CONFERENCE REPORT

"Growth and regeneration during development and aging"

Roscoff, France, May 22-26, 2023

President: **Claude Desplan,** Department of Biology, New York University, New York NY USA

Vice-President: **Allison Bardin,** Institut Curie, Paris

Introduction

A series of Jacques Monod Conferences centered on Developmental Biology started in 2012 with a Conference on the ***"Emergence and Evolution of Developmental patterns"*.** The aim of this conference was to bring together established leaders in the fields of Cell, Developmental and Evolutionary Biology, with a perspective in systems biology and mathematical modeling. This CJM brought together three seemingly distinct groups of people, developmental biologists, evolutionary biologists, and physicists. The same three disciplines were brought together in 2015 to discuss the latest advances in developmental biology for a meeting ***"Building, repairing and evolving biological tissues"*** that was discussing the generation of tissue patterns and shape under normal physiology, as well as in tissue repair and regeneration. Based on the success of this second conference, a third conference was organized about ***"Modeling Cell fate"*** that pushed even further the multidisciplinary aspects and the introduction of more quantitative approaches and mathematical modelling of developmental processes. The 2023 CJM conference, ***"Growth and regeneration during development and aging"*** focused on later stages of development and explored fundamental aspects of regeneration, homeostasis of tissue and the mechanisms of aging, when these processes no longer function properly. The program of the conference included six thematic sessions, each including speakers working in different model organisms and using different approaches.

The conference was organized along 6 themes:
(1) **Developmental control of Aging**
(2) **Transcription control and chromatin regulation of cell fate and aging**
(3) **Stem cells and their link with aging**
(4) **Developmental Patterning**
(5) **Regeneration**
(6) Senescence and Plasticity

Selection of speakers :
The invited speakers were selected based on their expertise in the particular topics central to the meeting that were organized in 6 sessions above. The organizers were careful to have gender balance among the invited speakers and to include diverse speakers in terms of seniority, geographical origin, seniority and other criteria for diversity. The CJM imposed a balance between invited speakers from France, Europe/UK and the rest of the world. Among the 27 invited speaker, 13 were females and 14 were males.
However, 10 slots were reserved for short talks by junior scientists and the organizers favored contribution by PhD students and postdocs. The choice was made by a committee made of the two organizers, a junior Faculty and a postdoc who were registered to the meeting and chosen once the deadline for abstracts was past. These two junior members were chosen by the organizers based on the quality of their abstract and were be speakers.

Conference statistics
The program comprised the following presentations:
- 2 plenary lectures by outstanding individuals (1h each), by Irene Miguel-Aliaga (FRS) from Imperial College in London and Peter Reddien from the Whitehead Institute at MIT, to open and close the meeting, respectively.
- 25 presentations by invited speakers (25 min + 5 min for questions)
- 10 short presentations selected from the abstracts (12 min + 3 min for questions)
- 20 3min-flash talks to present each of the two poster sessions; the presenters were also selected from the abstracts.
The flash talks were first initiated in 2015 and were designed to allow young scientists to gain experience in public speaking while advertising their poster. The flash talk slots were equally split between PhD students and post-docs.

7 invited/keynote speakers were from outside Europe,
9 were from Europe outside France, and
11 were from France.
Among the 10 selected speakers, 5 were from France and 5 were from Europe outside France.

For invited speakers, the female/male ratio was 13 women and 14 men.
For short talks, it was 6 women and 4 men

Each session was assigned a dedicated chair, chosen among applicants who had not been selected for an oral presentation.

There were two well-attended poster sessions, each lasting 2 hours. In addition, the poster room remained accessible until 22h for additional presentations and discussions. The

program also left ample opportunity for informal discussions amongst the participants both at lunchtime and dinner/post-dinner time.

We organized a visit to the Ile de Batz that allowed more informal fee time for interactions. The participants had also a free evening when dinner was not provided by the Station. This provided a nice platform for further informal discussions in smaller groups.

There was no Friday morning session and all participants took a taxi to Brest Airport or to the TGV in Morlaix.

Scientific program

The first evening was dedicated to a keynote lecture
Keynote Lecture #1: **Irene Miguel-Aliaga, FRS from Imperial College London.** She gave an overview of her work that elucidated how sex of the animal impact the development of the gut and thus food intake for reproduction in females. She elucidated how Tor signaling is required for this growth. She proposed the interesting model that the gut is in contact with other organs (ovary, testes, and trachea) to allow communication, thus implicating an important role for the shape of the gut.

