geometry of division. However, the cortex of extra stiff oocytes spontaneously polarize upon meiosis I entry, accumulating actin and Myosin-II in a flattened zone opposite as to where division will occur much later on. Directional cytoplasmic flows originate from this polarization zone, pushing inert objects such as oil droplets towards where division will occur. These flows seem to push the spindle as well towards the cortex opposite to the polarization zone, resulting in the spindle moving faster and often not along its long axis, with chromosomes misaligned just before anaphase. Other consequences such as aneuploidy, organelles distribution and fertilization efficiency are still to be explored.



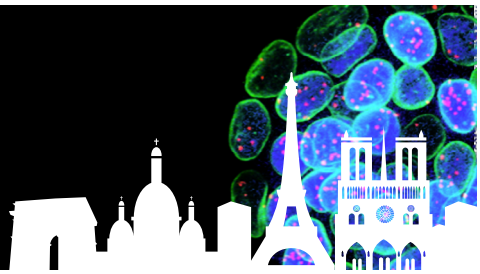
POSTER 69

Cédric SOLER

Moucaud Blandine, Elodie Prince, Elia Ragot, Yoan Renaud, Guillaume Junion, Krzysztof Jagla

Exploring tendon cell diversity and its contribution To muscle development

The musculoskeletal system consists of the assembly of distinct tissues. Among these tissues, tendons ensure the proper transmission of muscle contraction forces to the skeleton. While Drosophila melanogaster is a well-established model for understanding the cellular and molecular events involved in the conserved process of myogenesis, some studies have also highlighted common features in the development of muscle attachment sites between vertebrates and invertebrates. Here, we use the Drosophila leg system to decipher the mechanisms that control the coordinated development of tendon and muscle progenitors, which pattern the leg muscle architecture. Through transcriptomic analysis of Drosophila leg discs, we identified interacting partners between specific clusters of leg tendons and their corresponding subpopulations of myoblasts. Among these, we showed that the Amalgam (Ama)-Neurotactin (Nrt) interaction plays a crucial role in tendon-muscle reciprocal influence during development. Moreover, our data also highlighted a core genetic program common to the different clusters of tendon precursors, as well as gene expression signatures specific to each tendon, reflecting an unexpected diversity among tendon cell precursors from the early stages of development.



POSTER 70

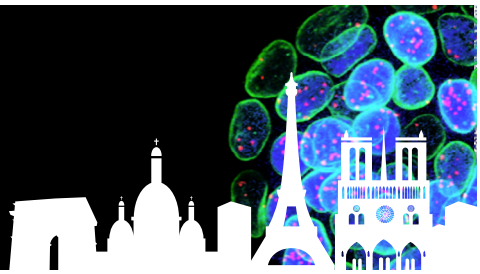
Eglantine SOUCAT

Sylvie Hudaverdian, Nathalie Prunier-Leterme, Romuald Cloteau, Gaël Le Trionnaire and Stéphanie Le Bras

L'Institut Agro Rennes-Angers INRAE IGEPP, France

Identification of asexual and sexual germarial cell identity markers during Pea aphid embryogenesis

Aphids exhibit reproductive polyphenism, which is a particular form of phenotypic plasticity. During the annual life cycle, genetically identical females reproduce asexually in spring and summer (via parthenogenesis) and sexually in autumn. At the beginning of autumn, asexual females are able to perceive and integrate the decrease in day length to eventually produce male and sexual female morphs. We hypothesize that differentiation between these three morphs occurs during embryonic development that is viviparous. This project aims to understand the cellular mechanisms involved in the differentiation of the two female morphs and to identify specific cell identity markers for the sexual and asexual ovaries. So far, no specific markers for sexual or asexual females during the embryonic stages have been identified. To fill this gap, we compared the spatio-temporal expression patterns of candidate genes in sexual and asexual ovaries. In situ hybridization demonstrated that at least five genes were specifically expressed in either asexual or sexual ovaries, in germ cells and/or somatic cells in adult and embryonic germaria. Among these genes, three patterns were notable in the two types of ovaries: i) specific expression during the first stages of embryogenesis, ii) specific expression during the last stages of embryogenesis, or iii) both. These results suggest that different genes are involved in the morphogenesis of sexual and asexual ovaries during embryonic development.



POSTER 71

Clémence THIANT

Joseph d'Alessandro, Benoit Ladoux, René-Marc Mège

Institut Jacques Monod, CNRS - Université Paris Cité, Paris, France

Transmission of front-back polarity in trains of cells

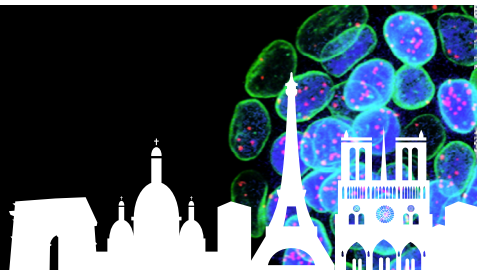
Collective cell migration is fundamental for many physiological processes such as development, but is also implicated in some pathological events like tumor metastasis.

At a single cell level, migration is first supported by the establishment of a front-back polarity, shaped by gradients of proteins and morphological changes. In a cell collective, such signals need to coordinate for efficient migration. However, despite biochemical and mechanical insights, how exactly this information of polarity is transmitted through the cell and then to its neighbor remains poorly understood.

Here, we used an optogenetic tool to activate the small RhoGTPase Rac1 at one extremity of a cell doublet, thereby defining a front. Coupled with traction force microscopy, this gives us insights of the mechanical state of the cells during migration. It led us to focus on the switch from non-activated to activated status to try to decipher more precisely how the Rac1 signal is transmitted through the single cell to the junction.

Next, we studied actin organization and dynamics as cells change direction during migration to gain understanding of what is happening within the two cells of a doublet and at the junction. In addition, we followed the evolution of molecular tension at the junction and at the extremities of doublets using an E-cadherin tension sensor.

Altogether these results suggest that cells might be more or less sensitive to polarity signals, their intrinsic state defining the response.



POSTER 72

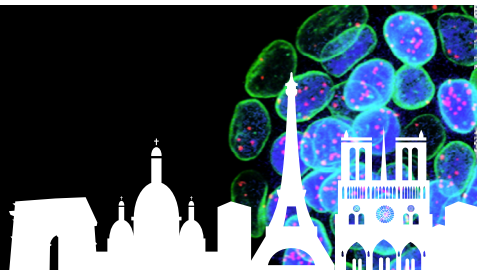
Tereza TORALOVÁ

Veronika Kinterová, Alexandra Rosenbaum Bartková, Shanjida Afrin, Andrej Susor, Radek Procházka, Jiří Kaňka

Institute of Animal Physiology and Genetics

The timing of maternal protein degradation is species-specific in mammals

At the beginning of mammalian preimplantation development all the mRNAs and proteins are of maternal origin and the embryo is transcriptionally silent. The timing of embryonic genome activation (EGA) is species-specific and varies between 2-cell stage and late 8-cell stage. The processing of maternal proteins during early mammalian embryogenesis undergoes strict rules concerning the selection of proteins and timing of degradation. Some proteins, the degradation of which is necessary for the correct course of EGA in one species, are preserved for a longer period in other species (CBX5, H1FOO...). After performing the expression analysis of selected proteins (DBF4B, TOPBP1, CDC25A, CDC6, PIASy, CBX5, TAB1), we found out that the selection for degradation seems to be driven by combination of protein sequence and embryo environment. Even protein homologs with high sequence conservation between species can be processed in a different way. Similarly, the degree of similarity in the timing of degradation does not correspond to the evolutionary relatedness of species. The timing of protein degradation is very similar in mouse and pig concerning the developmental stage in which the protein is degraded, regardless of the different timing of EGA. On the other hand, the course of protein degradation is highly distinct in quite relative species like pig and cow. Interestingly, long-term stored proteins include many proteins expressed in cell-cycle dependent manner. The localization of these proteins in preimplantation embryo (common cytoplasmic localization of otherwise nuclear proteins) suggests the possibility of switch to a non-functional state. In conclusion, the selection of maternal proteins to degradation and the timing of their degradation is clearly species-specific. Nevertheless, the precise mechanisms of these processes remains to be elucidated.
The work was supported by GAČR 23-05108S



POSTER 73

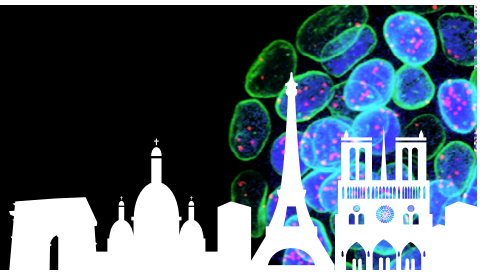
Bastien TOUQUET[1]

Clarisse Uwizeye[1a], **Sevan Belian**[1b], **Emilie Reuber**[1c], **Klemens Rottner**[2], **Isabelle Tardieux**[1]

1. Institute for Advanced Biosciences (IAB), Team Biomechanics of Parasite-Host Cell Interactions, CNRS UMR 5309, INSERM U1209, Université Grenoble Alpes, 38700 Grenoble, France.
2. TU Braunschweig Zoological Institute Molecular Cell Biology, Braunschweig, Germany
3. Present address a) CEA, Grenoble, France; b) Institut Pasteur, Paris, France; c) Max Planck, Berlin, Germany

Deciphering the dynamics interplay between the Toxoplasma invasive nanodevice and the host cell cortical cytoskeleton

The single-celled eukaryote *Toxoplasma* has evolved a morphotype called tachyzoite which is endowed with an impressive invasive capacity of most nucleated cells from a wide repertoire of homeothermic hosts, human included. Indeed, the several micron size and highly polarized cell relies on a unique actomyosin system to power active entry into target cells within only a few seconds. This rapid entry requires first the release of multi-unit protein hetero-complexes we referred as to the invasive device that within millisecond inserts in the bilayer and underneath cortex while organizing as an elastic torus, on which the parasite pulls to apply force. To fulfill such a force transmitting function and thus withstands the invasive force, the nanodevice must be stabilized into the cortical cytoskeleton but the details of this anchorage is largely elusive, in part due to the high-speed invasion process. We now tackle this enigma and have identified the main players and mechanisms that support transient anchorage, by designing a new experimental setting which slows down the invasion process and allows monitoring how the host cell actin machinery governs the anchorage process. Using fast live imaging combined with expansion microscopy and 3D modeling, and introducing a series of host cell lines deficient for the core machinery of actin polymerization, we report on a peculiar WASP-ARP2/3-actin based driven membrane protrusion that emerges at the nanodevice insertion site and powers a repulsive tube-like response of the cell when invasion is prolonged. We also identified a main contributor from the invasive nanodevice to such actin remodeling and force generation using parasite mutants and in vitro reconstitution assays. Collectively, this study uncovers the architecture of a unique microbial invasive nanodevice as a torus-like fold and its dynamics interplay with the cortical actin at the site of entry to guarantee host cell invasion.



POSTER 74

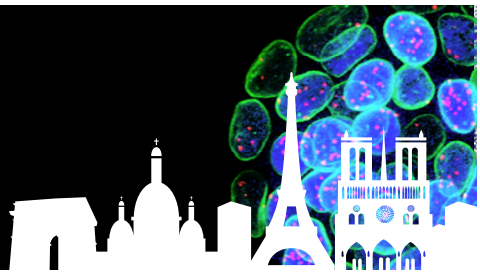
Marcos WAPPNER

Koichiro Uriu, Andrew C. Oates, Luis G. Morelli

IBioBA - MPSP - CONICET, Buenos Aires

The role of Delta-Notch in the synchronization of the zebrafish segmentation clock

Somitogenesis is a key step in vertebrate development during which a pattern of periodic segments form. These will be the precursors to repetitive tissue structures like vertebrae and ribs, among others. This pattern is thought to be an emergent phenomenon, arising from the coordination of individual genetic oscillators. Every cell in the undifferentiated tissue that will result in these somites expresses a network of self-repressing genes of the family her/hes, giving rise to a biochemical oscillator. These cells communicate the state of their oscillators to their neighbors through the Delta-Notch pathway, which enables the synchronization of the oscillations. In zebrafish in particular, the expression of the Notch ligand deltaC is regulated by Her, which activates Notch with a cyclic pattern governed by the oscillator. In the neighboring cell, activated Notch regulates the activity of the her oscillator, thus enabling communication between the states of the two oscillators, which enables synchronization. It has been shown that disrupting this pathway in embryos produces defective segmentation, which is correlated with a loss of synchrony. It has also been shown that loss-of-function mutants of another Notch ligand that is expressed during somitogenesis, DeltaD, forms defective segments. However, there is no evidence of transcriptional regulation of deltaD by the her oscillator, which prompts the question, what is its specific role in the synchronization of the oscillators?
In this work we employ a theoretical description of the components of the network and contrast predictions with published experimental results. The analysis reveals possible mechanisms through which DeltaD might be enabling the synchronization between cells, and further hints at experiments to test the different scenarios.



POSTER 75

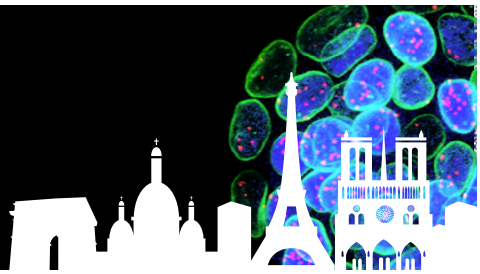
Michaela WOELK

Alex Smith, Milou Meeuse, Anca Walczak, Helge Großhans

Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

A gene regulatory network that supports organism-wide oscillatory gene expression to time development

Dynamic gene expression is at the heart of development. Yet, to build a tissue, organ or multicellular organism, the dynamics in many cells need to be coordinated. A striking example of this is seen in C. elegans larvae, where oscillations of thousands of genes can be observed at the whole animal level and across different tissues. Gene expression peaks occur in a fixed order for the affected genes, and always once per larval stage, with a ~7-hour period. Previously, we have shown that the oscillations are a result of rhythmic transcription and identified a small set of transcription factors required for rhythmic development. Yet, it has remained unknown how rhythmic transcription is achieved. Here, we characterize one of the previously identified transcription factors, GRH-1/Grainyhead, and show that it is required for oscillatory gene expression. Chromatin immunoprecipitation coupled to sequencing (ChIP-seq) combined with temporally highly resolved RNA-sequencing time courses reveals hundreds of direct GRH-1 targets and many more genes whose rhythmic expression it affects indirectly. Its direct targets include NHR-23/DHR3, another transcription factor required for rhythmic development. Genomics and quantitative time-lapse imaging data support the existence of a negative feedback loop where GRH-1 represses nhr-23 transcription, whereas NHR-23 promotes grh-1 transcription. Additionally, and at a different time scale, GRH-1 autoregulates by binding to its own promoter to repress transcription. We propose that the resulting gene regulatory network constitutes a core module of the C. elegans developmental clock that ensures proper temporal coordination of gene expression programs and developmental events to facilitate larval development.



POSTER 76

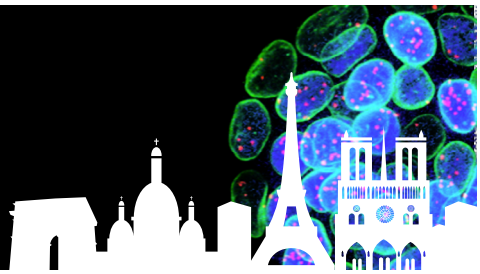
Maud WURMSER

Yvrick Zagar, Morgane Belle, Xavier Nicol

Institut de la vision, Sorbonne Université, Paris, France

Compartmentalized cAMP signaling modulates HUVEC migration in response to repulsive cues

Cues from the environment dictate cellular behaviors, including cell migration, that guides cells from their birth place towards a precise target location. To control their migration, cells detect attractive and repellent signals secreted in the environment. These cues are then processed and transduced into a mechanical response that leads to cell movement. Second messengers including cAMP, cGMP and calcium are central for signal transduction downstream of extracellular cues to translate them into a variety of cellular behaviors. However, how these ubiquitous signaling molecules can achieve specificity for their wide range of downstream effectors is elusive. We are investigating the features of second messenger signals induced by the repellent molecules Slits and ephrinAs, in a cell migration context, using human umbilical vein endothelial cells (HUVECs). Using wound healing and invasion assays, we first validated that HUVEC migration in vitro is sensitive to Slit2 and ephrinA1. We are now investigating the subcellular compartmentalization of second messengers as a mean to reach specificity for their downstream effectors. Our data using FLIM-FRET imaging suggest that Slit2 and ephrinA1 induce local cAMP signaling in small membrane compartments. To validate the role of local signaling in HUVEC migration, we are conducting in vitro assays using cells expressing a cAMP scavenger, thus enabling to buffer cAMP in different sub-cellular compartments.



POSTER 77

Iskra YANAKIEVA

Wolfram Pönisch*, Baptiste Vauléon, Belle Sow, Alex Winkel, Guillaume Salbreux, Ewa Paluch

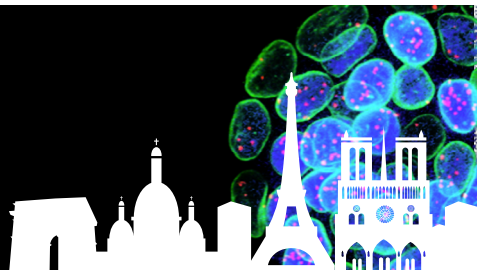
Department of Physiology, Development and Neuroscience, University of Cambridge, United Kingdom
**Co-First Author*

Role of cell shape fluctuations in cell spreading during epithelial-to-mesenchymal transition

Development entails series of cell state transitions, often coupled with cell shape changes. Studies suggest that, similarly to gene regulatory networks controlling cell state transitions, cell shape changes can be described as transitions between attractors. While gene expression changes driving state transitions have been extensively studied, how cells dynamically transition between shape attractors, and what molecular and mechanical changes underlie these transitions remains unclear.

We investigate cell shape dynamics in 3D during epithelial-to-mesenchymal transition (EMT), a key process in development and homeostasis, in which epithelial cells gain increased motility and spread morphology. To this end, we employ live-cell imaging and morphometric analysis. Our approach utilizes spherical harmonic descriptors to represent 3D shape trajectories in a low-dimensional morphospace. By modelling shape dynamics as a Langevin process, we infer the underlying stochastic morphodynamics. Our findings reveal that EMT-associated cell shape changes result from a change in morphospace potential upon EMT induction, indicating that the process can be described as a transition between morphospace attractors. Furthermore, cell shape fluctuations peak at the time of cell spreading suggesting that noise may facilitate the transition between attractor states. We dissect the origin of cell shape fluctuations using molecular perturbations of membrane and actin dynamics. Our findings suggest that efficient cell spreading in EMT requires a change in the balance of actin protrusivity, contractility, and membrane tension. To study actin reorganisation throughout EMT with high temporal and spatial resolution, we use structured illumination microscopy and lattice light-sheet microscopy.

Overall, by combining quantitative imaging, morphometric analysis and stochastic modelling with biomechanical measurements and molecular perturbations, our project creates a comprehensive understanding of the physical and biomolecular basis of EMT-associated cell shape change. Moreover, the description of cell shape changes using our stochastic inference approach provides a novel conceptual framework for investigations of cell morphology in general.



POSTER 78

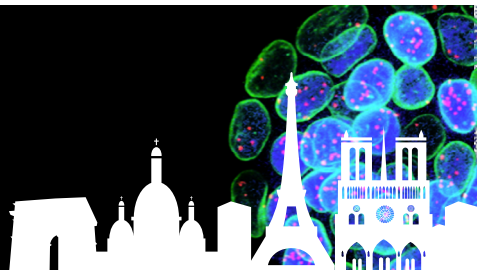
Hitoyoshi YASUO

Rossana Bettoni, Sophie de Buyl, Geneviève Dupont, Clare Hudson, Cathy Sirour, Géraldine Williaume

Sorbonne University CNRS/UMR7009, Villefranche-sur-Mer, France

Cell geometry, signal dampening, and a bimodal transcriptional response underlie the spatial precision of an ERK-mediated embryonic induction

We address the fundamental problem of how cells sense their position in a developing embryo to make cell fate decisions. Gradients of signalling molecules (=morphogens) have long been postulated to mediate such positional information. However, the morphogen system is conceptually inadequate when small groups of cells are concerned, as in the case of early embryogenesis of many invertebrates. Short-range or membrane-bound signalling molecules that operate only between neighbouring cells represent an alternative signalling strategy. In this context, the contact area with signal-emitting cells could play a critical role in controlling the signal strength in responding cells. Ascidian embryos may represent an extreme case of such a geometric control of cell induction. Embryos of this invertebrate chordate develop with stereotypic cell division patterns, such that cells adopt distinct developmental trajectories following well-documented cell lineages. We focus on the initial step of neural induction whereby precisely two out of eight ectoderm cells are induced as neural precursors. We have addressed how the spatial precision of this cellular induction is attained. Each cell in the ectodermal sheet exhibits a level of ERK activation that mirrors its area of surface contact with underlying FGF-expressing mesendoderm cells, with the neural precursors having largest areas of cell contact. This graded activation of ERK is converted into the threshold transcriptional response of an immediate-early gene, Otx, which is activated only in the neural precursors. Critical for this spatial precision is ephrin-Eph signals. A membrane-anchored ephrin ligand is expressed in ectoderm cells themselves and acts to dampen ERK activation levels across the ectoderm, maintaining levels of ERK below the critical threshold in non-neural ectoderm cells. Thus, ectoderm cells interpret antagonistic FGF and ephrin signals based on their unique geometries and adopt neural (Otx-on) or epidermal (Otx-off) fate via a threshold response.



POSTER 79

Mari W. YOSHIDA

Jesús M. López-Gay, Yohanns Bellaïche

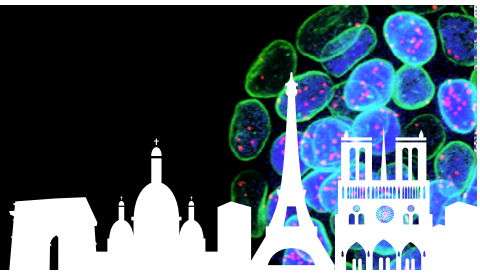
Institut Curie, Paris, France

Deciphering the temporal control of mechanosensing during development

Forming a functional tissue requires temporal control of its morphogenesis. Given that morphogenesis relies on the response of cells to mechanical forces, it is essential to determine whether and how cell mechanical responses vary over time during development. While an extensive body of work has outlined how mechanical forces control tissue deformation, an understanding of how the mechanical response of cells changes over developmental time is still lacking.

A key response of cells to mechanical forces entails the remodeling of the actomyosin cytoskeleton and the activation of the Hippo/YAP pathway. For instance, in the initial phase of Drosophila pupal notum morphogenesis, morphogenetic forces induce the formation of apical actomyosin stress fibers (SFs) in an apical cell area-dependent manner. SFs are anchored to adherens junctions and modulate cell proliferation and apoptosis by activating the Hippo/YAP pathway. Intriguingly, while mechanical stress remains high, this first phase of mechanosensing is followed by a second phase in which cells lack SFs.

To understand how the temporality of this mechanical responses is achieved, we first conducted a detailed characterization of SF dynamics and compared them between the two phases of tissue development. Interestingly, we found that the nucleation rate of SFs decreased in the second phase. We therefore aimed to understand how the nucleation rate is modulated over time. Towards this goal, we combined experiments and modeling to perform a comprehensive exploration of the role of cell geometry, Hippo/YAP feedback and systemic signaling in the temporal regulation of mechanosensing. Our work is expected to delineate how cell mechanics and developmental timing are coordinated during epithelial morphogenesis.



POSTER 80

Chenxi ZHOU

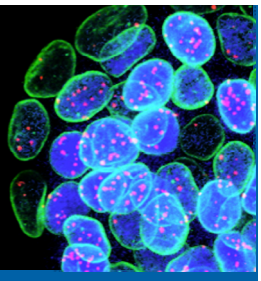
Laura Medina Cuadra, Méghane Sittewelle, Vincent Kappes, Anne H. Monsoro-Burq

Université Paris Saclay, CNRS UMR 3347, INSERM U1021 & Institut Curie Research Division, Orsay, France

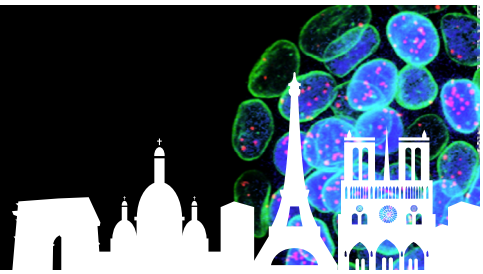
The glycolysis regulators PFKFB3 and PFKFB4 regulate cell migration in melanoma

Cell migration is promoted by numerous signaling pathways and processes, including Ras/phosphoinositide 3-kinase (PI3K) /Akt pathways and enhancement of aerobic glycolysis. However, the crosstalk between signaling and metabolism is still poorly understood. PFKFB1-4, are classical glycolysis regulators and highly express in multiple cancer cells[1]. Recently, our team found a non-canonical function of PFKFB4 as an AKT signaling regulator also necessary for cell migration both in neural crest and human melanoma[2,3,4]. In human melanoma, PFKFB4 directly interacted with ICMT and promoted the post-translational modification of Ras by ICMT, which is necessary for Ras/PI3K/AKT signaling activation[4]. Our team is expanding the study to PFKFB3, and comparing differences between PFKFB4 and 3. Interestingly, we found PFKFB4 localized in the cytoplasm, while PFKFB3 was predominantly located in the nucleus. Both PFKFB3/4 were necessary for melanoma cell migration, but the effect of PFKFB4 on cell migration was happening independently of glycolysis and was stronger/more consistent than that of PFKFB3. PFKFB4 depletion did not influence glycolysis levels while decreasing PFKFB3 did. The AKT pathways can regulate epithelial to mesenchymal transition transcription factors (EMT-TFs), acting via GSK3β which regulates SNAIL stabilization[5]. As PFKFB4 regulates AKT signaling, we examined how PFKFB4 knockdown affected EMT-TFs: lowering PFKFB4 resulted in decreased SNAI2 expression in melanoma cells, while PFKFB3 knockdown rather slightly increased TWIST1. Our study revealed a new function of PFKFB4, and indicated that PFKFB family members might function differently in cancer metastasis.

