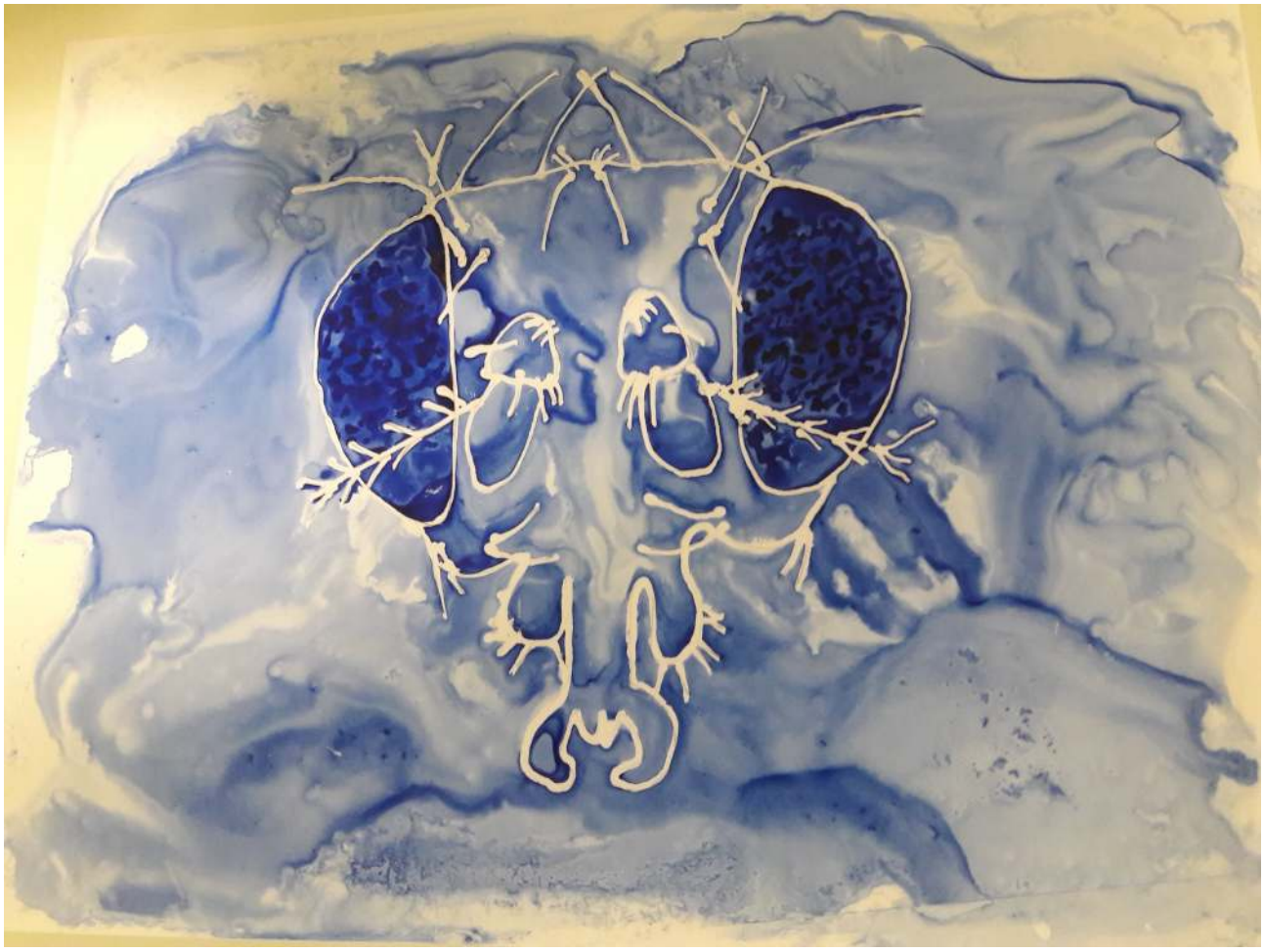
DIF-day 2018

Thursday, 14 June 2018
Collège de France, Amphitheater 5, Paris



COLLÈGE DE FRANCE
1530

DIF-day 2018 program

9:00 - 9:20	Reception
9:20 - 9:30	Welcome
	Session 1, Moderator: Michael Rera
9:30 - 9:50	**Romain Levayer** Mechanical cell competition induces cell elimination through compaction driven ERK downregulation
9:50 - 10:10	**Zvonimir Marelja** Lysosomal-derived cysteine stimulates autophagy via mitochondrial TCA cycle intermediates
10:10 - 10:30	**Flashtalks** Ana Maria Vallés, Juliette de Noiron, Stéphanie Soulé Pénélope Darnat, Dilyana Dimitrova
10:30 - 11:00	Coffee break
	Session 2, Moderator: Karine Narbonne-Reveau
11:00 - 11:20	**Alice Pavlowsky** A GABAergic Feedback Shapes Dopaminergic Input on the Drosophila Mushroom Body to Promote Appetitive Long-Term Memory
11:20 - 11:40	**Jacques Montagne** Interaction between Cancer progression and Social Environment
11:40 - 12:00	**Pierre Belichard** Starting a start-up in the start-up nation – is it worth trying ?
12:00 - 12:15	**Flashtalks** Alix Goupil, Karine Casier, Marina Antunes
12:15 - 14:15	Lunch break (organized at Collège de Fance)
	Session 3 Moderator: Antoine Guichet
14:15 - 15:05	**Keynote speaker: Benjamin Loppin** Epigenetic control of the oocyte-to-zygote transition in Drosophila
15:05 - 15:25	**Renata Basto** The centrosome biogenesis machinery orchestrates centrosome asymmetry and spindle orientation
15:25 - 15:45	**Radoslaw Ejsmont** LabDB - LIMS for Drosophila labs
15:45 - 16:15	Coffee break
	Session 4 Moderator: Juliette Mathieu
16:15 - 16:35	**Jean-René Martin** *ninaD*, a gene deregulated in the snoRNA mutant *jouvence* is involved in lipids and cholesterol metabolism in the gut and modulates lifespan in *Drosophila*.