Session 1. Developmental control of Aging
Chair: **Prashanth Rangan, Mt Sinai New York**

In this session, several speakers described the developmental events during aging.
- Bjorn Schumacher, CECAD, Cologne, described how, in C elegans, genome instability can be responsible for some of the aging mechanisms.
- Dario Riccardo Valenzano, from the Leibniz Institute on Aging, Fritz Lipmann Institute, Jena, gave an *EMBO YIP Lecture* where he presented his work on the very specific rapid development and aging of killifish that live in regions of Africa where ponds dry out in the summer season. He also discussed how the microbiome in the gut of the older fish leads to aging: replacing the microbiome with that of younger fish leads to delayed aging.
- Elvan Boke, from CRG Barcelona, also gave an *EMBO YIP Lecture* described how vertebrate oocytes accumulate protein aggregates and how mitochondria avoid accumulating damage by avoiding the formation of ROS in oocyte mitochondria.
- Benjamin Boumard, Ins Curie, Paris, described a very interesting phenomenon in which replication stress due to a mutation that is deficient for the production of nucleotides can be rescued in some tissues (imaginal disc in flies) by neighboring cells that are not mutant while other tissues (adult gut) are not. This is due to communication by gap junctions present in discs cells but not in gut cells.
- Gantas Perez-Mockus, from the Crick Institute, London (laboratory of JP Vincent) presented in a short talk the on timing of development of proliferation and how ecdysone is involved in controlling these cell divisions.
- Ninadini Sharma, MPI, Göttingen, Germany gave a dynamic short talk on the repair of DNA damage during aging of mammalian oocytes.
- Claude Desplan from NYU in New York discussed an original model of aging and rejuvenation: In some ant species, workers who normally have a much shorter lifespan (7 months) than queens (5 years) can in some conditions become pseudoqueens. In this case, they start laying eggs and their longevity increases dramatically to almost that of queens, in

spite of the metabolic cost due to egg production and high insulin levels. This appears to be due to the production of an anti-insulin that blocks the aging consequence of insulin without affecting its role in metabolism
This session was completed by a set of excellent flash-talks by students and post-docs, on subjects related to poster session #1.

Session 2. Transcription control and chromatin regulation of cell fate and aging
Chair: **Ursula Weber from Mount Sinai in New York**

In this session, speakers discussed the role of transcription and epigenetic mechanisms during development and aging.
- **Mounia Lagha, IGMM Montpellier** described her work on the Drosophila embryo using live imaging of transcription and translation, often at the single molecule levels. She could see how activation of transcription of zygotic genes depends on the localization of their mRNA at the apical or basal side of the nuclei. This demonstrated the power of new tools of visualization and the power of live imaging.
- Zayna Chaker, Biozentrum Basel, CH focused on adult neurogenesis and how physiological conditions like pregnancy can affect the recruitment of adult stem cells to produce neurons that migrate to the olfactory bulb and change the perception of odors.
- Wolfgang Kiel, Institut Curie, Paris described how C. elegans development is driven by genetic oscillations via sequential repression of temporal identity factors through microRNAs.
- Robert Johnston, Johns Hopkins, Baltimore demonstrate the power of human organoids to address questions specific to higher primates. By looking at human retinal organoids, he was able to identify how Thyroid hormone is able to contribute to the choice of color Photoreceptors between Blue-sensitive and Green-Red sensitive cone cells. He was then able to show that retinoic acid is implicated in the next choice between red and green photoreceptors that are the product of a recent gene duplication in primates
- Roger Revilla-I-Domingo, University of Vienna, Austria gave a short talk on stem cells and regeneration in an atypical model system *in early branching sponges.*
- **Luisa Cochella, Johns Hopkins, Baltimore** presented her work on the role of miRNA during morphogenesis in *C elegans*.

Session 3. Stem cells and their link with aging
Chair: ***Aurore L'honoré***

In this session, speakers described how stem cells are affected during aging and how this could be addressed
- **Allison Bardin, Institut Curie, Paris***,* went back to the role of genome instability, this time in the context of the Drosophila gut and the intestinal stem cells. She showed that somatic cells can become aneuploid for the X chromosome leading to ectopic activation of dosage compensation.
- **Fiona Doetsch, Biozentrum Basel** presented work on adult neural stem cell populations in mouse.
- **Giselle Cheung ISTA Vienna**, used a powerful lineage technique in mice (MADM) to decipher the generation of neural diversity in the superior coliculus. She was able to demaontrate that the 16 neural cell types present in the brain structure in the visual pathway are all generated by existing stem cell present in the tissue. Using technically involved “Patch-seq”, she was able to further show that none of the clones identified contained similar

