Research evaluation

# EVALUATION REPORT OF THE UNIT

LBD - Laboratoire de biologie du développement

## UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Sorbonne Université - SU,
Centre national de la recherche scientifique - CNRS,
Institut national de la santé et de la recherche médicale - Inserm

**EVALUATION CAMPAIGN 2023-2024**

GROUP D

Rapport publié le 25/04/2024

High Council for evaluation of research and highter education

In the name of the expert committee :

James Hombría Castelli-Gair, Chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

## MEMBERS OF THE EXPERT COMMITTEE

| | |
|---|---|
| **Chairperson:** | Mr James Hombría Castelli-Gair, Spanish National Research Council, Seville, Espagne |
| **Experts:** | Mr Markus Affolter, Biozentrum, Bale, Suisse<br>Ms Anna Castro, CNRS - Centre national de la recherche scientifique, Montpellier, France<br>Mr Guillaume Charras, University College London, London, Royaume-Uni<br>Ms Barbara Conradt, University College London, London, Royaume-Uni<br>Ms Alice Davy, CNRS, Toulouse, France (representative of CoNRS)<br>Mr Renald Delanoue, Inserm - Institut national de la santé et de la recherche médicale, Nice, France (representative of CSS Inserm)<br>Mr Francois Fagotto, université de Montpellier, France<br>Mr Stefan Hoppler, University of Aberdeen, Scotland, United-Kingdom<br>Mr Olivier Leprince, Institut national d'enseignement supérieur pour l'agriculture, l'alimentation et l'environnement - Institut Agro, Rennes-Angers, France<br>Ms Barbara Pernaute, Andalusian Centre of Developmental Biology CABD-CSIC, Seville, Espagne<br>Mr Cosmin Saveanu, Institut Pasteur Paris, Paris (representative of CoNRS)<br>Mr Claus Storgaard Sorensen, University of Copenhagen, Danemark<br>Mr Bertrand Vernay, Inserm, Strasbourg, France (representative of supporting personnel)<br>Mr Lucas Waltzer, CNRS, Clermont-Ferrand, France<br>Mr Elazar Zelzer, Weizmann Institute, Rehovot, Israel |

## HCÉRES REPRESENTATIVE

Mr Yacine Graba
Ms Marie-Josée Stasia

## REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr Philippe Agard, Sorbonne University
Ms Sandrine Betuing, Sorbonne University
Mr Patrick Blader, CNRS
Mr Thierry Galli, Inserm

# CHARACTERISATION OF THE UNIT

- Name: Developmental Biology Laboratory
- Acronym: LBD
- Label and number: UMR 7622
- Number of teams: 17
- Composition of the executive team: Director: Ms Sylvie Schneider-Maunoury until February 28, 2023; Deputy Director: Mr Thierry Jaffredo and Director since March 1, 2023 until December 31, 2024

## SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

## THEMES OF THE UNIT

The LBD's main topic of research is Developmental Biology using different models, including plants. The unit's teams also perform research using cell and tissue culture, including human cell lines, and have introduced organoids and organs on chips. There is a strong interest in mechanobiology and in techniques to analyse development applying single cell and single nucleus transcriptomics as well as spatial transcriptomics, epitranscriptomics and proteomics.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The LBD is composed of seventeen teams and five support and technological service platforms, comprising over 150 researchers (including engineers and technicians). LBD is located in the Sorbonne University campus (previously known as Université Pierre et Marie Curie, Paris 6), which is dedicated to biology, mathematics, physics, chemistry, and computer laboratories facilitating interdisciplinary interactions between units in the campus. The unit has been directed by Sylvie Schneider-Maunoury from May 2013 to March 2023, when Thierry Jaffredo previously acting as deputy director took over. The LBD is supported by Sorbonne University and the CNRS and host an Inserm ERL that includes four LBD teams.

Since 2014 LBD merged with another four units to form a research federation, the Institut de Biologie Paris Seine (IBPS). IBPS was initially directed by Michele Labouesse until March 2023 when the direction was taken over by Sylvie Schneider-Maunoury. This federation allows exploiting the multidisciplinary potential of the campus by associating units working on related topics including medicine, neuroscience, ageing, computational and quantitative biology, and physics at the interphase of biology, besides developmental biology. IBPS also supports shared core facilities including animal houses for mice and fish, imaging and flow cytometry, bioinformatics and protein engineering.

## RESEARCH ENVIRONMENT OF THE UNIT

The unit is integrated in the Institute de Biologie Paris Seine (IBPS) fostering interactions with units working on neuroscience, ageing, computation and quantitative biology, and soft matter physics providing a multidisciplinary approach. Technological platforms include facilities that have been recently expanded or refurbished and plant -greenhouse and growing rooms- facility, imaging (cellular imaging, electron microscopy, and flow cytometry), bioinformatics, and proteomics. LBD provides to the IBPS advanced techniques on single cell sequencing thanks to a 10X chromium device as well as nanopore sequencing capabilities, Next Generation Sequencing preparation, a laser micro dissection service and various devices providing an advanced analysis line for DNA and RNA. The multidisciplinarity at LBD has been reinforced by the Idex initiative i-Bio that started in 2020 to integrate several potentialities of IBPS. i-Bio supported interdisciplinary projects among various teams and helped to recruit one new team by providing a start-up package.

## UNIT WORKFORCE: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 12 |
| Maîtres de conférences et assimilés | 23 |
| Directeurs de recherche et assimilés | 13 |
| Chargés de recherche et assimilés | 15 |
| Personnels d'appui à la recherche | 38 |
| **Sous-total personnels permanents en activité** | **101** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 2 |
| Personnels d'appui non permanents | 7 |
| Post-doctorants | 5 |
| Doctorants | 41 |
| **Sous-total personnels non permanents en activité** | **55** |
| **Total personnels** | **156** |

## DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading "others".

| Nom de l'employeur | EC | C | PAR |
|---|---|---|---|
| SORBONNE UNIVERSITÉ | 35 | 0 | 23 |
| CNRS | 0 | 22 | 14 |
| Inserm | 0 | 6 | 1 |
| **Total personnels** | **35** | **28** | **38** |

# GLOBAL ASSESSMENT

The LBD (Laboratoire de Biologie du Développement) unit is specialised in Developmental Biology. Their research uses different models including plants, and they also perform research using cell and tissue culture, including human cell lines. In the last contract period, the unit has introduced organoids and organs on chips, and updated their research approaches by introducing single cell and single nucleus transcriptomics as well as spatial transcriptomics and has reinforced the study of mechanobiology by recruiting new teams with a physics background and introduced chips to model *ex vivo* the effects on development. This novel initiative will give the unit a unique strength, differentiating it from other units working in similar areas, and help them stay at the forefront of biology. It is important to increase efforts to make sure that junior groups joining the unit have a reduced lecture and administrative load when first arriving at the LBD, so they can settle as competitive research teams. The LBD is part of and plays a major role in the federative structure IBPS (Institut de Biologie Paris Seine), which promotes interdisciplinary research. IBPS includes four other research units and several technological platforms, and is supported by the i-Bio program (PIA idex, Sorbonne Université).

The unit's management by the director's is outstanding, favouring a smooth operation in a difficult context imposed by old infrastructures, as well as promoting a friendly atmosphere and cohesive spirit that makes the unit an attractive workplace. The coordination of the LBD with other IBPS units is well structured, and the integration of LBD in IBPS reinforces the available services and advanced technical platforms to which the unit has access.

The LBD benefits from an excellent national and international visibility (>150 invitations to conferences and seminars, organisation of 23 conferences), excellent attractiveness (recruitment of two teams, obtaining fivepermanent positions (1 Inserm, 2 CNRS and 2 SU, and training of 72 PhD students) and significant success in

national calls for projects (22 ANR, 1 INCA, and >30 charitable contracts). The influence of the unit's members is also demonstrated by strong participation in national (INSB Management, CoNRS 21 and 22, Inserm CSS1 and CSS2, CNU 65) and, in some cases, international (ERC, EMBO and Welcome trust panels) bodies.

The LBD scientific output is globally excellent, totalling >250 publications, including 160 on projects coordinated by members of the unit. The quality of the work carried out leads to a regular flow of publications in excellent to outstanding journals (Nature, Nature Cell Biology, Nature Commun, Molecular Cell, Developmental Cell, iScience, ELife, PNAS, JCB). Of particular note are significant advances in the mechanisms underlying asymmetric splitting (Nature Commun, eLife, JCB), the understanding of muscle lineages (Nature Commun), the discovery of a hemogenic bone marrow endothelium in the late fetus and young adult (Nature Cell biology), and the mechanical control of axial elongation, a key stage in animal development (Nature, eLife).

The contribution of research activities to society is excellent for a basic research unit. Although the teams are mostly focused on basic research, they have a strong input to society. The LBD makes a major contribution to Sorbonne University's teaching and training activities. The activities of some teams, particularly those working on plants, have an economic impact, with numerous interactions with national and international private companies (Limagrain, Syngenta, BASF), cifre doctoral contracts (3), patent applications (5) and the creation of the "Auxoway" start-up. The unit also hosts an Inserm ERL (4 teams in the unit) which promotes a network of clinical interactions. Finally, all teams are involved in outreach activities targeting society (Déclics, Vie ma vie de chercheur, conferences for the general public (>40), TV and radio broadcasts (7).

