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Meeting report: Third Franco-Japanese developmental biology meeting “New Frontiers in developmental biology: Celebrating the diversity of life”

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Summary

The French and Japanese Developmental Biology Societies, teaming up with Human Frontier Science Program, were eager to meet back in person in November 2022 in the lovely city of Strasbourg. Top scientists in the developmental biology field from France and Japan, but also from United States, United Kingdom, Switzerland or Germany shared their exciting science during the 4 days of this meeting. Core fields of developmental biology such as morphogenesis, patterning, cell identity, and cell state transition, notably at the single cell level, were well represented, and a diversity of experimental models, including plants, animals, and other exotic organisms, as well as some in vitro cellular models, were covered. This event also extended the scope of classic scientific gatherings for two reasons. First the involvement of artists during the preparation of the event and on site. Second, part of the meeting was open for the general public through a series of outreach events, including a music and video presentation through projection mapping at Rohan palace, as well as public lectures.

KEYWORDS

early development, process; fate specification, process; patterning, process; genomics, process; genetics, process

The lead organizers, Sophie Jarriault, Shigeo Hayashi and Guntram Bauer, together with their supporting organizing teams, prepared a rich scientific program divided in eight sessions that we will briefly detail bellow. The first session was entitled “Building an organism: Patterning and scaling during embryogenesis & organogenesis.” It illustrated the multifaceted aspects of the embryonic development field. Topics included organismal chirality explored at the molecular level notably on the emergence for left–right asymmetry in the snail and *Drosophila* (Kuroda et al., 2016) (Reiko Kuroda, Chubu University; Asuka Yamaguchi, Osaka University), evolution of mesoderm formation in the echinoderm (Barone & Lyons, 2022) (Vanessa Barone, UC San Diego), force feedback regulation (Jérôme Gros, Institut Pasteur

or the influence of cell-to-cell heterogeneity and differential growth in quail embryo morphogenesis (Benazeraf et al., 2017; Romanos et al., 2021) (Bertrand Benazeraf, MCD/CBI Toulouse). The existence of intermediate cell stages and dynamic decision making required for harmonization of fates after tissue morphogenesis of the *Drosophila* trachea was also discussed (Sakaguchi et al., 2021) (Takefumi Kondo, Kyoto University) as well as the translational control during maternal to zygotic transition (Ludivine Fierro, Sapporo University). Keynote Speaker, Yoshiko Takahashi (Kyoto University) presented her studies on the mechanisms driving gut peristaltic contractions during embryonic development of chicken (Shikaya et al., 2022; Yagasaki et al., 2022). These contractions, propagating like waves, are crucial

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for proper transit. Surprisingly, peristaltic pulses are initiated before food intake from the embryonic day 12 and gradually synchronize into wave patterns. Using gut organoid model embedded in microcavities in combination with calcium imaging and optogenetic manipulation, her team showed that Interstitial Cells of Cajal have a central role to synchronize contraction of Smooth Muscle Cells. Jerome Gros (Institute Pasteur) presented his work on the involvement of mechanical forces to generate feedbacks between the patterning of gene expression and morphogenesis during the process of quail gastrulation (Saadaoui, Rocancourt, Roussel, Corson, & Gros, 2020). He showed collective cell movements similar to fluid dynamics that generate a pattern of high-tension regions and highly contractile regions. Mechanical forces, via the opposite effects of tension (inhibition) and contractility (induction) could control gene expression in a similar manner than Turing's molecular reaction-diffusion model (Caldarelli, Chamolly, Alegria-Prévo, Gros, & Corson, 2021). Thus, illustrating how mechanical forces can be a central driver for gastrulation and enable very fast regulation of gene expression.