16:35 - 16:55	**Daniel Vasiliauskas** Natural variation of retinal mosaic
16:55 - 17:15	**Isabelle Becam** The GPCR Smoothened binds and regulates the RNA-binding protein Smaug
17:15 - 17:35	**Alain Debec**: Out of Drosophila
17:35 - 17:55	Flash-talk award celebration
17:55 - 19:30	Refreshments

Abstracts

Romain Levayer, Institut Pasteur, 15-min-talk

Mechanical cell competition induces cell elimination through compaction driven ERK downregulation

The plasticity of developing tissues relies on the adjustment of cell survival and growth rate to environmental cues. This includes the effect of mechanical cues on cell survival. Accordingly, compaction of an epithelium can lead to cell extrusion and cell death. This process was proposed to contribute to tissue homeostasis but also to facilitate the expansion of pretumoral cells through the compaction and elimination of the neighbouring healthy cells. However we know very little about the pathways than can trigger apoptosis upon tissue deformation and the contribution of compaction driven death to clone expansion was never assessed *in vivo*. Using the Drosophila pupal notum and a new live sensor of ERK, we show that tissue compaction induces cell elimination through the downregulation of EGFR/ERK pathway and the upregulation of the pro-apoptotic protein Hid. The activation of the oncogene Ras in clones can also downregulate ERK and activate apoptosis in the neighbouring cells through their compaction, which contributes to Ras clone expansion. The sensitivity of EGFR/ERK pathway to mechanics and its role in the fine tuning of cell elimination could play a more general role during tissue homeostasis and tumour progression.