Due to the retirement of several groups, the unit contemplates restructuring by merging the remaining LBD teams with some groups from other IBPS units to generate a new unit named "Development, Adaptation and Ageing" (Dev2A). This is an intelligent strategic move that will merge the LBD teams with excellent basic research profiles with other teams with a stronger technological output. Among various advantages, the merger will increase the number of plant groups, reinforcing this area of research in the unit, and could gain full affiliation to Inserm.

# DETAILED EVALUATION OF THE UNIT

## A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report criticised the unit was not publishing in the most prestigious journals of the field, making it less attractive to international students:
The unit has improved the quality of its production with four publications in Nature Commun., 2 Cell Reports, 2 Journal of Cell Biology, 2 PLoS genetics, 2 Development, 2 eLife, and publications in Nature Cell Biology, Journal of neuroscience, iScience, Journal of Cell Biology, PNAS, EMBO reports, Nature, The plant journal, Nucleic Acid Research, Science Advances and Molecular Cell. The unit also has advertised two new positions and has had a good response obtaining applications from France and abroad, indicating it is attractive to international researchers.

The previous report also said that the socio-economical activities were discreet:
The LBD has increased the number of patents to five and has created a startup company, Auxoway. On the educational side, the unit members have participated in numerous activities for the public.

Finally, the report criticised that in some teams, students did not get a first author publication at the time of defense:
This problem has not been solved, arguing that the three-year period when the thesis is supposed to be finished does not provide enough time for publishing a paper of sufficient quality to appear in a top journal. It is a problem still to be solved, as the student's future depends on it.

## B - EVALUATION AREAS

### EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

#### Assessment on the scientific objectives of the unit

The unit has a clear scientific focus, developmental biology, using various model organisms. Recently, it has reinforced the study of mechanobiology recruiting new teams with a physics background and introduced chips to modulate *ex vivo* the effects on development. This novel initiative will give the unit a unique strength, differentiating it from other units working in similar areas. The unit also focuses on techniques to analyse development applying single cell and single nucleus transcriptomics as well as spatial transcriptomics, epitranscriptomics and proteomics.

#### Assessment on the unit's resources

Funding and technical and human resources were assesed as exellent. The unit benefits from a critical mass of researchers, although the loss of support staff may become an issue very soon. Recurrent funding by the CNRS and SU averaged 460 k€/year over the reporting period, representing 20% of the unit's total budget. The unit optimaly exploited its resources by setting up multiple technical facilities (Microexplo laboratory, laser dissection, transcriptomics and proteomics, transgenesis and genome editing facility).

## Assessment on the functioning of the unit

The unit's organisation resulting from an efficient and stable direction is outstanding. Activities of well-acting committees (Direction team, Laboratory council, group leader board, health and safety and ad-hoc committees) contribute to the harmonious functioning of the unit. The organisation of other issues like animal welfare, computer protection, psychosocial risks, green committee and research training are well-structured. The unit's coordination with other IBPS units and IBPS technology platform is well-structured, favouring a smooth operation.

### *1/ The unit has set itself relevant scientific objectives.*

#### Strengths and possibilities linked to the context

The unit has a series of objectives spanning the various established areas of the developmental biology discipline: signalling, gene regulation, epigenetics etc. Besides this, the unit has started exploring new topics that will allow staying at the forefront of biology. Most recent is the effort on the application of massive sequencing to development through single cell and spatial transcriptomics, as well as in mechanobiology and on the fabrication of biomimetic organs on chips. This latter area of research has received a donation that has been used to establish the "Microexplo Laboratory", dedicated to control physicochemical measurements of the cellular environment that enable the fabrication of biomimetic organs-on-chips. As a result, the unit has the potential to become a reference on mechanobiology research.

#### Weaknesses and risks linked to the context

The unit focuses on many different aspects of biology and that may result in some teams being isolated because of their topic. For example, during most of the period of evaluation there was only one team working in plants.

### *2/ The unit has resources adapted to its activity profile and research environment, and makes use of them.*

#### Strengths and possibilities linked to the context

The unit benefits from a critical mass of researchers.

The unit is regularly supported by the CNRS and SU with a recurrent annual funding that averages 460 k€/year over the reporting period, representing 20% of the unit total budget, highlighting the success of teams in obtaining external funding. Four teams in the unit the belong to an Inserm ERL.

The unit has good resources to assist research and has set up a large number of technological facilities. It created a unique "Microexplo laboratory" to enhance work of mechanobiology thanks to a donation complemented with the unit's own funds, and has the resources to use single cell technology with a 10xChromium device. The unit has acquired a laser dissection equipment for spatial single cell approaches, providing transcriptomics and proteomics services. There are cell culture rooms with an area used for human tissue and lentivirus treatment. An additional cell culture room is available for manipulation of pluripotent stem cells and organoids. There is a transgenesis and genome editing facility for zebrafish and *Xenopus*. The unit also has a green house for plant cultures.

The unit can make use of the IBPS core facilities which include imaging facility (with flow cytometry services, image analysis and a variety of advanced confocal microscopes), electron microscopy, bioinformatics, protein engineering, etc. The unit itself has a cleaning service and media solution facilities, a facility for the preparation of *Drosophila* and *C. elegans* culture media.

#### Weaknesses and risks linked to the context

The outdated infrastructure of the building and the scarcity of funds allocated to the renovation of rooms, plus the decrease of technical human resources, results in a sizeable part of the unit's budget being employed for the renovation of installations and for the recruitment of technical personnel.

The loss of support staff may become a serious issue. For example, although the bioinformatic support is excellent, it is currently overworked, not being able to support the different teams as often as required.

### *3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, the environment, ethical protocols and the protection of data and scientific heritage.*

## Strengths and possibilities linked to the context

The director and deputy director are assisted by the laboratory council and the group leader board. The laboratory council takes decisions on LBD policy, recruitment, management, technical facilities and is consulted on the annual budget.

The group leader board is in charge of scientific strategy, especially in the selection and creation of new research groups or requests for new permanent positions for technicians, engineers, or university teachers.

A staff council is involved in the development of the technical and administrative staff. Other committees are set up to organise annual events, including retreats and annual celebrations.

A health and safety committee oversees that all regulations are followed. The LBD's local Health and Safety Committee is composed of the Director, staff representatives, the Health and Safety Officers, representatives of the SU Health and Safety Department and the CNRS Delegation Régionale (DR02), and the SU Preventive Medicine physician. This committee meets at the request of the Head of the Department or LBD members. There are three Safety Officers who advise and support LBD employees in the application of health and safety measures and in the area of occupational health. All new personnel arriving in the unit for more than 6 months are required to attend the obligatory Health and Safety course in addition to specific training for the work they perform in the laboratory.

All LBD members can make use of the IBPS "listening and mediation centre" which provides a space for advice and internal mediation.

The LBD has (almost) achieved gender equality, with 43% female group leaders at the level of professors and research directors.

The organisation of other issues like animal welfare, computer protection, psychosocial risks, green committee and research training are well-structured.

A major green agenda success is the building's renovations funded by SU to make it energy efficient.

## Weaknesses and risks linked to the context

The age of the building starts to be a problem with the requirement of expensive repairs and renewals.

There is no specific Gender Equality committee. Although the unit is very equilibrated at the PI level, it would be good to have such a Gender Equality committee to consider other important issues.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The unit members' international visibility and recognition is excellent, with team leaders being frequently invited to and organising national and international conferences and workshops, and participating to Scientific Advisory Boards, international grant selection panels and Editorial Boards in various specialised journals. External funding has been excellent, yet mostly national. The outstanding organisation of the unit and its services makes the LBD a very attractive place to do research. The unit attracted two new teams, obtained five permanent research positions and trained 72 PhD students. Attractiveness for post doctoral fellows remained limited.

*1/ The unit has an attractive scientific reputation and is part of the European research area.*

*2/ The unit is attractive because for the quality of its staff support policy.*

*3/ The unit is attractive through its success in competitive calls for projects.*

*4/ The unit is attractive for the quality of its major equipment and technical skills.*

### Strengths and possibilities linked to the context for the four references above

The international recognition of the unit members is reflected by the unit's members being frequently invited (>150) to National and international conferences, (EMBO meetings and workshops, Gordon Conferences and Cold Spring Harbor Conferences).

The team members have also organised in average two national or international conferences per year, including EMBO workshops French Developmental Society meetings (in some cases joint with the sister Japanese society).

The PIs are also recruited to scientific advisory boards and participate in selection committees of French, UK and EU grant panels. They are also selected to local, national (Direction of CNRS biologie, CoNRS 21 et 22, Inserm CSS1 and CSS2, CNU 65) and international institutions (ERC, EMBO et Wellcome trust panels) and participate in the editorial boards of various specialised journals including Cells, Frontiers in Cell and Developmental Biology, Frontiers in Developmental Epigenetics, Plant, Nucleic Acid Research and BMC Genomics among others.