The next session was "Regeneration & stem cells, aging, senescence." In this session, six speakers showed their results regarding the dynamics of gene expression in stem and progenitors cells from various tissues, such as during ectomesenchyme specification (Zalc et al., 2021) (Antoine Zalc, Cochin Institute), homeostasis of the intestine (Hayot, Massonot, Keime, Faure, & Golzio, 2023) (Mathieu Massonot, IGBMC Strasbourg), regeneration of the fin in zebrafish (Cudak, Lopez-Delgado, Keil, & Knopf, 2023) (Franziska Knopf, Center for Regenerative Therapies TU Dresden & Center for Healthy Aging, Medical Faculty TU Dresden) and aging process (Aiko Sada, Kumamoto University). Thereby illustrating beautifully how we need to expand our understanding of cell differentiation potential. HFSP keynote speaker, Penney Gilbert (University of Toronto) showed how physical stresses modify muscle stem cell responses to biochemical niche cues, using an original *in vitro* system developed in her laboratory. Cultured in normal laboratory conditions, muscle stem cells (MuSCs) fail to proliferate efficiently and lose their regenerative capability (Gilbert et al., 2010). Therefore, her team established new methods using bioengineered substrates to recapitulate key biophysical and biochemical niche features, that allow them to stabilize MuSCs in the dish. She also shared new insights on how the native three-dimensional tissue exerts spatiotemporal control on muscle stem cell fate (Jacques et al., 2022; Moyle, Davoudi, & Gilbert, 2022). Hironobu Fujiwara (RIKEN BDR) identified the origin of hair follicle stem cells and established new model of cell fate determination, called the "telescope model." He showed the dynamic lineage progression and transcriptome changes in the entire epithelium of the mouse hair follicle during embryonic development, by combination of marker-independent long-term 3D live imaging and single-cell transcriptomics analysis. In this "telescope model," the precursors of different epithelial lineages form 2D concentric patterns. Each concentric ring extending to form longitudinally aligned, 3D cylindrical compartments as the telescope, that allow compartmentalization of hair follicles tissue and stem cell formation at the same times (Morita et al., 2021; Morita & Fujiwara, 2022). Aiko Sada (Kumamoto University) presented her

work on the dynamics of skin epidermal stem cells during adult tissue homeostasis and aging in mice. She discovered two populations of cells acting in compartmentalized regions as Stem Cells (SC): one slow-cycling clones and the other fast-cycling clones (Sada et al., 2016). Interestingly, slow- and fast-cycling SC undergo distinct aging processes: slow-cycling clones expand into the fast-cycling SCs territory, while the number of fast-cycling clones gradually declines during skin aging (Raja et al., 2022). Fibulin 7, an extracellular matrix protein, was identified as a crucial player to maintain proper microenvironment for SC population maintenance (Raja et al., 2022).

The third session was "Developmental processes modelled in a dish: stem cells, blastuloids and organoids." In this session, six speakers showed their new findings using 2D or 3D *in vitro* reconstituted systems allowing to study for example: how patterned cells with differential expression impact auto-organization processes of confined tissues (Shariati et al., 2019) (Ali Shariati, University of California), how interfacial surface tension changes translate into epithelium elongation (Katia Barrett, IBDM Marseille), evolution of the pluripotent stem cell in the rabbit (Bouchereau et al., 2022) (Nathalie Beaujean, Stem-Cell and Brain Research Institute), as well as how cell-interactions in co-cultures of myoblasts and fibroblasts favor muscle differentiation (Rosa Nicolas, Institut Biologie Paris-Seine). Satoru Okuda (Kanazawa University) notably presented how mechanical forces play a key role for generating optic cup formation, by developing a versatile computational model of 3D multicellular dynamics at single-cell resolution combining it with 3D culture system of pluripotent stem cell-derived optic-cup organoid. His study illustrates how mechanical forces act a key role as feedback regulator to establish the robustness of organogenesis as the optic cup (Okuda et al., 2018). Rafael Carazo Salas (University of Bristol) presented their multiplexed live visualization system, called ORACLE, a powerful tool to enable quantitative monitoring of cell fate dynamics at the single-cell resolution during human pluripotent stem cells reprogramming (Kim, Ren, Casanova, Piddini, & Salas, 2021). He also presented a deep learning enhanced morphological profiling approach, called DEEP-MAP, that is allowing to robustly map, and predict cell fate dynamics in real-time without cell state-specific reporters (Ren et al., 2021). H el ene Vignes (IGBMC Strasbourg), SFBD Thesis 2022 Prize, presented her findings performed in the Vermot Lab with respects to mechanical force contribution in the process of zebrafish heart morphogenesis, using notably beautiful and challenging quantitative high-resolution microscopy in beating hearts (Vignes et al., 2022).