[1] Kotowski K., et al., Cancers (Basel), 2021 Feb 22;13(4):909.
[2] Pegoraro, C., et al., Nat Commun, 6, 5953 (2015).
[3] Ana Leonor Figueiredo., et al., Development, 2017; 144 (22): 4183–4194.
[4] Méghane Sittewelle., et al., Life Science Alliance, 2022
[5] Jin Young Kim., et al., The FEBS Journal, 279 (16): 2929-2939, 2012



FRIDAY, OCTOBER 18TH
2:00 - 3:45PM
POSTER SESSION 2



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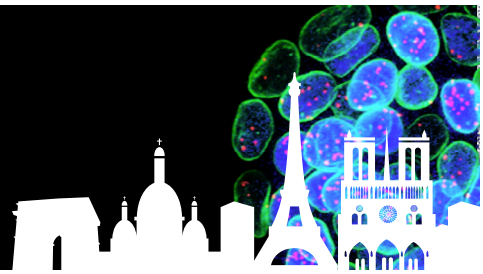
82	ALIÉ	Alexandre	Cellular and molecular characterization of stolonial budding in the planktonic tunicate Thalia democratica (Thaliacea, Salpida)
83	ALPAR	Lale	Keeping it together: How Toll-2 shapes the Drosophila neck
84	ALVES	Marine	Evolution of Arf small G proteins and membrane trafficking establishment
85	BALAVOINE	Guillaume	Stem cells and evolution
86	BANOS	Ghislain	Engineered 3D muscle constructs for modeling Duchenne Muscular Dystrophy and high-throughput screening of novel therapeutics
87	BARDOT	Boris	Pax3, a master Neural Crest specifier, regulates Geminin expression
88	BASU	Soham	Extracellular matrix modulates morphogenesis across scales in a sea anemone
89	BEAUJEAN	Nathalie	Viable chimeric rabbits with a high contribution of induced pluripotent stem cells
90	BEREZENKO	Anastasiia	The role of parentally provided RNAs in zebrafish transgenerational thermal tolerance.
91	BLEUZEN	Anaïs	Human engineered skeletal muscle derived from iPSC for the modeling of neuromuscular disorders and the development of a screening cellular platform
92	BORENSZTEIN	Maud	X-chromosome reactivation in development
93	BORGHI	Nicolas	Epithelial density controls cell migration through a Focal Adhesion-nucleus mechanotransduction pathway
94	BROU	Christel	Proteomic landscape of tunneling nanotubes reveals CD9 and CD81 tetraspanins as key regulators



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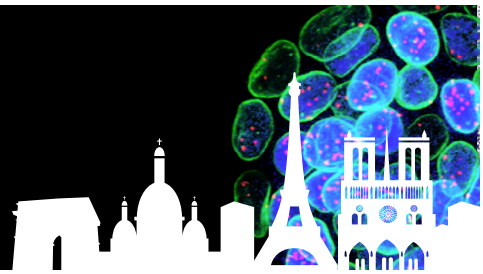
96	CADART	Clotilde	Polyploidy in Xenopus lowers metabolic rate by increasing cell size
97	VAN WESTENDORP	Demi	Notch signalling: A new player in the inflammation/regeneration coupling
98	CHANET	Soline	Impact of Confinement on Germ Cells Activity
99	COLLINET	Claudio	Endocytosis imparts regionalized sensitivity to uniform ligand-mediated activation of contractility
100	COUX	Rémi-Xavier	How to make Primitive Endoderm: a tale of pioneer transcription factors and fragile nucleosomes
101	CROZET	Flora	Dissecting ERK mechanotransduction in living epithelia
102	DANG	Thanh Mai Julie	Understanding the role of the tubulin code on organism-wide functions
103	DE GIORGIO	Ettore	Tissue size adjustment during morphogenesis in Drosophila melanogaster
104	DE HAAN	Diede	Reconstructing the ancestral architecture of animal cells
105	DELFINI	Marie-Claire	RIPOR2 promotes multinucleation of melanoma cells downstream of the RAS/ERK oncogenic pathway
106	DELPIERRE	Julien	Exploring the scaling of morphogenetic processes with animal size.
107	DUBEY	Sushil	Mechanical stresses govern myoblast fusion and myotube growth
108	DUFOUR	Sylvie	Non-Canonical Function of Glutaminase Cooperates with Wnt Signaling to Drive EMT in Neural Crest Cell
109	DUFOURD	Joey	Identification of TELS1, a telomere stabilization protein in stem cells
110	FAGOTTO	Francois	The cellular and biophysical basis of Xenopus mesoderm intercalation



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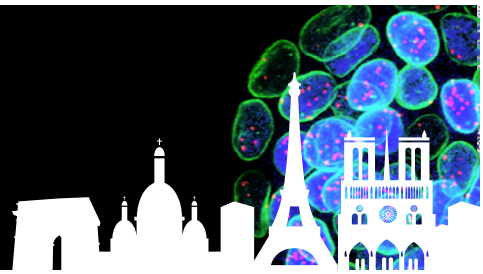
111	FIGUEIREDO	Catarina	How developing tissues compensate for unwanted cell death: Lessons from the zebrafish retina
112	FISCHER	Evelyne	Unequal mitochondrial segregation during mitosis initiates asymmetric fate choices in neural stem cells progeny
113	FUHS	Thomas	Structure, mechanics, and dynamics of biological systems studied by AFM
114	GATTOBIGIO	Futura	NODAL signaling is required for blastocyst development in the mouse
115	GAUDIN	Raphael	Characterization and identification of new antiviral molecules and targets associated to the endoplasmic reticulum
116	GÉLIN	Matthieu	Development of a synthetic hydrogel to study the invasion of glioblastoma cells
117	GOULOIS	Alison	TRIM71 RNA repressor activity in stemness: insights into congenital hydrocephalus
118	GREEN	David	Relative contributions of positional information, Notch signaling and tissue mechanics in Neuroblast specification in the early Drosophila embryo
119	INFANTE	Elvira	Mechanoregulation of glioblastoma cell survival
120	JOUNEAU	Alice	A conserved 3D model of epiblast morphogenesis in mammals
121	JOURNOT	Robin	Symmetry breaking and self-organization of bi-layered epithelia are orchestrated by conserved signals during development and regeneration
122	KAIVOLA	Jasmin	Mechanical stimulation reverses oncogenic properties in ECM-enriched vocal fold cancer
123	KHORUZHENKO	Antonina	Bidirectional ion transport plays an important role in the regulation of thyroid intrafollicular lumen size
124	KURZAWA	Laëtitia	Contractile forces direct the chiral swirling of minimal cell collectives



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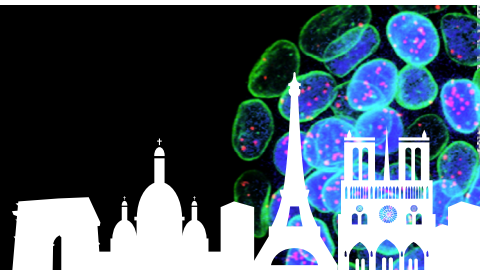
126	LÉGER	Joseph	The transcription factor MF is necessary and sufficient to specify the ILC fate in lymphoid progenitors
127	LOPEZ-GAY	Jesus	Mechanosensing buffers rapid junction length changes in epithelial tissues.
128	MALLART	Charlotte	Regulation and function of cytoplasmic F-actin networks in early embryos.
129	MAVRAKIS	Manos	Genetically encoded reporters of actin filament organization in living cells and tissues
130	MAYRAN	Alexandre	Cadherins modulate the self-organizing potential of gastruloids
131	MICOUIN	Adèle	PI3K/AKT signalling orchestrates ICM maturation and proper epiblast and primitive endoderm specification
132	MIGNOT	Julien	Development of therapeutic strategies for Volumetric Muscle Loss repair based on innovative hydrogels associated with human MuSC
133	MIYAZAWA	Hidenobu	Unraveling a signaling role of glycolysis in regulation of developmental timing in mammalian embryos
134	ORTICA	Sara	Establishment of the Notch3 signaling pattern within the neural stem cell population of the adult zebrafish telencephalon
135	PEREA-GOMEZ	Aitana	New insights into the initiation and maintenance of mammalian ovarian development
136	PICCIOTTO	Cara	Symmetry breaking and fate divergence during lateral inhibition in Drosophila
137	POIDOMANI	Etienne	Investigating pre-comitment in the cell fate decision of cortical progenitors
138	POSERN	Guido	Control of epithelial tissue (re-)generation by the actin-regulated transcription factor MRTF-A



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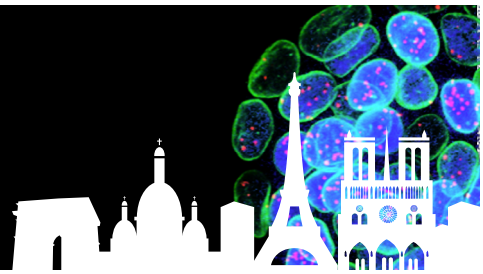
140	QUENEC'HDU	Ronan	Development and morphogenesis of the mouse extra embryonic parietal endoderm: implication of the transcription factor GATA6
141	RAASCH	Katharina	A novel in vitro tubular model to recapitulate features of distal airways: the bronchioid
142	RAFFAELLI	Ana	Extracellular matrix mechanics regulates BMP signalling through a switch in epithelial organisation in human pluripotent stem cells
143	ROSFELTER	Anne	The establishment and the mechanical role of the epithelium's simple columnar organization in the cellularizing and gastrulating Drosophila embryo.
144	SACHDEVA	Meenu	The role of stiffness and cell adhesion molecules in the process of forebrain roof plate invagination
145	SAGET	Bérénice	Deciphering the role of the amino-acid transporter SNAT8 in the developing retinal pigment epithelium and neural retina
146	SCHATKA	Magdalena	GATA4 and NKX2.5 regulate Nkx2.5 expression through a conserved enhancer element during early heart development
147	SENOUSSI	Anis	Revealing trajectory-specific transcriptional dynamics during zebrafish gastrulation using single-cell metabolic RNA labeling
148	SHAJAHAN	Shireen	Z-DNA drives Zscan4-dependent chromatin reorganization to induce and safeguard totipotent stem cell identity
149	SINGH	Anurag Kumar	MRTF-A gain-of-function in mice impairs homeostatic renewal of the intestinal epithelium



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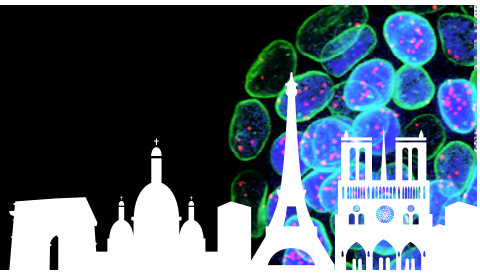
151	THOMAS	Valentine	Unraveling the interplay between Tau aggregates and autophagy-lysosomal dysfunction
152	THURNER	Larissa	From extracellular cues to building a lung-like epithelium: mechanical forces in shaping tissues
153	TOZER	Samuel	Mib1 asymmetry in neurogenic divisions relies on ciliogenesis-regulated anchors and mitotic relays
154	VEITS	Nisha	Genetic perturbations in energy metabolism affect developmental speed in the fly eye
155	VERTUEUX	Anaïs	ORP3, and the Importance of Lipid Transport Proteins in Mitosis
156	VIGNES	Hélène	Understanding the impact of intra-tumor heterogeneity found in metaplastic breast cancer on tumor progression
157	WARIN	Julie	FROM PLURIPOTENT STEM CELLS TO INTERVERTEBRAL DISC PROGENITOR CELLS: A RECONSTRUCTION BASED ON SINGLE-CELL TRANSCRIPTOMICS
158	WIEGERING	Antonia	A differential requirement for ciliary transition zone proteins in human and mouse neural progenitor fate specification
159	WODRASCKA	Fanny	Impact of RhoA-mediated contractility at the multi-cellular scale in cell extrusion process in MDCK epithelia
160	ZOLLO	Noemi	A novel RNP compartment allows mouse oocytes to adapt translational levels during late growth



POSTER 81

Neha AHUJA

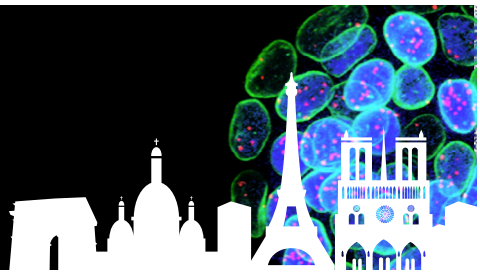
Tyler Bierschenk, Chris Chaney, Caitlin Maynard, Sophie Voss, Jinlong Lin, Kevin Dean, Thomas Carroll, Ondine Cleaver

UT-Southwestern Medical Center, Irving, Texas, USA

Building pancreatic tubes: the hippo modulator merlin is required for pancreatic development

A central goal of regenerative medicine (RM) is building organs in a petri dish, to then be used for therapeutic purposes. There is a particular need for RM strategies for the pancreas due to the prevalence of diabetes. Our goal is to uncover mechanisms of pancreatic organogenesis using murine in vivo and ex vivo approaches.

Pancreatic development relies on de novo lumenogenesis, wherein cells establish an apical membrane through vesicular trafficking and undergo apical constriction, giving rise to a microlumen. These microlumens fuse to give rise to an epithelial plexus, which harbors islet progenitor cells. How do cells coordinate the formation and fusion of lumens? We hypothesized that mechanical stimuli arising from apical constriction during lumen formation acts as a cues to guide plexus formation. To test this hypothesis, we focused on Merlin, a key regulator of the Hippo pathway, which senses mechanical cues. We conditionally deleted Merlin from the murine pancreas and found that loss of Merlin leads to severe defects, including an expansion of ductal and endocrine cell populations, and a concomitant failure of plexus formation. To investigate the role of Merlin in microlumen formation, we utilized a 3D-sphere forming assay that enables live imaging of lumenogenesis. We found that spheres deficient in Merlin are not able to open. To evaluate the role of Merlin in establishing the apical membrane, we utilized a novel live imaging system that enables us to track individual vesicles in explant culture. Intriguingly, we found that Merlin is required to restrain vesicular trafficking. Our current work focuses on understanding how Merlin is regulated through actomyosin tension and identifying the downstream targets for Merlin in pancreatic epithelium. This work provides insight into how pancreatic tubes are built in vivo, how beta cell mass is determined, and highlights the need to consider mechanics in RM approaches.



POSTER 82

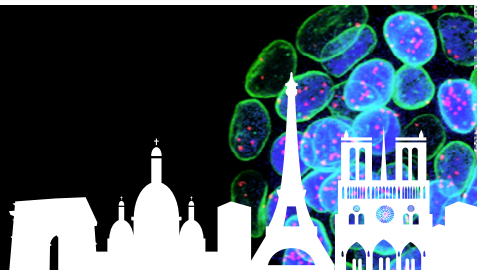
Alexandre ALIÉ

Léa Bastid-Solinas, Manon Boosten, Dany El Gharbi, Sonia Lotito, Camille Duval, Gauthier Lorillard, Théo Chavanis, Stefano Tiozzo

LBDV-UMR7009, CNRS, Villefranche-sur-mer, France

Cellular and molecular characterization of stolonial budding in the planktonic tunicate Thalia democratica (Thaliacea, Salpida)

Salps (order Salpida) belong to the tunicate subphylum, our closest invertebrate relatives, in which many species can either regenerate their body entirely and/or reproduce from strictly somatic cells. Salps are holoplanktonic tunicates that play a fundamental ecological role in the world's oceans, where they form vast seasonal swarms, or blooms. This seasonal demographic explosion is explained by a very short life cycle that includes an asexual reproduction phase, during which an individual produces hundreds of clones in just a few days. This mode of reproduction, known as stolonial budding, is achieved using a special organ called a stolon. To better understand the link between salp demography and asexual reproduction, we are studying the molecular and cellular mechanisms of stolonial budding in the species Thalia democratica, as well as the impact of seasonal environmental fluctuations on these mechanisms. We have identified several populations of stem cells residing at the base of the stolon, whose role is to provide the tissue required for the continuous production of clones. Using histology and confocal imaging techniques, we are describing how these stem cell populations are established during development. In addition, using a single-cell RNAseq approach, we are reconstructing the transcriptomic trajectories accompanying cell differentiation during budding. Finally, by combining multi-year monitoring of the Thalia democratica population with aquarium experiments, we have shown a positive correlation between the rate of budding and the abundance of salps under environmental conditions (T° and food) favourable to the formation of blooms. These results therefore begin to reveal a possible link between the environment and stem cell activity, impacting the demography of these planktonic organisms.



POSTER 83

Lale ALPAR

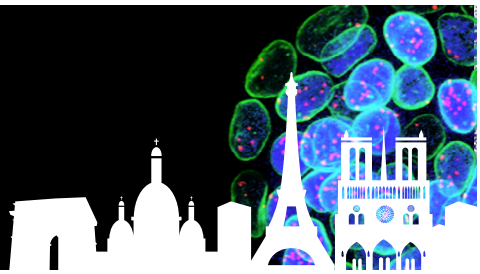
Rémi Pigache, Stéphane Pelletier, Priscillia Pierre-Ellies, Mehdi Ech-Chouni, Adrien Leroy, Floris Bosveld, Yohanns Bellaiche

Institut Curie, UMR3215/U934, Paris, France

Keeping it together: How Toll-2 shapes the Drosophila neck

Forming the 3D shape of an organism requires large scale tissue changes, such as epithelial folds. The forces driving these changes have to be sufficiently large, and accurately positioned and timed. Consequently, the tissue has to maintain its integrity and continue developing under the impact of these mechanical forces. A large scale epithelial fold forms the Drosophila neck, the position of which is defined by the homeotic gene Deformed (Dfd). We have shown that this folding is driven by the concerted action of tissue curvature and a regional tension build-up within the Dfd homeotic domain (Villedieu et al, 2023). Here we would like to address how a homeotic domain maintains its shape and integrity, while ensuring coherent movement, under increasing tension.

Tension increases gradually within the neck domain over several hours prior to neck folding, in which actomyosin distribution, cell shape and behavior are dynamic. Moreover, both cell and tissue shape appear to follow a stereotypical progression, suggesting the presence of a mechanism that control cell and tissue geometry in this phase of increasing tension. Here we describe a role for the Toll-like receptor Toll-2 in ensuring correct tissue geometry during neck morphogenesis. In the absence of Toll-2, the Dfd homeotic domain fails to assemble properly into its characteristic shape. This initial defect in homeotic domain geometry is followed by further defects in cell and neck folding dynamics, seemingly independent of the initial problems in neck assembly. This suggests a dual role for Toll-2, both prior to and during neck folding. Collectively, our results hint at an interplay between homeotic gene expression, cell adhesion and contractility, that function together to form and maintain the characteristic shape of the neck domain. Altogether, our work provides important insights on the mechanisms linking tissue identity and geometry with its subsequent morphogenesis.



POSTER 84

Marine ALVES

Mandeep Sivia, Marek Eliáš, Julie Ménétrey, Joel Dacks and Catherine Jackson

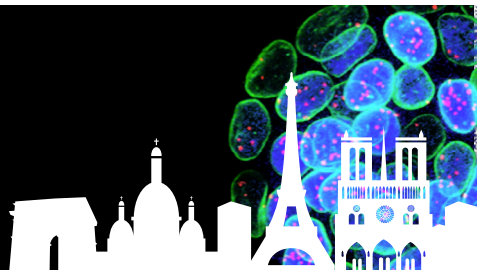
Institut Jacques Monod, CNRS, Paris, France

Evolution of Arf small G proteins and membrane trafficking establishment

How eukaryotes arose from their prokaryotic ancestors is one of the most important questions in biology. How this transition occurred remains unclear. However, it is generally accepted that eukaryotes arose from the symbiosis of an archaeum and a bacterium. The discovery of the Asgard archaea supports this theory. Archaea have proteins that were previously found only in eukaryotes. These include proteins implicated in intracellular trafficking such as the Arf GTPases. We have identified a group of prokaryotic Arf-related proteins (ArfR) in the Asgard archaea, from which all eukaryotic Arf family proteins have arisen.

Arf GTPases control numerous processes in the cell, notably vesicle trafficking, cytoskeleton-membrane interaction, and movement of organelles. The inactive GDP-bound form confines the N-terminal amphipathic helix (AH), released in the active GTP-bound form, allowing the Arf protein to bind membranes and recruit effectors to carry out downstream functions. We have shown that the Asgard ArfR proteins use the same mechanism for membrane binding as eukaryotic Arf family proteins, dependent on the N-terminal AH. Our results suggest that the common ancestor of the Asgard archaea and eukaryotes already possessed ancestral Arf proteins.

To better understand the evolution of Arf family proteins, we are using bioinformatics approaches to predict ancestral protein sequences. We are starting with reconstruction of the Arf1 and Arf6 common ancestor. Arf1 localizes and functions at the Golgi apparatus, whereas Arf6 localizes and functions at the plasma membrane. In mammalian cells and yeast, I have shown that two predicted ancestral sequences localize to both the Golgi and the plasma membrane, therefore possessing characteristics of both Arf1 and Arf6. We are exploring the domains involved in these localizations and we will express the predicted proteins in arf1 temperature-sensitive yeast strains, to determine whether they possess essential Arf1 functions in yeast. Our data provides information on the evolution of the Arf GTPase family.



POSTER 85

Guillaume BALAVOINE

Institut de Neurosciences Paris-Saclay CNRS, Paris, France

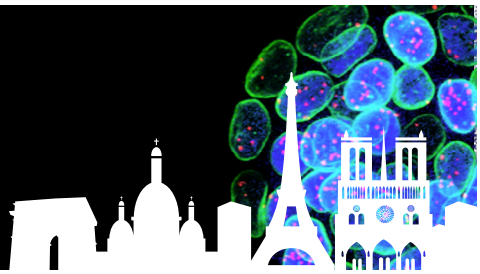
Stem cells and evolution

Adult stem cells are present in most animals and play crucial roles in growth, homeostasis, regeneration, and occasionally, asexual reproduction. These cells vary considerably in their potency and location. Some animals possess pluripotent stem cells, capable of giving rise to various cell types, while others have lineage-restricted adult stem cells, limited to producing cells within a particular lineage. The regeneration of body parts and organs in animals involves either the action of stem cells or the process of cell dedifferentiation, where specialized cells revert to a more primitive state.

In this talk, I will review the different categories of animal adult stem cells and their potential roles in growth and regeneration across diverse animal groups, from sponges to vertebrates. Understanding the variety and function of these stem cells provides insights into their evolutionary significance and practical applications in medicine and biology.

One fascinating example is the characterization of posterior stem cells in the annelid Platynereis. Through transgenesis experiments, we established the lineage restrictions of these cells. Unlike planarians, another group of spiralians, where growth is based on pluripotent stem cells, Platynereis demonstrates growth driven by lineage-restricted posterior stem cells. In contrast, regeneration in Platynereis appears to be predominantly based on cell dedifferentiation, forming a regeneration blastema—a mass of cells capable of growth and differentiation. The process of lineage restriction is also prominent in regeneration.

This talk will further discuss hypotheses about the evolution of stem cells, particularly concerning their roles in regeneration. By comparing different animal models, we can trace the development and specialization of stem cells and their pivotal functions in repairing and renewing tissues.



POSTER 86

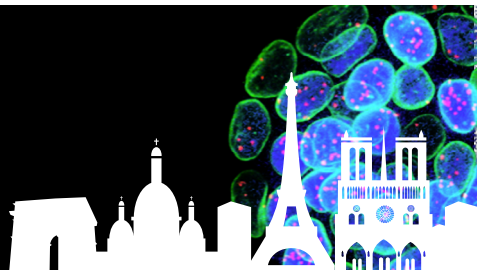
Ghislain BANOS

Anaïs Bleuzen, Teoman Ozturk, Julien Mignot, Thomas Boudou, Olivier Stephan, Frédéric Relaix, Hélène Rouard, Nathalie Didier

Univ Paris Est Créteil, INSERM, EFS, IMRB, F-94010 Créteil, France

Engineered 3D muscle constructs for modeling Duchenne Muscular Dystrophy and high-throughput screening of novel therapeutics

With the rapid advances in gene therapy and the constant need to rapidly test new drug candidates, the development of reliable in vitro skeletal muscle models reproducing the main features of muscular disorders has become essential and is therefore an active area of research in tissue engineering. We have developed innovative biomimetic hydrogels (Hd-7KP) favoring the differentiation and the fusion of muscle stem cells (MuSC), as well as the formation of unidirectionally aligned and mature myofibers in vitro. Taking advantage of the properties of these hydrogels, we developed 2 approaches to engineer skeletal muscle tissue in vitro : (1) a 3D-Monolayer Model in which MuSC-derived myofibers are generated between 2 layers of hydrogel, and (2) a 3D-Muscle Model based on PDMS-micropillar technology that enables longer cultures and force measurement by live imaging and. Using these 2 approaches, we aim to model Duchenne Muscular Dystrophy (DMD), a X-linked neuromuscular disorder caused by mutations in the DMD gene encoding Dystrophin protein, for which therapeutic options are still missing. We purified MuSC from WT or R-DMDdel52 (exon 52 deletion) rat muscles as source of cells. Using our 3D-Monolayer Model, we first observed that WT rat MuSC (rMuSC) differentiated on our hydrogels formed perfectly aligned and mature myofibers expressing adult Myh genes (Myh 1, 2, 4 and 7) and exhibiting regular striations of sarcomeric a-Actinin, peripheral myonuclei and AChR clusters. We noticed that DMD myofibers exhibited a reduced size, an increased number of branchings and diffuse AChR clusters compared to WT myofibers. By RT-qPCR, we observed a reduced expression of Ttn, Ryr1 and Myh genes, and more markedly of the fast Myh2 gene in DMD myofibers compared to WT myofibers. Using our 3D-Muscle Model, we showed that 3D-DMD muscles have impaired spontaneous contractile activity with tetanic phases. Similarly, upon electrical stimulation, 3D-DMD muscles exhibit reduced amplitude of contraction and decreased specific force compared to 3D-WT muscles. Finally, we are now investigating the effect of AAV-microdystrophin treatment on the defects observed in 3D-DMD muscles.