Several teams at the LBD have hosted international scientists in their laboratories for visits ranging from one to six months from University of Cambridge, UK (1 month in 2018 and 2019), University of Mexico (6 months in 2017), University of Chile (for 6 months). One team welcomed three PhDs (from Brazil and China) for one year and several visiting scientists (from Poland, India and Turkey) for shorter periods (1-4 months).

The LBD receives a high number of PhD fellowships from the doctoral school, that add to those obtained from funded projects and charities. Seventy two PhD students were trained during the period of evaluation.

Help is provided to prepare grant applications by discussions of the project and interactions among PIs.

The unit has developed a new line, reinforcing it with equipment for mechanobiology and single cell genomics and related techniques. Although some equipment is funded by Inserm and CNRS via institutional funds, the largest part came from a donation.

The organisation of services in the unit makes the LBD a very attractive place to work: there are services to assist all teams by organising media preparation for flies and worms, a service for transgenesis and genome editing for *Xenopus* and fish, laser microdissection for transcriptomics and proteomics, and a washing facility shared with other IBPS units that offer a robust system providing a smooth assistance to all teams. Three cell culture

rooms are available to work with *Drosophila*, vertebrate cell cultures and a third one for pluripotent stem cells and organoids. There is a histology facility providing support for sections. Finally, a green house is available for the only group, although it will be shared with other IBPS units.

During the period of reference, the unit recruited two teams and obtained five permanent positions (1 Inserm, 2 CNRS et 2 SU).

The unit teams were successful in obtaining local and national grants (including 22 ANR, 1 INCA, et >30 charity grants), averaging 2 M€/year.

## Weaknesses and risks linked to the context for the four references above

The international visibility of the unit may be diluted due to its belonging to different substructures. Some researchers may know LBD, others IBPS, others Sorbonne University while others will now have to remember Dev2A. The unit should aim to have a single corporative image that is remembered and should have a modernised webpage.

The teams' international funding could be improved, in particular through application to ERC grants.

Attraction of post doctoral fellows remains limited.

It would be important to expand the recruitment process with external calls.

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

### Assessment on the scientific production of the unit

The overall scientific production of the unit is excellent with a third of the teams assessed as excellent to outstanding or outstanding. The unit is highly productive with over 250 publications for the reporting period. The scientific production has increased in quality as assessed by the number of publications in multidisciplinary high-profile journals, reflecting the unit's scientific exploration of new areas and the use of advanced techniques. This should open possibilities to raise even further the level of scientific production.

*1/ The scientific production of the unit meets quality criteria.*

*2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*

*3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

### Strengths and possibilities linked to the context for the three references above

The unit's overall scientific output is excellent, with a third of the teams assessed as excellent to outstanding or outstanding. The unit produces >250 publications, including 160 on projects coordinated by members of the unit.

The scientific production of the unit has increased in quality as assessed by the number of publications in multidisciplinary high-profile journals and in highly respected specialised journals. These include four publications in Nature Communications, two Cell Reports, two Journal of Cell Biology, two PLOS genetics, two Development, two eLife, and one publication in Nature Cell Biology, Journal of Neuroscience, iScience, Journal of Cell Biology, PNAS, EMBO reports, Nature, The Plant Journal, Nucleic Acid Research, Science Advances and Molecular Cell.

The increased publication quality is a reflection of the interest and originality of the unit's scientific exploration of new areas of biology such as mechanobiology and the use of advanced techniques in single cell and positional cell transcriptomics. The use of organs on chips can open new niches to the unit that may attract new talent.

Of particular note are significant advances in the mechanisms underlying asymmetric cell division (Nature Commun, eLife, JCB), the understanding of muscle lineages (Nature Commun), the discovery of a hemogenic bone marrow endothelium in the late foetus and young adult (Nature Cell Biology), and the mechanical control of axial elongation, a key stage in animal development (Nature, eLife).

### Weaknesses and risks linked to the context for the three references above

One risk is the highly competitive environment in which the unit operates, with other units in the Paris area working in similar areas being capable of attracting the best postdocs and students by offering better start-up packages. This is however compensated by the size of the LBD, which gives a critical mass, offering a competitive research environment.

The variety of topics studied in the unit, may result in some groups becoming more isolated due to their research thematic (for example, there was only one plant team in the unit for most of the reporting period).

The very high teaching load of the university professors and assistant professors may severely challenge their scientific production and, in consequence, that of the teams and of the unit. Besides having general administrative tasks, the average teaching load of teacher-researchers is 220-230 hours per year (much more than the 192 hours normally due), decreasing the time that can be dedicated to research.

Although the unit teams have increased the number of papers published in prestigious journals with respect to the previous periods, there is still room for further improvement.

## EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

### Assessment on the inclusion of the unit's research in society

Focusing on basic research the unit fully exploit its potential for contribution of research activities to society. The unit is strongly involved in teaching and training activities as part of the Sorbonne University. Unit members also largely participate in open science events for the public. The Inserm ERL teams promote a network of clinical interaction, and one group filed a patent focusing on the improvement of haematopoietic grafts. The team working on plants has an important economic impact, with numerous interactions with national and international private companies and patent deposition. Globally considered, this is an excellent contribution for a basic research unit.

*1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*

*2/ The unit develops products for the cultural, economic and social world.*

*3/ The unit shares its knowledge with the general public and takes part in debates in society.*

The LBD, with a majority of permanent teaching researchers, makes a major contribution to SU's teaching and training activities.

The activities of some teams, particularly those working on plants, have an economic impact, with numerous interactions with national and international private companies (Limagrain, Syngenta, BASF), cifre doctoral contracts (3) and patent applications (5).

The unit also hosts an Inserm ERL (4 teams in the unit) which promotes a web of clinical interaction.

### Strengths and possibilities linked to the context for the three references above

The unit teams are mostly focused on basic research and are strongly involved in teaching and training activities at the Sorbonne University.

The unit members participate in open science events for the public (Fete de la Science; Declics, Vie ma vie de chercheur, conferences for the public (>40), TV and radio broadcasts (7)). One team leads the participation of Sorbonne University in the open science collaborative project iGEM for competitions in synthetic biology and education using microorganisms.

On the economic side, some teams in the unit are more active. The plant group has filed several patents (4), implemented several interactions with national and international private companies (Limagrain, Syngenta, BASF) accompanied by cifre doctoral contracts (3) and created a startup company (Auxoway) for the use of cold plasma in agriculture to increase the seed's germinative properties and protect them from pathogens. The unit also hosts an Inserm ERL (4 teams in the unit) which promotes a network of clinical interaction. One group filed a patent focusing on the improvement of haematopoietic grafts.

## Weaknesses and risks linked to the context for the three references above

None identified

# ANALYSIS OF THE UNIT'S TRAJECTORY

Coincident with the closure of six teams due to the imminent retirement of several team leaders, the unit is planning to restructure during the next contract. LBD will disappear as such and the twelve LBD remaining teams (one of them of new creation after the coalescence of two of the closing teams under the leadership of two senior staff members) will merge with teams from other existing units of the IBPS: four teams from the Biology of Aging and Adaptation (B2A) unit that will close, and two teams from the Neurosience unit (Neuroscience Paris Seine (NPS) to create the "Development, Adaptation and Ageing" (Dev2A) unit.

Dev2A will continue to be affiliated to Sorbonne University and the CNRS and possibly to Inserm (final decision pending). The new unit will be composed of a similar number of teams (19) as the current LBD and a total of about 250 permanent and non-permanent staff. The objective of the new unit is to increase the fundamental knowledge on the mechanisms underlying healthy life, and allow developing strategies for tissue repair, identifying therapeutic targets to treat pathologies, and understanding the impact of environmental stresses relevant to sustainable development. This change to a more applied view is accompanied by the request to become affiliated to Inserm (National Institute of Health and Medical Research), whose goal is to improve the health by advancing knowledge of life and disease, innovation in treatment, and public health research.

The new unit will have four main thematic axes, with some teams working in several of them: 1-Stem cells, differentiation and regeneration; 2- Morphogenesis; 3- Plasticity and adaptation to the environment; 4- Chromatin, RNA and heredity. The different teams already have experience in those four areas on which they have published excellent or outstanding work. This reorganisation will reinforce plant research with the incorporation of two plant teams that will join the only plant team previously at the LBD. The establishment of productive interactions among Dev2A teams is backed by the collaborations already established among many of the future unit's teams, which are already publishing joint papers and co-directing PhD thesis.

The mergers of B2A and NPS with LBD in the new Dev2A unit will increase the unit's strength in technology transfer, facilitating the generation of spinoff companies. The unit will maintain a high level of research models including plants (*Arabidopsis* and *Solanum* species), *C. elegans*, *Drosophila*, zebrafish, *Xenopus*, mice and even humans (induced pluripotent stem cells (iPS) derived organoids and organ on Chip techniques).