Zvonimir Marelja, Institut Imagine, 15-min-talk

Lysosomal-derived cysteine stimulates autophagy via mitochondrial TCA cycle intermediates

Organisms respond to variation in food availability to maintain metabolic homeostasis. Upon nutrient supply, the kinase of the lysosomal nutrient sensing machinery, mechanistic Target of Rapamycin Complex 1 (mTORC1), stimulates cellular anabolic processes to support cell growth, differentiation, and proliferation by phosphorylating its target molecules including 4E-BP1 and S6K. Upon fasting, cells meet their metabolic needs through nutrient remobilization from internal sources by mTORC1 inactivation that leads to induction of autophagy. By examining Drosophila knockout mutants lacking the lysosomal cystine transporter cystinosin (ctns[1]) we observed developmental delay and reduced survival in starved but not fed conditions. Moreover, levels of cysteine, pyruvate and all TCA cycle intermediates were specifically reduced in starvation. Accordingly, the administration of these metabolites rescued ctns1 starvation phenotypes. In agreement with the central role of the Drosophila fat body in the global starvation response, fat body-specific knockdown of ctns recapitulated the starvation sensitivity of ctns[1] animals. Starved fat body cells without cystinosin showed inadequately elevated mTORC1 signalling with a subsequent failure to induce autophagy whereas cystinosin overexpression stimulated autophagy via mTORC1 downregulation in fed condition. Finally, low doses of rapamycin caused a significant improvement of survival of ctns[1] flies upon fasting. Thus, cystinosin is upstream of a starvation response pathway that links cysteine with mTORC1 via the TCA cycle.

Ana Maria Vallés, Collège de France (CIRB), 2-min-flash-talk

Isolation of the Piwiless pocket, the 2-8 cell cyst compartment in the germarium of Drosophila

Transposable elements (TEs) account for 20% of the *Drosophila* genome. Their mobilization in germ cells can have dramatic consequences by causing mutations and chromosomal rearrangements transmitted to next generations. Thus silencing of TEs in the germline is preserved by piRNAs, a class of 23-28 nt long PIWI-associated small RNAs. However, in the mitotic region of the germarium, reporters for TEs silencing indicate that the repression seem to be alleviated or weaker in this region (Dufour et al. 2014). This small region also coincides with lower levels of Piwi proteins, thus the name Piwiless pocket. Whether there is higher levels of endogenous TEs expression in this region remains to be determined. So, why is there a small window in the germarium where silencing of TEs is relaxed. The function of such "de-silencing" is mysterious. To investigate the role of TEs during the time when silencing is alleviated we isolated the Piwiless compartment for high-throughput analysis of gene expression. For this, we used fluorescence activated cell sorting to isolate BamGFP and RFPwcd expressing cells. Wcd is not expressed in the Piwiless pocket and thus served as control. This approach offers a powerful tool to perform studies on isolated Drosophila germline cells thereby providing insights into the molecular mechanisms underlying TEs regulation during early development.

Juliette de Noiron, Université de Versailles-Saint-Quentin-En-Yvelines, 2-min-flash-talk

Drp1 regulation during Rbf1-induced apoptosis in Drosophila

Rbf1, the Drosophila homolog of the Retinoblastoma (Rb) tumor suppressor protein, like Rb, is a transcriptional co-factor able to induce apoptosis in proliferative cells. Our team characterized part of the molecular events explaining this activity. Indeed, we showed that this pro-apoptotic activity relies in part on the transcriptional repression of *buffy*, the unique *Drosophila* anti-apoptotic member of the *bcl-2* family. Buffy usually inhibits by physical interaction at the mitochondria the pro-apoptotic member of the Bcl 2 family Debcl. Rbf1 overexpression allows Debcl activation and triggers a cascade of mitochondrial events such as mitochondrial fission. We show for the first time that an interaction between Debcl and the dynamin-like protein Drp1 triggers mitochondrial fragmentation in Drosophila. In mammals, Drp1 can oligomerize around mitochondria to induce mitochondrial fission. Drp1 localization,oligomerization and fission activity are tightly regulated according to the cell type or physiological state through a large range of post translational modifications (PTM) that might condition its interaction with its mitochondrial membrane receptors. Even if many studies investigated the regulation of Drp1 activity, this remains far from being completely elucidated. In Drosophila, almost nothing is known about Drp1 regulation. Our study focuses on Drp1 *Drosophila* homolog regulation. To this end, we use genetic and cellular approaches to identify partners and PTM of Drp1 allowing its interaction with Bcl-2 family members in apoptotic conditions.