POSTER 87

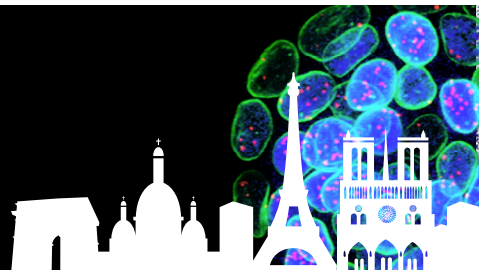
Boris BARDOT

Anthony Rabate, Chenzi Zhou, Subham Seal, Anne-Hélène Monsoro-Burq

Paris-Saclay University Institut Curie - Centre de Recherche - UMR3347/U1021, France

Pax3, a master Neural Crest specifier, regulates Geminin expression

Neural crest cells (NCC) are a multipotent stem cell population that undergo epithelial-mesenchymal transition (EMT) to migrate and invade the developing embryo, colonize various tissues and differentiate into multiple cell types such as peripheral sensory neurons and glia, melanocytes or craniofacial skeletal cells. Recently, we have described complex genetic programs at single-cell resolution, which preside over the choice of fate in the developing ectoderm and activate the EMT and migration programs. Candidate genes have been identified that may play a major role in NCC, regulating not only fate choice and migratory behavior, but also their genomic stability. One of these candidate genes codes for Geminin (GMNN). This protein is well-known to play a key role in ensuring genome stability by inhibiting DNA re-replication, notably through its interaction with CDT1. GMNN also helps maintaining the self-renewal capacity of many stem cells by regulating gene transcription via its interaction with specific transcription or chromatin remodeling factors like Brahma. Spatial transcriptomics and in situ hybridization data in xenopus indicate that GMNN is expressed in Neural Crest (NC) during key developmental events and that its expression is positively regulated by Pax3, a master NC specifier.



POSTER 88

Soham BASU[1,2]

Alexandre Paix[3], Petrus Steenbergen[1], Jonas Hellgoth[4], Suat Özbek[5], Anna Kreshuk[4], Aissam Ikmi[1]

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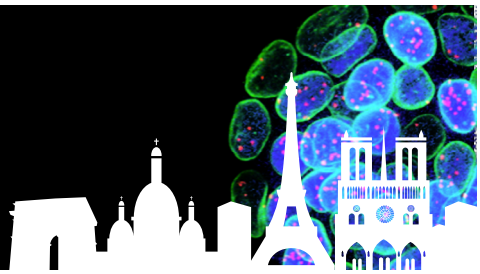
2. Collaboration for Joint PhD Degree between EMBL and Heidelberg University, Faculty of Biosciences, 69117 Heidelberg, Germany
3. Department Algal Development and Evolution, Max Planck Institute for Biology, Tübingen, Germany
4. Cell Biology and Biophysics Unit, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
5. Centre for Organismal Studies, Heidelberg University, Germany

Extracellular matrix modulates morphogenesis across scales in a sea anemone

Biological systems during development slowly transition from an environment with only intracellular communication to an environment that actively integrates the extracellular matrix (ECM), a substrate that provides the tissue a mechanochemical context. We wanted to understand how an organism builds up its ECM, and the reciprocal feedbacks it establishes with the tissue to coordinate morphogenesis. We pursued the establishment of the basement membrane in the starlet sea anemone Nematostella vectensis, owing to its simplified tissue architecture composed of outer ectodermal and inner endodermal layers. Using CRISPR-Cas9 mediated endogenous tagging of collagen IV and following up with quantitative imaging, we observe a constant local amount and thickness of the ECM across the entire body column throughout early morphogenesis. We found out that prior to gastrulation the future endodermal tissue continuously produces collagen IV. The emergent patterns in the basement membrane are directly controlled by the developing muscular organization. Using pharmacological perturbations, we established a control over ECM degradation and assembly, and found a direct effect on the dynamics of body axis elongation. Furthermore, we observed cryptic leakages at the aboral end in control and in animals with reduced ECM at the termination of axial elongation. Using further experiments, we confirmed the role of ECM in coordinating tissue rearrangements that facilitate axial elongation across organismal scales. At the aboral end, the ECM requires local remodeling while the tissue prepares an active muscular valve that permits the cryptic opening of a secondary opening at high internal pressure. Our findings shed light to intrinsic tissue-matrix feedbacks that help modulating morphogenesis across scales.



POSTER 89

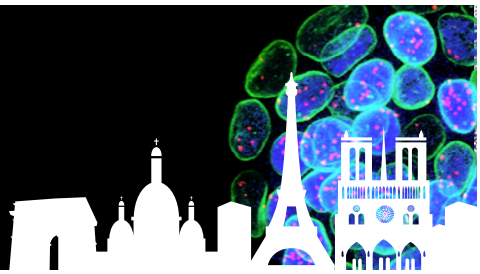
Nathalie BEAUJEAN

Florence Perold, Hong Thu Pham, Pijoff Yannicke, Marielle Afanassieff, Pierre Savatier

Stem cell and Brain Research Institute, INRAE, Bron, France

Viable chimeric rabbits with a high contribution of induced pluripotent stem cells

Viable systemic chimeras with pluripotent stem cells have never been achieved in non-rodent species. To overcome this hurdle, we used rabbits as a model system. We conducted an unbiased screening of a cDNA library encoding a panel of 36 pluripotency factors and identified KLF2, ERAS, and PRMT6. The expression of these factors enables rabbit induced pluripotent stem cells to self-renew in a culture medium free of FGF2 and supplemented with LIF, activin A, PKC and WNT inhibitors. The reprogrammed cells acquired the transcriptomic, epigenetic, and functional features of naive pluripotency, including the ability to colonize the epiblast in host embryos. Remarkably, using a subset of reprogrammed cells expressing CD75 at a high level, we produced chimeric fetuses and newborns with a high contribution from induced pluripotent stem cells in all major organs. Additionally, we successfully generated chimeric male and female young rabbits. These results provide the first demonstration of viable chimeras in a non-rodent species, paving the way for the generation of new disease models with complex genetic traits.



POSTER 90

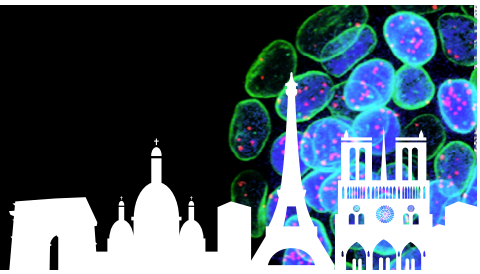
Anastasiia BEREZENKO

Dragan Stajic, Irene Adrian-Kalchhauser

Institute for Fish and Wildlife Health, Vetsuisse Faculty, University of Bern, Länggassstrasse 122, 3012 Bern, Switzerland

The role of parentally provided RNAs in zebrafish transgenerational thermal tolerance

Non-genetic inheritance (NGI) is the inheritance of alterations in gene expression without changes in the underlying DNA sequence. NGI has been observed in a wide range of animal species and even in humans, has been postulated to facilitate adaptation to rapidly changing conditions, and is recognized as a key factor in a population's health.
Among the various factors involved in NGI, RNA plays a particularly interesting role. Maternally provided RNA orchestrates the early development of numerous species including vertebrates, and paternally provided RNA has been shown to mediate stress phenotypes. However, the precise role of maternal and paternal RNAs in epigenetic inheritance during early development and their impact on further adaptation to changing environmental conditions remains unknown.
We study the response of parental RNA contributions in zebrafish with temperature as a stimulus. We investigate the molecular response of fish to heat at the level of paternal and maternal RNA, as well as the physiological response of fish to heat experienced by their parents, and then attempt to establish functional links between the two responses. We want to understand which regulatory pathways and gene regulatory mechanisms are involved in NGI in fish, how they affect offspring behavior and physiology, and for how long parental exposures remain transmittable.



POSTER 91

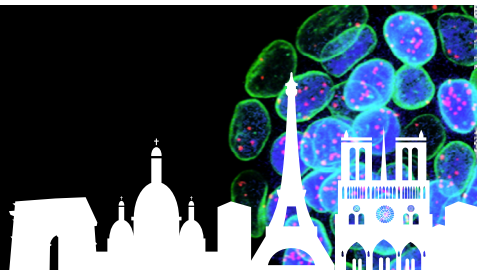
Anaïs BLEUZEN

Ghislain Banos, Teoman Ozturk, Julien Mignot, Hélène Rouard, Frédéric Relaix, Nathalie Didier

Univ Paris Est Créteil, INSERM, EFS, IMRB, F-94010 - Créteil (France)

Human engineered skeletal muscle derived from iPSC for the modeling of neuromuscular disorders and the development of a screening cellular platform

Rapid advances in gene therapy and drug discovery for the treatment of neuromuscular disorders have exacerbated the need to develop standardized and miniaturized cellular platforms reproducing the structural and functional characteristics of native skeletal muscle. Accordingly, important progress has been made in the field of skeletal muscle engineering, notably by moving from 2D models to more sophisticated 3D models, combining myogenic cells with biomaterials. For this purpose, human induced pluripotent stem cells (hiPSC) are of great interest, since they can be easily amplified, unlike muscle stem cells (MuSC), they give access to cells carrying various human disease genetic mutations and allow the engineering of isogenic models. However, to date, protocols for myogenic differentiation of hiPSC remain suboptimal, leading to poor enrichment of myogenic cells, and immature progenitor cells with reduced fusion capacity. Our lab has developed innovative hydrogels that greatly promote MuSC fusion and enable the engineering of 3D muscle constructs with highly mature and organized myofibers in vitro. Taking advantage of these hydrogels, we are now seeking to transfer this technology to the production of human 3D muscle from hiPSC. For this purpose, we successfully differentiated 3 hiPSC lines derived from 3 different cell types (Fibroblasts, PBMCs and Myoblasts) into myogenic progenitors. In line with the literature, we obtained variable levels of myogenic cell purity, evidenced by the proportion of CD56, CD29, PAX7 and MYOD positive cells. Importantly, we observed that flow cytometric purification of CD56+ cells considerably enriched our cultures in myogenic progenitors, thus improving the fusion index. Lastly, we noticed that differentiation of hiPSC-derived myogenic progenitors on our hydrogels significantly improved their fusion efficiency and the maturation of the myofibers obtained. Given these encouraging results, our objective is to generate 3D human muscles to model neuromuscular disorders, such as Duchenne Muscular Dystrophy, and provide high-throughput screening platforms.



POSTER 92

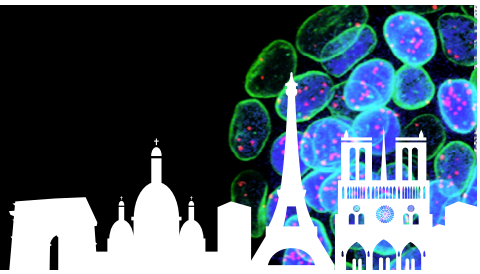
Maud BORENSZTEIN

Clara Roidor, Yolanda Moyano Rodriguez, Laurène Syx, Christel Picard, Karim Chebli

IGMM, Université of Montpellier, CNRS, Montpellier

X-chromosome reactivation in development

In mammals, the formation of gamete precursors, the primordial germ cells (PGCs), leads to the repression of the somatic program and the expression of germline-specific genes, accompanied by a profound epigenetic remodeling. The reprogramming includes: genome-wide demethylation, important redistribution of histone marks, erasure of the genomic imprints, and, in females, X-chromosome reactivation.
The inactive X chromosome (Xi) undergoes reprogramming through the loss of Xist long non-coding RNA coating, followed by the erasure of repressive chromatin marks and biallelic expression of X-linked genes. Despite this knowledge, little is known about the gene-activation dynamics and the mechanisms involved during Xi reactivation in vivo. To explore the chromosome-wide kinetics of Xi reactivation, we are using in vivo single-cell allele-specific RNAseq during PGC development. We show that X-linked genes are sequentially activated as it was previously described for the inner cell mass of the blastocyst and iPSCs but with different dynamics and requirements. In PGCs, we saw a reactivation dependency on Xist RNA loss, repressive chromatin marks, and genomic location.
We are now performing further explorations both in vivo and in vitro to better understand the mechanisms underlying Xi reprogramming in the context of female development. Together, these investigations open up the way for a better understanding of the in vivo requirements for epigenetic reprogramming in general.



POSTER 93

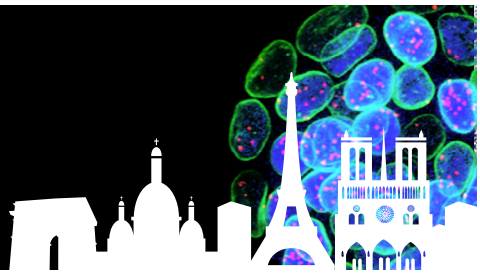
Nicolas BORGHI

Louis Laurent*, Thomas Germier, Helena Canever, Nicolas Audugé, Philippe Girard, François Sipieter

Institut Jacques Monod, CNRS, Paris, France
**First Author*

Epithelial density controls cell migration through a Focal Adhesion-nucleus mechanotransduction pathway

The perception of cell density within a cohesive tissue is thought to underlie the regulation of tissue growth, homeostasis and regeneration in multicellular organisms. However, the mechanisms by which cells sense and adapt their behaviour to their density within the tissue remain largely unknown.
To address this question, we used genetically encoded biosensors of protein mechanics and enzymatic activity, genetic and pharmacological perturbations and quantitative fluorescence microscopy on cultured model epithelia to study mechanotransduction pathways downstream of cell density.
We found that epithelial cells respond to decreased density by increasing the size of their focal adhesions, leading to mechanical relaxation of the mechanotransducer Vinculin and release of its competitive binding with the Focal Adhesion Kinase (FAK) and the Extracellular Signal-Regulated Kinase (ERK). As a result, FAK can directly bind and activate ERK within a cytoplasmic complex. Cytoskeletal tension applied to the LINC (Linkers Of the Nucleoskeleton and Cytoskeleton) complexes then facilitates Importin-7-dependent nuclear translocation of the two kinases.
In the nucleus, ERK contributes to chromatin decompaction and post-translational modifications. In addition, the low density favours translocation to the nuclear envelope of the mechanosensitive phospholipase PLA2, an ERK target that is phosphorylated in proportion to the nuclear localization of ERK. Finally, PLA2 activity promotes cell migration within the epithelium.
Overall, our results support a model in which epithelial cell density controls cell migration via a pathway involving ERK and PLA2 and a combination of mechanically gated interactions and activities from adhesion complexes to the nuclear envelope.



POSTER 94

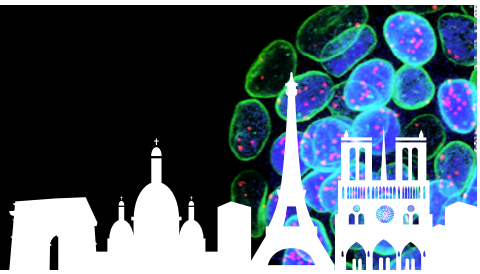
Christel BROU

Roberto Notario Manzano*, Thibault Chaze, Eric Rubinstein, Esthel Penard, Mariette Matondo, Chiara Zurzolo

Institut Pasteur
**First Author*

Proteomic landscape of tunneling nanotubes reveals CD9 and CD81 tetraspanins as key regulators

Tunneling nanotubes (TNTs) are open actin- and membrane-based channels, connecting remote cells and allowing direct transfer of cellular material (e.g. vesicles, mRNAs, protein aggregates) from cytoplasm to cytoplasm. Although they are important especially in pathological conditions (e.g., cancers, neurodegenerative diseases), their precise composition and their regulation were still poorly described. Here, using a biochemical approach allowing to separate TNTs from cell bodies and from extracellular vesicles and particles (EVPs), we obtained the full composition of TNTs compared to EVPs. We then focused to two major components of our proteomic data, the CD9 and CD81 tetraspanins, and further investigated their specific roles in TNT formation and function. We show that these two tetraspanins have distinct non-redundant functions: CD9 participates in stabilizing TNTs, whereas CD81 expression is required to allow the functional transfer of vesicle in the newly formed TNTs, possibly by regulating docking to or fusion with the opposing cell.



POSTER 95

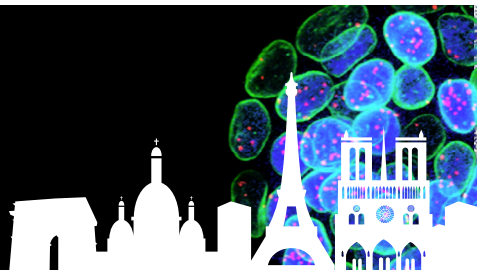
Stéphane BRUNET

Adrian Candelas*, Benoit Vianay, Matthieu Gelin, Lionel Faivre, Jerome Larghero, Laurent Blanchoin, Manuel Théry

Human Immunology, Pathophysiology, Immunotherapy, INSERM Unit 976, Institut de Recherche St Louis, AP-HP, Hôpital Saint-Louis, Université Paris Cité. Paris, France
**First Author*

Heterotypic interactions promote asymmetric division of human hematopoietic stem and progenitor cells

Homed within the bone marrow, Hematopoietic Stem and Progenitor Cells (HSPCs) can self-renew or differentiate to give rise to all cell types of the hematopoietic system. HSPC can undergo asymmetric division, a key process in stem cell biology. Nevertheless, the external cues of the microenvironment or niche that drive these divisions have not been identified. Using engineered microwells as "minimalist niches", we here show that heterotypic interactions with specific stromal cells do promote asymmetric division of human HSPC. Upon interaction in interphase, HSPCs dramatically polarize with the centrosome, the Golgi apparatus, and lysosomes positioned close to the site of contact. Subsequently, during mitosis, the spindle is oriented perpendicularly to the plane of contact. The division gives rise to siblings with unequal amounts of lysosomes and of CD34 differentiation marker. Such asymmetric inheritance generates heterogeneity in the progeny, which is likely to be a key contributor to the plasticity of the early steps of hematopoiesis.



POSTER 96 & FLASH TALK

Clotilde CADART

Juliane Bartz, Gillian Oaks, Martin Ziyuan Liu, Rebecca Heald

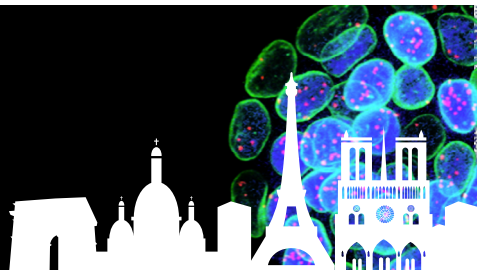
Institut Cochin, Inserm U1016, Paris, France

Polyploidy in Xenopus lowers metabolic rate by increasing cell size

Although polyploidization is frequent in development, cancer, and evolution, impacts on animal metabolism are poorly understood.

We generated triploid Xenopus laevis embryos and showed that triploid tadpoles are made of fewer, larger cells than diploids and consume oxygen at a lower rate. To understand the underlying basis of such decrease, we developed a mathematical framework to quantify the energy budget of tadpoles and combined it with quantitative measurements of the energy allocated to proliferation, growth, and maintenance. We show that treatments altering biosynthesis pathways and plasma membrane ionic pumps such as the Na+/K+ ATPase abolish the metabolic difference across ploidies. We propose that the increase in cell size in triploids causes a decrease in total cell surface area and a reduction of costs associated with production and activity at the plasma membrane which explains the overall lower metabolic rate. Crucially, comparison of three Xenopus species that evolved through polyploidization reveals that metabolic differences emerge in development only once cell size scales with genome size. Thus, cell size increase, not ploidy or genome size, causes the reduction in embryo metabolic rate.

Ongoing work now investigate the connection between energy expenditure, ploidy, and cell size from single cells to whole-embryos.



POSTER 97

Demi VAN WESTENDORP[1]

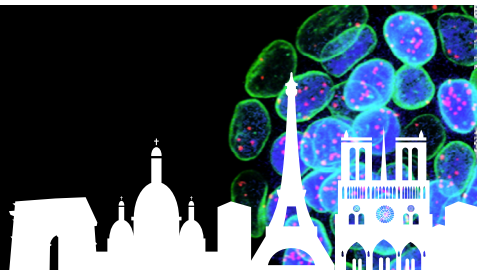
Xavier Guillonneau[2] , Patrick Pla[1]*, Muriel Perron[1]*

1. Institut des Neurosciences Paris-Saclay (NeuroPSI), France
2. Institut de la Vision, France

Notch signalling: A new player in the inflammation/regeneration coupling

Mammals have limited retinal regenerative capacity compared to fish and amphibians where Müller cells are the main source of stem cells in the adult retina. The neuroinflammatory response controlled by microglia has been reported as a regulator of Müller cell-derived regeneration. However, the signalling pathways involved in the inflammation/regeneration coupling remain elusive. The Notch pathway plays a role in Müller cell-derived regeneration in the fish and chick but is less understood in mammals. Recent studies have focused on the cell-autonomous role of Notch signalling in Müller cells, and have neglected the possible indirect role of Notch in microglia on Müller cell proliferation.

Hence, we sought to characterise the Notch pathway within retinal microglia and determine its role in inflammation-dependent Müller cell proliferation. Using immunomagnetic cell separation, we confirmed that microglia in the mouse retina express components of the Notch pathway which are modulated upon injury in an ex vivo model of degeneration. We also modulated either Notch or inflammation and analysed the effect on one another. We discovered the presence of a negative feedback loop. Our data suggest that: the Notch pathway has an anti-inflammatory effect and inhibits Müller cell proliferation. Reciprocally, pro-inflammatory cytokines would inhibit Notch gene expression. Altogether, our results support a model in which the Notch pathway inhibits the inflammatory response required for Müller cell-dependent retinal regeneration.



POSTER 98

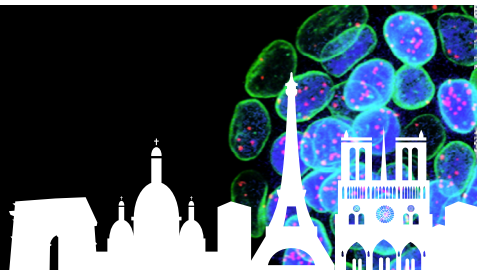
Soline CHANET

Jean-René Huynh

Center for Interdisciplinary Research in Biology (CIRB), College de France, CNRS, INSERM, Université PSL, Paris, France.

Impact of confinement on germ cells activity

In all animal species, development of the female gamete requires the formation of a structure called ovarian follicle in mammals, where the germ cells are surrounded by a layer of somatic cells. In Drosophila melanogaster the functional equivalent of the ovarian follicle is an egg chamber. Egg chambers are continuously produced by the germarium, a structure located at the anterior of the ovaries that contains both germline stem cells and somatic stem cells. Within the germarium, a group of 16 interconnected germ cells is surrounded by a layer of somatic cells leading to the individualization and budding of a new egg chamber. This morphogenetic process is called encapsulation. Recently, we showed that germ cells are not passive but actively generate cortical contraction waves during encapsulation. A defect in this cortical contractility leads to defects in the formation of egg chambers. We are now investigating the mechanisms regulating cortical activity in germ cells during encapsulation. It has recently been shown in a wide variety of eukaryotic cells that physical confinement can be an essential factor for inducing cortical contractility and amoeboid-like differentiation (with appearance of blebs). We are currently investigating whether the germarium is a confined environment and whether the confinement of germ cells by the somatic cells which surround them at the time of encapsulation, acts as a mechanical signal to trigger and/or maintain their cortical activity. In favor of this hypothesis, preliminary results indicate that, when germaria are dissociated, germ cells isolated from somatic cells round up and their cortical contractility is greatly reduced. When confinement is artificially restored, cortical contractility reappears in germ cells.



POSTER 99

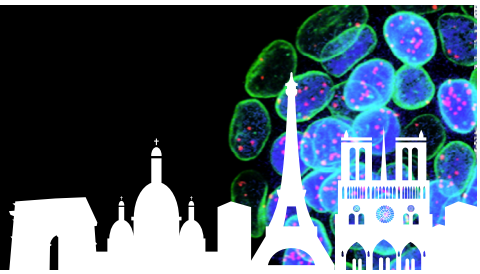
Claudio COLLINET

Gayatri Mundhe*, Valentin Dunsing, Jean-Marc Philippe, Élise Da-Silva & Thomas Lecuit

Institut de Biologie du Développement de Marseille, Marseille, France.
**First Author*

Endocytosis imparts regionalized sensitivity to uniform ligand-mediated activation of contractility

Tissue morphogenesis is driven by patterned active forces, such as mechanical tension due to actomyosin contractility. Patterns of contractility are either controlled by regionalized biochemical cues or can emerge as self-organized through mechanochemical feedback on contractility and cell-ECM interactions. During morphogenesis of the Drosophila posterior endoderm, genetic patterning through the localized expression/secretion of the GPCR ligand Fog controls the activation of apical Myosin-II (MyoII) and tissue invagination in the posterior-most primordium region, the primordium. Subsequently, a wave of MyoII activation and tissue invagination propagates anteriorly in a self-organized manner. A mechanochemical 3D cycle of deformations involving integrin-mediated cell adhesion to the overlying vitelline membrane, amplification of MyoII contractility and subsequent cell detachment underlies wave propagation.
Here, we investigated the specific role of Fog-GPCR signalling during wave propagation. Using mosaic mutants and tissue-specific expression of membrane-tethered Fog, we found that Fog-induced GPCR signalling is also required during wave propagation. We demonstrate that Fog produced in the primordium diffuses to the region of wave propagation, forming an intracellular gradient, activating MyoII and inducing cell invagination. This suggests that Fog acts as a morphogen to activate MyoII at a distance. Consistently, the range and amplitude of an exponential gradient of MyoII depend on both Fog production in the primordium and on its extracellular clearance by GPCR endocytosis. Strikingly, however, endogenous YFP-tagged Fog is uniformly distributed in the extracellular space. Using FCS, we measured Fog diffusion during wave propagation. We found that the amount of a slow-diffusing fraction of Fog detectable at the cell apical surface is distributed as a gradient and it is tuned by GPCR endocytosis.
Altogether, we show that Fog acts tissue non-autonomously to activate MyoII during wave propagation and that GPCR endocytosis shapes a travelling gradient of Fog activity during wave propagation.