sequences of neurons, suggesting that stochastic choices occur during the neurogenesis of this structure, which is sharp contrast with the precisely orchestrated production of cortical neurons demonstrated by the same lab (Simon Hippenmeyer) also using MADM.
- **Camille Lafage, Univ. Grenoble Alpes, INSERM U1216** gave a short talk on the role of early aging of stem cells in Huntington disease.
- **Dan Ohtan Wang, RIKEN, Kobe & NYU Abu Dhabi** described very powerful behavior devices to study the reaction of mice to different stimuli. She also described her investigations of RNA modifications and how mutations of 'readers' of these modifications can affect the nervous syytem.
- Pura Muñoz Cànoves, Altos Labs, San Diego addressed the very pertinent question of regeneration/rejuvenation, focusing on muscles: is it possible to improve regeneration of aged muscles stem cells that are usually quiescent. Their capacity at regeneration might decrease with age due to proteostasis and mitophagy.
- Abderrahman Khila, IGF Lyon uses a very original model organism, the water strider that displays extremely elongated limbs whose length differs between segments. He uses comparative genomics and RNAi manipulations to identify the factors for this extreme growth.

Session 4. Developmental Patterning
Chair: **Mireille Galloni**

This session provided specific insights into the contribution of developmental patterning to generate shape and cell diversity.
- **Olivier Hamant, ENS Lyon** gave a fairly theoretical talk on the function of noise and robustness in plant morphogenesis focusing on the role of mechanical stress that contributes to the positioning and shape of leaves.
- **Fabienne Lescroart, Marseille** presented the first of two talks on cardiac specification and the cardiopharyngial mesoderm with the formation of two heart fields.
- **Maheva Andriatsilavo, Institut du Cerveau-Paris Brain Institute (ICM)** gave a short talk on the work of the lab on the stochastic events that lead to axon targeting and how a give neuron is presented with several choices to extend axons in different directions, then choosing one branch to extend.
- Pauline Spéder, Institut Pasteur, focused her attention on stem cell niches using the Drosophila brain as a powerful model system. She could show that glial cells contribute to the niche and how in particular, cortex glia wraps entire lineages.

Session 5. Regeneration
Chair: **Patrick Steinmetz**

This session provided a general update on the mechanisms of regeneration in a variety of model- and non-model organisms, from fish to ascidians to shark and a variety of vertebrates.
- **Lionel Christiaen from SARS in Bergen, Norway** described how the ascidian Ciona can serve as a powerful system to study heart regeneration. Its very simple structure and the knowledge of the cells that generate the heart fields. He presented the work form his lab in which a single progenitor divides to give rise to a pharyngeal and a cardia progenitor. In particular, he described how the common progenitor is 'primed' to express the appropriate gene after the next cell division, and how cell cycle is important to coordinate this event.

- **Guo Huang from UCSF**, presented the role of Thyroid hormone in regeneration and why different species of animals with widely different sizes. He tested Kleiber's law for scaling of metabolism with bodyweight and how this changed when animals became homeotherm. He showed that the inhibition of thyroid hormone and the adrenergic pathway increases the regenerative capacity of the heart as well as decreasing body temperature.
- **Hernan Lopez-Schier, NYU Abu Dhabi, UAE,** focused on regeneration of the lateral line of the zebrafish and how the Notch signaling pathway can allow the initially stochastic orientation of sensory cells to detect the water movements become set in two different directions.
- **Agnés Boutet, from the Laboratory of Integrative Biology of Marine Model in local Roscoff,** described how sharks deal with the high salt concentration of the marine environment. She focused on the development of the nephrons of these animals that can regenerate, a property that was lost in higher fish.
- **Patrick Lemaire, Institute of Biological Sciences, Montpellier** took an unusual view of ascidian development and discussed how the lineage-based development has been conserved over extremely long evolutionary distances while the genomes changed much more rapidly.
- Michael Averof, IGF Lyon addressed the important question of the relationship between regeneration and development: does regeneration recapitulate development? He used the amphipod Parhyale and its great ability to regenerate (multiple times) its limb. By comparing gene expression between new and regenerative leg formation, he could show that the two processes do not use the same strategy. This serves as an important system to compare the two gene regulatory networks.

<u>Senescence and Plasticity</u>
Chair: **Khaled Tighanimine**

- Han Li, Institut Pasteur, Paris talked about senescence that is the consequence of various stresses that affect cell cycle while plasticity is a positive response to the external stimuli. Can somatic cells can acquire plasticity exhibit plasticity, especially during aging and cancer.
- Michael Rera, Institut de Biologie Paris Seine, asked whether aging was a continuous phenomenon or instead had different phases responding to different stimuli. One can use markers of aging (aging clock) or study short-lived model system to address this question.
- Anadika Rajive Prasad, University College London gave a short talk on neuronal differentiation in the optic lobe of Drosophila: There, precursor cells are induced to enter a pro-neural phase and then neural differentiation. She mentioned how transcription as well as post-transcriptional regulation can affect these processes.
- Bill Keyes, IGBMC, Strasbourg, presented his work on senescent cells produce fragments (“senescent-cell adhesion fragments”), that are transferred to neighboring cells, contributing to inflammation in aging.