Stéphanie Soulé, Lucille Mellottée and Jean-René Martin
Institut des Neurosciences Paris-Saclay (Neuro-PSI), 2-min-flash-talk

The mutation of jouvence, a new small nucleolar RNA expressed in the enterocytes affects the length of the gut.

Longevity is a complex biological processes influenced by genetic and environmental factors, and is often related to neurodegenerative lesions in aged organisms. Though several genes and metabolic factors play a role in longevity and neurodegeneration, the underlying biological mechanisms, ranging from molecular to organismal levels, still remain largely unknown. In the last few years, JR Martin lab has characterised a new small nucleolar RNA (snoRNA), named *jouvence* (*jou*), and show that its mutation reduces the lifespan and leads to neurodegenerative lesions, in aged flies. A transgene containing the genomic region of *jou* rescues longevity and neurodegeneration in mutant flies. *In-situ* hybridisations have revealed that *jou* is expressed in specific gut epithelial cells (enterocytes), while its targeted expression in these cells is essential and sufficient to rescue and extend lifespan. Thus, to assess the role of *jouvence* in the gut and to analyse if the mutation of *jouvence* leads to some damages in the gut, as a first step, we have measured the length of the gut. I will present the results from these measurements in mutants as well as in different “rescued” transgenic fly lines.

Pénélope Darnat, Institut de Biologie Paris Seine (IBPS Jussieu), 2-min-flash-talk

Cyclin A as a novel link between cell proliferation and cell polarity

Cell proliferation and planar cell polarity are two processes among others required for morphogenesis. It is known that the impairment of cell proliferation induces cell polarity defects and vice versa. The nature of the mechanisms by which these processes crosstalk remains barely understood. I aim to study how proteins involved in cell cycle interact with those regulating planar cell polarity. These links are studied in asymmetric cell divisions, which generate cell fate diversity, through polarization of precursor cells. As a model system, we used the polarized cell divisions occurring in the formation of the *Drosophila melanogaster* bristle. We have shown that CyclinA (CycA), a cyclin essential for the entry into mitosis, acts as a bridge between cell proliferation and planar cell polarity. Indeed, we have observed that a pool of CycA was asymmetrically localized at the apical-posterior cortex of the precursor cells during mitosis. This particular CycA asymmetric localization was abolished when the planar cell polarity was disrupted in *frizzled* and *disheveled* mutants. Using a Proximity Ligation Assay (PLA), we have also displayed the physical interaction between CycA and Frizzled. More importantly, cell divisions are misoriented under a cycA loss of function condition as well when CycA was ectopically localized at the cell cortex. Together, these data unravel the involvement of this asymmetric CycA localization in cell division orientation and, highlight a new function never observed in other systems for this cell cycle factor.

Dilyana Dimitrova, Margarita Angelova, Bruno Da Silva, Cyrinne Achour, Jozef Gecz, Matthias Shaefer, Christophe Antoniewski, Clemént Carré, Institut de Biologie Paris Seine (IBPS Jussieu), The University of Adelaide, Australia and Medical University of Vienna, Austria, 2-min-flash-talk

RNA methyltransferase mutant links tRFs to small non-coding RNAs

tRNA fragments (tRFs) are 18-26 nucleotide small RNAs derived from specifically cleaved mature tRNA transcripts. In *Drosophila melanogaster*, our team has discovered a conserved tRNA methyltransferase and linked it to accumulation of specific tRFs and disregulation of the three small non-coding RNA pathways (sncRNA) i.e. si-, mi- and piRNA. Dysfunctions in the human ortholog cause a specific case of Intellectual Disability (ID). The mutant flies exhibit intriguing phenotypes, such as ovarian size reduction, decreased viral resistance, and most importantly, increased transposon levels in heads. Therefore, our results support an unexpected link between RNA modifications, sncRNA pathways, tRFs, and disease etiology, such as ID. We are currently investigating the functional and mechanistic conservation in ID patient cells carrying mutations in the corresponding tRNA methylase.