Altogether, the committee appreciates the effort for local restructuring at a pertinent time point in the IBPS unit evolution, in particular in the context of a strong loss of critical mass at the LBD, and supports the challenge proposed to create an environment for improved synergy between basic and translational research.

# RECOMMENDATIONS TO THE UNIT

## *Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit*

A committee should be created to suggest new equipment needs and renewals.

The committee encourages the unit to try to find alternative funding sources for the update and renovation of their infrastructures so that it does not detract from funds that are better used for new equipment or to provide for start-up funds to attract to the unit promising team leaders with potential to obtain international grants.

## *Recommendations regarding the Evaluation Area 2: Attractiveness*

One weakness is the existence of three levels of organisational structures that dilute the international visibility of any one of them: (LBD, B2A) now Dev2A integrated in IBPS and integrated the Pierre et Marie Curie Campus at Sorbonne University. This detracts from the existence of a unique, well-known, trademark for the unit. It may be interesting to reinforce IBPS and keep all other units as departments.

In between, a modernised webpage could help visibility of the new Dev2A unit.

The committee encourages the unit to aim for more international projects, especially ERC.

The committee encourages the unit to announce the recruiting policy of new teams as international calls. This may help to recruit outstanding young team leaders that could successfully apply for international projects.

## *Recommendations regarding Evaluation Area 3: Scientific Production*

The committee encourages the unit to try to find ways to balance the teaching and administrative load, a situation that negatively affects the scientific production of some teams. It is urgent to find solutions to reduce the burden of teaching and the administrative duties. This is especially important for team leaders having arrived recently to the unit.

The new unit teams are encouraged to publish papers in more prestigious journals, even if this results in a lower quantitative output. This is a trend that has already been started by the LBD and is important to maintain now that teams from other units with different publishing strategies join into the Dev2A unit.

## *Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society*

LBD's contributions to society are excellent for a basic research unit, but basic science outreach could be further promoted. This could be achieved by having a dedicated person in the unit or at the IBPS level.

# TEAM-BY-TEAM OR THEME ASSESSMENT

**Team 1:** Seed Biology – Seed Biology

Name of the supervisor: Mr Christophe Bailly

## THEMES OF THE TEAM

The team investigates cellular and molecular events associated with the regulation of germination and dormancy and how this is influenced by environmental conditions. The focus was on the role of oxidative and oxygen signalling, epigenetic, post-transcriptional and -traductional mechanisms using the model plant Arabidopsis together with sunflower and barley as crop models

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hceres report (italics) were:

*1- Given the quality and originality of the work, team members should aim for publications in higher impact journals.* Eight out of team's 35 research articles were published in the highest regarded journals in Plant Sciences (Genome Biol., J. Integr. Plant Biol.; New Phytol., Plant Physiol.).

*2- The study of the role of central metabolism and physical properties of the seed, as well as the building of a model integrating the different levels of analysis will require novel expertise, which is currently missing in the team. To secure the feasibility of the project, the team should establish collaborations to gain support in bioinformatics, biophysics and modeling.* The team focused on its research on the cellular and regulatory events controlling seed germination rather than the role of central metabolism and physical properties *per se*. The team established a successful collaboration on the effects of cold plasma on seed germination with the Laboratoire de Physique des Plasmas (Sorbonne University). It is not clear whether the teams also resorted to ad hoc external collaborations (such as IPS2, Papso) to analyse omics data. However, it recently initiated a collaboration with J Bernardes, a bioinformatician at CQBL (Sorbonne University).

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 2 |
| Maîtres de conférences et assimilés | 3 |
| Directeurs de recherche et assimilés | 0 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 2 |
| **Sous-total personnels permanents en activité** | **8** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 1 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 0 |
| Doctorants | 8 |
| **Sous-total personnels non permanents en activité** | **10** |
| **Total personnels** | **18** |

# EVALUATION

## Overall assessment of the team

The team has an excellent to outstanding publication record with some articles in highly regarded journals and an outstanding attractivity due to their strong links with the seed industry. The quality of the team is overall excellent to outstanding. The team clearly stands out by the outstanding quality of its interactions with the seed industry, leading to new knowledge and solutions to improve seed performance in the field.

## Strengths and possibilities linked to the context

The team is well established and outstanding recognition in the field for its work on oxidative signalling and post-translational regulation of seed germination. This is attested by four articles in high level journal and 9 articles published with foreign co-authors (Canada, Spain, Brazil), the coordination of one ANR grant (RNASEED) and participation in another ANR (Isistor, 125 k€)). Thanks to is strong reputation among the seed industry, the team has an outstanding capacity to obtain grants to perform collaborative research on seed crops, representing five contracts (85 k€) and to provide services to solve problems for the industry (3 contracts, 230 k€). The team successfully supervised twelve PhD students, leading to at least one publication for those who graduated or the creation of one the start-up (Auxoway) and/or best presentation prises in meetings. Outstanding supervision is also seen by the industry (ANR Price Biostim, 1 cifre fellowships) and international PhD students (4 Chinese Council Scholarships and one Brazilian student). The team was also successful in recruiting four permanent staff from CNRS and SU, including one technician, one engineer, one CNRS researcher and one associate professor. Team members were invited to give lectures in 8 international conferences and also organised one international conference. The team contributed to the promotion of seed science by holding two editorial responsibilities in international journals. The team also includes a member of the Academie d'Agriculture de France.

The team has been particularly productive with 35 peer-reviewed articles, including 21 as first or co-/corresponding author (among them 2 *Plant Physiol.*, 2 *New Phytol.*, 1 J. Integr. Plant Biol. 2 *Plant Cell and Environ., 1 J. Exp. Bot. and 2 Plant J.*) plus 8 reviews, involving all members of the team. This is excellent considering the team's size and its activity profile including teaching, administrative responsibilities within SU and significant collaborations with the seed industry. The team made two significant contributions to the understanding of regulation of germination/dormancy in response to the environment. The team's major contribution was the demonstration of the involvement of mitochondria being a major ROS producer and environmental sensor and its retrograde signalling in the regulation of germination/dormancy. A link between ROS homeostasis and chromatin compaction during germination was also discovered. This is highly original and opens new research avenues in the redox regulation of chromatin organisation. The second significant contribution is the characterisation of post-transcriptional regulatory mechanisms controlling seed germination/dormancy, including the roles of mRNA decay and the N-end rule of the proteolysis in seed responsiveness to oxygen and ethylene.

The non-academic activities of the team are outstanding. The team clearly stands out by the quality of its interactions with the seed industry, leading to new knowledge and solutions to improve seed performance in the field. This was attested by several contracts for collaborative research on sunflower, maize and herbicides and services to major companies both in France and the Netherlands, resulting in joint publications and 5 patents/declaration of invention. The team has been also very active in promoting the importance of seeds to the general public through publications, conferences, presence in the media and organising 4 continuing education courses for the industry. A PhD thesis in collaboration with cold plasma physics experts at SU led to one patent and one declaration of invention and the creation of a start-up company (Auxoway) aiming at deploying solutions to the agriculture using cold plasmas.

## Weaknesses and risks linked to the context

So far, the lack of a strong bio-informatics support did not allow the team to valorise some of their -omics data (RNAseq) in publications or in databases or exploit them beyond a descriptive analysis. This has impeded the team from having an integrated view on how the different layers of regulation control seed germination and dormancy.

## Analysis of the team's trajectory

The five-year research strategy is consistent with previous achievements of the team. The project rational relies on the research environment and platforms provided by IBPS and SU (cellular imaging, Nanopore technology)

and on a secured budget of 622 k€. The project is structured in three axes, each bearing several questions: 1) the understanding of the phosphor-regulation of TCP1 and ROS responsive transcription factors in the regulation of germination; 2) How non-coding RNAs and mRNA modifications/fate play an active role in seed germination (supported by the ANR RNASEED) and 3) how ROS modulates the regulation of chromatin components/modifiers in the control of germination. Although highly competitive, axes 2 and 3 are original as the field of research is largely unexplored in seeds, which is excellent. Next to this, the team intends to pursue its collaborative work with the seed industry, in particular in the recently granted ANR PRCE (BIOSTIM) in which they are studying the effects of endophytes on seed germination. This project might open new research perspectives for the team.

## RECOMMENDATIONS TO THE TEAM

Considering the team's size and the teaching/administrative duties by four out of five researchers, attention should be paid to strike a balance between academic and applied research in order to aim at a steady production of high-level publications that develop new concepts in seed biology.

To develop the novel research questions dedicated to ncRNA epigenetic mechanisms, the team should increase its collaboration with DEV2A teams.

To develop statistical and mathematical models using machine learning to design novel regulatory network, the team should rely on external expertise through a strong collaboration.