POSTER 100

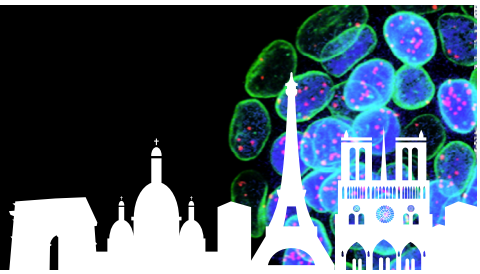
Rémi-Xavier COUX

Agnès Dubois, Almira Chervova, Nicola Festuccia, Inma Gonzalez, Sandrine Vandormael-Pournin, Michel Cohen-Tannoudji and Pablo Navarro

EPIC Unit, Developmental and Stem Cell Biology department, Institut Pasteur Paris

How to make Primitive Endoderm: a tale of pioneer transcription factors and fragile nucleosomes

Before implantation, the mammalian embryo divides actively while specifying three multipotent cell types. Embryonic cells must then acquire and maintain their transitory identity while dividing rapidly. Cell identity is normally transmitted epigenetically; however, the canonical epigenetic regulators are dispensable for early development and preimplantation development is instead controlled by a network of transcription factors (TF). Pioneer TFs that engage their DNA recognition motif within closed chromatin to activate new regulatory elements promote differentiation are thus essential for cell fate decisions. However, the complexity, binding dependencies and temporal effects of their action remain unclear. We dissected how the pioneer TF GATA6 triggers Primitive Endoderm (PrE) differentiation from pluripotent cells. We showed that transient GATA6 binding exploits accessible regions to decommission active enhancers and promotes pluripotency gene silencing. Simultaneously, GATA6 targets closed chromatin and initiates an extensive remodeling culminating in the establishment of fragile nucleosomes flanked by ordered nucleosome arrays and increased accessibility. This is directly enhanced by rapidly expressed PrE TFs (SOX17) and by repurposing of the pluripotency TFs OCT4/SOX2 for differentiation. Furthermore, GATA6 mediates the replacement of essential nuclear receptors and pioneer TFs for PrE differentiation, from ESRRB to ESRRA. Therefore, pioneer TFs orchestrate a complex gene regulatory network involving many if not all available pioneer TFs, including those required to support the original identity of differentiating cells.



POSTER 101

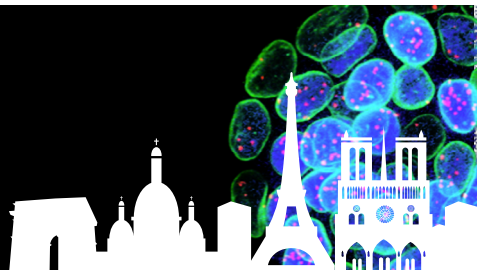
Flora CROZET

Fabiana Cerqueira-Campos, Florence Levillayer, Romain Levayer

Institut Pasteur, Levayer group, Department of Developmental and Stem Cell Biology UMR 3738, Paris, France

Dissecting ERK mechanotransduction in living epithelia

The interplay between mechanical cues and the modulation of cell signaling pathways is an essential underpinning of epithelial plasticity to changing environments that maintains the functional and architectural integrity of tissues. Our group recently identified the EGFR-ERK pathway as an emerging mechanotransducer that regulate the spatiotemporal distribution of cell death in the Drosophila pupal notum, a monolayer epithelium. Local tissue stretch/compaction results in a transient increase/decrease in ERK activity respectively, and a corresponding effect on cell survival. To further dissect ERK mechanotransduction in epithelia, we are characterizing the cellular parameters and molecular regulators that couple mechanics to ERK activity in the pupal notum in vivo. By decoupling cell tension from cell geometry using a local increase/decrease in cell contractility induced by optogenetics (opto RhoGEF or RhoGAP, respectively), our data tend towards a variation in ERK activity based on cell tension rather than cell shape. At the molecular level, we have identified the ubiquitin ligase Cbl as an emerging regulator of ERK activity and sensitivity to mechanics, probably acting through trafficking and degradation of EGFR. Preliminary data in Cbl RNAi cells, however, show no effect on steady-state EGFR localization, without ruling out an alteration in EGFR trafficking and turnover. By combining functional screens, mechanical tissue perturbation (optogenetics and laser ablation) and live quantitative imaging, this study aims to establish a multi-scale understanding of the coupling between mechanics, variation in ERK activity and cell survival in epithelia. It is particularly relevant in pathological contexts, such as tumor cells, where the ERK pathway can be co-opted under mechanical stress and affect tissue integrity.



POSTER 102

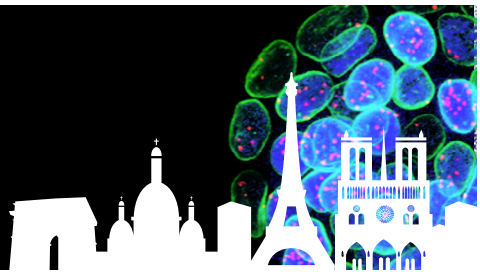
Thanh Mai Julie DANG

Filippo Del Bene

Sorbonne Université, INSERM U968, CNRS UMR 7210, Institut de la Vision, Paris, France

Understanding the role of the tubulin codeon organism-wide functions

Microtubules, fundamental elements of the eukaryotic cytoskeleton, play crucial roles in processes such as cell division, motility and intracellular transport. Despite their diverse functions, microtubules share a remarkably uniform structure composed of nearly identical building blocks constituted of tubulin proteins. Posttranslational modifications of tubulin are emerging as regulators of microtubule functions, a concept known as the 'tubulin code'. However, the precise impact of these tubulin modifications on an organism homeostasis throughout its lifespan, as well as their potential link to cellular malfunctions and disease, remains elusive. To address these questions, we have developed zebrafish mutant lines that lack functional enzymes responsible for the primary post-translational modifications observed in neurons, namely polyglutamylation, acetylation, and detyrosination. Using the unique readouts available in zebrafish, our aim is to explore the intricate mechanisms influenced by these tubulin post-translational modifications. This investigation encompasses microtubule-dependent processes like axonal transport and neuronal activity, which we intend to analyze through in vivo experiments, ultimately connecting molecular, cellular and functional biology using calcium imaging. In the following poster, we will introduce the various zebrafish mutant lines that we have generated, along with an overview of the upcoming study's structure.



POSTER 103

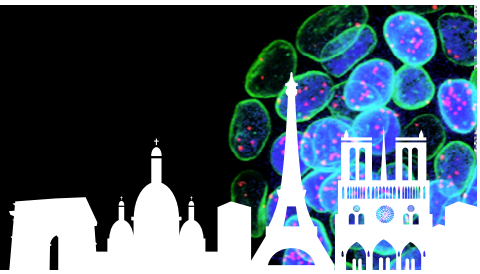
Ettore DE GIORGIO

Pierre Leopold

Institut Curie, CNRS UMR 3215 / INSERM U934, Paris, France

Tissue size adjustment during morphogenesis in Drosophila melanogaster

The control of organ size mainly relies on precise autonomous growth programs. However, organ development is subject to random variations, called developmental noise, best revealed by the fluctuating asymmetry observed between bilateral organs. The developmental mechanisms ensuring bilateral symmetry in organ size are mostly unknown. In Drosophila, null mutations for the relaxin-like hormone Dilp8 increase wing fluctuating asymmetry, suggesting that Dilp8 plays a role in buffering developmental noise. In a previous project from the lab, we showed that size adjustment of the wing primordia involves a peak of dilp8 expression that takes place sharply at the end of juvenile growth. Wing size adjustment relies on a cross-organ communication involving the epidermis as the source of Dilp8. We identify ecdysone signaling as both the trigger for epidermal dilp8 expression and its downstream target in the wing primordia, thereby establishing reciprocal hormonal feedback as a systemic mechanism, which controls organ size and bilateral symmetry in a narrow developmental time window. In this work, we analyze this time window with high temporal resolution to determine exactly when the size adjustment occurs. Using genetic labelling, confocal microscopy, and dissection techniques we built in our lab, we evaluate several parameters such as tissue volume, cell number and cell size of the pupal wing precursors. We find out that the tissue volume adjustment between left and right wings occurs only in two hours, exactly when important morphogenetic events occur. Now we are interfering with these morphogenetic events to analyze their impact on size adjustments. In this way, we will be able to evaluate a correlation between size adjustment and morphogenesis.



POSTER 104

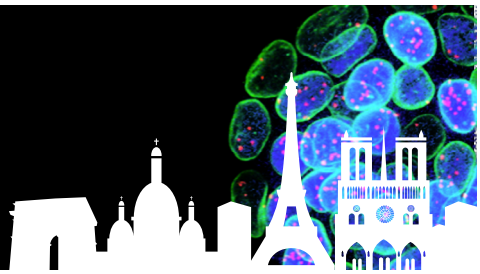
Diede DE HAAN

Thibaut Brunet

Institut Pasteur, Paris, France

Reconstructing the ancestral architecture of animal cells

The evolution of multicellular complexity in animals involved crucial innovations, including coordinated cell contractility, which underlies tissue morphogenetic processes such as epithelial bending. Epithelia are composed of polarized cells that adhere to one another and to a basal membrane through adhesion complexes, and often have microvilli on their apical side. Interestingly, similar cellular structures are observed in choanoflagellates, the closest living relatives of animals, suggesting that the architectural foundation of such cells was established before the evolutionary divergence of these two groups.
Choanoflagellates are a group of aquatic microeukaryotes known for their ability to switch between different cellular states, including sessile and colonial forms. They are characterized by an apical collar complex, a central flagellum encircled by microvilli, used for locomotion, mechanosensation, and feeding. The homology between the choanoflagellate and animal collar complexes is supported by the conservation of flagellar and microvillar genes and structural components. Thus, although the understanding of animal cell morphogenesis is primarily within a multicellular context, the foundational cellular architecture and mechanisms likely originated in a unicellular ancestor.
Our goal is to describe how choanoflagellate cell and colony morphology are regulated to uncover the origins of key cellular architectures in animals. We study a recently isolated choanoflagellate species, Choanoeca flexa, which exhibits emergent collective behavior. Cells form sheet colonies through intercellular links at the microvilli and can switch between swimming and feeding conformations via collective apical constriction, reminiscent of animal tissue morphogenesis. Despite its evolutionary and functional significance, little is known about the structure, patterning, and remodeling of the apical collar complex, and the nature of intermicrovillar links remains entirely unexplored. By integrating various imaging techniques, we aim to bridge gaps in resolution and field of view to dissect the ultrastructure and biogenesis of this complex, focusing on intermicrovillar links and the morphology of colonies.



POSTER 105

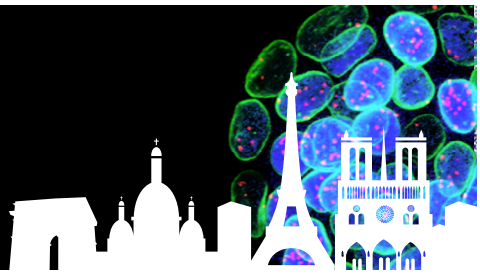
Marie-Claire DELFINI

Axelle Wilmerding*, Aurélie Richard, Nicolas Macagno, Estelle Hirsinger, Tarek Gharsalli, Caroline Gaudy, Lauranne Bouteille, Nathalie Caruso, Delphine Duprez, Yacine Graba, Souhila Medjkane, Heather Etchevers

Department of Cells and Tissues, Instituto de Biologia Molecular de Barcelona, Consejo Superior de Investigaciones Cientificas (IBMB-CSIC), Parc Cientific de Barcelona, C/Baldiri i Reixac 20, 08028 Barcelona, Spain
**Frist Author*

RIPOR2 promotes multinucleation of melanoma cells downstream of the RAS/ERK oncogenic pathway

Multinucleation promotes cell heterogeneity and aneuploidy associated with poor patient outcome for a variety of tumor types including melanoma. However, the molecular mechanisms that lead to multinucleation of tumor cells remain not fully understood. In this study, we combined in vivo experiments using chicken embryo as in vivo vertebrate model, human cell culture and human skin biopsies, and bioinformatic analysis including single-nucleus RNA sequencing. We present evidence that RIPOR2/FAM65B, the atypical RhoA inhibitory protein described as being expressed during development in syncytiotrophoblast and skeletal muscle cells at the stages when they become multinucleated, is ectopically expressed in human developing melanoma downstream of the RAS/ERK oncogenic pathway at the onset of the pathology, and favors multinucleation including in melanoma tumor cells. These findings unveil that RIPOR2/FAM65B might therefore represent a therapeutic target of early-stage cancer lesions to limit aggressiveness of melanoma and other solid tumors in which it is ectopically expressed thanks to the oncogenic activation of ERK.



POSTER 106

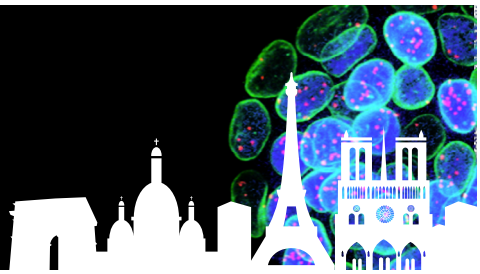
Julien DELPIERRE

Aurélien Villedieu, Boris Guirao, Fabian Gärtner, Floris Bosveld, Yohanns Bellaïche

Institut Curie, CNRS, Paris, France

Exploring the scaling of morphogenetic processes with animal size

The scaling of biological structures with organism size can be observed across metazoans. In animals, this phenomenon is visible during development and ensures the preservation of the structure-function relationship in the adult despite a large physiological variation of individual sizes. This phenomenon has been mainly studied through the lens of morphogen gradient scaling, but it remains unclear how tissue flows scale to ensure that similar shapes are reached among animals of different sizes. In this study, we explore this fundamental question during collective cell migration in Drosophila epithelial tissue by studying morphogenesis across a broad range of animal sizes. We found that the velocity of collective migration linearly scales with the animal size to ensure that the traveled distance matches the size of the tissue. By combining genetic perturbation and physical modeling, we explored whether and how the scaling of a morphogenetic field enables the scaling of tissue flow velocity to match animal size. Overall, our study delineates how similar shapes emerge during development regardless of animal size.



POSTER 107

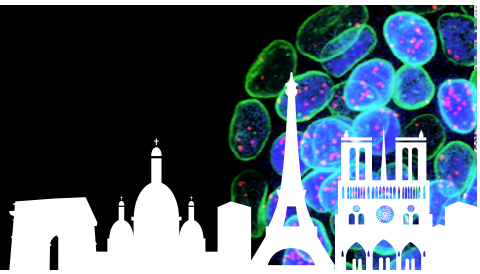
Sushil DUBEY

Yoann Le Toquin, Aleksandra Ardaševa, René-Marc Mège, Amin Doostmohammadi, Christophe Marcelle, Benoît Ladoux

Institut Jacques Monod, CNRS, Université Paris Cite, Paris, France

Mechanical stresses govern myoblast fusion and myotube growth

The way shape of organs and embryos emerges and self-organize during development has been a fundamental question in biology. Myogenesis, the formation of skeletal muscle tissue, is a key process during embryonic development. Myoblast fusion where individual myoblasts merge to form myotubes is critical for myogenesis during embryonic development as well as for muscle repair in the adult. Myoblast fusion is a complex process that relies on cell-cell interaction, cell adhesion, and cytoskeletal remodeling and membrane fusion. Despite numerous studies on the signals and the downstream effectors implicated in myoblastfusion, its mechanical regulation remains an open question. Here, we investigated this question by observing primary myoblasts cultured on deformable substrates and show that myoblasts rearrange and realign themselves to form long oriented domains that leads to singularities(topological defects). We observed that fusion of myoblasts cells is primarily associated with the locations of singularities that correspond to hotspots of high compressive stresses. As the system evolves over time through the process of fusion that result in growth of the myotubes, the number of defects decrease by annihilation followed by long-range cellular alignment. These results are accompany by a considerable increase in isotropic stresses. By impairing fusion and myotube growth through biochemical perturbations, we show that these effects are reversed, demonstrating the role of myotube growth in the self-organization of the cell population. Altogether, our results highlight the crucial importance of the physical properties of cell populations and mechanical forces in regulating complex morphogenic events.



POSTER 108

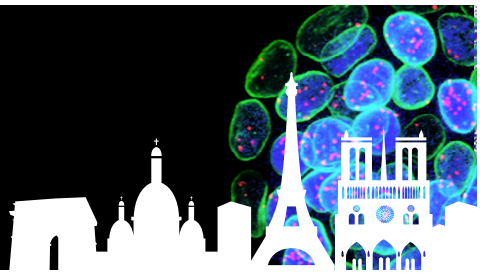
Sylvie DUFOUR

Nioosha Nekooie-Marnany*, Alwyn Dady, Frédéric Relaix, Roberto Motterlini, Roberta Foresti, and Jean-Loup Duband

Institut Mondor de Recherche Biomédicale, INSERM, Créteil, France
**First Author*

Non-Canonical Function of Glutaminase Cooperates with Wnt Signaling to Drive EMT in Neural Crest Cell

Metabolic reprograming has been linked to epithelium-to-mesenchyme transition (EMT) in cancer cells, but how it influences EMT in normal cells remains largely unknown. Here, using metabolic profiling and in vivo - in vitro strategies, we explored how metabolism drives transition from delamination to migration in trunk neural crest cells (NCC), an important progenitor cell population of the vertebrate embryo. We report that delamination exhibits a quiescent metabolic phenotype whereas migration is characterized by OXPHOS-driven metabolism coupled to distinct expression of metabolic, EMT and developmental genes. We uncover a novel role for glutamine and its catabolizing enzyme glutaminase (GLS) in delamination. Specifically, glutamine is required for nuclear translocation of GLS, which interacts and cooperates with beta-catenin, a major player of Wnt signaling, to regulate EMT gene expression during delamination.



POSTER 109

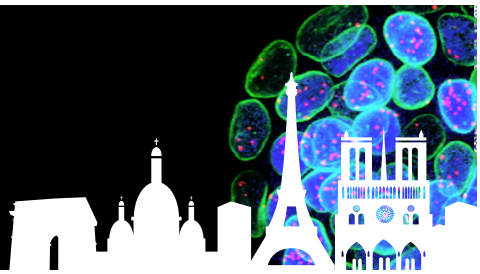
Joey DUFOURD

Mathieu Tardat, Sandrine Sauzet, Gabrielle Pozo, Yen Huyhn, Serge Urbach, and Jérôme Déjardin

IGH, CNRS, Montpellier, France

Identification of TELS1, a telomere stabilization protein in stem cells

Telomeres are long stretches of repeated sequences that are located at the end of linear eukaryotic chromosomes. Consequently, telomeres are particularly sensitive to double strand break DNA damage sensors. Telomeres are bound by a complex of proteins known as shelterins for protection against illegitimate repair mechanisms. In addition to telomere protection, shelterins play a critical role in telomere length maintenance and replication. The current model proposes that their protection against illegitimate fusions with other telomeres is achieved through a unique shelterin protein: TRF2. Specifically, TRF2 is involved in the formation of the t-loop, a lariat-like structure allowing invasion of the 3' overhang in the double stranded part of the telomeric DNA to escape detection by DNA damage sensors. In MEFs Terf2 loss of function causes: loss of the t-loop, triggering of the DDR, and subsequent fusion events between telomeres, suggesting that t-loops are protective structures at telomeres. However, TRF2 possesses other protective functions such as inhibition of cNHEJ through its iDDR domain. Therefore, it is unclear whether t-loops are protective by themselves or if other TRF2 intrinsic mechanisms protect telomeres. Interestingly, recent studies suggest that telomere integrity and t-loops are maintained in Terf2 KO mESCs, arguing for a protective function of the t-loop and suggesting that an alternative mechanism of t-loop formation occurs in pluripotent cells. Complementary to these investigations our results show that TELS1, a newly identified telomere protein, is essential for t-loop stabilization in mESCs. In absence of TELS1 and independently of the status of TRF2, t-loops are no longer formed, without induction of DNA damage or telomere fusions. These results therefore suggest that neither TRF2 nor t-loops are involved in telomere protection in mESCs. Finally, our results suggest that t-loops regulate overhang access to important factors such as the telomerase. Hence t-loops negatively regulate telomere length.



POSTER 110

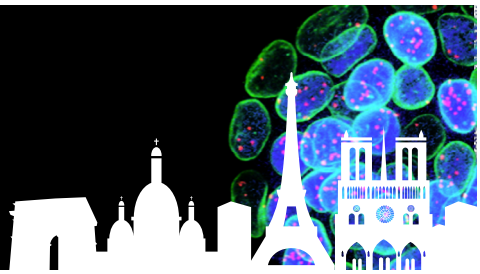
François FAGOTTO

David Rozema, Leily Kashkooli, Artur Ruppel, Christine Fagotto-Kaufmann

CRBM-University of Montpellier and CNRS, Montpellier, France

The cellular and biophysical basis of Xenopus mesoderm intercalation

Mesoderm involution during Xenopus gastrulation represents the prototype of collective migration of a coherent mesenchymal tissue. It crucially relies on cells actively exchanging contacts with their neighbours. Importantly, cell rearrangement of this mesenchymal-like tissue does not involve the classical mode of "T1 transition" described in epithelia monolayers, but on a distinct type of intercalation based on differential migration, which remains poorly understood. To get to the core of this process, we have combined embryo/tissue analysis with minimalistic in vitro approaches. We have made the following key discoveries: 1) Mesoderm tissue dynamics are stimulated by controlled repression of actomyosin contractility, thus opposite to the classical view of intercalation; 2) We have identified RhoA regulators that become specifically expressed in the gastrulating mesoderm, and are necessary and sufficient for its migration; 4) We show that cell-cell contact remodelling involves fast reversible cadherin disengagement through a mechanism of peeling and lateral diffusion. 3) Furthermore, we have succeeded at reconstituting intercalation in a minimal system of cell quadruplets, allowing the first direct measurement of force dynamics through TFM. Altogether, our approach unveils unique characteristics of mesoderm dynamics, which are markedly different from the standard epithelial models. We postulate that these findings will widely apply to morphogenesis of mesenchymal tissues.



POSTER 111 & FLASH TALK

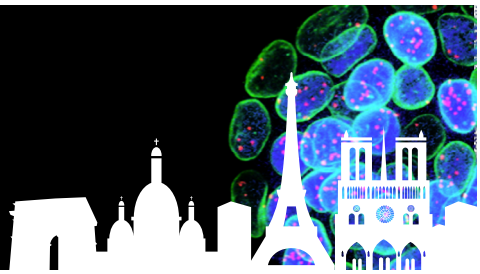
Catarina FIGUEIREDO

Caren Norden and Mauricio Rocha-Martins

Instituto Gulbenkian de Ciência, Oeiras, Portugal

How developing tissues compensate for unwanted cell death: Lessons from the zebrafish retina

Embryos are often exposed to genetic and environmental stressors that induce cellular damage, culminating in unwanted cell death. Thus, embryos require protective mechanisms to ensure organ size and function. Developing tissues can counteract unwanted apoptosis via compensatory proliferation. While key molecular regulators of apoptosis-induced compensatory growth have been identified in invertebrates, it remains unclear whether similar capabilities exist in vertebrates. More broadly, whether and how survivor cells modify their developmental trajectory to rescue organ size remains an important knowledge gap. We leverage the live imaging capabilities of the developing zebrafish retina to investigate the cellular mechanisms of compensatory growth. Embryos subjected to a strong and prolonged heat stress exhibited extensive apoptosis in the retinal neuroepithelium. Despite the high variability in cell death dynamics, a significant portion of the retina often became occupied by apoptotic cells, causing severe loss of tissue integrity and reduction of eye size. Remarkably, dead cells were efficiently cleared out and most embryos recovered in just 4 days, forming laminated retinas of sizes comparable to unperturbed controls. Compensatory growth occurred without a general delay in tissue differentiation and coincided with the neurogenic phase. Notably, live imaging revealed that, in the presence of cell death, most neurogenic progenitors undergo self-renewing divisions, a behaviour not observed in control embryos. Thus, a simple change in the outcome of neurogenic divisions may compensate for early loss of progenitor cells, helping to counteract size defects. Our findings suggest that previously underappreciated cellular plasticity confers self-correction capabilities to the developing retina. Future work will uncover how these transient amplifying divisions are regulated to ensure recovery at the tissue scale.



POSTER 112

Evelyne FISCHER

Bunel Benjamin*, Goiame Rosette, Morin Xavier

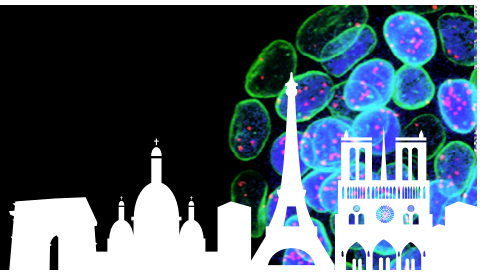
IBENS INSERM U1024 - CNRS UMR8197, Paris, France
**First Author*

Unequal mitochondrial segregation during mitosis initiates asymmetric fate choices in neural stem cells progeny

The differentiation of neural cells at the «right place and right time» is fundamental to ensure the development of functional circuits. Asymmetric division of neural stem cells is a key player during neurogenesis, allowing the sequential production of neurons while maintaining a progenitor pool. However, we still know little about the identity of the fate determinants whose unequal inheritance during progenitor division initiates a different identity between two sister cells. Recent studies have shown that the unequal segregation of age-selective or dysfunctional mitochondria during mitosis influence daughter cell fate (eg. proliferative capacity) in a non-neural context in vitro. In the mouse neocortex, experimental modulation of mitochondrial dynamics during a limited time window after mitosis influences the choice of progenitor versus neuronal fate. Therefore, we postulate that unequal mitotic mitochondrial distribution could initiate the acquisition of this differential fate during neurogenesis.

Using live imaging of fluorescent mitochondrial reporters in the chick embryonic neural tube, we show that mitochondrial distribution during mitosis ranges from equal to very unequal, with a relative frequency that mirrors that of symmetric and asymmetric divisions during development. Accordingly, functional challenges that promote or delay neurogenic divisions shift the mitotic distribution towards inequality or equality, respectively. Strikingly, live fate tracking of sister cell pairs shows unequal mitochondrial distribution in most asymmetric divisions, with the smallest mitochondrial pool preferentially inherited by the future neuron. Remarkably, mitochondrial inheritance is equal in symmetric divisions (both proliferative or neurogenic). Finally, direct manipulation of mitochondrial transport to force their unequal distribution in proliferative progenitors is sufficient to alter the identity of their progeny, with the daughter cell inheriting the smallest pool of mitochondria becoming a neuron.

Altogether, these observations characterize the unequal segregation of mitochondria as a cell fate determinant, and provide a new insight into mitochondrial regulatory roles during neural development.