Keynote lecture #2: **Peter W. Reddien from Whitehead Institute at MIT in Boston** concluded the meeting with a presentation that described in exquisite details the mechanisms of regeneration in Planaria: He addressed how neoblasts, the universal stem cells, can regenerate all body parts: They can produce a large variety of specialized stem cells (maybe 125 types) that expressed specific transcription factors and are distributed throughout the body and might move to reconstruct the missing parts.

General comments

There were 78 participants to the Conference, including an almost equal representation of principal investigators, post-docs and research associates/PhD students. Selected applicants originated from multiple different European Countries, USA, and Japan. The overall quality of the talks was outstanding, and each presentation was followed by a large number of questions that led to stimulating discussions, which often had to be interrupted to remain on schedule. All 6 oral sessions and 2 poster sessions were very well attended, to a large extent due to the geography of Roscoff as a venue. Its cozy and small size was integral to the very interactive atmosphere that prevailed during the meeting, fostering extensive informal scientific exchanges. It was also extensively followed on Twitter with dynamic messaging and photos from the meeting. The success of the conference could be judged from the request by most participants, during the final discussion session, that another meeting be held in the future. The chairs and co-chairs received a significant number of messages conveying the happiness of the participants and the desire to return in three years. The different views of development and regeneration should justify the future organization of another version of this conference and its maintenance every 3 years beyond this. Allison Bardin, who was the vice-chair of this conference will chair the 2026 conference, pending approval by the CNRS. Lionel Christiaen from SARS in Bergen was co-opted by consensus to be the co-chair of the next conference (2026?) and hopefully the chair of the later meeting (2029?).

Final program of the conference

"Growth and regeneration during development and aging"

May 22-26, 2023 in Roscoff

Monday May 22, 2023

15:30-20:00 *Arrival / Registration*
19:00-19:30 *Cocktail*
19:30-20:45 *Dinner*
21:00-21:15 Opening and welcome
21:15-22:00 **Keynote 1: Irene Miguel-Aliaga, Imperial College London**
Changing Guts

Tuesday May 23, 2023

Session 1 - Developmental control of Aging

08:45-09:15 Bjorn Schumacher, CECAD, Cologne
Genome Stability in Reproduction and Aging: New Insights from C. elegans

09:15-09:45 Dario Riccardo Valenzano, Leibniz Institute on Aging, Fritz Lipmann Institute, Jena
EMBO YIP Lecture
Evolution and Ecology of Aging,

09:45-10:15 Elvan Boke, CRG Barcelona,
EMBO YIP Lecture
Evading Ageing: Mitochondrial and Proteostatic Adaptations in Oocytes

10:15-10:30 Benjamin Boumard, Ins Curie, Paris
Sharing of nucleotide precursors via gap junctions can protect cells from replication stress

10:30-11:00 coffee break

11:00-11:15 Gantas Perez-Mockus, Crick Institute, London
Proliferation control by a temporal gradient of a steroid hormone"
11:15-11:30 Ninadini Sharma, MPI, Göttingen, Germany
Impact of maternal aging on the DNA damage repair landscape in mouse oocytes.
11:30-12:00 Claude Desplan NYU, New York
Are longevity and reproduction compatible?
12:00-12:30 5 x 5min flash talks (from sessions 1-3)

13:00-14:15 Lunch

14:30-16:00 **Poster session A; Sessions 1-3** (w/coffee)

Session 2 - Transcription control and chromatin regulation of cell fate and aging
16:00 -16:30 Petra Hajkova, MRC, London Institute of Medical Sciences
Resetting and Maintenance of Epigenetic Information in the Context of Mammalian Germ Line
16:30-17:00 Mounia Lagha, IGMM Montpellier
EMBO YIP lecture
Gene Expression Dynamics during the Awakening of the Zygotic Genome
17:00-17:15 Zayna Chaker, Biozentrum Basel, CH
Spatio-temporal recruitment of adult neural stem cells during pregnancy for transient neurogenesis
17:15-17:30 Wolfgang Kiel, Institut Curie, Paris
Circadian rhythm orthologs drive post-embryonic pulsatile miRNA transcription in C. elegans
17:30-17:45 short break
17:45-18:15 Robert Johnston, Johns Hopkins, Baltimore
Generating neuronal diversity in human retinal organoids
18:15-18:30 Roger Revilla-I-Domingo, University of Vienna, Austria
Regeneration in the sponge Suberites domuncula and the evolutionary origin of stem cell differentiation
18:30-19:00 Luisa Cochella, Johns Hopkins, Baltimore
Quantitative Control of Morphogenesis by a Deeply Conserved miRNA Family