**Team 2:** Mechanics of Neuronal Development

Name of the supervisor: Ms Marie Bréau

## THEMES OF THE TEAM

The team studies the role of mechanical forces on neuronal migration and on axon growth. The aims are the identification of the origin of the forces as well as their interpretation at the level of the development of the neural system and the resulting functional consequences.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was established in 2018, they were not evaluated in the previous report.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 0 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **3** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 1 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **4** |
| **Total personnels** | **7** |

## EVALUATION

### Overall assessment of the team

This is an excellent young team with very high potential. The team tackles a problem that has not been addressed in the past, defining an original research line. They have already made significant progress, and have published two important papers, demonstrating that they can make excellent contributions and move ahead to gain a better understanding of the origin of the mechanical forces shaping the developing neural networks. In addition, the group edited review volumes and wrote reviews on this topic, taking a lead in the field and participating in shaping its future.

### Strengths and possibilities linked to the context

The visibility and attractivity of the team are excellent to outstanding. Members of the team are invited to present their work at conferences and the team organised a symposium on neuromechanics. The team successfully applied to ANR JCJC and was a partner in a NIH RO1 grant. The team has already grown since it started in 2018, and two new permanent staff members have joined. The team's attractivity is excellent, two PhD students and two postdoctoral fellows were recruited. Importantly, a permanent researcher, who was a

postdoctoral fellow in the team, has been stabilised in the group with an Inserm position. Furthermore, the group will be joined by a professor in 2024.

The scientific production of the team is excellent. As a postdoc in the lab of Schneider- Maunoury, Marie Bréau, the group leader, has initially made the interesting observation using the zebrafish system and live imaging that mechanical forces shape the developing olfactory system (Nat Commun, 2017). This research topic built the basis for the establishment of the team in 2018, and they have already made very important progress in addressing issues of where the forces originate and in a different context, what the functional consequences of mechanical forces can be (EMBO Rep, 2022 and Dev Cell, 2023). While building on their strength (zebrafish and live imaging), the team has already initiated several collaborations with excellent groups to strengthen their biophysical expertise, their experimental skills (laser ablation) as well as the introduction of novel and innovative technologies (engineered oil droplet sensors).

The group has organised a symposium on neuromechanics, and group members have contributed to events organised in schools.

### Weaknesses and risks linked to the context

The group has had a very productive start, not only because they published two papers in highly visible journals, but because they already add very important new ideas and concepts to the emerging research field that they co-initiated. To maintain this productivity, they need to obtain additional funding and recruit the next generation of students. Considering the excellent start of the team, this should be possible.

### Analysis of the team's trajectory

As it looks, the group knows very well what they need to do to further tackle the origin, interpretation and consequences of mechanical forces on the development and function of the nervous system. They have initiated collaborations that help them to tackle the important questions using avant-garde technology, in order to tackle emerging questions in a comprehensive manner.

## RECOMMENDATIONS TO THE TEAM

The team should continue the efforts and participate in shaping this novel and very interesting topic of research.

The team should look for support from all available sources, and try to join forces with a theoretician physicist.

Since the topic is novel and the group leader has made some of the initial observations regarding to mechanical input on neuronal development in an in vivo system, the group is ideally positioned to remain at the forefront of the field in the coming years, and their effort should be supported as much as possible.

The role of each team member should be clarified, in particular with regard to the co-direction of the different projects

**Team 3:** Transgenerational Epigenetics & Small Rna Biology

Name of the supervisor: Mr Clément Carre / Ms Laure Teysset

## THEMES OF THE TEAM

The team's research is divided in two main axes related to small RNA (sncRNA) biology and transposable element control: i) RNA methylation's impact on gene regulation and ii) study of the environmentally-induced epigenetic conversion of a PIRNA cluster.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous Hceres report (italics) were:

*1- To increase their international recognition and visibility by publishing in higher impact journals and attend international meetings*. The team has increased its international visibility, attending numerous international meetings in which the team leaders were invited speakers or had selected talks and establishing international collaborations. They have published in highly respected journals (Nucleic Acids Res, eLife) and already have a publication in 2023 (Sci Adv).

*2- To hire more post-doctoral researchers and attract collaborators from abroad*. The team has secured funding for a future postdoc and has established international collaborations. One of the team leaders has participated as a partner in an international grant.

*3- To secure funding to develop projects involving genome wide technology and to attract postdocs*
the team has successfully secured funding from different sources. This has allowed it to secure funding for one postdoc for the upcoming period.

*4- To request close mentoring of the two principal investigators from the LBD*. Progress in this recommendation is not directly mentioned in the written document. However, the successful transition engaged by the team in term of publications and funding suggests this might not be necessary for the upcoming period. Moreover, in addition to the team leaders, two experienced and recognised researchers are present and their expertise will be helpful in that aspect.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 1 |
| Maîtres de conférences et assimilés | 2 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 0 |
| Personnels d'appui à la recherche | 2 |
| **Sous-total personnels permanents en activité** | **6** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 4 |
| **Sous-total personnels non permanents en activité** | **4** |
| **Total personnels** | **10** |

# EVALUATION

## Overall assessment of the team

The team's research lines are of major interest and the results arising from them are contributing substantially to our knowledge of small RNA biology. The team shows an excellent scientific production and the team's visibility has increased substantially and is now also excellent. The training capabilities of the team are outstanding in terms of PhD students; however, they are still limited in the number of postdoctoral fellow trained. The team is actively involved in outreach activities aimed to engage with the general public.

## Strengths and possibilities linked to the context

The team has shown an excellent visibility and attractiveness during the period under evaluation and has successfully consolidated itself as an expert in the field of small RNA biology, in particular within the two main research areas that they lead: small RNA epigenetic modifications and PIRNA regulation. The team has developed a strong national and international visibility with team members being invited speakers or selected for talks at five international and fourteen national meetings, courses and seminars. The team leaders have also been involved in the organisation of seven local meetings, participate in expert committees and act as reviewers for renowned journals. The outcome for PhD student supervision is outstanding for the evaluated period: three PhD students have completed their PhD, all of them having at least one first author research article and having co-authored other research and/or review publications. All three students have found research related positions (2 as postdocs and 1 in industry) within months of PhD completion. They currently have three PhD students in progress. The team has successfully secured funding during the period under evaluation and for the following four years, with a team member being coordinator of grants from National and Local sources (1 ANR, 1 Emergence-SU, 2 IBPS- Action Incitative) and from Charity Associations (2 ARC, 2 FMR-Genomics, 1 La Ligue Regional Contre le Cancer), and partner in an international grant (DFG).

The team has an excellent scientific production in the field of RNA biology, with nine research articles and five reviews/books chapters since 2017. This includes publication in renowned journals (RNA, NAR, eLife) as well as publications in collaboration with national and international teams. Both research lines have made important contributions of general interest to this field during the evaluated period that are already leading to additional insightful discoveries. Their research on sncRNA biogenesis led to a major finding on the role of two *Drosophila* RNA Nm methyltransferases (Trm732 and Trm734, homologues of the human FTSJ1) on tRNA modification (NAR, 2020), whereas the second research line, focused on PIRNA regulation, has led to the unravelling of important ways of regulation of PIRNA cluster activity (eLife 2019). Importantly, the scientific production seems to be shared between the members of the team, with an outstanding contribution from students and all tenured researchers showing a leading role in contributing to scientific production.

The team regularly participates in outreach activities to engage with the general public, these include writing a book chapter on transposable elements for students, participating in a film for all audiences based on a scientific expedition and presentations at elementary schools.

## Weaknesses and risks linked to the context

Although they seem to successfully attract PhD students, they did not train any postdoctoral fellow during the period under evaluation. The national and international visibility through meeting attendance and grant proposal seems to mostly rely on one of the team leaders.

Although the team has proven highly productive, the elevated teaching responsibilities together with the lack of more independent researchers (postdoctoral fellows) may represent a challenge to remain at the cutting edge of each topic.

The team has not developed partnerships with industry.

## Analysis of the team's trajectory

The team was created in 2018 from the merge of two different teams and has now consolidated two main lines of research based on the expertise and synergy between both team leaders. Both research lines are focused on small non-coding RNA biology and are highly complementary, which should benefit the success of the proposed projects.

For the following period they propose two main research lines well founded on their recent findings. The first project is based on their investigation on the involvement of an Nm MTase (the human FTSJ1) in the biogenesis of multiple sncRNA in Drosophila and its link to neurodevelopmental processes in human patients, this is already well supported by their recent publication in Life Sci Alliance (Brazane et al 2023). The proposed research aims at elucidating the mechanisms behind the observed FSTJ lack of function phenotype by using a combination of IP, state of the art sequencing techniques (Direct RNA sequencing, RiboMethSeq) and loss of function screening in *Drosophila*. In addition, they plan to develop further their ongoing collaborations to extend their studies to human patients' cell lines knock-out for FTSJ1, which will provide a translational view to their research. The second project is also well supported by their previous findings on PIRNA cluster activation and the effect of KDM3 mutation (recently published in Sci Adv, Casier, Autaa et al 2023). For the following period they aim at looking into the genetic pathways involved in PIRNA cluster determination by exploring the mechanism behind the KDM3 mutant phenotype on PIRNA cluster activation, investigating what makes endogenous regions susceptible to become PIRNA loci in the absence of KDM3 and determining which are the PIWI/PIRNA components required to activate a PIRNA cluster through generations.