Alice Pavlowsky, ESPCI, 15-min-talk

A GABAergic Feedback Shapes Dopaminergic Input on the Drosophila Mushroom Body to Promote Appetitive Long-Term Memory

Memory consolidation is a crucial step for long-term memory (LTM) storage. However, we still lack a clear picture of how memory consolidation is regulated at the neuronal circuit level. Here, we took advantage of the well-described anatomy of the *Drosophila* olfactory memory center, the mushroom body (MB), to address this question in the context of appetitive LTM. The MB lobes, which are made by the fascicled axons of MB intrinsic neurons, are organized into discrete anatomical modules, each covered by the terminals of a defined type of dopaminergic neuron (DAN) and the dendrites of a corresponding type of MB output neuron (MBON). We previously revealed the essential role of one DAN, the MP1 neuron, in the formation of appetitive LTM. The MP1 neuron is anatomically matched to the GABAergic MBON MVP2, which has been attributed feedforward inhibitory functions recently. Here, we used behavior experiments and *in vivo* imaging to challenge the existence of MP1-MVP2 synapses and investigate their role in appetitive LTM consolidation. We show that MP1 and MVP2 neurons form an anatomically and functionally recurrent circuit, which features a feedback inhibition that regulates consolidation of appetitive memory. This circuit involves two opposite type 1 and type 2 dopamine receptors in MVP2 neurons and the metabotropic GABAB-R1 receptor in MP1 neurons. We propose that this dual-receptor feedback supports a bidirectional self-regulation of MP1 input to the MB. This mechanism displays striking similarities with the mammalian reward system, in which modulation of the dopaminergic signal is primarily assigned to inhibitory neurons.

Jacques Montagne, Institut de Biologie Intégrative de la Cellule (I2BC), 15-min-talk

Interaction between Cancer progression and Social Environment

The influence of oncogenic phenomena on the ecology and evolution of animal species is fast becoming an important research topic. Here, we exposed adult *Drosophila*, with colorectal-like tumors, to different social environments. Flies kept in isolation exhibit faster tumor progression than flies kept in homogeneous groups. More importantly, we also found that tumorous flies, kept in homogeneous groups, develop tumors at a lower rate compared to heterogeneous groups, where a single tumorous fly was kept with other non-tumorous conspecifics, suggesting a strong impact of social group composition on tumor growth. Finally, we show that flies can discriminate between individuals at different stages of tumor development and selectively choose their social environment accordingly. Control flies actively avoid flies with tumor but only at the later stages of tumor development, whereas tumorous flies display strong social preferences for tumorous flies in the early stages of tumor development. Our study demonstrates the reciprocal links between cancer and social interactions, as well as highlighting how sociality impacts health and fitness in animals and its potential implications for disease ecology and ecosystem dynamics.

Pierre Belichard, Societé Enterome, 15-min-talk

Starting a start-up in the start-up nation – is it worth trying ?

It is becoming very trendy to create a start-up when you are a talented scientist having the sense that your invention could become the topic of an investment to be further developed. You have anyway to ask to yourself a lot of questions before other do for you. This presentation will help you to better understand these fundamental questions. What is a product ? Could my science become such a product thanks to benchmark and market studies ? What you need to create a start-up? People and money only ? Who does what: CSO, CEO, CTO, CFO, Lawyers… outsourcing or not? Funding beyond start-up competitions and early public money?