Fourth session was "Single cell analyses: heterogeneity, epigenetics status and GRNs." In this session, six speakers showed their finding on fate acquisition in various organisms notably using the popular single-cell multiomics approach: during endocrine cell differentiation (Sarah Jimenes, IGBMC Strasbourg), along Schwann cell precursor trajectories (Maria Kastriti, Vienna Center for Brain Research) or more surprisingly during spider embryo body patterning (Akiyama-Oda, Akaiwa, & Oda, 2022) (Yasuko Akiyama-Oda, JT Biohistory Research Hall). Regarding neurogenesis, the role of apoptosis (Gabriel Krasovec, National University of Ireland Galway) as well as histone marks (Pierre Cattenoz, IGBMC Strasbourg) were

presented. Alex Schier (University of Basel) presented the single-cell reconstruction of developmental trajectories during embryonic development in zebrafish using large-scale single-cell RNA sequencing (Farrell et al., 2018). Using this dataset, gene modules with similar function and expression dynamics can be extracted. Critical transcription factors related to these differentiation modules are then analyzed by CRISPR knock-out and single cell sequencing. Siobhan Brady (University of California, Davies) showed the unexpected role of the exodermis in tomato root development, by using single cell RNA-seq analysis. It is considered that suberin is a hallmark of endodermal differentiation, but she found that suberin is absent in the tomato endodermis during normal development. Instead, suberin was present in the exodermis, a cell type that is absent in the model organism *Arabidopsis thaliana*. She uncovered genes driving exodermal suberization and described its effects on drought responses in tomato, suggesting that a control of the degree of exodermal suberization could be a new strategy for breeding climate-resilient plants (Cantó-Pastor et al., 2022). Keynote speaker, Michalis Averof (Institut de Génétique Fonctionnelle de Lyon) showed a comparison of global transcriptional dynamics between the adult leg regeneration process and the normal embryonic leg development of *Parhyale hawaiiensis*. If regenerating animals have the ability to reproduce body parts, whether the regeneration mirrors the development or not remains an open question in most regenerative species. In the presented case, embryonic development of the leg and regeneration use similar sets of genes, but the temporal patterns in which genes are deployed are different and cannot be systematically aligned. These results suggest that regeneration is not the simple repetition of development. The same body part can be formed either via independent mechanisms or by shared core mechanisms hidden within the global transcriptomics dynamics (Almazan, Cevrim, Musser, Averof, & Paris, 2022; Sinigaglia et al., 2022).

Fifth session was “Robustness and plasticity of cells and developmental processes.” In this session, six speakers illustrated how cell fate is robustly set in living models notably during a natural transdifferentiation in *C. elegans* (Riva et al., 2022) (Christelle Gally, IGBMC Strasbourg), junctional remodeling within the *Drosophila* Wing (Ikawa, Ishihara, Tamori, & Sugimura, 2023) (Kaoru Sugimura, University of Tokyo) or limb patterning (Rushikesh Sheth, University of Basel Medical School). Marie-Anne Felix (Institut de Biologie de l'École Normale Supérieure) showed how a developmental system responds to mutational perturbations. To evaluate how developmental genetic biases affect phenotypic evolution, her laboratory characterized animals which had been subjected to random mutation starting from eight distinct wild isolates of the nematode species *C. briggsae*, *C. elegans*, *Oscheius tipulae* and *O. onirici*. They identified the fastest evolving cell fate in vulva precursor cells, which differs between the two nematode genera and matches the corresponding fast phenotypic evolutionary rate. By identifying the underlying mutations, they showed that a broad mutational target is the cause of the high mutational variance (Besnard et al. 2020). Fengzhu Xiong (Gurdon Institute, University of Cambridge) showed how tissue mechanics promote robustness of morphogenetic progress, using chicken axial elongation models

(Xiong, Ma, Benazeraf, Mahadevan, & Pourquie, 2020). In this meeting, he presented tissue force microscopy experiments illustrating how the pace of elongation is accommodating to external pushing or pulling forces, a process thought to be dependent on cell density (Chan et al., 2023). Yuuki Ishita (Hiroshima University) was offered a Best Presentation Prize for her work on the discovery of a novel gene associated with the predatory feeding, which is an evolutionary novel trait of the nematode *Pristionchus pacificus* (Ishita, Chihara, & Okumura, 2021). HFSP keynote speaker, Christine Cheung (Nanyang Technological University, Singapore) presented her work in a pre-recorded talk on pathological endothelial cell behaviors using patient-derived endothelial models under inflammatory conditions (Ng et al., 2022).