Both projects are well supported by the team's previous research, they ask relevant questions of broad interest for the scientific community and in particular for the understanding of small RNA biology and function in development and disease. The proposed studies seem feasible considering the team expertise, the number of stable positions within the team and the ongoing collaborations. In addition, the team has secured funding for this research for the following four years and they have ongoing applications for funding.

## RECOMMENDATIONS TO THE TEAM

Although the scientific production and overall achievements of the team seem at a high standard, given the heavy teaching duties of the team members they should consider the recruitment of more experienced researchers (postdoctoral fellows) beyond the one that they have already secured funding for. In this regard, achieving a good international visibility for both team leaders may contribute to the attraction of international students and postdocs through competitive calls.

**Team 4:** Muscle And Tendon Formation And Repair

Name of the supervisor: Ms Delphine Duprez

## THEMES OF THE TEAM

The team studies how the musculoskeletal system develops, with a special focus on the development of muscles and tendons and on muscle-tendon interaction, as well as the underlying mechanical and molecular signals. The insights they obtain by studying this system are then utilised to address questions in regeneration and repair of these tissues. The team employs state of the art technologies for in vitro and in vivo studies using the chicken as a model organism.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- It is important for all staff scientists to define their contribution to the overall goal of the team and to continue to raise external grants to fund these contributions.* The team has secured sufficient funding for its main projects. Altogether, it raised more than 1M € during the last contract.

*2- It will be important to continue to unify the focus of the team and avoid an excess of small and diversified projects, to build the focus upon Sections II and III, and to ensure real collaboration between staff scientists in the team. The team should avoid the temptation to diversify into too many fields.* The team has improved its focus by clearly formulating three main projects.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 3 |
| Personnels d'appui à la recherche | 2 |
| **Sous-total personnels permanents en activité** | **7** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 0 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **4** |
| **Total personnels** | **11** |

# EVALUATION

## Overall assessment of the team

This is a leading team in the field of musculoskeletal research and muscle-tendon development. The team has an excellent to outstanding visibility and attractivity. It's strategy to focus on basic research related to a specific human syndrome has high impact and has led to an excellent to outstanding scientific production. The team's non-academic activities, including outreach activities, are diversified and valuable.

## Strengths and possibilities linked to the context

The team has an excellent to outstanding visibility and recognition in the field of musculoskeletal development. During the contract, five PhD students were trained by the team. Currently, there are two PhD students and one postdoc in the team. Most PhD students published as first authors, which is excellent. The team has a strong capacity to lead research projects with full-time tenured researchers, university teacher/researchers and physicists. The team leader has an excellent capacity to obtain research grants totalling more than 1M €, including from national agencies, two ANR grants as Coordinator and two ANR grants as partner, two AFM and SU iBio and SU-Initiative. The team also obtained one grant from Aviesan Itmo Cancer and SU-Initiative for FOUCHARD, as Coordinator. The team's visibility is also attested to by regular invitations of the leader and other members to scientific meetings, such as Gordon Research Conference, EMBO and ORS. In addition, team members participated in committees such as Scientific Committee Inserm, Hceres committees, Chair and Vice-Chair of the SFBD.

The scientific production is excellent to outstanding. In the last 5 years, the team has focused its research on the genetic program that regulates muscle and tendon development and the interface between them. Their publications provide a new understanding of the process by which muscle and tendon attach during development. These studies were published with team members as first/last co-authors in leading journals (*Development and Nature Communications)*. In addition, the team contributed to a number of collaborative publications. Altogether, during the period of evaluation, the team published an impressive 21 publications (including research articles and reviews) and two preprints in bioRxiv.

The non-academic activities of the team are excellent. The team is involved in workshops with local schools and high school students, interview to French TV programs, and presentation of the profession of Teacher-Researcher.

## Weaknesses and risks linked to the context

There is concern about the load of research administration and university teaching, which is 40%.
Such a heavy load can influence the productivity of the group.

## Analysis of the team's trajectory

For the next contract, the team will focus on muscle-tendon connection. The team will identify the principles underlying the development of these important tissues and utilise the obtained knowledge to study tendon pathologies and fibrosis. The team will increase the resolution of the understanding of the musculoskeletal system by uncovering the mechanisms that allow different regions of the muscle to have specific functions. This direction is extremely interesting, as it promises to reveal new principles in the development and function of organ systems. The team will capitalise on single-nucleus RNA sequencing data they have already obtained from different developmental stages in chicken and mouse embryos to identify regionalisation within the developing muscle. Specific effort will be made to identify local molecular mechanisms that regulate the specification of myonuclei at the tips of myofibers to establish myotendinous junctions. The findings of this study may contribute to the understanding of muscular dystrophies, where transcriptional changes in myonuclei at the muscle-tendon interface have been reported.

Another goal of the team is to increase the resolution of understanding connective tissue subtypes. The term connective tissue has long been used to describe a variety of fibrous tissues that serve different functions, such as tendon, muscle, ligaments and more. The difference in functions implies the existence of different genetic programs that regulate each tissue specifically. The team has already obtained single-cell RNA-seq data from chicken and mouse limbs at different developmental stages. Using these data, they have identified molecular

signatures of different fibroblast populations. These signatures may serve as the basis for identifying the genetic programs that instruct the formation of various types of connective tissue.

Mechanical regulation is vital for normal musculoskeletal development. The team has contributed to this concept by demonstrating the role of mechanical signals in muscle and tendon development. One of the central open questions in this context is the identity of the molecular signals that are activated by mechanical signals and the genetic programs these signals control. The team has established snRNA-seq datasets of limb cells under immobilisation conditions during foetal development. Using these data, they seek to fill this knowledge gap.

Previously, the team has made a seminal discovery that during myotendinous junction development, fibroblasts are recruited to the myotubes at the site under regulation of the BMP signalling pathway. Now, the team suggests using 2D and 3D co-culture systems of myoblasts and tendon fibroblasts, which they have already developed, to determine the conditions that allow in vitro formation of the myotendinous junction. The results of this project may be highly beneficial in the context of the treatment of sport injuries.

Connective tissues relay biochemical and mechanical signals to neighbouring tissues in both normal physiology and disease. Using tendon fibroblasts and stromal fibroblasts of pancreatic adenocarcinoma, the team will aim to distinguish between the contributions of fibroblasts versus extracellular matrix and fluid in this function and to uncover the effect of the mechanical environment of the cell on matrix organisation.

The future trajectory is clear and achievable. The team will employ state-of-the-art methodology to implement all the above projects. They have extensive preliminary data and the required skills and know-how to ensure their success. Although these projects address basic science questions, the expected findings may be valuable for future disease-oriented research. One minor weakness is the last aim, namely “Mechanisms of mechanical homeostasis of connective tissues”, which seems somewhat less clear and developed than the other aims. Nevertheless, it is likely the team will know how to further develop this project and exploit the expected results.

Overall, the very interesting and promising new directions in this research plan are expected to produce important discoveries in the field of musculoskeletal studies.

## RECOMMENDATIONS TO THE TEAM

This excellent team plays a central role in the research of musculoskeletal development. Especially exciting is the concept of regionalisation, an area that could lead to important new discoveries in the field. The committee only recommend pursuing this excellent activity.

**Team 5:** C. elegans Heredity And Development

Name of the supervisor: Mr Vincent Galy

## THEMES OF THE TEAM

The team investigates the mechanisms that eliminate paternal mitochondria after fertilisation with the ultimate goal of studying the physiological roles of uni-parental mitochondrial inheritance. As a model system, the team uses *C. elegans*.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- maintain the quality of the research and increase the productivity through improved focus and the involvement of a larger team.*
*2- recruit postdocs and students and make sure the team members really work as a team.*
*3- complete the ongoing screens full speed and validate the mutants identified.*

These recommendations have been addressed partially. The quality of the research has been maintained, the focus has been improved by dropping the germline project, and the team is about to get one more permanent researcher-teacher, which will increase the number of research-teachers with an HDR to three. In addition, one postdoc was recruited for two years, and the team currently has two PhD students. The productivity of the team has increased to a certain degree.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 0 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **3** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **2** |
| **Total personnels** | **5** |

# EVALUATION

## Overall assessment of the team

The team works on a fundamentally important process and continues to do pioneering work, endowing the team with a very good to excellent visibility. They have developed new unique tools for the analysis of this process, making it likely that significant progress will be made in the next period, which will increase scientific production assessed as very good for the reporting period. The team is engaged in teaching and training and contributes to the local and national C. elegans community but non-academic and outreach activities are limited.

## Strengths and possibilities linked to the context

The team's visibility and attractiveness is very good to excellent. The team pioneered studies on the elimination of paternal mitochondria after fertilisation using C. elegans as a model, and it continues to do critical and innovative work on this fundamental process. For this reason, the team has visibility and is attractive to researchers, postdocs and PhD students: a third permanent researcher-teacher with HDR will join the team in 2024 and during the last period, one postdoc and two PhD students joined the team. The team successfully applied for funding from the ANR. By organising regular scientific meetings and workshops, the team also plays an important role in the C. elegans community nationally as well as in the Paris region.