Alix Goupil, Institut Curie, 2-min-flash-talk

Identifying the principles that maintain aneuploidy at tolerable levels in the Drosophila brain

Development of multicellular organisms requires the coordination of cell proliferation, death and differentiation to assemble functional organs of the correct size. In this context, one important level of control is to maintain a stable genome content. Variations to the diploid content, whole chromosome loss or gain, known as aneuploidy, are associated with a variety of human diseases. Currently, the frequency of aneuploid cells in the brain remains debatable. Further, a quantitative view and the mechanisms underlying its genesis is also missing. Additionally, since the frequency of aneuploid cells has to be tightly controlled to avoid decreased fitness and pathological status, it is utterly important to understand how these cells are identified and eliminated to be kept at low frequency maintaining thus brain homeostasis. (1) To assess the frequency of aneuploidy, we follow chromosome loss *in vivo* using a recently developed method in *Drosophila* that combines the well-established Gal4/Gal80 inhibition system with GFP expression. (2) In parallel, to ascertain the mechanisms by which chromosomes are gained or lost during cell division in the developing brain, we assess mitotic errors by live imaging of wild-type *Drosophila* brains and use the strength of *Drosophila* genetic manipulation to model chromosome loss. (3) Subsequently, we will identify pathways responsible for aneuploid cells elimination. This project will generate, for the first time, a quantitative cartographic view of aneuploidy at the level of the developing wild-type brain, providing mechanistic insight into the genesis of physiological aneuploidy during development.

Karine Casier, Institut de Biologie Paris Seine (IBPS Jussieu), 2-min-flash-talk

Environmentally-induced epigenetic conversion of a piRNA cluster

Transposable elements (TEs) activity is repressed in animal gonads by PIWI-interacting RNAs (piRNAs), a class of small RNAs produced by specific loci made of TEs insertions and fragments. Current models propose that these loci are functionally defined by the maternal inheritance of piRNAs produced during the previous generation, raising the question of their first activation in the absence of piRNAs. Taking advantage of an inactive cluster of P-element derived transgene insertions, we show here that raising flies at high temperature (29°C) instead of 25°C results in a rare but invasive epigenetic conversion of this locus into an active piRNAs producing one. The newly acquired epigenetic state is stable over many generations even when flies are switch back to 25°C. The silencing capacities, piRNA production and chromatin modifications of the cluster are all identical whether conversion occurred by maternal piRNA inheritance or by high temperature. We also demonstrate that in addition to high temperature, a single homologous transgene inserted elsewhere in the genome is required to activate the locus. We thus have identified a minimal system of three components to create a stable piRNA producing locus: 1) a locus with multiple TE derived sequences; 2) a euchromatic copy of these sequences and 3) elevated temperature. Altogether, these data report the first case of the establishment of an active piRNA cluster by environmental changes. It highlights how such variations of species natural habitat can become heritable and shape their epigenome.

Marina Antunes, Institut Jacques Monod, 2-min-flash-talk

Regulation of Smoothened trafficking by the HH signalling pathway

The HH signalling pathway is crucial in early development across metazoan and its deregulation leads to birth defects and cancer. Smoothened (SMO) is a G protein-coupled receptor whose activation is required for HH signal transduction and, consequently, pathway activation. SMO activation is regulated by its localization and post-translational modifications, e.g. phosphorylation and ubiquitination. In absence of HH, SMO is inhibited at the PM, which leads to its internalization and degradation, whereas when HH is present, SMO accumulates at the PM, is hyperphosphorylated and becomes active. Nonetheless, the precise order of the events that lead to SMO activation and the role of HH in it are not well understood and this is the basis of my PhD project: it concerns the study of SMO trafficking and its regulation by the HH signaling pathway in *Drosophila melanogaster*. In order to study this, I am going to focus on two main aims that consist of understanding how, in the context of the HH signaling pathway, 1) SMO localization to the plasma membrane is regulated and 2) SMO apical-basal distribution is regulated. The two aims will be accomplished by employing Cl8 cells and the wing imaginal disc (WID) epithelium as research models. The wing imaginal disc is a polarized epithelial tissue where the HH signaling pathway is activated. Within this tissue, where there is HH, SMO distribution appears to be enriched in the basolateral domain; where there is no HH, SMO appears to be enriched apically