The sixth session was “Dynamics processes, imaging advances and new models in developmental biology.” In this session, six speakers showed dynamics of developmental process using novel imaging tools or novel techniques such as cell spatial confinement using droplet microfluidics (Kohler et al., 2022) (Timo Kohler, University of Cambridge) enabling to identify Plakoglobin as a pluripotency factor, cell doublets and chiral rotation in relation with cell cytoskeleton organization (Tomoki Ishibashi, RIKEN BDR) or single-cell lineage tracing of axis stem cells during body axis formation to show their bipotency (Guillot, Djefal, Michaut, Rabe, & Pourquie, 2021) (Charlène Guillot, University of Clermont Auvergne—iGReD). In an EMBO YIP lecture, Mounia Lagha (Institut de Génétique Moléculaire de Montpellier) presented her work on the kinetics of gene expression during the awakening of the zygotic genome *Drosophila*. In living embryos, the spatio-temporal precision in gene expression is monitored by imaging the flow of information along the central dogma (MS2/MCP system for transcription and SunTag/scFv for translation). Discontinuities (bursting) and heterogeneities seems to be the rule for these processes (Dufourt et al., 2021; Pimmett et al., 2021). Yoshikatsu Sato (Nagoya University) presented an application of microfluidics in the field of plant development which enabled to demonstrate the developmental flexibility of tip-growth. Plant cells grown inside 1 μm sized chambers are guided toward the gaps using microdevices which are customized for each cell type (Yanagisawa et al. 2017). He also showed a novel DNA-labeling dye, called Kakshine, that has high DNA specificity and membrane permeability, allowing the staining of nuclear or mitochondrial DNA suitable for live cell imaging (Uno, Sugimoto, & Sato, 2021). Gilles Dupouy (Institut de biologie moléculaire des plantes de Strasbourg) was offered a Best Presentation Price for his work on the role of actin and microtubule cytoskeleton in nucleus shape and positioning during the process of root hair growth in *Arabidopsis Thaliana* using a recently established microfluidic chip design (Singh et al., 2021).

Seventh session was “Ontogeny, evolution, trajectories & transition states of cellular identities.” In this session six speakers discussed their findings and re-questioning classic concepts of cell fate acquisition. This included detective phylogenetic work to find out the developmental and evolutionary origins of tetrapod neck muscles (Eglantine Heude, Muséum National d'Histoire Naturelle de Paris) or understand the transcriptional convergence at work for vertebrate skeletal cells

3rd Franco-Japanese Developmental Biology Meeting New Frontiers in Developmental Biology: Celebrating the Diversity of Life

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SCIENTIFIC PROGRAM

KEYNOTE SPEAKERS

Michalis Averof
IGFL | France

Penney Gilbert
University of Toronto | Canada

Christine Cheung
NTU | Singapore

Yoshiko Takahashi
Kyoto University | Japan

INVITED SPEAKERS

Igor Adameyko
Karolinska Institute | Sweden
Vienna Medical University | Austria

Hironobu Fujiwara
Riken BDR | Japan

Aiko Sada
Kumamoto University | Japan

Vanessa Barone
UC San Diego | USA

Jérôme Gros
Institut Pasteur | France

Yoshikatsu Sato
Nagoya University | Japan

Siobhan Brady
University of California | USA

Mounia Lagha
IGMM | France

Alex Schier
Harvard University | USA
University of Basel | Switzerland

Rafael Carazo Salas
University of Bristol | UK

Olivier Pertz
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IRCMS et Kanazawa University | Japan

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ABSTRACT | REGISTRATION DEADLINE
July 15th 2022

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FIGURE 1 Poster of the meeting.