The team's scientific production is very good. The team's work is highly original and significantly contributes to our knowledge of uni-parental mitochondrial inheritance, a process that turns out to be very challenging to dissect genetically and molecularly. The team has developed unique tools, including genetic and imaging-based tools, which allows them to follow mitochondrial inheritance and to study it quantitatively. From the team's analyses during the last period, it has emerged that the process is highly robust. None of the factors identified by the field so far as implicated in the process, blocks uni-parental mitochondrial inheritance when knocked-down. Importantly, in contradiction to published studies, the team demonstrated that two 'marks' on sperm mitochondria, which had been proposed to be required for the selective removal of paternal mitochondria (i.e. ubiquitylation and loss of mitochondrial membrane potential), are not acting as such (iScience 2020, review in Adv Anat Embryol Cell Biol 2019). Finally, in collaboration with one lab in the USA, the team identified the protein FNCD-1 as involved in the specific elimination of sperm mitochondria (Dev Biol 2019). These publications form the basis of the biochemical approaches the team plans to use in the future in parallel to genetic approaches to elucidate pathways involved in paternal mitochondrial elimination. These biochemical approaches are done in collaboration with colleagues in Paris and Nice. Based on the new knowledge of the robustness of the process, the team has designed innovative genetic screens that are highly likely to elucidate novel mechanisms and pathways involved in uni-parental mitochondrial inheritance in *C. elegans*. In the future, they also plan to do some mouse work, as the researcher-teacher joining in 2024 will bring expertise in early mouse development. Finally, the scientific production is balanced across the team with, postdocs and PhD students as authors on the team's publications.

The team significantly contributes to university-level teaching and actively engages in improving and updating the curriculum by designing new courses.

## Weaknesses and risks linked to the context

The document provided does not allow an assessment of non-academic activities and the extent of participation to scientific meetings.

The new screens and the biochemical approaches planned are very promising; however, there is still the risk that they will not lead to the identification of new 'players' that will lead to increased knowledge and publications.

## Analysis of the team's trajectory

The team's trajectory is positive and going into the right direction. The team is working on a very important process i.e. uni-parental mitochondrial inheritance that turns out to be extremely difficult to study and to mechanistically dissect. It occurs during a very specific and very short period of time during development (right after fertilisation), it affects a small number of mitochondria in a large 'sea' of maternal mitochondria (i.e. the paternal ones) and the team has shown that the process is also genetically highly robust. This means that it is very challenging to study at the cell biological level, the biochemical level and also genetically. In addition, based on high profile publications from competing teams, the field made assumptions about mechanisms involved that turned out to not be correct. During the last period, the team has shown much endurance and not only revised or corrected the literature but made good progress on increasing our understanding of this fundamental progress, which is highly conserved but essentially not understood. In addition, during the last period, the team has generated original and unique tools (genetic screens) and tested new approaches (biochemical approaches) for the identification of pathways and players involved, which are very promising. Based on this, much progress can be expected in the next period.

# RECOMMENDATIONS TO THE TEAM

The team should continue to work on the recruitment of postdocs and PhD students to have enough capacity to perform the screens and follow up mutants identified and to perform the biochemical approaches and analyse the factors uncovered.

The team needs to improve their visibility by presenting at international conferences.

The team (PI as well as other permanent members of the team) should continue to apply for funding especially in light of the team's plans to initiate studies using mouse as a model.

The team's involvement in teaching is excellent but they should also consider outreach activities with the general public.

**Team 6:** Cell Cycle And Cell Determination

Name of the supervisor: Mr Michel Gho

## THEMES OF THE TEAM

Using *Drosophila melanogaster*, the team has been studying the relation between cell cycle and cell fate acquisition in the nervous system. They have developed a system, the posterior thorax of the Drosophila pupa, where they can observe the formation of mechanosensory organs with spatial and temporal precision. By manipulating the timing of cell division, they can observe how temporal effects on neurogenesis affect animal behaviour. They are also analysing how the cell cycle regulators affect planar cell polarity of the thorax bristles.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- Given the conceptual impact of the team's data in the field, recognised and important in our understanding of cell identity acquisition, it should be possible to publish in higher impact journal and obtain more substantial funding.* This has been achieved. Most of the proposed projects have been published in excellent journals (Nature Communications (2022), eLife (2022) and Nature Cell Biology (2023).

*2- Being more pro-active and attract more students at the PhD level.* There has been a significant increase in the number of PhD students. In the previous evaluated period there had been only one defended thesis and one in progress. In the current evaluated period there have been three defended theses and two in progress.

*3- To secure funding or establish strong collaboration before pursuing the transcriptomic project*. It is unclear if the transcriptomic project was started.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 2 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 0 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **5** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **0** |
| **Total personnels** | **5** |

# EVALUATION

## Overall assessment of the team

The work of this team is characterised by the elegance of their approach, exploiting a very simple and accessible neural model developed by them over the years. The scientific production of the team for the reporting period has been excellent with the publications in highly visible -journals (Nature Commun, eLife). The quality of the research however did not translate into the expected visibility and attractivity. The team is closing down due to the retirement of the team leader, it would be important that the remaining staff members are able to continue exploiting this elegant model.

## Strengths and possibilities linked to the context

The team has had a regular and important conceptual impact in our understanding of cell identity acquisition, providing an excellent scientific visibility at the national level.

The scientific production of the team is excellent. The use of a very accessible model (specification and formation of the highly stereotyped sensory elements that give rise to the adult thoracic bristles of the fly) allows the analysis neurogenetic processes with great temporal and spatial resolution. The production of this team is characterised by the elegance of their approach, exploiting a very simple and accessible neural model developed by them over the years.
In these last years they have completed and published most of the projects they had proposed.
1- Study of the relationship between cell cycle and cell polarity. They found that Cyclin A (Cyca, a regulator of M phase) localises precisely in the apical posterior position of the cell and this depends on PCP regulators with which Cyclin A physically interacts. Conversely the mutation or mislocalisation of Cyca results in the abnormal orientation of cell division. They found that Cyca intracellular localisation is controlled by the PCP organisers and, in turn, Cyca contributes to the positioning of the posterior spindle pole during cell division (Nature Communications 2022). This project will be followed up once the team closes by the "Heterochromatin, cell fate and exposome" team. This team will absorb the staff from the closing team.
2- Analysis of the antero-posterior wave of mitosis of the sensory organ precursor cells forming the mechano-sensory bristles. The team has studied how the sensory organ precursors giving rise to the homogeneous array of bristles in the *Drosophila* thorax mature. They found that they do not divide simultaneously but that there is a controlled temporal wave in the divisions that will affect the maturation timing. Neighbouring sensory precursors mutually inhibit their division. However, when the precursors in the anterior lateral position finally divide, they relieve the inhibition from their immediate neighbours, leading to a temporal wave of division and maturation that will affect axonogenesis timing. Such non simultaneous axonogenesis is necessary for controlling the animal's behaviour (eLife (2022) 11; e75746.). This work beautifully links neural specification timing to behavioural output.
3- In a final collaborative project, the team studied how the neural sensory organs recruit an epithelial cell to the sensory organ that increases the signalling output - Nat Cell Biol. (2023).

## Weaknesses and risks linked to the context

The team members are very highly involved in teaching and have not been able to create a sufficient mass to exploit their excellent model.

With the exception of an ANR support 2022, the team has been underfunded and have not recruited postdocs to allow them pursue many of their interesting projects.

The team low international visibility does not credit the quality of their research.

## Analysis of the team's trajectory

The team is closing down. Its permanent staff members are joining another team in the Unit. Two researchers will co-direct a new team "Heterochromatin, cell fate and exposome" in the next five-year contract.

# RECOMMENDATIONS TO THE TEAM

The team has done excellent work. Now that it is closing down due to the retirement of the team leader, it would be important that the remaining staff members are able to continue exploiting this model.

**Team 7:** Dynamic and Multiscale Processes of Auto-Organisation in Tissue Morphogenesis

Name of the supervisor: Mr Mathieu Hautefeuille

## THEMES OF THE TEAM

The team aims to develop microfluidic platforms integrating physiologically realistic physical environment (e.g. substrate stiffness, luminal pressure, shear stress) to reconstitute liver sinusoids/hepatic lobules on a chip. Another aim is to develop an "organ on chip" with vascularisation to investigate the influence of microvessel mechanics on the tissue they vascularise. For this, the team aims to recapitulate the processes of self-organisation taking place during development rather than arranging already differentiated cells into a 3D environment.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was recently established and was not evaluated in the previous report.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 1 |
| Maîtres de conférences et assimilés | 0 |
| Directeurs de recherche et assimilés | 0 |
| Chargés de recherche et assimilés | 0 |
| Personnels d'appui à la recherche | 0 |
| **Sous-total personnels permanents en activité** | **1** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 1 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **1** |
| **Total personnels** | **2** |

## EVALUATION

### Overall assessment of the team

The team recently joined the unit and still needs to consolidate its funding and human resources. The proposed projects are original and innovative. They rely on state-of-the-art biomedical engineering techniques and have an excellent potential. Although the impact of the team leader work has not yet reached a very high level, he has been very productive in his past environment and he secured a very good level of funding in challenging conditions to set up his lab. Some funding has been obtained in the French system, collaborations have been established, and a new state of the art facility has been created. Overall, this is encouraging.