Benjamin Loppin, Laboratoire de Biométrie et Biologie Évolutive (LBBE), plenary talk

Epigenetic control of the oocyte-to-zygote transition in Drosophila

The oocyte-to-zygote transition involves complex cytoplasmic and nuclear reorganization events that are entirely controlled by maternal products synthesized during oogenesis. In sexually reproducing species, the formation of a diploid zygote additionally requires the transformation of the fertilizing sperm nucleus into a DNA replication-competent male pronucleus. We have recently performed a shRNA-based genetic screen in Drosophila to identify new maternal-effect genes involved in zygote formation. Our screen identified several members of a conserved histone demethylase complex, which appears critical for the formation of the zygote by specifically promoting sperm chromatin remodeling. Our results suggest that the oocyte-to-zygote transition relies on a specific subset of maternal gene products whose expression is tightly regulated in female germ cells by key epigenetic modifiers.

Renata Basto, Institut Curie, 15-min-talk

The centrosome biogenesis machinery orchestrates centrosome asymmetry and spindle orientation

Defects in mitotic spindle orientation (MSO) disrupt the organization of stem cell niches impacting tissue morphogenesis and homeostasis. Mutations in centrosome genes reduce MSO fidelity leading to tissue dysplasia causing several diseases such as microcephaly, dwarfism and cancer. Whether these mutations perturb spindle orientation solely by affecting astral microtubule nucleation or if centrosome proteins have more direct functions in regulating MSO is unknown. To investigate this question we analysed the consequences of deregulating Plk4 (the master centriole duplication kinase) activity in *Drosophila* asymmetrically dividing neural stem cells. We found that Plk4 functions upstream of MSO control orchestrating centriole symmetry breaking and consequently centrosome positioning. Mechanistically, we show that Plk4 acts through the Spd2 phosphorylation, inducing centriole release from the apical cortex in two different ways. Overall, this work not only reveals a novel role for Plk4, but also links the centrosome biogenesis machinery with the machinery controlling MSO.

Radoslaw Ejsmont, Institut du Cerveau et de la Moelle Epinière (ICM), 15-min-talk

LabDB - LIMS for Drosophila labs

I will present the LabBD - an open source, modular Laboratory Inventory Management System that features a Drosophila-specific module with many features (vial management, stock management, cross management, automated labeling solution, integration with FlyBase, etc.)

Stéphanie Soulé, Lucille Mellottée and **Jean-René Martin**, Neuro-PSI, 15-min-talk

***ninaD*, a gene deregulated in the snoRNA mutant *jouvence* is involved in lipids and cholesterol metabolism in the gut and modulates lifespan in *Drosophila*.**

The identification of a new *Drosophila* H/ACA-type small nucleolar RNA (*jouvence*) in the epithelium of the gut reveals that it is essential for lifespan determination. Its mutation reduces lifespan, increases neurodegeneration, and induces metabolic disorders as the hypertrophy of fat body (increase of triglycerides and cholesterol). The targeted expression of *jouvence* in enterocytes is sufficient to rescue these defects. To characterize the role of *jouvence* in the gut, a transcriptomic analysis (RNA-Seq) was performed on gut. It reveals that several genes are deregulated in mutants, the majority being involved in lipids uptake and/or metabolism. Among them, *ninaD*, a CD36 homologue known to participate in the uptake of high density lipoprotein cholesteryl-ester in mammal is particularly deregulated. However, in *Drosophila*, apart its function in 🚲-carotene metabolism and vision, its role in the gut metabolism remains to be clarified. RT-qPCR revealed a significant increase in mRNA level of *ninaD* in mutants, while the targeted expression of *jouvence* in the gut rescues it. Moreover, in *jouvence* mutant, the targeted expression of a RNAi against ninaD in the gut decreases the mRNA level of *ninaD* and restores the metabolic parameters, as well as it increases lifespan. These results suggest a role of *ninaD* in the lipids and cholesterol uptake or metabolism, which consequently affects lifespan. The regulation of *ninaD* level in the gut could therefore be considered as an effective strategy to extend lifespan, and protect against the decline of parameters associated to aging. These data raise the possibility that *jouvence* could represent a new therapeutic candidate to improve aging, and fight against metabolic disorders.