19:30-21:00 Dinner

Wednesday May 24, 2023
Session 3 Stem cells and their link with aging
08:45-09:15 Allison Bardin, Institut Curie, Paris
Genome Stabilty of Stem and Progenitor Cells during Aging
09:15-09:45 Fiona Doetsch, Biozentrum Basel
Regulation and Diversity of Adult Neural Stem Cells
09:45-10:15 Giselle Cheung ISTA Vienna
Multipotent Progenitors Instruct Ontogeny of the Superior Colliculus
10:15-10:45 coffee break
10:45-11:00 Camille Lafage, Univ. Grenoble Alpes, Inserm, U1216
Premature aging of Neural Stem Cells in Huntington's disease
11:00-11:30 Dan Ohtan Wang, RIKEN, Kobe & NYU Abu Dhabi
Reading the m6A RNA Methylation Signals in Neurons and at Synapses

11:30-12:00 Pura Muñoz Cànoves, Altos Labs, San Diego
Promoting Regeneration of Aged Muscles
12:00-12:30 Abderrahman Khila, IGF Lyon
Molecular, ecological and evolutionary mechanisms of extreme growth variation in a water strider

13:00-14:00 Lunch

14:30-17:00 Excursion to 'Ile de Batz'
Session 4 Developmental Patterning
17:30-18:00 Olivier Hamant, ENS Lyon
How Transcriptional Noise and Mechanical Conflicts Contribute to Organ Shape Reproducibility
18:00-18:30 Fabienne Lescroart, Marseille
Early Specification of the Cardiopharyngeal Mesoderm: Multiple Roads to the Heart and Head Muscles
18:30- 18:45 Maheva Andriatsilavo, Institut du Cerveau-Paris Brain Institute (ICM)
Probabilistic axon targeting dynamics lead to individualized brain wiring
18:45-19:15 Pauline Speder, Institut Pasteur
Building the neurogenic niche, one block at a time

***Free evening** (Restaurants close early in Roscoff)*

Thursday May 25, 2023
Session 5 Regeneration
08:45-09:15 Lionel Christiaen, SARS Bergen
Cardiac Development and Whole Heart Regeneration in a Simple Chordate
09:15-09:45 Guo Huang, UCSF, San Francisco
Neurohormonal Control of Organ Regeneration: Insights from Platypus, Anteaters, Bats and Whales
09:45-10:15 Hernan Lopez-Schier, NYU Abu Dhabi, UAE
Long-term homeostasis of complex patterns in regenerating organs
10:15-10:45 coffee break
10:45 -11:00 Agnés Boutet, Laboratory of Integrative Biology of Marine Model, Roscoff, France
Vertebrate kidney regeneration: insights from a shark"
11:00 -11:30 Patrick Lemaire, Institute of Biological Sciences, Montpellier
Growth, Apoptosis, Regeneration, Signaling Gradients: Everything the Ascidian Embryo Can Do Without…
11:30-12:00 Michael Averof, IGF Lyon
Does Regeneration Mirror Development?
12:00-12:30 5 x 5min flash talks (from themes 4-6)

13:00-14:15 Lunch

14:30-16:00 **Poster session B; Sessions 4-6** (w/ coffee)

Session 6 Senescence and Plasticity
16:00-16:30 Han Li, Institut Pasteur, Paris
New tricks of an Old Player: Senescence-Induced Cellular Plasticity in Health and disease
16:30-17:00 Michael Rera, Institut de Biologie Paris Seine

	Two phases for better understanding ageing
17:00-17:15	Anadika Rajive Prasad, UCL, London
	Post-transcriptional regulation enables rapid changes in gene expression at the onset of neuronal differentiation
17:15-17:45	Bill Keyes IGBMC, Strasbourg
	Cellular Senescence in Development and Aging
18:00-18:45	**Keynote 2: Peter Reddien, Whitehead Institute, MIT Boston**
	Fate Choice in Planarian Regeneration
18:45-19:15	Discussion about the next CJM
19:30-22:00	*Drinks & Banquet*

Friday May 26, 2023 - morning

Departure	*08:40: Bus to Morlaix*
	09:10: Bus to Brest