POSTER 113

Thomas FUHS

Alexander Dulebo, André Körnig, Dimitar Stamov, Thomas Henze

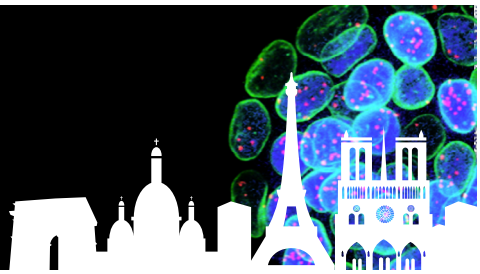
Bruker Nano GmbH, JPK BioAFM Business, Berlin, Germany

Structure, mechanics, and dynamics of biological systems studied by AFM

Mechanobiology encompasses a range of studies on the mechanotransduction between growing cells and their microenvironment. Active forces in biological systems define the interactions between single molecules, growing cells and developing tissues. Over the last three decades atomic force microscopy (AFM) has become an indispensable tool for characterisation of samples from single molecules to complex living systems, featuring cells and tissues.

We will further introduce the concept of automated large area multiparametric characterization of densely packed cell layers and highly corrugated tissue samples, where full automation, smart mechanical sample analysis, multiple scanner technology, and optical integration is critical for data throughput and reliable correlative microscopy. We will discuss how these developments, in combination with advanced optical microscopy techniques, can overcome the inherent drawbacks of traditional AFM systems for characterizing challenging biological samples.

We will also introduce the most recent high-speed tip-scanning atomic force microscopy (AFM) developments that enable kilohertz linerate imaging and visualization of molecular dynamics by enabling temporal resolution on the sub-100-milisecond scale. Such developments are critical for studying of cells which adapt their shape and react to the surrounding environment by a dynamic reorganization of the F-actin cytoskeleton. We will demonstrate how cell spreading and migration in living KPG-7 fibroblasts and CHO cells, can be studied with high-speed AFM and associated with spatially resolved cytoskeletal reorganization events.



POSTER 114

Futura GATTOBIGIO

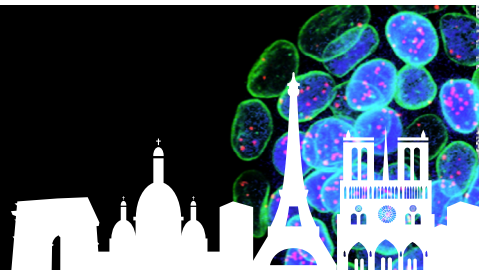
Nicolas Porchet, Annalisa Fico, Katia Boutourlinsky, Peta Bradbury, Jean-Léon Maître, Gabriella Minchiotti, Claire Chazaud, Jérôme Collignon

Institut Jacques Monod, Université Paris Cité, CNRS, Paris, France

NODAL signaling is required for blastocyst development in the mouse

Preimplantation development in the mouse begins at the zygote stage (embryonic day E0.5) and lasts 4 days, during which cell divisions and cell differentiation lead to the establishment of 3 cell populations - the trophectoderm, the primitive endoderm and the epiblast - which form a blastocyst capable of implanting in the uterus. Several morphogens are expressed during blastocyst formation, but for some of them, their role in this process is not yet fully understood. This is notably the case of the TGF family member NODAL.
NODAL expression begins in the inner cell mass (ICM) of the compacted morula (E2.75), and is dynamically regulated in the epiblast and primitive endoderm cells that derive from the ICM once the blastocyst is formed, up to the time of implantation (E4.5). However, to date, no requirement for NODAL has been identified before peri and post-implantation stages. This is despite the fact that all components of the SMAD2,3-dependent ACTIVIN/NODAL signaling pathway are also present in preimplantation embryos. The fact that ACTIVIN also is expressed in preimplantation embryos, and that both ligands are expressed by the uterus of pregnant females, raised the possibility that the absence of zygotic NODAL might be compensated at these early stages

Indeed, we found that E2.5 Nodal -/- embryos cultured ex-utero for 48h form blastocysts consisting solely of a layer of TE surrounding a lumen with few or no inner cells, thus revealing an important role of NODAL in the establishment and maintenance of ICM derivatives. We will present a detailed characterization of the ontogeny of this phenotype and of the distinct roles of NODAL and ACTIVIN at these stages.



POSTER 115

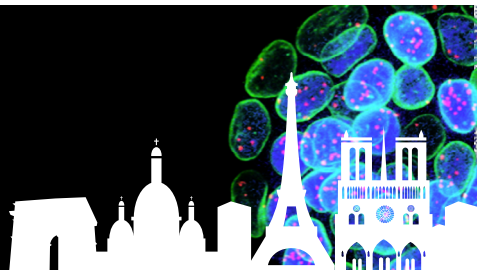
Raphael GAUDIN[1,2]*

Gaia Cogrossi[1,2]*, Aurélie Hirschler[3], François Delalande[3], Valériane Gaxotte[3], Emma Partiot[1,2], Vincent Lucansky[1,4], Maika S. Deffieu[1,2], Christine Carapito[3], Yonis Bare[1,2], William Bakhache[1,2]*

1. Institut de Recherche en Infectiologie de Montpellier (IRIM), CNRS, 34293 Montpellier, France
2. Université de Montpellier, 34090 Montpellier, France
3. Laboratoire de Spectrométrie de Masse Bio-Organique, IPHC, UMR 7178, CNRS-Université de Strasbourg, ECPM, Strasbourg, France.
4. Comenius University in Bratislava, the Jessenius Faculty of Medicine in Martin (JFMED CU), Biomedical Center Martin, Mala Hora 4C, 036 01 Martin, Slovakia.

Characterization and identification of new antiviral molecules and targets associated to the endoplasmic reticulum

The recent pandemic of COVID-19 highlighted the necessity for better preparedness against emerging pathogens, including the ones we have not encountered yet. To this end, the development of broad-spectrum antivirals represents an important therapeutic strategy requiring further research. One of the best ways to address this need is to develop host-targeting antivirals, as our current arsenal is scarce. Here, we synthesized a series of proprietary molecules, and found molecules exhibiting potent broad-spectrum antiviral activity against several coronaviruses, flaviviruses and bunyaviruses. In particular, we identify that the molecule RG10b had strong antiviral activity against SARS-CoV-2, impairing viral replication in the endoplasmic reticulum (ER). Live cell imaging analyses showed that RG10b perturbs ER dynamics, while ER stress was not found to be a major process driving RG10b's antiviral activity. To unbiasedly assess the potential targets of RG10b, we then searched for potential host protein interactors using thermal proteome profiling, and identified several proteins associated to ER-associated degradation (ERAD) among our top hits. Interestingly, the knock down of two ERAD genes resulted in increased expression of viral protein expression, suggesting that the endogenous ERAD pathway may interfere with SARS-CoV-2 replication. Together, our work has important implications for antiviral research and may also provide a new approach to modulate the unfolded protein response.



POSTER 116 & FLASH TALK

Matthieu GÉLIN

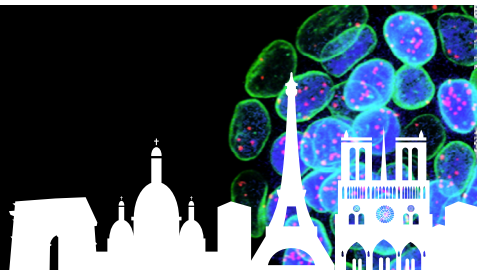
Jérôme Wong, Yekta Kesenci, Hugo Siefried, Emmanuel Terriac, Jean-Christophe Olivo-Marin, Samy Gobaa, Sandrine Etienne-Manneville

Institut Pasteur, Polarité cellulaire, Migration et Cancer, Paris, France

Development of a synthetic hydrogel to study the invasion of glioblastoma cells

Cancer invasion is a landmark event that transforms a locally growing tumor into a systemic, metastatic, and life-threatening disease. Its invasive character is one major contributor to the poor prognosis of glioblastomas (GBM), which are incurable primary brain tumors. GBM cells, which migrate away from the tumor core, evade surgery and radiotherapy and initiate recurrence, while tumor invasion is in itself the main cause of death. In parallel, numerous studies underscore the pivotal role of the tumor microenvironment in facilitating this invasive behavior.

Therefore, deciphering the invasion's mechanisms is crucial for developing anti-invasive therapies that complement and enhance conventional therapeutic approaches. To address this challenge, we propose a novel approach utilizing bioengineered, fully defined 3D matrices mimicking tissue environments coupled with advanced cell imaging offering high temporal and spatial resolution. Additionally, we have developed a new computational analysis of cell deformations, pressures, and forces to analyze simultaneously passive and active mechanical properties of invading GBM cells. In the future, we hope to use this tool to determine how intermediate filaments integrate these properties to promote tumor cell invasion.



POSTER 117

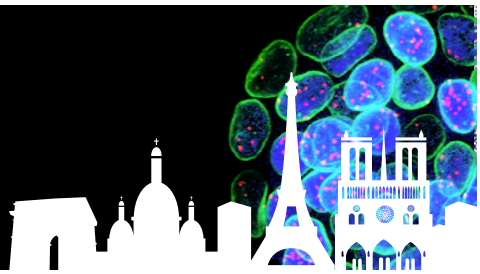
Alison GOULOIS

Thomas Welte, Daniel Hess, Helge Grosshans

Friedrich Miescher Institute for biomedical research, Basel, Switzerland

TRIM71 RNA repressor activity in stemness: insights into congenital hydrocephalus

Development relies on a proper balance between the maintenance and differentiation of stem and progenitor cells. A conserved regulator of stem cell fates is the RNA-binding protein TRIM71. Abundant during early development and essential for embryonic viability, it plays a key role in brain formation. Heterozygous mutations in its RNA-binding domain trigger human congenital hydrocephalus (CH), a neurodevelopmental disorder caused by precocious differentiation of neuroprogenitors. Recently, in mouse embryonic stem cells (mESCs), we discovered that TRIM71 degrades its targets by binding specific hairpin motifs in the 3′ untranslated region and recruiting TNRC6 with its associated RNA-degradation machinery. Here, we show complementary evidence that TRIM71 forms oligomers via its B-Box domain which turns out to be essential for RNA and cofactor binding. Accordingly, oligomerization of wild-type and CH-mutant proteins reduces target repression by impairing both binding events. Therefore, we suggest that in neural progenitor cells, such heteromeric formations result in precocious upregulation of key targets responsible for premature neurogenesis in the embryo.



POSTER 118

David GREEN

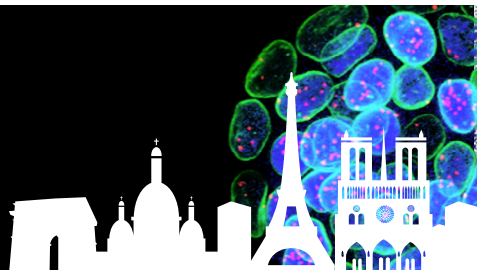
Khallil Mazouni, Ulrich Tepass and Francois Schweisguth

Institute Pasteur, Paris, France

Relative contributions of positional information, Notch signaling and tissue mechanics in Neuroblast specification in the early Drosophila embryo

The early fly embryo is an excellent model to study how genetic activity and mechanical forces, constrained by geometry, are integrated to build complex multicellular structures. During early Drosophila neurogenesis, a highly reproducible spatial pattern of neural precursor cells, or neuroblasts (NBs). forms as the embryo extends along the Anterior-Posterior (AP) axis via cell-cell intercalation, in a process known as GermBand Extension (GBE). NBs emerge from groups of cells located at stereotyped positions along the AP and Dorso-Ventral (DV) axes. Inhibitory signalling by Notch ensures that a single NB per proneural cluster adopts a NB fate. However, the relative significance of positional information, lateral inhibition and mechanical forces in NB selection during GBE remains to be investigated.

To study whether positional information and mechanical cues could bias NB selection, we performed live imaging and back-tracked presumptive NB throughout GBE. Apical morphology, such as cell perimeter, did not correlate with NB fate adoption. In contrast, our preliminary data indicated that early expression of the proneural gene lethal of scute (lsc), monitored using live imaging of lsc transcription correlated with adoption of the SOP fate. This suggests that positional information provides a strong bias for fate selection before the onset of GBE. How changes in cell-cell contacts during GBE contribute to define the proneural cluster cells to be excluded from the NB fate by Notch remains to be investigated.



POSTER 119

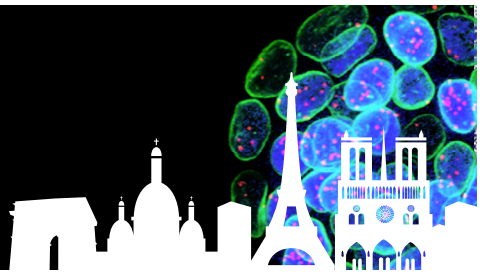
Elvira INFANTE

Terriac E., Khalil S., Siegfried H., Gelin M., van Bodegraven E.J. and Etienne-Manneville S.

Institut Pasteur, CNRS, Paris, France

Mechanoregulation of glioblastoma cell survival

Glioblastoma multiforme (GBM) is one of the most aggressive and common brain tumours, with a very poor prognosis. The standard therapeutic approach is surgical resection - which remains difficult due to the risk of post-resection neurological deficits - followed by radiotherapy and treatment with temozolomide. Nevertheless, virtually all patients with GBM suffer a relapse. Understanding the molecular mechanisms that characterise this cancer's aggressiveness, progression and resistance to current treatments is essential to developing effective therapies. It is now recognized that the interaction between the microenvironment and the mechanical properties of GBM influences cellular adaptation, tumour heterogeneity and resistance to treatment. Among the best characterized molecular player that respond to mechanical forces exerted on and by the cells is the intermediate filaments vimentin. Vimentin provide structural and mechanical support to cells and maintain the shape of cells and nuclei. Single-cell transcriptomic analysis of glioblastoma previously identify alterations in vimentin expression in GBM patients. Here, by combining multidisciplinary techniques, we discovered an unconventional impact of cell compression in promoting GBM cell survival to DNA damage and revealed the key role of vimentin in buffering compression-induced nuclear responses.



POSTER 120

Alice JOUNEAU

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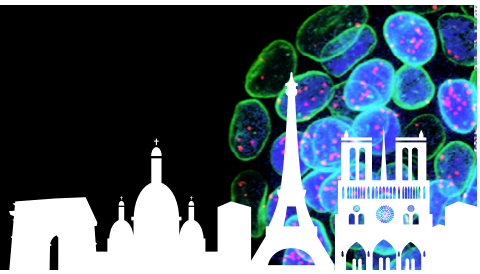
Université Paris-Saclay, UVSQ, INRAE, BREED, 78350 Jouy-en-Josas, France
**First Author*

A conserved 3D model of epiblast morphogenesis in mammals

Pluripotency is the capability of cells to differentiate into all cell lineages. In vivo, cells of the epiblast gradually acquire this ability by undergoing a morphogenetic event, characterized by cell polarization and arrangement into a 3D rosette that eventually forms a lumen, the pro-amniotic cavity. During this process, significant alterations occur in the transcriptome and metabolism. These processes are intertwined in both space and time, but their exact hierarchy and interconnections still remain poorly understood. Embryonic stem cells (ESCs), the in vitro substitute of early epiblast cells, self-organise into a rosette structure when cultured in 3D along with a hydrogel composed of basement membrane proteins. We show that pluripotency rapidly changes from a naïve to a primed state as early as cell polarization. Metabolic genes are also dynamically regulated as well as the activity of the mitochondria, assessed by the mitochondrial membrane potential measured in living cells. Interestingly, such a morphogenesis seems to be well conserved in another mammalian species that normally do not form a pro-amniotic cavity in vivo: indeed, we show that bovine pluripotent cells also form a rosette followed by luminogenesis when cultured in 3D. Such a system thus constitutes a platform to investigate conserved mechanisms in the development of the pluripotent epiblast.



POSTER 121 & FLASH TALK

Robin JOURNOT

Mathilde Huyghe, Alexandre Barthelemy, Hugo Moreira, Jakub Sumbal, Marisa M. Faraldo, Silvia Fre

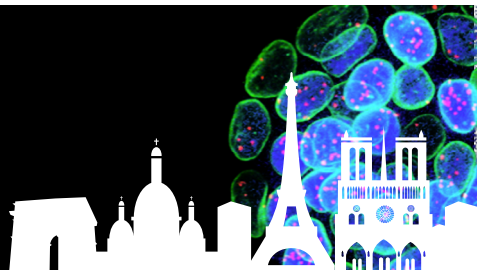
Institut Curie, PSL University, Sorbonne Université, CNRS UMR3215, Inserm U934, Genetics and Developmental Biology, 75005 Paris, France

Symmetry breaking and self-organization of bi-layered epithelia are orchestrated by conserved signals during development and regeneration

Organ development relies on intricate molecular mechanisms that guide initially identical cells to differentiate into specialized cell types within defined spatial patterns. During regeneration, cell organization has to be reestablished to guarantee tissue function. However, the mechanisms orchestrating these processes in bi-layered glandular epithelia are underexplored. Specifically, the coordination between tissue architecture and cell fate specification remains enigmatic.

To address these questions, we employed in vitro organoids and ex vivo embryonic tissue culture models, coupled with single-cell quantitative imaging techniques, to comprehensively investigate the molecular mechanisms governing self-organization and symmetry breaking in four bi-layered epithelia (mammary, lacrimal, salivary and prostatic gland) in the context of embryonic development and regeneration. We demonstrate that p63 and Notch signals are the key determinants of cell fate in all these tissues, and identify the Hippo/YAP pathway as the regulator of the timing of cell fate commitment. Indeed, we found that YAP activity is spatially patterned and represents an essential step for symmetry breaking in bi-layered epithelia.
We identified in this work an elegant mechanism coupling positional cues with molecular signaling to form and maintain fate patterns. This study unveils the inherent capacity of individual cells to self-organize, culminating in the formation of intricate multicellular structures wherein differentiated cell types occupy precise positions to fulfill their tissue-specific functions.

Conserved signals orchestrate self-organization and symmetry breaking of bi-layered epithelia during development and regeneration. Journot et al. (In preparation)



POSTER 122 & FLASH TALK

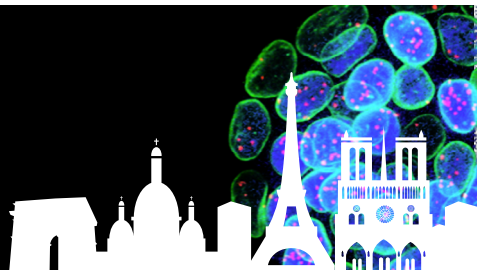
Jasmin KAIVOLA

Karolina Punovuori, Megan Chastney, Yekaterina A. Miroshnikova, Fabien Bertillot, Hind Abdo, Fabian Krautgasser, Jasmin Di Franco, James R. Conway, Gautier Follain, Antti Mäkitie, Heikki Irjala, Sami Ventelä, Hellyeh Hamidi, Roberto Cerbino, Giorgio Scita, Sara A. Wickström and Johanna Ivaska

Turku Bioscience Centre,University of Turku, Finland

Mechanical stimulation reverses oncogenic properties in ECM-enriched vocal fold cancer

In healthy individuals, phonation causes vibration of the vocal folds which is essential for vocal fold homeostasis. However, with age and cancer progression, the tissue becomes less elastic and stiffens resulting in immobility of the vocal fold epithelium. Surprisingly, mechanobiology of the vocal fold epithelium and its cancers is almost fully unexplored. Our data demonstrate that fibronectin and multiple collagens are upregulated in vocal fold cancer patient tissues samples compared to normal tissue. Furthermore, atomic force measurements of freshly isolated vocal fold tissue reveal a marked increase in tissue stiffness in cancer. Comparing patient derived cancer cells representing T1 and T3 cancers (histopathologically classified as mobile and immobile), we uncover that mechanical manipulation by stretching and vibrating cells leads to a decrease in oncogenic nuclear β-catenin levels in vocal fold cancer cells. Moreover, nuclear YAP levels are downregulated by vibration and a negative regulator of YAP, Angiomotin like protein-2 (AMOTL) expression is increased in response to vibration. Finally, exploration of a large VFC cancer patient cohort reveals an increase in ECM content with increasing cancer T-stage, high ECM content correlating positively with nuclear YAP levels and high YAP being associated with significantly lower survival. Collectively our data show that through regulation of integrin-mediated cell-ECM interactions, cytoskeleton coupled cell-cell mechanics and modulations in the hippo-signaling pathway, mechanical stimulation promotes reversion of vocal fold cancer cells toward a less malignant state.



POSTER 123

Antonina KHORUZHENKO

Françoise Miot, Xavier De Deken, Renaud Beauwens & Alain Boom

Université Libre de Bruxelles, Belgium

Bidirectional ion transport plays an important role in the regulation of thyroid intrafollicular lumen size

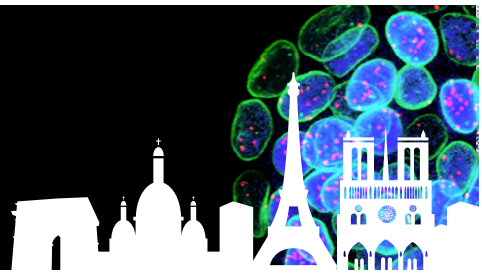
Background: Thyroid structure including the follicle size is closely related to its function. There are evidence that ion channels play an important role in maintaining/regulating the size of the intrafollicular lumen.

Aim: This study aimed to reveal ion channel involvement in the regulation of the follicular lumen size in rat thyroid follicles cultured in Matrigel.

Methods: Culture of functionally active rat thyroid follicles in Matrigel, immunofluorescent analysis, confocal microscopy, western blot analysis, statistical analysis.

Results: It was observed that an increase of glucose concentration in growth media to 22 mM caused a robust increase of the intrafollicular lumen of thyroid follicles cultured in Matrigel. Inhibition of glycolysis by 3PO completely canceled the above-mentioned effect of high glucose. Furthermore, it was observed by western blot that high level of glucose caused the activation/phosphorylation of p70S6K1 indicating activation of mTOR. In agreement, rapamycin and Torin 1 also abolished the effect of high glucose on thyroid intrafollicular lumen size, indicating the implication of mTOR signaling and a prominent role of glycolysis. On the other hand, high glucose did not alter Tg, T4 production, 125I binding. However, several inhibitors such as Ani-9, TAO1, cftr inhibitor-172, bumetanide completely annihilate the effect of glucose treatment indicating that high glucose increases primarily chloride secretion by the basolateral Na-K-2Cl cotransporter and the apical chloride channels ANO1 and CFTR. Sodium and water followed by electrical and osmotic coupling respectively. However, inhibition of the activity of the epithelial sodium channel (ENaC) channels by amiloride and benzamil led to a significant increase in the size of the intracellular lumen in normal glucose but not in high ambient glucose.

Conclusion: These data suggest that at normal glucose, the secretory flux is matched by a reabsorptive flux driven by Na reabsorption through ENaC while high glucose concentration drives an increase in chloride secretion.



POSTER 124

Laëtitia KURZAWA[1]

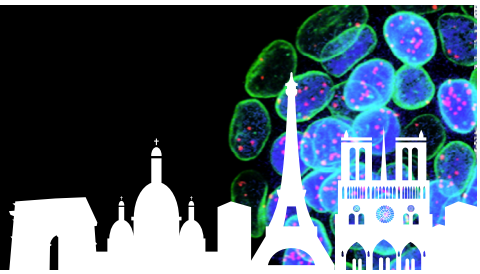
Ghina Badih[1], **Alexandre Schaeffer**[2], **Benoit Vianay**[1], **Pauline Smilovici**[1], **Laurent Blanchoin**[1], **Manuel Théry**[2]

1. Université Grenoble Alpes, CEA, CNRS, UMR5168, Interdisciplinary Research Institute of Grenoble, CytoMorphoLab, 38054 Grenoble, France
2. PSL, CNRS, CEA, ESPCI, IPGG, UMR8231, CytoMorphoLab, France

Contractile forces direct the chiral swirling of minimal cell collectives

Chirality is a conserved biological feature with critical implications in tissue morphogenesis and embryonic development. In culture, large multicellular groups exhibit spontaneous chiral symmetry break when moving collectively on micropatterned surfaces. Although several studies have shown that actin network integrity and acto-myosin network contractility participate to the establishment of the chirality of the movement, the exact contribution of contractile forces to the directionality of the chiral bias in collectives remains to be elucidated.

Here we studied the contractile forces produced by a minimal collective constituted of a pair of endothelial cells. We first show that cell doublets confined on disk-shaped micropatterns undergo spontaneous and persistent chiral swirling, displaying a mild but robust clockwise (CW) bias, as the one observed in bigger collectives. This bias could be amplified or reversed by modulating contractile forces. Traction force measurements revealed that large forces tend to drive counter-clockwise (CCW) rotation whereas low forces rather favor a CW rotation. Furthermore, the study of heterotypic doublets indicates that the speed and direction of the rotation is determined by the more contractile cells within the doublets. This study thus sheds new light on the importance of the generation and integration of mechanical forces within a small collective in the determination of its chiral rotation.



POSTER 125 & FLASH TALK

Marie LEBEL

Sharon Rabiteau, Pragati Sharma, Tiphaine Deshayes, Olivier de Thier, Philippe Dru, Jean-Francois Flot, Alexandre Alié, Stefano Tiozzo

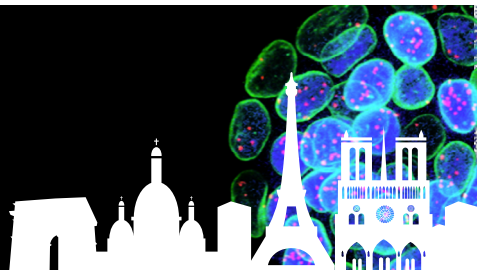
LBDV UMR 7009, Sorbonne Université, Villefranche-sur-Mer, France

Exploring cellular origins and differentiation during non-embryonic development with the single cell RNAseq atlas of B. schlosseri budding

Colonial tunicates are the only chordates that can asexually reproduce by building a functional adult body from a few somatic cells. This process, known as budding, bypasses embryogenesis and originates from little-characterized epithelial and mesenchymal cells. Budding partially co-opts embryonic mechanisms, yet operates within a distinct developmental context. In tunicates, in addition to sexual reproduction, over half of the species can undergo budding, which has been independently acquired at least seven times.

To better understand the mechanisms underlying the potency to generate a new individual from somatic cells, we employed the laboratory model Botryllus schlosseri. By generating a chromosome-level reference genome and applying single-cell transcriptomics, we produced an atlas delineating the cellular constituents involved across successive developmental stages of peribranchial budding in B.schlosseri, spanning from its onset to morphogenesis.