Daniel Vasiliauskas, Institut des Neurosciences Paris-Saclay (Neuro-PSI), 15-min-talk

Natural variation of retinal mosaic

Natural variation of the nervous system has been largely unexplored in *Drosophila*. In human retina the ratio of different subtypes of cone photoreceptors shows considerable variation between individuals; about 10% of men are entirely missing a cone subtype and are colour blind; and, the majority of retina neurodegenerative diseases have a genetic basis and can also be viewed as natural variants. We set out to ask whether similar variation exists in *Drosophila melanogaster*. In the fly, the differentiation program of photoreceptor neuron subtypes, which results in the expression of different Rhodopsins (Rh), is relatively well understood. It culminates in mutually exclusive expression of blue-sensitive Rh5 and green-sensitive Rh6 in the R8 photoreceptors. Thus, in order to phenotypically “capture” natural perturbations in most steps of the photoreceptor differentiation we examined Rh5/Rh6 expression in wild-derived fly lines. Among ~200 highly inbred and sequenced lines of the *Drosophila* Genomic Reference Panel, we identified at least 10 distinct phenotypes (e.g. shifts in Rh5-R8 vs. Rh6-R8 ratio, Rh5/Rh6 co-expression, loss of Rh5 expression, and retinal degeneration) affecting approximately 15% of the lines. We found that three of the phenotypes were due to novel mutations in Rh5 itself (analogous to human colour-blindness) and in key regulators of photoreceptor differentiation, spineless (transcription factor) and melted (repressor of the Hippo pathway in the R8).

Isabelle Becam, Institut Jacques Monod, 15-min-talk

The GPCR Smoothened binds and regulates the RNA-binding protein Smaug
A challenge in developmental biology is understanding how signaling systems are integrated into the cell regulatory machinery. The conserved RNA binding protein Smaug/Samd4 controls the fate of many mRNAs during fly development. In mammals, it is involved in synapse biology, muscle development and osteogenesis. Smaug/Samd4 proteins repress the expression of target mRNAs via the recruitment of protein partners that destabilize these transcripts and/or prevent their translation. However, very little is known about how Smaug/Samd4 activity is regulated. Here we show that the Drosophila Smaug protein interacts and colocalizes with Smoothened (SMO), a G-protein coupled receptor required for the transduction of the Hedgehog (HH) signalwhich controls metazoan development and oncogenesis. We demonstrate that activated SMO regulates Smaug by inducing its phosphorylation, altering its subcellular localization, reducing Smaug protein levels and attenuating its mRNA repressive activity. These data highlight an unexpected relationship between HH/SMO signaling and post-transcriptional regulation of gene expression.

Alain Debec, Michael Lang, Romain Perronet and Mathieu Molet, Institut Jacques Monod and Sorbonne Université - iEES Paris, 15-min-talk

Out of Drosophila : A new model for the study of cell division derived from a primitive Australian ant with a single chromosome.
The mechanism of mitosis is a key problem of biology and medicine. However the complex karyotypes of most species makes the analysis of this phenomenon difficult. In this project, we propose to establish a new experimental model able to simplify such analysis.
We have undertaken in March 2018 an expedition to Australia to collect specimens of a very special endemic ant, *Myrmecia croslandi*. These ants are the only animal species known on earth to have the simplest karyotype of n=1 in the haploid males. 15 colonies (each with a queen and hundred of workers) have been taken and established in Paris. The goal will be, starting from dissociated embryos, to create the first animal cell line with only one chromosome. This cell line will be of essential value for many cell biologists and geneticists as a new biological system for studying cell division.

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