(Patrick Tschopp, University of Basel) as well as work revealing the rich regional molecular patterning at work defining fish eye organization (François Agnès, Paris-Saclay Institute of Neuroscience) and ultra-sensitivity in ascidian neural induction via activator-repressor competition for same binding sites (Clare Hudson, LBDV IMEV Sorbonne Universities; Guillaume et al., 2021; Bettoni et al., 2023). Igor Adameyko (Karolinska Institute) showed fine spatiotemporal trajectories of cell fate decisions in mouse neural crest lineage, using single-cell and spatial transcriptomics with statistical analysis of branching trajectories. The classical view of neural crest EMT (epithelial to mesenchymal transition), as an abrupt process resulting from the activation of a gene regulatory network, might be erroneous. Pre-EMT neural crest cells express genes associated with neural plate border and neural tube identity. More advanced neural crest cells down-regulate the expression of neural tube markers and increase the expression of neural crest cell-specific genes, indicating that the transition from pre-migratory to migratory neural crest cells is more gradual and complex than initially thought and that gating at the bifurcation fork might exist (Kastriti et al., 2022; Soldatov et al., 2019). Oliver Pertz (Institute of Cell Biology, Switzerland) showed dynamics of MAPK signaling during tissue homeostasis and development, examining the single-cell measurements of ERK activity dynamics using an ERK biosensor and also optogenetically control of MAPK signaling. He found that during tissue homeostasis and development, stochastic ERK pulses as well as collective ERK waves allow tissue level coordination of ERK pulse frequencies in single cells within epithelial tissues. High, medium and low ERK pulse frequencies are then decoded into proliferation, quiescence/survival and apoptosis fates. This explains how self-organization of signaling can coordinate fate decision in time and space (Dessauges et al., 2022; Ender et al., 2022).

The final session was entitled “Ensuring the next generation: Meiosis, mitosis & germ cells,” thus bringing us to the singular totipotent cells at the origin of all. Topics included some study of the mechanisms at the origin of germline transcriptional regulation in *C. elegans* (Rodríguez-Crespo, Nanchen, Rajopadhye, & Wicky, 2022) (Chantal Wicky, University of Fribourg) or a description of the spatial patterning of piRNA complexes in *Drosophila* germ cells (Hirono Kina, Institute of Molecular Embryology and Genetics of Kumamoto University). Marie-Hélène Verlhac (Collège de France) showed how cytoplasmic forces linked to actin cytoplasmic networks instruct nucleus position within the mouse oocyte but also promote nuclear envelope fluctuation, thus impacting the transcriptional status of over 250 genes and the splicing activity within liquid-like nuclear speckles. These actin related forces are thus key for proper oocyte maturation process. This mechanism of nucleoplasm agitation via cytoplasmic cytoskeleton related forces has been conserved during evolution, being also observed in *Drosophila* oocytes (Al Jord et al., 2022).

In addition to this rich scientific program, the lead organizers decided to deeply anchor this event in society. First, it was supported by the Consul General of Japan who notably made us the pleasure to open the scientific meeting in person with his kind Welcome Speech. Second, two public conferences (presented by Chris Bowler, École Normale Supérieure de Paris and Shigeru Kuratani, RIKEN BDR) were programmed targeting a general audience. Additionally, a few citizens

could join scientific sessions of the meeting for a deeper immersion into science! Younger public was reached on one side via the invitation of high school students for conferences and private discussion sessions with scientists on the site of the meeting; on the other side scientists visited primary schools on the first morning, enabling children to discover some of our animal models of study.

Arts was also included throughout the meeting as two collaborations had been initiated early on. Frist with a scientific illustrator enabling us to build a real visual identity for the meeting (Figure 1) and second with an art's school in Strasbourg, for a partnership



FIGURE 2 Presentation of artistic scientific books presenting different model organisms.



FIGURE 3 Kakemono with details on the genesis of one of the artistic scientific books.



FIGURE 4 Picture of the opening of the video mapping event.

project with scientists to create artistic scientific books presenting model organisms used in biology (Figures 2 and 3). These books were exposed side by side with scientific posters and accessible to all citizens within the Palais Universitaire of Strasbourg. But the most astonishing event took place at night in a courtyard adjacent to the Cathedral of Strasbourg with an artistic video mapping happening! What a show at night! Sound and light projections as well as a whole scenery caught the eye not only of us, scientists sometimes overexcited to recognize our own images in a poetic context, but also of passing people stopping to observe how organisms emerge from one zygotic cell with the pop's eye of the artist (Figure 4). This event was freely accessible to all passing citizen and even advertised throughout Strasbourg as short movies were visible on displays of several tram stations! Have a look and enjoy too!

<https://www.youtube.com/watch?v=jewWB5lhSeo>

Meeting URL

<https://www.sfb2022jsdb.com/>

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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