This atlas displays distinct 37 clusters encompassing all major cell types, and a branching topology pointing to the developmental trajectories of different cell populations, such as different types of blood cells, germline, bodywall and cardiac muscles, epidermal and neural cells, gut epithelia and endostyle cells.
A more detailed sub-clustering, coupled with the expression of early budding markers such as Nk4 and Vim, pointed to a relatively small population of cells that are involved in the budding onset. Through trajectory inference analyses, we can now explore in detail the signaling and gene regulatory networks during the onset of budding and differentiation of the various lineages.
The datasets generated provide a novel high-resolution genomic and transcriptomic description of non-embryonic development in a chordate, as well as an extensive source of information to investigate the budding mechanisms in B. schlosseri and, by comparing with other species, start to understand the multiple acquisitions of this character.



POSTER 126

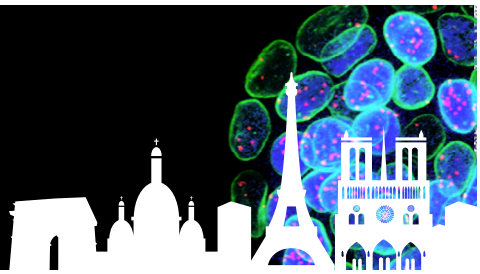
Joseph LÉGER

Raoudha Fadhloun, Devin Kenney, Avinash Bhandoola, Christelle Harly

Nantes Université, Inserm UMR 1307, CNRS UMR 6075, Université d'Angers, CRCI2NA, Nantes, France
LabEx IGO «Immunotherapy, Graft, Oncology», Nantes, France

The transcription factor MF is necessary and sufficient to specify the ILC fate in lymphoid progenitors

Helper innate lymphoid cells (ILC) play important functions in immunity and tissue homeostasis, but their development remains poorly understood. In this study, we characterized novel early developmental intermediates that enable us to investigate the mechanisms underlying the initiation of ILC specification. We identified new epigenetic and transcriptional candidate controllers of ILC development and investigated the functional relationships between known controllers. We identified a transcription factor as a candidate initiator of ILC specification, upstream of all other known controllers. We showed that this factor is required for the initiation of ILC specification, thus establishing this controller as the earliest known requirement during ILC development. We further showed that its forced expression in mouse lymphoid progenitors in vitro triggered a developmental process that recapitulated known steps of ILC development, and lead to the generation of all adult ILC. Mechanistically, we showed that this factor induced expression of key controllers of ILC development. This specific factor thus resides at the apex of a hierarchy of transcription factors important for ILC development, and is necessary and sufficient to impose the ILC fate.



POSTER 127

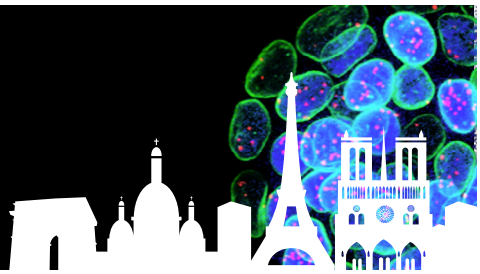
Jesus LOPEZ-GAY

Inès Cristo, Isabelle Gaugue, Stéphane Pelletier, Stephane Rigaud, Edouard Hannezo and Yohanns Bellaïche

Institut Curie, PSL Research University, CNRS UMR 3215, INSERM U934, F-75248 Paris Cedex 05, France
Sorbonne Universités, UPMC Univ Paris 06, CNRS, CNRS UMR 3215, INSERM U934, F-75005 Paris, France.

Mechanosensing buffers rapid junction length changes in epithelial tissues

The regulation of cell-cell junction length is a critical aspect of epithelial tissue development, homeostasis, and proper organ function. Cell-cell junctions can undergo rapid changes in length over short periods of time, but over longer timescales, they tend to maintain a consistent length in developing tissues. In this study, we investigated the dynamics of cell junction length regulation and its relationship with E-Cadherin levels and cytoskeleton dynamics. Our findings reveal that rapid events of junction lengthening are associated with localized decreases in E-Cadherin levels, followed by a subsequent increase in MyoII. This increase in MyoII is controlled by the mechanosensing RhoGEF Cysts, as no MyoII increase is observed in the absence of Cysts. Consequently, rapid junction length changes are not buffered, E-Cadherin local decreases remain unresolved for longer times, and therefore junction lengths are not robustly maintained. Additionally, we discovered that this actomyosin-dependent mechanism works in conjunction with the Spectrin complex, which interacts with the actomyosin network and plays a crucial role in reducing the occurrence of localized E-Cadherin decreases. Taken together, our findings suggest a mechanosensing process driven by Cysts at the actomyosin cortex that, in combination with the Spectrin complex, contributes to the regulation of junction length in epithelial tissues.



POSTER 128

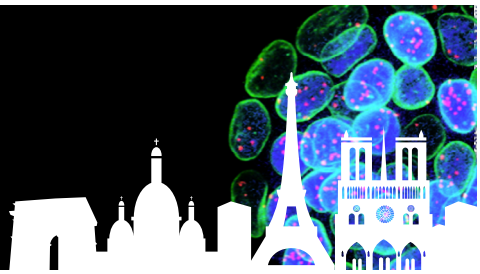
Charlotte MALLART

Nicolas Minc

Université Paris Cité, CNRS, Institut Jacques Monod, Paris, France.

Regulation and function of cytoplasmic F-actin networks in early embryos

Cytoplasmic F-actin network dynamics and flows are being increasingly recognized as key players in various developmental processes such as spindle positioning in mouse oocyte, phase segregation in zebrafish embryos and polarity establishment during Drosophila oogenesis. For instance, recent findings in sea urchin zygotes, suggest that F-actin contributes up to 50-70% of cytoplasm viscoelasticity, with important implications for the stabilization of the mitotic spindle in the center of these large cells and consequent symmetric first division. However, the nature and organization of those bulk F-actin networks remain poorly characterized, due to the difficulty of imaging filaments deep inside large eggs and embryos. Using high-resolution microscopy and dynamic live imaging, we captured with unprecedented details cytoplasmic F-actin network drastic rearrangements all along the cell cycle, and linked them with changes in the viscoelastic properties of the cytoplasm. Our initial data suggest that actin filaments could act in promoting cytoplasm stiffness and viscosity by connecting with intracellular crowding organelles, like yolk granules, thereby regulating their dynamics and the rheology of the entire cytoplasm. Using freely available image analysis tools, we are getting closer to segmenting complex F-actin networks from live images and to extract crucial information such as filament length and connectivity. Overall, this project tackles the challenge of in-depth imaging of cytoplasmic F-actin networks in vivo to connect cytoplasmic F-actin architecture and dynamics with the mechanical properties of the cytoplasm. This work will have broad implications to cell mechanics in general, and to other actin-dependent processes like cell migration, polarity and adhesion.



POSTER 129

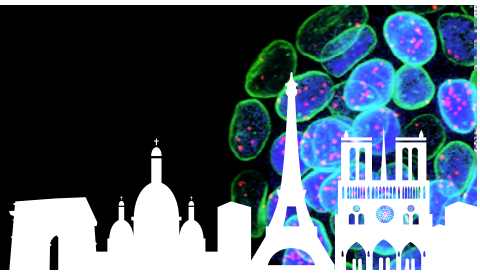
Manos MAVRAKIS

Carla Silva Martins, François Iv, Shashi Kumar Suman, Thomas C. Panagiotou, Clara Sidor, María Ruso-López, Camille N. Plancke, Shizue Omi, Maxime Gomes, Alexander Llewellyn, Sourish Reddy Bandi, Laurie Ramond, Federica Arbizzani, Caio Vaz Rimoli, Frank Schnorrer, François Robin, Andrew Wilde, Loïc LeGoff, Jean-Denis Pedelacq, Stéphanie Cabantous, Sergio A. Rincon, Cristel Chandre, Sophie Brasselet

Institut Fresnel, CNRS, Marseille, France

Genetically encoded reporters of actin filament organization in living cells and tissues

The cytoskeletal protein actin is crucial for cell shape and integrity throughout eukaryotes. Actin filaments perform essential biological functions, including muscle contraction, cell division and tissue morphogenesis. These diverse activities are achieved through the ability of actin filaments to be arranged into diverse architectures, but a detailed appreciation of the dynamic organizational state of the actin filaments has been hindered by available tools. Fluorescence polarization microscopy is uniquely placed for measuring actin organization by exploiting the sensitivity of polarized light excitation to the orientation of fluorophores attached to actin filaments. By engineering constrained fluorescent protein fusions to widely used actin localization reporters, we have succeeded in developing novel genetically-encoded reporters for non-invasive, quantitative measurements of actin filament organization in living cells by fluorescence polarization microscopy. We show examples of actin organization measurements in living mammalian cells in culture, as well as in vivo in fission yeast, C. elegans and Drosophila.



POSTER 130

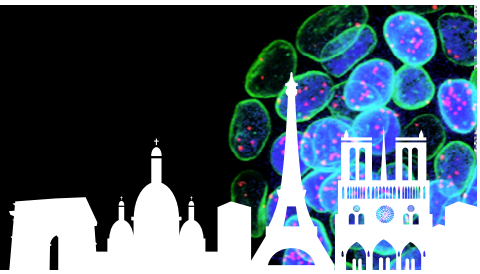
Alexandre MAYRAN

Dominique Kolly, Lucille Lopez-Delisle, Romaniuk Yuliia, Maxine Leonardi, Anne-Catherine Cossy, Theo Lacroix, Amandia Ana Rita, Pierre Osteil and Denis Duboule

Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Cadherins modulate the self-organizing potential of gastruloids

Gastruloids have recently emerged as an efficient four-dimensional model for studying some aspects of post-implantation embryonic patterning. They undergo gastrulation-like processes leading to the self-organization into highly reproducible biological objects. Here, we sought to uncover the molecular and cellular mechanism underlying this remarkable property. We report that self-organization competence is associated with a cell-specific coordination of a Cadherin switch. We find that N-Cadherin hinders gastruloids morphogenetic competence, for its inactivation leads to the formation of trunk-like structures in absence of extra-cellular matrix analogues. In contrast, E-Cadherin repression by Snai1 is critical for self-organization: Snai1 establishes a cell-specific repressive pace by triggering the repression of a pluripotency-associated transcription program and its chromatin landscape, thus allowing a proper transition from E- to N-Cadherin to occur. Altogether, this work establishes a molecular mechanism that integrates the exit from pluripotency and the pace of cell differentiation, leading to the observed self-organizing potential of gastruloids.



POSTER 131

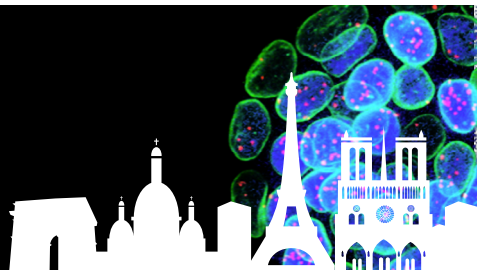
Adèle MICOUIN

Anna Geiselmann, Sandrine Vandormael-Pournin, Vincent Laville, Almira Chervova, Sébastien Mella, Pablo Navarro and Michel Cohen-Tannoudji

CNRS UMR3738, Epigenomics, Proliferation, and the Identity of Cells, Department of Developmental and Stem Cell Biology, Paris, France

PI3K/AKT signalling orchestrates ICM maturation and proper epiblast and primitive endoderm specification

The inner cell mass (ICM) of early mouse embryos is specified into Epiblast (Epi) and primitive endoderm (PrE) lineages during blastocyst formation. The antagonistic transcription factors (TFs) NANOG and GATA6 in combination with FGF/ERK signalling are central actors in ICM fate choice. However, what initiates the specification of ICM progenitors and whether other factors are involved in this process is not fully understood yet. Our aim is then to understand how key transcription factors integrate signalling pathways to drive the specification of ICM progenitors. Interestingly, we recently discovered that PI3K/AKT pathway is not only important for the maintenance and survival of Epi and PrE-progenitors after their formation but also acts as an upstream regulator orchestrating the molecular events required for both EPI and PrE specification. Using pharmacological inhibition, we demonstrate that PI3K/AKT enables the formation of a functional ICM capable of giving rise to both the EPI and the PrE: it maintains the expression of the TF NANOG, which specifies the EPI, and confers responsiveness to FGF4, which is essential for PrE specification. Our observations thus identify PI3K/AKT signalling as an upstream regulator orchestrating the molecular events required for both EPI and PrE specification.



POSTER 132

Julien MIGNOT

Teoman Ozturk, Frédéric Relaix, Hélène Rouard, Nathalie Didier

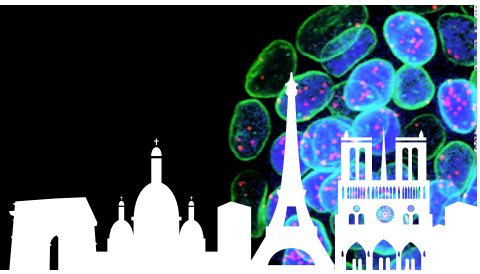
Université Paris Est Créteil, INSERM, EFS, Créteil, France

Development of therapeutic strategies for Volumetric Muscle Loss repair based on innovative hydrogels associated with human MuSC

Introduction: Adult skeletal muscle has remarkable regenerative capacity relying on resident muscle stem cells (MuSC). Upon injury, MuSC supported by the other cell types of their surrounding niche are able to completely repair the muscle tissue. However, in case of massive ablation of muscle mass, also known as Volumetric Muscle Loss (VML), the biophysical and cellular cues orchestrating the muscle regenerative process are lost, leading to the replacement of muscle tissue by fibrosis, and therefore chronic functional deficits. Despite the incidence and severity of VML injuries, treatment options remain limited and most of the patients suffer from chronic disability. Accordingly, extensive work is made in the field of muscle tissue engineering to elaborate transplantable 3D muscle constructs, in order to repair these complex injuries and enable functional recovery of the injured muscle.

Results: We are developing strategies aiming at stimulating muscle regeneration and limiting the formation of fibrotic tissue in case of severe muscle lesions. We generated and characterized a surgical mouse model of VML using of a 5 mm biopsy punch that enables the removal of 20% of the quadriceps muscle in a reproducible manner. After 2 weeks, we observed that muscle regeneration was strongly compromised leading to the accumulation of fibrous tissue, validating our surgical model of VML. We have developed biocompatible hydrogels mimicking the topographic and biomechanical properties of the native muscle and favoring the differentiation and the fusion of MuSC. We showed that the transplantation of these hydrogels at the site of VML lesion, greatly stimulates muscle regeneration and limit the formation of fibrous tissue compared to non-transplanted muscle. Taking advantage of these hydrogel, we are now exploring the therapeutic potential of the association of these hydrogels with competent myogenic cells to repair VML lesion.

Conclusion: We developed hydrogels able to stimulate muscle regeneration and restrain fibrosis, even is the case of massive ablation of muscle tissue. We anticipate that these innovative hydrogels could be of great interest for regenerative medicine approach.



POSTER 133

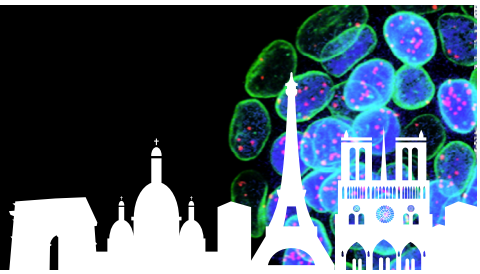
Hidenobu MIYAZAWA

Jona Rada, Alexander Aulehla

EMBL, Developmental Biology Unit, Heidelberg, Germany

Unraveling a signaling role of glycolysis in regulation of developmental timing in mammalian embryos

How metabolism interacts with genetic programs to determine phenotype is a fundamental yet unresolved question. It is increasingly clear that metabolism impacts gene expression and signal transduction, while fueling biological processes by providing energy and biomass. However, how metabolism plays an instructive rather than a permissive role during embryonic development remains unclear. In this meeting, we will present that glycolytic flux controls the timing of mouse presomitic mesoderm (PSM) development via regulating Wnt signaling rather than cellular bioenergetic state.
Vertebrate embryos undergo periodic segmentation of the PSM. This temporal periodicity is controlled by a molecular clock known as the segmentation clock, comprising of the Notch, Wnt, and FGF signaling pathways in mice. Since we previously revealed the necessity of active glycolysis for ongoing PSM segmentation, our primary interest was to reveal whether and how glycolysis plays an instructive role in this context. We first revealed that glycolytic flux controls the segmentation clock period in an anti-correlated manner. To probe for a signaling role of glycolysis, we employed a dynamical systems approach and demonstrated metabolic entrainment of the segmentation clock with periodic pulses of the glycolytic sentinel metabolite fructose 1,6-bisphosphate (FBP). Notably, periodic FBP pulses first synchronized Wnt signaling oscillations before Notch signaling oscillations, revealing a glycolysis-Wnt signaling axis. Critically, using genetics, we provide direct evidence that this glycolysis-Wnt signaling axis controls the segmentation clock period in a non-bioenergetic manner. Combined, our work demonstrates a glycolysis-FBP-Wnt signaling axis controlling developmental timing of mouse embryo mesoderm segmentation.



POSTER 134

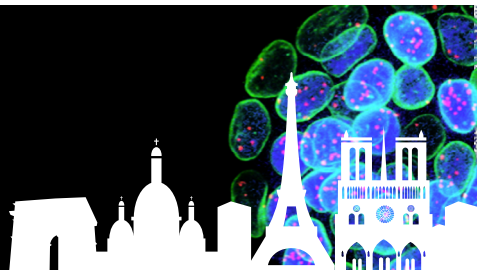
Sara ORTICA

Nicolas Dray, Laure Bally-Cuif

Institut Pasteur, Paris, France

Establishment of the Notch3 signaling pattern within the neural stem cell population of the adult zebrafish telencephalon

In the adult vertebrate brain, new neurons and glia are generated by pools of adult Neural Stem Cells (NSCs). The zebrafish dorsal telencephalon is enriched in adult NSCs: they are mainly quiescent, but can activate and re-enter the cell cycle, to maintain the NSC pool and permit neuronal production. The balance between quiescence and activation is controlled by Notch3 signaling, which gates cell cycle entry. The mode of action used by Notch3 to regulate this process is poorly understood for now, due to the lack of tools precise enough to capture signaling variations.
To overcome this limitation, we generated two transgenic lines where the C-terminus of the Notch3 receptor is tagged with fluorescent proteins, either via CRISPR/Cas9 technology, or with a recombined BAC harboring the tagged version of notch3. With these lines, it is possible for the first time in a vertebrate model to follow Notch3 protein localization and measure signaling activation after nuclear translocation of the intracellular domain, in real time in vivo as well as after immunostaining.
We are now taking advantage of these lines to investigate in detail the mechanisms of Notch3 signaling involved in the regulation of the NSC homeostasis in the dorsal telencephalon. We are particularly interested in understanding the link between Notch3 ligands, signaling dosage and targets in the maintenance of adult NSC population. Both families of Notch ligands, Delta and Jagged, are indeed expressed in our system. It has been reported that these two families can control Notch mode of action, shaping the signal patterning via either lateral inhibition (Delta) or lateral induction (Jagged). We will use our reporter lines to look at the changes in NSC activation and stemness after loss of function of the different ligands, to better describe and understand Notch3 role in our system.



POSTER 135

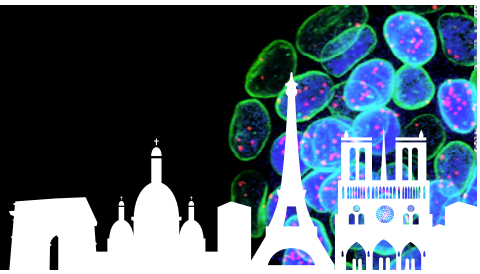
Aitana PEREA-GOMEZ

Furong Tang, Elodie Grégoire, Natividad Bellido-Carreras, Kheira Bouzid, Magali Dhellemmes, Aurélie Lardenois, Aurélie Despoux, Chloé Mayère, Serge Nef, Frédéric Chalmel, Marie-Christine Chaboissier

Université Côte d'Azur, CNRS, Inserm, iBV, France

New insights into the initiation and maintenance of mammalian ovarian development

In mammals, sex determination is the process that allows the formation of a testis or an ovary from an undifferentiated gonad initially identical in XX and XY embryos. In XY gonads, the male determining pathway is driven by the Y-linked gene Sry. SRY activates the expression of the transcription factor SOX9 and of a downstream genetic cascade that orchestrates testicular differentiation and morphogenesis. Our group has recently identified the long-sought ovarian determining factor, the -KTS variant of Wilms Tumor Supressor (WT1), that initiates the genetic cascade leading to the formation of an ovary in XX embryos. Loss of function of WT1 -KTS prevents ovarian development in XX individuals whereas an excess of WT1 -KTS in XY embryos induces precocious ovarian differentiation, prevents the activation of Sry and leads to male-to-female sex reversal.
We had previously demonstrated that once the ovarian program is launched, its maintenance requires the function of Rspo1. RSPO1 belongs to the R-Spondin family of secreted proteins that promote WNT/β-Catenin signaling by inhibiting the internalization and degradation of WNT ligand/receptor complexes. By using a new mouse model for conditional mutation of Rspo1 at different time points we have defined the critical temporal window of RSPO1 requirement during ovarian development. In addition, we have found that expression of steroidogenic enzymes and androgen receptor are among the earliest phenotypic defects in XX Rspo1 mutants. Through pharmacological and genetic inhibition of androgen receptor, we have established that abnormal activation of the androgen signaling pathway in XX Rspo1 mutant gonads promotes female-to-male sex reversal. Our work brings new insights into the mechanisms of primary sex determination and ovarian differentiation in mammals and into the etiology of Differences in Sex development (DSD) in human patients.



POSTER 136

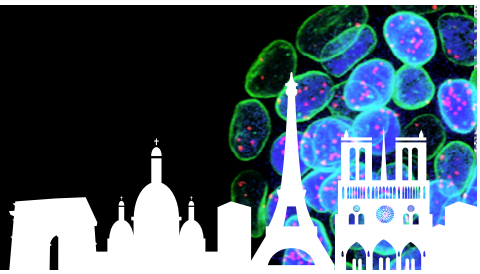
Cara PICCIOTTO

Minh-Son Phan, Jang-mi Kim, Lydie Couturier, Nisha Veits, Khallil Mazouni, François Schweisguth

Institut Pasteur, Paris, France

Symmetry breaking and fate divergence during lateral inhibition in Drosophila

Many tissues across many species form regular patterns of two distinct cell fates. A well-studied model to mediate binary fate decisions during development is lateral inhibition via Notch signaling. Lateral inhibition describes an intercellular negative feedback loop, that is proposed to amplify small stochastic differences in Notch activity over time. In neurogenesis, lateral inhibition singles out neural precursor cells from clusters of proneural cells, which are initially equipotent to become neural through the expression of proneural transcription factors. So far however, the temporal dynamics of symmetry breaking were not studied using live imaging.
Here we are using the abdomen of Drosophila as a model to study when and how symmetry breaking occurs on single-cell level. Using quantitative live imaging, we monitored the accumulation of the transcription factor Scute (Sc), used as a surrogate for proneural competence and adoption of the Sensory Organ Precursor cell (SOP) fate.
We found that fate symmetry breaking occurred early at low Sc levels. Fate divergence was not preceded by a prolonged phase of low or intermediate level of Sc accumulation. Analysis of Sc dynamics in wild-type and experimental contexts further revealed that cell-to-cell heterogeneity promoted fate divergence. Unexpectedly, lateral inhibition defects were also observed in roughly 10% of all SOPs. These were corrected via cellular rearrangements. We further observed that SOP emergence takes place at low levels of Notch activity, shortly after the onset of Notch inhibitory signaling and that expression of Notch target genes were preceded by expression of Sc. In sum, our data indicate that cell-to-cell heterogeneity in Sc levels underlies stochastic fate choice in the abdomen and experimentally support the intercellular negative feedback loop model.



POSTER 137

Etienne POIDOMANI

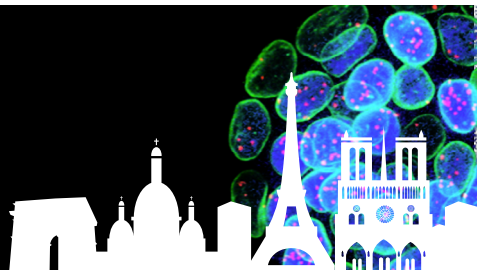
Alexandre Baffet

Curie Institute, Paris, France

Investigating pre-comitment in the cell fate decision of cortical progenitors

The human cortex is a complex structure that arises during embryonic development. Most neurons are present at birth, and several neurological disorders take root in development. Yet, human cortical development and several of its fundamental mechanisms are not fully understood. Amongst these, the precise mechanisms regulating whether progenitors choose to renew or differentiate (their cell fate decisions) are unknown. In particular, it is unclear whether apical radial glia (aRG), the progenitors of the neocortex, have equal output probabilities, or if they are pre-committed to certain types of divisions. In other words, is an aRG cell more likely to undergo the same type of division it has already gone through at the previous generation? Moreover, if a cell is artificially pushed towards a specific cell fate decision, can it revert back after the stimulation, or does it stay locked into a pre-committed lineage?

These questions are difficult to address with clonal methods, as the precise history of sequential divisions is largely lost. To answer these questions, we use a correlative microscopy technique in mouse brain slices that enables live tracking of dividing progenitors, and fate determination after fixation and immuno-staining. We here further implemented this method to track two successive divisions before fixation, in order to correlate cell fate decisions of aRG cells at the n+1 and n+2 generations. Morever, we established a pulse-chase assay to test whether artificial fate commitment of aRG cells towards a differentiation route is reversible, or if cells remain locked in this state. I will present this ongoing work aimed at better understanding the regulation of cell fate decisions in the developing neocortex.



POSTER 138

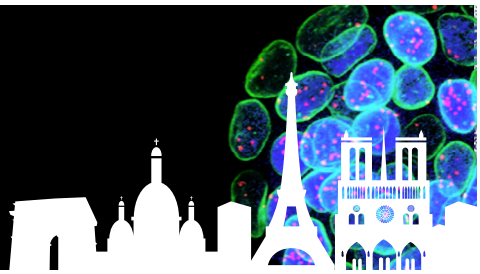
Guido POSERN

Anurag Singh, Anna Burova, Markus Moser, Ines Block

Institute for Physiological Chemistry, University of Halle,Germany

Control of epithelial tissue (re-)generation by the actin-regulated transcription factor MRTF-A

The actin-regulated transcription factor MRTF-A represents a central relay in mechanotransduction and controls a subset of SRF-dependent target genes. Despite its expression, its role in epithelial cells and during morphogenetic development is not well understood. Moreover, gain-of-function studies in vivo are lacking. To address this, we generated a conditional MRTF-A transgenic mouse model and started characterizing the effects of activated MRTF-A in the intestine and the mamma. Specific expression in the intestinal epithelium caused an erosive architectural distortion, villus blunting, cryptal hyperplasia and colonic inflammation, resulting in transient weight loss. Activated MRTF-A resulted in depletion of intestinal stem cells and reduced populations of all differentiated cell types in both murine guts and in primary 3D organoids generated from the transgenic animals. We observed a defective cryptal compartment and impaired self-renewal of the intestinal epithelium by MRTF-A gain-of-function. In addition, epithelial polarization of the enterocytes was altered. Our results suggest that activated MRTF-A in the intestinal epithelium shifts the balance between proliferation, differentiation and apoptosis.
Using WAP-Cre mice to activate MRTF-A in the bilayered mammary epithelium showed that transgenic mice fail to feed their offspring, but the pups survived in foster care. This demonstrated a functional failure in the mammary gland of the transgenic mother animals. Preliminary experiments suggest that expression of activated MRTF-A results in smaller acini, and luminal cells adopt myoepithelial traits while maintaining luminal markers. How activated MRTF-A may impair mammary differentiation and the feeding function will be discussed.



POSTER 139

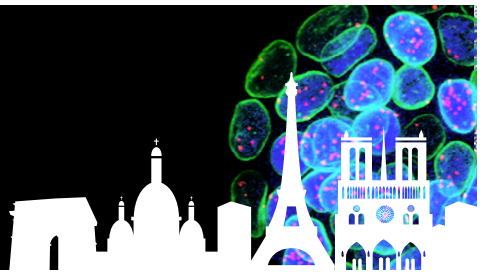
Mary PRESSÉ

Antoine Zalc

Institut Cochin, INSERM, CNRS, Université Paris Cité, Paris, France

Deciphering the molecular mechanisms controlling the re-emergence of pluripotency programs in cranial neural crest cells

During embryonic development, cells gradually restrict their differentiation potential, notably through the decrease in the proportion of opened chromatin and the increase in DNA methylation. This leads to a reduction both in the variety of genes expressed and in the potency of each cell. Thus, it has long been thought that once cells are committed to a germ layer and a specific fate, they were unable to spontaneously give rise to cell types different from their lineage of origin. However, cranial neural crest cells (CNCC) appeared as an exception, since those cells, although ectoderm-derived, are able to give rise to a large diversity of derivatives that build the face, including bones and cartilages, which are usually classified as mesoderm-derived. In a recent study, the lab demonstrated CNCC broader differentiation potential is due to the re-expression of pluripotency factors, including Oct4, in CNCC precursors. To better understand the mechanisms underlying CNCC expanded differentiation potential, we are focusing on Oct4 – the main pluripotency programs organizer – and setting up several strategies to understand the molecular regulation of Oct4 re-expression. To this end, we are modeling CNCC in vitro to identify conditions in which this population re-expresses Oct4 or not, and determine the transcriptional differences between them. In addition, we are establishing a mouse model to isolate and study pre-migratory CNCCs using single cell RNA-seq and ATAC-seq. Combining in vitro, ex vivo and in vivo approaches, we will decipher the mechanisms by which pluripotency programs are re-activated in vivo.



POSTER 140

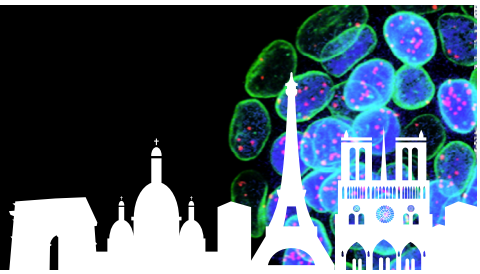
Ronan QUENEC'HDU

Nicolas Allegre, Bhasman Goswami, Caroline Vachias, Yvonne Scholte Op Reimer , Pierre Osteil, Nicolas Rivron, Claire Chazaud

Institut Génétique, Reproduction et développement (iGReD), INSERM/CNRS/UCA, Clermont-Ferrand, France

Development and morphogenesis of the mouse extra embryonic parietal endoderm: implication of the transcription factor GATA6

At the time of implantation in the maternal uterus, around 4.5 days of development, the mouse embryo performs the first epithelial-to-mesenchymal transition (EMT). At this stage, the epithelium of the primitive endoderm (PrE) differentiates into visceral endoderm (VE), which remains epithelial, and into the parietal endoderm (PE) whose mesenchymal cells that progressively cover the mural trophectoderm. PE formation has been little studied due to its co-occurrence with implantation. We show that the transcription factor GATA6 is highly present in PE cells, suggesting a role in their differentiation. By looking in vivo with specific markers of PrE, PE and EMT, we show that PE cells perform an EMT while still retaining some polarity markers such as pERM and aPKC, demonstrating a partial EMT. Live imaging is also carried out to track the origin of PE cells and their movements. In parallel, we carried out functional analyses with Gata6 conditional deletion and/or overexpression in embryos and in embryoid bodies derived from embryonic stem cells. We are currently carrying out transcriptomic analyses on embryoid bodies. Altogether, my project enables to further understand how PE is formed, with a focus on the role of GATA6 in this process.



POSTER 141

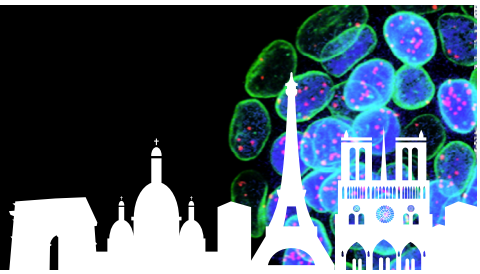
Katharina RAASCH[1,2]

Elise Maurat[1,2,*] , Alexander M. Leipold[3], Pauline Henrot[1,2,4], Maeva Zysman[1,2,4], Renaud Prevel[1,2,4], Thomas Trian[1,2], Tobias Krammer[3], Vanessa Bergeron[5], Matthieu Thumerel[1,2,4], Pierre Nassoy[6], Patrick Berger[1,2,4], Antoine-Emmanuel Saliba[3,7], Laetitia Andrique[5], Gaëlle Recher[6], Isabelle Dupin[1,2,8]

1. Univ-Bordeaux, Centre de Recherche Cardio-thoracique de Bordeaux, U1045, CIC1401, Pessac, France
2. INSERM, Centre de Recherche Cardio-thoracique de Bordeaux, U1045, CIC1401, Pessac, France
3. Helmholtz Institute for RNA-based Infection Research (HIRI), Helmholtz-Center for Infection Research (HZI), Würzburg, Germany
4. CHU de Bordeaux, Service d'exploration fonctionnelle respiratoire, Service de réanimation, Service de chirurgie thoracique, France
5. VoxCell Facility, TBMcore UAR CNRS 3427, INSERM US 005, Univ-Bordeaux, France
6. Laboratoire Photonique, Numérique et Nanosciences, UMR 5298 CNRS, Univ-Bordeaux, France
7. University of WÜrzburg, Faculty of Medicine, Institute of Molecular Infection Biology (IMIB), WÜrzburg, Germany
*8. Institut universitaire de France (IUF). * equal contribution (co-1st author)*

A novel in vitro tubular model to recapitulate features of distal airways: the bronchioid

While numerous in vitro airway models already exist, none of them gathers all characteristics for an ideal distal bronchial organoid, together with a tubular geometry. This hinders full understanding of the mechanisms of lung development, associated diseases and ultimately drug discovery. Working with the Cellular Capsule Technology, we developed a so-called bronchioid model, using an innovative tubular cell-based assay and human bronchial adult stem cells derived from clinical samples. We produced a tubular scaffold made of alginate gel, that drives the spontaneous self-organisation of epithelial cells. Fine control of the level of contraction is required to obtain a model of distal bronchiole, with physiologically relevant shape and size. 3D imaging, gene expression and single-cell RNA-seq analysis of bronchioids made of bronchial epithelial cells demonstrates the tubular organization, the formation of epithelial junctions, as well as differentiation into ciliated and goblet cells. Ciliary beating is observed, at a decreased frequency in bronchioids made of cells from patients with respiratory diseases. The bronchioid can be infected by rhinovirus. An air-liquid interface is introduced, that modulates gene expression.
We provide here a proof of concept of a perfusable bronchioid, with proper mucociliary and contractile functions. We are currently integrating mesenchymal cells into the model to investigate epithelial-mesenchymal interactions. Key advantages of our approach, such as the air-liquid interface, the lumen accessibility, the recapitulation of pathological features and possible assessment of clinically pertinent endpoints, will make our pulmonary organoid-like model a powerful tool for fondamental and pre-clinical studies.



POSTER 142

Ana RAFFAELLI

Tom Wyatt, Ewa Paluch, Kevin Chalut

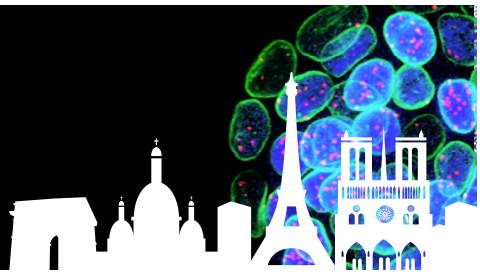
Department of Physiology, Development & Neuroscience; Cambridge Stem Cell Institute, University of Cambridge

Extracellular matrix mechanics regulates BMP signalling through a switch in epithelial organisation in human pluripotent stem cells

Historically, most research on cell fate induction was focused around biochemical signals, however, it is now clear that mechanical signalling from the extracellular matrix (ECM) also influences cell fate. For example, in human pluripotent stem cells (hPSCs), softening of the substrate increases mesoderm differentiation. We investigate the mechanisms underlying this phenomenon.

To investigate the role of mechanical environment on hPSC fate, we exposed these cells to various stiffnesses using polyacrylamide hydrogels and subjected the cells to mesoderm-inducing BMP4 signal. We found that on soft substrates, hPSCs exhibit higher levels of BMP signalling activity. We showed that increased BMP signalling starts with lower Focal Adhesion Kinase (FAK) activation, and consequently lower activation of PI3K. Lower FAK-PI3K activity on soft substrates causes a less evenly-organised epithelium, in comparison to a more hexagonal cellular arrangement on stiff substrates. We hypothesised that these morphological changes represent alterations of epithelial functional properties. Indeed, a tight junction (TJ) protein Claudin-6 displays reduced junctional localisation in response to lower FAK-PI3K activity on soft substrates. Concomitantly, we also observed lower activity of apical actomyosin, whose force regulates TJ barrier. Finally, we asked whether these differences in TJ organisation are indicative of differences in epithelial permeability. To directly assess this, we exposed live cells to fluorescent dextran. We found that on soft substrates, hPSC epithelia exhibit higher permeability to BMP4-sized dextran. We are now investigating how alongside permeability, epithelial polarity is also affected in response to the substrate.

Together, our work identifies a mechanism through which mechanical signalling from the substrate intertwines with biochemical signalling to affect cell fate in hPSCs. We are also aiming to investigate whether such mechanism is involved in initiation of gastrulation during basement membrane remodelling. In general, our findings impact our understanding of the role of ECM properties on biochemical signalling in fate transitions.



POSTER 143

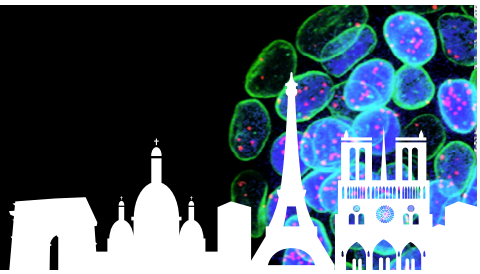
Anne ROSFELTER[1]

Ian David Estabrook[2], **Anna Erzberger**[2,3], **Yu-Chiun Wang**[1]

1. RIKEN Center for Biosystem Dynamic Research (BDR)
2. Cell Biology and Biophysics Unit, European Molecular Biology Laboratory (EMBL)
3. Heidelberg University

The establishment and the mechanical role of the epithelium's simple columnar organization in the cellularizing and gastrulating Drosophila embryo

Epithelial tissues are the building blocks of animal bodies. Highly polarized epithelial tissues typically exhibit two packing organizations, the simple columnar epithelium (SCE) or the pseudostratified epithelium (PSE). The critical feature that distinguishes between the two is whether the nuclei are located in a uniform position along the apico-basal axis of the cells as in the SCE, or randomized positions, as in the PSE. What cellular and mechanical principles orchestrate these organizations, and whether they have distinct functional and mechanical advantages remains poorly understood. The epithelium of the pre-gastrulating Drosophila embryo displays a SCE. Nuclear mis-positioning has been observed in mutants of genes related to cell surface mechanics, nucleo-cytoskeletal connection and microtubule dynamics. The mutants' tissue morphology resembles that of a PSE, providing a unique opportunity to elucidate both the mechanical principle of the transition between SCE and PSE and the functional relevance of each organization in the context of morphogenesis. In particular, several epithelial folds form with distinct cellular and mechanical mechanisms during Drosophila gastrulation, one major unknown question is whether the columnar organization is necessary for fold formation. Overall, we aim to understand (i) how epithelial organization is established and maintained, and (ii) whether the SCE organization serves a specific purpose, especially, whether it can influence folding. To do so, we compare mutants with a PSE-like state with WT embryos using a combination of high-resolution microscopy, quantitative analysis of nuclear and cellular morphology, and theoretical modeling.



POSTER 144

Meenu SACHDEVA

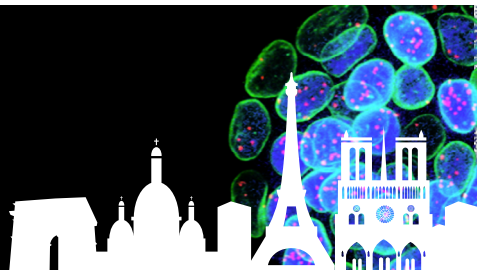
IIT Kanpur, India

The role of stiffness and cell adhesion molecules in the process of forebrain roof plate invagination

The invagination of the forebrain roof plate leads to the division of the single telencephalic vesicle into two cerebral hemispheres. Disruption of this process often leads to a congenital disorder known as holoprosencephaly (HPE). While loss-of-function mutations in several genes have been linked to HPE, there are very few mechanistic insights available. Because the invagination of the roof plate is conserved between birds and mammals, we leveraged the chick (Gallus gallus) embryo as a model system to address this limited mechanistic understanding.

The roof plate, a two-layered structure composed of neuroepithelium and overlying mesenchyme, requires coordinated interplay for invagination. To understand the driving forces behind this morphogenesis, we employed Atomic Force Microscopy (AFM) to measure the stiffness of each layer. Tissue stiffness is often linked to cell adhesion molecule (CAM) expression. This prompted us to screen for CAM expression patterns in the developing chick forebrain roof plate. This analysis revealed differential expression of Cadherins, a CAM family.

We focused on N-Cadherin and R-Cadherin, functionally manipulating their activity. This resulted in abnormal forebrain development, with evagination (outward folding) replacing invagination and mesenchyme separation from the neuroepithelium. We further measured roof plate stiffness under normal conditions and after CAM manipulation. The results support our theory that differential stiffness plays a significant role in invagination. Additionally, we propose a potential mechanism for interaction between the neuroepithelium and mesenchyme. Overall, this work sheds light on the mechanism of forebrain roof plate invagination and identifies the novel regulatory role of Cadherins in mediating differential stiffness, a crucial driver of this process.



POSTER 145

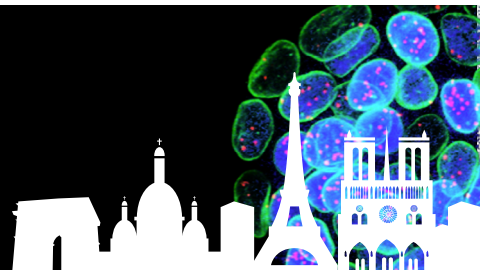
Bérénice SAGET

Virginie Chotard, Cécile Jouffret, Yvrick Zagar, Céline Nanteau, Bruno Gasnier, Olivier Goureau et Alexandra Rebsam

Institut de la Vision, Sorbonne Université, Paris, France

Deciphering the role of the amino-acid transporter SNAT8 in the developing retinal pigment epithelium and neural retina

During development, the retinal progenitor cells (RPCs) in the neural retina are in contact with the retinal pigment epithelium (RPE). The RPE matures and pigments early on, and impacts retinal neurogenesis. In mouse models of albinism, early defects in RPE cells, causing hypopigmentation, lead to a delay in neurogenesis and ultimately important visual deficits such as low visual acuity, nystagmus and a lack of 3D vision. However, how the RPE affects the RPCs during development is still unknown.
Recently, an interesting candidate emerged from the identification of the FHONDA syndrome, a very rare genetic disease with the same visual deficits as albinism but without hypopigmentation. We have previously shown that the mouse model of FHONDA also recapitulates most retinal and visual deficits present in mouse models of albinism. The protein impacted in this disease is SNAT8, an understudied amino acid transporter. We found that SNAT8 is expressed in the RPE at embryonic stages in mouse and could thus be a downstream target important for both FHONDA syndrome and albinism. We show that SNAT8 is located in the lysosomes of non-pigmented HeLa cells, the organelles closest to melanosomes, and could therefore play a role in signaling within the RPE to regulate retinal neurogenesis.
To study the subcellular localization of SNAT8 and to identify its substrates, we are using hiPSC-derived RPE cells. Furthermore, we have generated a human in vitro model using CRISPR-Cas9 to obtain a non-sense mutation in the causative gene of the FHONDA syndrome and assess the impact of this SNAT8 loss of function on hiRPE cells.

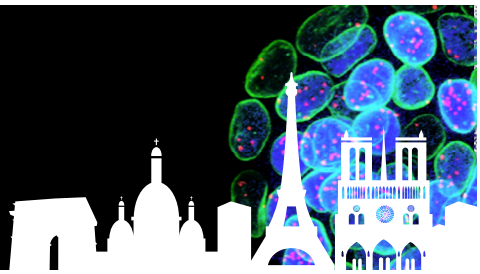


POSTER 146

Magdalena SCHATKA

GATA4 and NKX2.5 regulate Nkx2.5 expression through a conserved enhancer element during early heart development

Within an embryo, the heart is the first organ to form as its circulatory function is essential for both development and postnatal life. Past research has identified a complex network of numerous genes and pathways involved in heart formation, with dysregulation often leading to congenital heart disease. Therefore, understanding the mechanisms of cardiogenesis is crucial. The transcription factor NKX2.5 is a key regulator of heart development, with mutations causing severe defects, however, its upstream regulation is not fully understood. For this reason, we investigate the regulation of this gene within early heart development by characterising a conserved cis-regulatory element (CRE) associated with Nkx2.5. We demonstrate that this enhancer not only is functionally conserved across human, mouse, chicken and frog, but is also regulated by GATA4, another major cardiac transcription factor. Using ATAC-Seq data from chicken cardiac progenitor cells, several transcription factor binding sites were identified. Site-directed deletions within a reporter construct tested the individual and combined effect of these sites on Nkx2.5 expression in-vivo. The results of this were verified using preliminary CUT&RUN data, which confirmed interactions between GATA4, NKX2.5 and the CRE. This supports the hypothesis of GATA4 as an upstream regulator and an autoregulatory loop involving NKX2.5, a mechanism previously thought to be exclusive to mammals.



POSTER 147

Anis SENOUSSI

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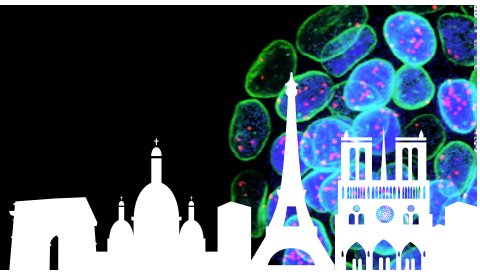
MDC Berlin,Germany

Revealing trajectory-specific transcriptional dynamics during zebrafish gastrulation using single-cell metabolic RNA labeling

Every time an egg is fertilized, the cellular diversity of an animal must be rebuilt from scratch. Therefore, a central question in developmental biology is how cells differentiate to acquire distinct fates. During zebrafish gastrulation, this process is highly regulated and relatively fast, leading to the emergence of cellular diversity from a single fertilized egg. A combination of genetics, molecular biology, and microscopy approaches has led to fundamental discoveries. In recent years, single-cell genomics has enabled the analysis of transcriptional differentiation trajectories at an unprecedented scale and resolution. However, it remains unclear how transcription and mRNA degradation rates are coordinated and regulated during development in a developmental trajectory-specific manner.

This study aims to measure mRNA dynamics using a novel methodology that combines single-cell RNA sequencing and labeling with biochemical nucleoside conversion and sequencing (scSLAM-seq) in zebrafish embryos. This approach creates a detailed temporal atlas of single-cell RNA changes, moving towards a dynamic view of differentiation. We generated a comprehensive single-cell RNA sequencing atlas of zebrafish gastrulation at high temporal and cell type resolution. We constructed single-cell developmental trajectories based on transcriptomic similarities and RNA velocity, identifying driver genes regulated in a trajectory-specific manner. Utilizing temporal information from labeling, we identified cell types with high transcriptional activity and computed genome-wide mRNA dynamics for each developmental trajectory.

Coupled with traditional developmental biology and recent single-cell and spatial genomics technologies, our study provides insights into how mRNA dynamics shape cellular differentiation within the spatiotemporal complexity of embryonic development.



POSTER 148

Shireen SHAJAHAN

Yann Loe-Mie, Marion Salmon-Legagneur, Tatiana Traboulsi, Anne Dejean, Jack-Christophe Cossec

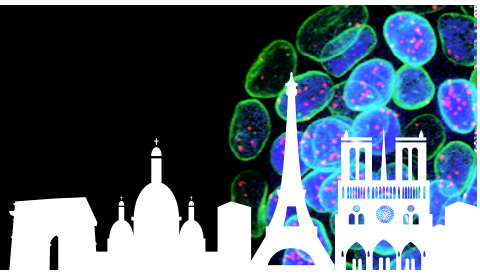
Institut Pasteur, INSERM, Sorbonne Université, Paris, France

Z-DNA drives Zscan4-dependent chromatin reorganization to induce and safeguard totipotent stem cell identity

Mammalian development involves a sequence of cell fate decisions leading to restricted developmental potential and increased specialization. This progression is marked by gradual potency loss, significant transcriptome changes, and extensive chromatin remodeling. Totipotent 2-cell (2C) embryos are defined by a unique transcriptional signature and a relaxed chromatin organization (global hypomethylation, poor chromatin compaction, increased chromatin accessibility). However, how 2C embryos safeguard their strict cell identity in a permissive chromatin conformation remains poorly understood.

The spontaneous conversion of mouse embryonic stem cells (mESCs) to a 2C-like state, called 2C-like cells (2CLCs), provides a convenient in vitro model system to study totipotent-like characteristics, as they share several features with 2C embryos. To investigate genome-wide chromatin interactions, chromosome conformation capture experiments (Hi-C) were conducted in both mESCs and 2CLCs. While the global chromosome architecture remained stable between the two cell populations, we identified new large interacting regions specific to 2CLCs, mostly located towards one end of numerous chromosomes. DNA-FISH experiments showed that these specific interactions localize to the nuclear periphery of 2CLCs, associated with a histone mark switch from active in ESCs to repressive in 2CLCs preventing transcriptional activation in these regions. The formation of these chromatin interactions depends on Zscan4 family proteins, a chromatin factor expressed specifically at the 2C stage. Intriguingly, Zscan4 has been shown to bind to motifs predisposed to adopt a Z-DNA conformation, characterized by a left-handed double helix. We detected the presence of Z-DNA in 2CLCs, and their induction significantly increased the proportion of 2CLCs displaying chromatin conformations akin to spontaneous 2CLCs.

In summary, we propose a two-step mechanism in which the formation of Z-DNA induces the emergence of 2CLCs, followed by their relocation to the nuclear envelope in large Zscan4-dependent chromatin domains that might be crucial for securing totipotency within a globally permissive chromatin environment.



POSTER 149

Anurag Kumar SINGH

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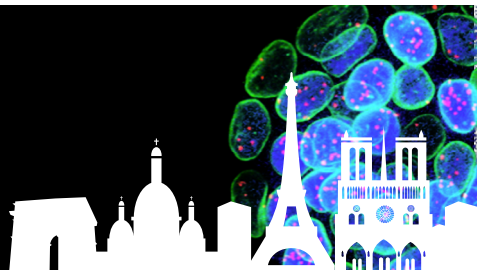
MRTF-A gain-of-function in mice impairs homeostatic renewal of the intestinal epithelium

The actin-regulated transcription factor MRTF-A represents a central relay in mechanotransduction and controls a subset of SRF-dependent target genes. However, gain-of-function studies in vivo are lacking. Here we characterize a conditional MRTF-A transgenic mouse model. While MRTF-A gain-of-function impaired embryonic development, induced expression of constitutively active MRTF-A provoked rapid hepatocyte ballooning and liver failure in adult mice. Specific expression in the intestinal epithelium caused an erosive architectural distortion, villus blunting, cryptal hyperplasia and colonic inflammation, resulting in transient weight loss. Organoids from transgenic mice repeatedly induced in vitro showed impaired self-renewal and defective cryptal compartments. Mechanistically, MRTF-A gain-of-function decreased proliferation and increased apoptosis, but did not induce fibrosis. MRTF-A targets including Acta2 and Pai-1 were induced, whereas markers of stem cells and differentiated cells were reduced. Our results suggest that activated MRTF-A in the intestinal epithelium shifts the balance between proliferation, differentiation and apoptosis.



POSTER 150

Baptiste TESSON

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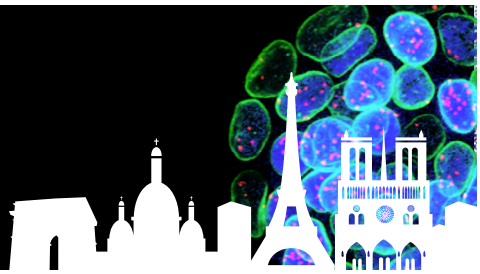
**Co-First Author*

Patterned cell displacement and adhesion drives epithelial folding

Folding is a crucial morphogenetic event that transforms a 2D epithelial sheet into a 3D structure. We explored the mechanisms of tissue folding during Drosophila wing morphogenesis by focusing on wing hinge shaping. The wing hinge forms the junction between the thorax and the wing blade. Beyond its role in wing articulation, its compaction during pupal morphogenesis is essential for wing blade elongation. However, the mechanisms underlying this compaction and its role in wing function remain unclear. In this poster, we show that the hinge compaction is anisotropic and localized to specific hinge domains. We identify that the compaction in a specific subregion emerges from the folding of the hinge epithelium, and we delineate how genetic patterning of extracellular matrix deposition and cell displacement promote fold dynamics and positioning. Interestingly, this hinge fold individualizes the alula, a structure required for the correct articulation of the wing. Our results highlight how genetic patterning and collective cell flow provide a simple design principle shaping an organ subunit, while ensuring the global morphogenesis and functionality of the whole organ.



POSTER 151

Valentine THOMAS

Chiara Zurzolo, Christel Brou

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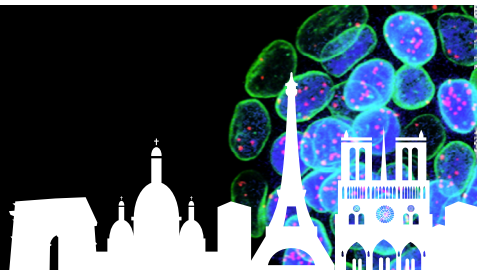
Unraveling the interplay between Tau aggregates and autophagy-lysosomal dysfunction

Neurodegenerative diseases like Alzheimer's and Parkinson's have been associated with the pathological aggregation of misfolded proteins. In both diseases, respectively, Tau and α-synuclein seed and spread from cell-to-cell in a prion-like manner. Previous data suggests that aggregate-containing cells are dysfunctional in the autophagy-lysosomal pathway, leading to aggregates persistence and neurodegeneration. More precisely, we and others have shown that exogenous α-synuclein fibrils accumulate in lysosomes in human and mouse neuronal cells (SH-SY5Y and CAD cells), resulting in their swelling and decreased activity (measured by lysotracker labelling and cathepsins activity measures). However, in the case of Tau, we previously reported that endogenously formed repeated-domain (RD)-Tau aggregates were recognized as autophagic cargos but failed to be delivered to lysosomes. Yet, whether aggregates are not degraded because they are intrinsically resistant to degradation or because they impair the autophagy-lysosomal pathway still remains an open question. Our study aims to better characterize the fate of full-length (FL)-Tau aggregates and whether these cause autophagy-lysosomal disruption. In human SH-SY5Y neuronal cells, we stably overexpressed soluble or aggregated P301S-FL-Tau-mClover3 based on a Tet-off system. Using immunofluorescence and western blotting approaches, we show that in these cells lysosomes are affected in their morphology (bigger), positioning (more peripheral). However, unlike in the presence of α-synuclein aggregates, they are still labeled with lysotracker, suggesting that their acidification is not impaired. Intriguingly, we found that FL-Tau-mClover3 silencing by doxycycline doesn't revert this lysosomal phenotype, suggesting that the simple overexpression of FL-Tau modifies lysosomes irreversibly. Moreover, we observe that aggregates are more stable than soluble proteins and are not targeted to autophagy-lysosomal degradation. We are currently studying the mechanisms governing Tau aggregate formation, maintenance, and downstream effects on lysosomes, notably via lysosome purification and immunoprecipitation, in comparison to α-synuclein.



POSTER 152

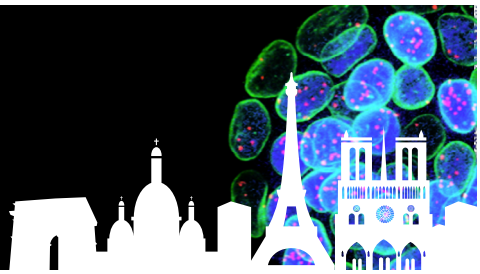
Larissa THURNER

Aritra Misra, Athanasios Pasias, Mari Tolonen, Jakub Sedzinski

NNF Centre for Stem Cell Medicine - reNEW, Copenhagen University, Copenhagen, Denmark

From extracellular cues to building a lung-like epithelium: mechanical forces in shaping tissues

How can a uniform pool of stem cells create patterned tissue with functionally distinct cell types? Such a process can be observed in emerging lung-like epithelia, such as the developing frog skin (Xenopus laevis). In here, progenitor cells become specified while simultaneously the tissue undergoes formational changes and acquires its final architecture. Gene regulatory networks have been extensively studied in this context, however how extracellular cues influence cell fate and patterning remains largely unknown. In the developing frog skin, transcriptomic profiling revealed a drastic and temporary increase of extracellular matrix protein hyaluronan (HA). We hypothesized that HA could be a crucial regulator of differentiation and tissue formation by exerting hydrostatic pressure. With the help of perturbation studies, we could observe a change in cell type proportions and an altered architecture of the epithelial sheet. Additionally, life-imaging data indicates differences in how progenitor cells dynamically interact with their surrounding cells. To further explore HA's function in regulating stem cell fate and tissue morphogenesis, we are currently investigating the molecular basis of this process. We aim to understand what molecular players mediate these signals and how they are translated into the cell's behaviour. In summary, our findings underscore the critical role of forces of the extracellular environment in shaping lung-like epithelia. Knowledge on how cells interact with their environment and the consequence of it, is key in understanding how to build a tissue.



POSTER 153

Samuel TOZER

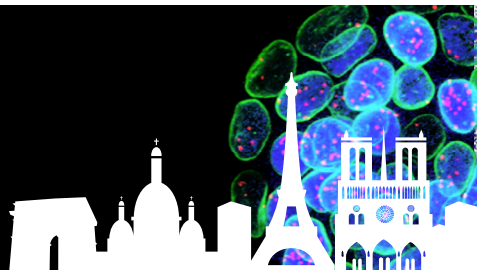
Bojana Djelic*, Rosette Goiame, Xavier Morin

IBENS, CNRS, Paris, France
**First Author*

Mib1 asymmetry in neurogenic divisions relies on ciliogenesis-regulated anchors and mitotic relays

Asymmetric divisions of progenitor cells are crucial for prolonged neurogenesis during nervous system development in vertebrates. The inheritance of differently aged centrosomes was shown to correlate with asymmetric cell fate decision. Centriolar satellites, enriched at the "young" newly-duplicated centrosome, are anchoring points for the Notch regulator Mindbomb1 (Mib1), mediating its preferential inheritance by the prospective neuron following division, therefore driving differential Notch activity and fate acquisition. This project aims to determine the basis of asymmetry establishment in interphase and its maintenance throughout mitosis.

Contrary to cell lines where they have been described as an amorphous cloud of proteins surrounding the centrosome, PCM1-positive centriolar satellites are strongly enriched at the daughter centriole in vertebrate neural progenitors. Surprisingly, they do not appear to rely on active transport to be recruited but rather on a combination of aggregation (through liquid-liquid phase separation (LLPS)) and direct interaction with the centrioles. Our data indicate that the anti-ciliation protein Cp110, actively excluded from the mother centriole, is required to anchor PCM1 and Mib1 to the daughter centriole. This highlights the ability of the ciliogenic program to polarize centrosomal organization, creating the conditions to instruct asymmetric cell fates. However, centriolar satellites are dispersed during mitosis and can no longer serve as Mib1 centrosomal anchors. We hypothesize that another interactor, pTBK1, enriched at both centrosomes during mitosis allows the local reattachment of Mib1 to centrosomes. In addition, our data suggest that Mib1's ability to oligomerize during mitosis is fundamental to maintain the integrity of the Mib1 pool. Thus, Mib1 asymmetric inheritance in neural progenitors would rely on different anchors in interphase and mitosis but also different physical properties (LLPS in interphase and self-oligomerization in mitosis).



POSTER 154

Nisha VEITS

Y. Guo, J. He, K. Mazouni, M. Bres, C. Mestdagh, Y. Yan, F Schweisguth

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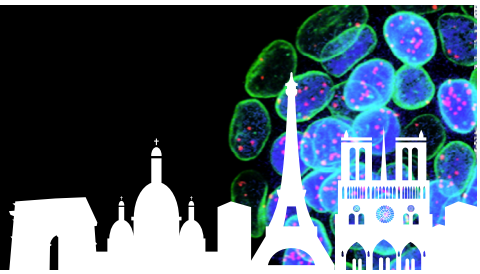
Genetic perturbations in energy metabolism affect developmental speed in the fly eye

The various developmental decisions underlying the making of animals are temporally ordered and occur at a stereotyped speed in each species. How developmental speed is genetically encoded is not known. Here, we use the developing Drosophila eye to address this issue. The adult eye forms via a differentiation front that sweeps through the eye imaginal disc at a constant speed. While the regulatory logic underlying the progression of this differentiation front is well understood, how speed is regulated is not known. Using a tissue-specific RNAi assay that allows us to monitor variations in the progression speed of the front independently of physiological cues acting at the organismal level, we looked for genes required for the timely progression of the front. This small screen identifies several genes involved in energy metabolism, including several components of the mitochondrial Electron Transport Chain (ETC). Using an ATP sensor, we found that ATP levels remained constant upon ETC inhibition due to increased glycolysis. Using scRNAseq we found that expression of the Lactate dehydrogenase (Ldh) gene was increased upon ETC inhibition in the undifferentiated cells anterior to the differentiation front. This compensatory response was required to regenerate NAD+ to fuel glycolysis. Increasing the rate of NAD+ regeneration using a bacterial NADH oxidase or adding NAD+ precursor in the food suppressed the delayed progression of the front upon defective ETC. Additionally, inhibiting NAD+ synthesis via the salvage pathway slowed the progression of the front. We conclude that energy metabolism regulates developmental speed and suggest that free NAD+ levels may be limiting for proper speed in the Drosophila eye.



POSTER 155

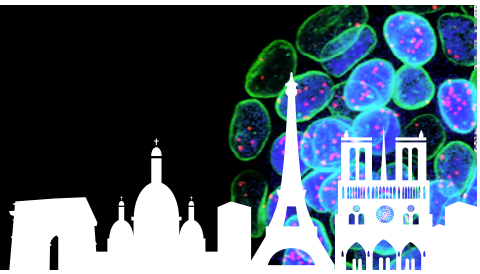
Anaïs VERTUEUX

Agathe Verraes, Christie Ouaddi & Jean-Marc Verbavatz

Institut Jacques Monod, Université Paris Cité, Paris, France

ORP3, and the importance of lipid transport proteins in mitosis

Phosphoinositides are lipids with multiple functions. They can recruit cytoskeletal nucleating factors to exert force on their resident membranes. During cell division, phosphoinositides, especially PIP2 form dynamic patterns at the plasma membrane, providing a transmission line to the cytoskeleton, necessary from chromatin segregation to abscission. Multiple kinases and phosphatases remodel phosphoinositides at membranes, partially explaining their regulations. Lipid transport at membrane contact sites (MCS) also contribute to the lipid composition of cell membranes, particularly phosphoinositides. MCS consist of the apposition of membranes from distinct organelles, where lipid transport proteins foster intermembrane transfer of lipids. However, the regulation of phosphoinositide transport at MCS in cell division remains unexplored.
ORP3 is a lipid transfer protein binding PIP2 and transporting PI4P from the plasma membrane (PM) to the ER. ORP3 harbors two binding domains to the ER protein VAPA: a canonical domain (FFAT1) and a phospho-inducible domain (FFAT2). I have shown that ORP3 depletion leads to various mitosis and ploidy defects. During mitosis, the localization of ORP3 is spatially and temporally regulated. ORP3 is mostly cytoplasmic during interphase and shifts to the ER in a VAPA-dependent and FFAT2-phosphorylation manner in prometaphase. ORP3 KO or KD is correlated to chromosome alignment and condensation defects along the mitotic furrow, suggesting a defective distribution of polarity complexes located at the plasma membrane. During telophase, ORP3 is concentrated at the cytoplasmic bridge. It may contribute to PIP2 regulation by depleting PI4P, the PIP2 substrate at the PM. Accordingly, a non functional mutant of ORP3 unable to transport PI4P accumulates at the bridge, suggesting accumulation of PIP2. In conclusion, ORP3 localization regulates PIP2 and PI4P distribution at the PM at different steps during mitosis, which is crucial to allow proper chromosome transmission to the daughter cells.



POSTER 156

Hélène VIGNES

Andreas Schoenit, Lucas Anger, Elisabetta Marangoni, Philippe Chavrier, René-Marc Mège, Benoit Ladoux, Carine Rossé

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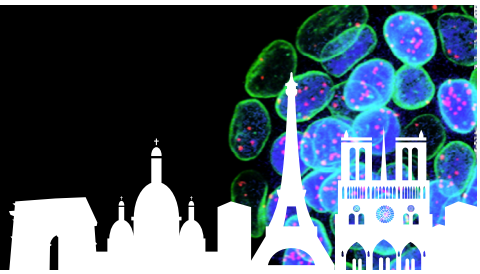
Understanding the impact of intra-tumor heterogeneity found in metaplastic breast cancer on tumor progression

Cancers, particularly breast cancers, exhibit significant intra-tumoral heterogeneity, which poses considerable therapeutic challenges. Metaplastic breast cancer, despite its rarity, manifests enhanced aggressiveness and poor prognostic outcomes, largely attributable to its heterogeneous nature. It is characterized by the coexistence of distinct tumor subpopulations with both epithelial and mesenchymal cancer cells. Our hypothesis is that this spatial intra-tumoral heterogeneity favors tumor progression via a cooperation between the different subpopulations of cancer cells. To investigate this, patient-derived xenografts (PDXs) from two originally distinct patients are used to obtain primary cell cultures in the form of tumoroids. Upon culturing the tumoroids on a substrate (glass coated with fibronectin or type I collagen), the preservation of the two excepted sub-populations, epithelial and mesenchymal, as well as their spatial segregation, is observed. Our findings reveal that the epithelial subpopulation expresses E-cadherin (E-cad+) and is surrounded by mesenchymal cells negative for E-cadherin (E-cad-). Interestingly, epithelial cells exhibit invasive behavior through collective cell migration at the interface with mesenchymal cells. They infiltrate either beneath the mesenchymal cells on glass, or within a gel of type I collagen. This result suggests that the presence of mesenchymal cells is necessary for inducing invasion. A competitive dynamic exists at the interface between the two subpopulations, since at the expense of the expansion of the epithelial cells, the mesenchymal cells detach from the substrate (extrusion phenomenon) and also form 3D multilayer cell structures locally at the interface. We observed that the formation of these multilayered structures, that could promote tumor growth, is associated with an increase in secreted fibronectin by mesenchymal cells that may help to glue the cells together. We are currently investigating whether these aggregates of mesenchymal cells confine the epithelial cells inducing their invasive behavior (mechanical contribution) or whether some biochemical are also needed to guide the invasive behavior of the epithelial cells (biochemical contribution). In summary, our findings suggest that the presence of different cancer subpopulations within the same tumor may play a pivotal role in breast tumor progression.



POSTER 157 & FLASH TALK

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From pluripotent stem cells to intervertebral disc progenitor cells: a reconstruction based on single-cell transcriptomics

During embryonic development, the notochord act as signaling structure, essential for forming the axial skeleton among others. In particular, the notochordal cells (NC) actively participate in the formation of the intervertebral disc (IVD), and subsequently reside in its center. NC are key regulators of the IVD homeostasis, and their loss during childhood has been linked to the onset of disc degeneration. With no effective treatments available yet, NC hold promise for cell-based therapies (Bach et al. 2022, Front. Cell Dev. Biol.). Understanding the molecular regulation of NC specification and maturation into IVD progenitors during embryogenesis and throughout life is crucial.

Based on knowledge from mouse developmental biology, we defined a protocol to differentiate human induced pluripotent stem cells into notochordal-like cells (NLCs), relying on a fine-tuned balance of WNT/β-catenin, NODAL/SMAD2/3, and BMP/SMAD1/5/8 signaling. Our recent work has described the molecular signature of the notochord using single-cell RNA sequencing from both in vitro human stem cells and in vivo human native notochord (8 weeks GA) (Warin, Vedrenne et al. 2024, iScience). By selectively inhibiting the TGF-β pathway, we reduced cellular heterogeneity during in vitro differentiation. Our novel time course scRNA-seq dataset will uncover the transcriptomic landscape of notochordal lineage specification, pinpointing the gene networks driving cell fate decisions in vitro.

We are pursuing our research by identifying critical cues to preserve NLCs embryonic identity, guiding their maturation towards a rejuvenating phenotype, and explore their full potential using 3D culture systems. These insights are necessary for developing models to study and regenerate diseased disc-tissue.

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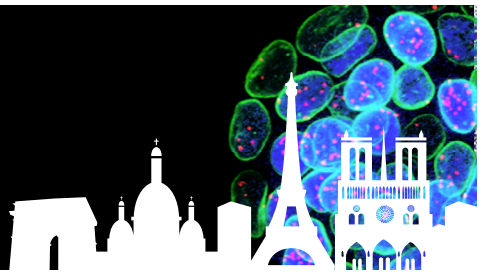

POSTER 158

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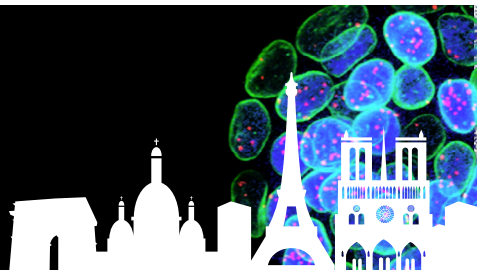
A differential requirement for ciliary transition zone proteins in human and mouse neural progenitor fate specification

Although cilia are widely distributed in the developing CNS, their dysfunction in humans leads to region-specific defects in neurodevelopmental ciliopathies such as Joubert syndrome, which is characterized by a distinctive brain malformation («molar tooth sign») involving the cerebellum and brainstem [1]. The pathogenetic mechanisms linking ciliary dysfunction to such specific neurodevelopmental defects are largely unknown. Here, emerging approaches of hiPSC-based organoids offer new opportunities to study the context-specific role of primary cilia in a human development.
By using mESC- and hiPSC-derived spinal organoid approaches, we identified species- and progenitor type-specific differences in the function of the ciliopathy proteins RPGRIP1L and TMEM67. We show that spinal organoids derived from Rpgrip1l mutant mESCs faithfully recapitulate the loss of cilia on neural progenitors, the strong reduction of SHH signaling and the loss of motoneurons (MNs) observed in mutant mice. In contrast, hiPSC-derived neural progenitors mutant for RPGRIP1L or TMEM67 present cilia, activate SHH signaling and produce MNs. Remarkably, we show that human RPGRIP1L-deficient spinal organoids show anteroposterior patterning defects thereby adopting hindbrain instead of spinal identities. Temporal transcriptome analysis revealed that the anteroposterior specification defect arises in early axial progenitors. Interestingly, cilia are absent from RPGRIP1L-deficient axial progenitors indicating a progenitor-type specific role for TZ proteins in cilia formation. Candidate signaling pathways that could be controlled by cilia in early axial progenitor cells and regulate anteroposterior pattern formation are WNT, RA or FGF signaling. [2]
In summary, our study uncovers distinct functions for ciliopathy proteins in humans and mice and a novel role for RPGRIP1L and cilia in human axial progenitors. These findings have important implications for understanding the role of cilia in human spinal cord and hindbrain development, that could be implemented in the pathogenic mechanisms of neurodevelopmental ciliopathies.

[1] Doi: 10.1016/S1474-4422(13)70136-4
[2] Doi: 10.1101/2024.02.28.582477



POSTER 159

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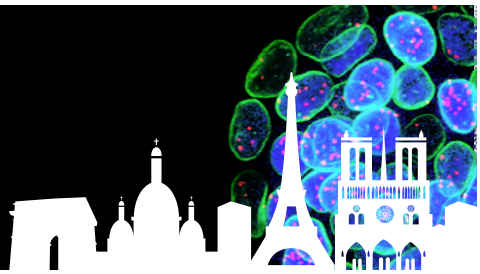
Impact of RhoA-mediated contractility at the multi-cellular scale in cell extrusion process in MDCK epithelia

Cell extrusion is one of the mechanisms allowing abnormal or supernumerary cells to be eliminated from epithelia in order to control the integrity of the tissue. Mechanical stresses in epithelial tissue, such as induced by cell compaction or topological defects, have been shown to trigger the initiation of extrusion events. However, the details of decision-making during mechanically-induced extrusions remain poorly known. In particular, why a specific cell is extruded out of a crowded epithelium is still not well understood, neither is the fate of extruded cells. They can activate apoptotic pathways before being removed from the tissue or can be extruded alive: what are the mechanisms that regulate these different outputs ? We address this question through a combination optogenetic and microscopy techniques.
Optogenetics approaches are combined with Traction Force Microscopy experiments to take the quantitative aspect of the tool to a higher level. Optogenetics are used in this project as local mechanical force tuners: by controlling RhoA activation and subsequent myosin contraction, they allow us to trigger cell contractility in a local and semi-quantitative manner. the inference of physical parameters such as traction forces associated with our optogenetics system allow us to study precisely the role of mechanical forces in cell extrusion.
Combining optogenetics and TFM enabled us to show that enhancing cell contractility by stimulating cells increases rate of extruding cells and that those events involve the neighboring-less-contractile cells. It also show that mechanically induced cell extrusions have an increased probability to be independent of caspase-3 activation as compared to unstimulated cells. Moreover, these extruded cells are increasingly oriented at the basal side of the tissue and show a delayed onset of apoptosis as compared to apically extruded ones. Altogether, these results show a strong relationship between cell contractility, the apico-basal orientation of cell extrusions and the fate of extruded cells.



POSTER 160

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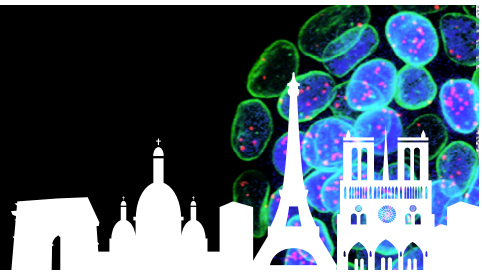
A novel RNP compartment allows mouse oocytes to adapt translational levels during late growth

Oocytes are large cells which accumulate maternal stores during their growth in the ovary to sustain their development. We uncovered the presence of a previously undescribed cluster of organelles and ribonucleoproteins adjacent to the nucleus in the cytoplasm of growing mouse oocytes, which is absent in fully grown oocytes.

This peculiar structure shares some morphological features with the Balbiani body, a well-characterized cytoplasmic compartment present in the oocytes of several vertebrates that preserves maternal stores. In mouse oocytes the presence of a Balbiani body is controversial, but the resemblance of this novel structure with the Balbiani body described in other organisms raises questions about its role in mouse oocytes. We showed using immunofluorescence, live imaging and electron microscopy that this cluster is well connected to the cytoskeleton through microtubules and intermediary filaments, and enriched in ribosomes and membranous organelles including mitochondria, endoplasmic reticulum and Golgi complex. Just like the Balbiani body, this cluster also contains typical ribonucleoproteins, usually associated with mRNAs storage and timely regulation. Mass spectrometry analysis of the isolated cluster as well as RNA sequencing comparing growing oocytes with or without the cluster strongly argue for a role of this novel structure in protein synthesis. These observations are further supported by measures of dry mass of oocytes with or without the cluster. We are currently validating a novel function for this transient structure, appearing at the end of oocyte growth, in promoting a burst of translation to cope with the rapid size increase and avoid cytoplasmic dilution, therefore maintaining the oocyte developmental potential.



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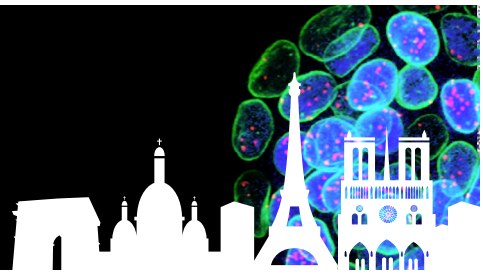

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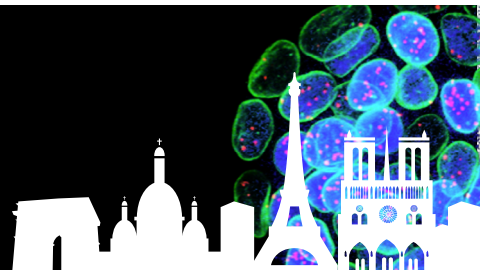

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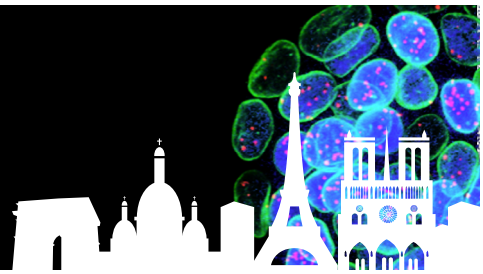

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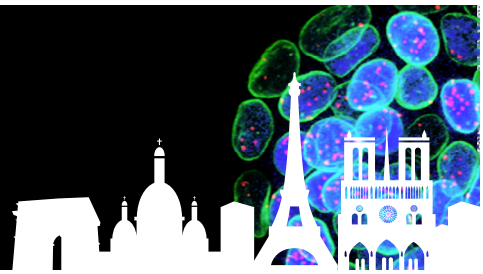

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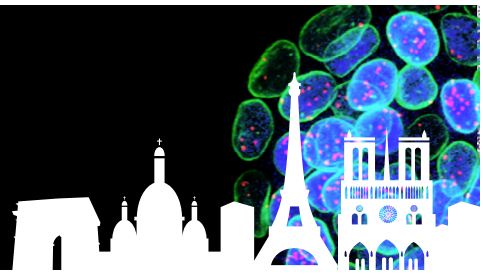

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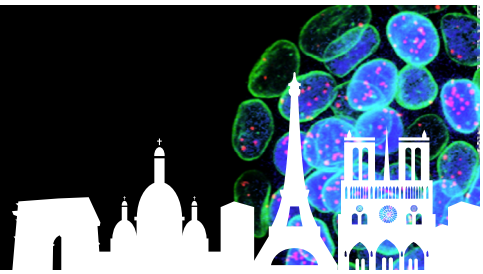

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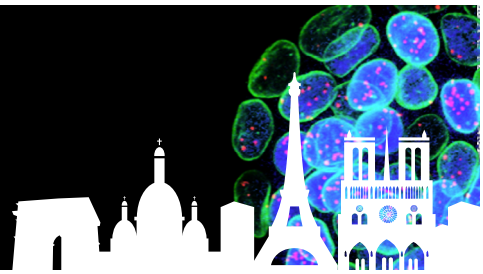

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