### Strengths and possibilities linked to the context

The team was created in 09/2021 following a call from Sorbonne University to recruit a new professor in developmental biology. The team leader obtained a start-up package from IBPS +LBD (40k€), funding from idex

i-Bio (180k€), and DIM-ELCIIT (308k€). With some of this funding, he established a new collaborative making space dedicated to microfabrication and microfluidics at IBPS, which will be used by multiple teams. In his previous position in Mexico, the team leader obtained substantial funding. His current team consists of one PhD student with another ongoing at his previous position. The team leader obtained young academic award from UNAM (Mexico, 2017) and was invited to two international meetings in Mexico (2019). Altogether, this provides this young team with an excellent visibility.

The team was recently created at LBD/IBPS, rendering the assessment of its scientific production within its new environment premature. The team aims to develop organs on a chip with a philosophy of building to understand. These organs on a chip can be used as alternatives to animal models both for mechanistic studies examining the influence of the environment on physiology and drug testing. A key feature of their strategy is to build vascularised organs using guided-biochemical differentiation and interplay with physical environmental forces within microfluidic channels. The team has established an interesting model to form vasculature without 3D embedding / hydrogels using endothelial cell lines. A follow-on goal is to develop a vascularised liver on chip. Together these platforms will enable the study of the barrier function in capillary networks and liver sinusoid response to hypertension in the initiation of pathologies such as fibrosis and fatty liver disease. The team's thematic are a very good fit with other teams interested in mechanical signalling during development/mechanobiology at IBPS/LBD/Dev2A. A number of clinical collaborators have been identified. With a total of 21 publications (including 9 as PDC) during this period, the PI has been very productive. However, most of the publications originate from work at his former institute (UNAM, Mexico; 17 publications). This is to be expected given the challenges of establishing a new laboratory.

The team leader has excellent interactions with the society: he contributes to outreach (including creation of a Youtube channel) and valorisation (3 patents in Mexico). He is very active in outreach to the general public through a number of media (radio, TV, Youtube, public appearances).

## Weaknesses and risks linked to the context

The team leader has recently arrived in LBD and the team has not yet published work in this new environment.

Previous research has not yet achieved a strong impact (modest citation levels) and studies were published mostly in specialised journals in the field of biomedical engineering. This is partly to be expected given the goals of the team and the profile of the team leader, which is more oriented towards engineering.

The team is very small: only the team leader and two PhD students (1 in France and 1 in Mexico).

The team leader has heavy teaching duties. This will slow progress.

Past project and achievements are not very well described. The strategies for guiding developmental processes to self-organise on a chip are not very clearly described. It is not clear what the state of advancement is.

## Analysis of the team's trajectory

The team leader originally established his team in Mexico. During this time, he secured significant funding and created a laboratory with expertise in microfluidics and microfabrication. This led to a substantial number of publications despite relatively modest levels of staffing. In September 2021, the team leader was recruited to LBD/IBPS and he has since worked on establishing his lab there. Since then, the team leader has been very active in applying to and obtaining funding. This allowed the creation of a new collaborative making space that will benefit many teams within IBPS but also serve as main platform for the team leader. He has recruited one PhD student and made connections with potential clinical and biology collaborators locally and internationally. Altogether, this is an encouraging start.

Going forward, the team wishes to build on their established expertise to create new organs on a chip. For this they propose a new strategy based on the interplay between biochemical guidance of differentiation and interplay with physical forces (shear stress, substrate stiffness, luminal pressure). This combination should harness the self-organising properties of stem cells by replicating development and ensure optimal spatial and temporal differentiation. They propose to focus on two models: capillaries and liver sinusoids. Preliminary work has taken place on these models but optimisation still remains to be done before they can be used for scientific discovery. The models will then be used in collaboration with clinicians and biologists to investigate basic questions about capillaries and liver in normal physiology and the establishment of disease. In addition to answering basic scientific and medical questions, these devices will reduce the need for animal experimentation.

The technological project is timely and ambitious with a clear focus on microvessel development but the underlying biological questions could be better defined and the state of advancement more clearly stated. With many collaborations on different sub projects, there is a risk of dispersion, particularly for such a small team.

# RECOMMENDATIONS TO THE TEAM

The team needs to secure longer term funding by applying for national and international grants. This will allow them to recruit staff at all levels of expertise (PhD, post-doc, technical staff…) to reach a reasonably competitive size / critical mass.

The team should focus on a small number of well-chosen collaborations until it has grown sufficiently to support all of the planned work and avoid diversion from its main project.

It would be extremely useful to reduce the teaching load of the PI during the next two years.

In addition to publications in lab on a chip and bioengineering journals, the team should leverage its expertise to investigate fundamental physiological and pathophysiological processes – potentially in collaboration with clinicians and basic biologists. This will allow them to publish their work in broader audience journals, gain further visibility as well as aid in recruitment and funding.

**Team 8:** Migration and Differentiation of Hematopoietic Stem Cells

Name of the supervisor: Mr Thierry Jaffredo /Mr Charles Durand

## THEMES OF THE TEAM

The team focuses on the formation of hematopoietic stem cells (HSCs) and the relationship to their microenvironment using zebrafish, chicken, mouse as *in vivo* model systems as well as human cells.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- train and mentor more PhD students and post-docs.* During this mandate, the team hosted 5 PhD (3 ongoing) and 2 post-docs, which is still somewhat limited considering the size of the team.

2- *all staff should raise external grant.* This has on the whole been achieved.

3- *focus on the core of its projects.* This recommendation was not clearly been put into practice.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 1 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 3 |
| **Sous-total personnels permanents en activité** | **7** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 1 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **4** |
| **Total personnels** | **11** |

## EVALUATION

### Overall assessment of the team

The team has made several important discoveries and developed original lines of research in the field of HSC development, leading to excellent to outstanding publications. The visibility of the team is excellent, with a strong network of collaborations both at the national and international level. The team obtained very considerable levels of funding through national grants and was able to attract young researchers. Its attractiveness is excellent. It is also well involved in valorisation and transfer of knowledge to the society.

## Strengths and possibilities linked to the context

The visibility and attractivity of the team is excellent. This is a very well-established team, which is also part of Inserm-affiliated team (ERL U1115). The team is well recognised for his pioneering work in the field of HSC emergence, leading to many collaborative projects with renowned scientists and publications in high profile journals. The team organised a number of international/national meetings (Fondation des Treilles 2017, French society for Stem Cell Research/FSSCR 2018-2021). Collectively, they were invited to very good number of conferences or seminars. The team secured an excellent level of funding (~1.4M€) through national grant agencies (3 ANR including 1 as coordinator, 1 Inserm plan cancer, 1 CNRS prematuration, 1 AP-HP SU) and charities (1 FRM, 1 Fondation de France, 2 Gefluc). It was able to provide career development and was also able to attract new talent. The team plays an important role in the LBD unit and the wider IBPS: it invested in single-cell technologies (10X Chromium of the IBPS hosted in the team) and is responsible for the Laser microdissection platform in the unit and the FACS platform at the IBPS. A particular strength of the team in an international context is the breadth of established experimental systems (zebrafish, chick, mouse and human cells) and experimental approaches (microdissection to single-cell transcriptomics) that they can deploy to address their scientific questions about the haematopoietic tissue.

The scientific production of the team is excellent to outstanding. The team made several highly significant findings during this period, such as the identification of secreted vesicles by the hematopoietic niche cells that are specifically recognised by HPC and deliver specific RNA in those cells; they also extended the notion of hemogenic endothelium to late foetus and young adults in vertebrates (chicken and mice). They recently developed embryoid bodies that allow in vitro development of human HSC and presomitic cultures to push the cells toward an hemogenic endothelium fate; they also moved toward scRNA-seq, spatial transcriptomics and artificial intelligence approaches to define the stem cell niche identity and heterogeneity. Their work resulted in the publication of 15 research articles (including 4 as main author), with several high-profile publications (Nature Cell Biology, J Cell Biol).

The team has developed excellent pathways for contributing to the wider society. It filed one declaration of intent for a patent for the improvement of hematopoietic graft. Their projects have strong translational potential for in vitro production of human HSC and transplantations (coll. Tenon Hospital) as well as for the understanding of LSC interaction with their microenvironment. The team is labelled by the SIRIC Cancer (INCA) and it has links with St Antoine Hospital haematology department (1 MD post-doc from this department hosted in the team 2016-2017). Both PIs are involved in teaching at SU and the team had a very good investment in outreach activities. One PI is engaged in scientific lobbying at the European level (EHA roadmap).

## Weaknesses and risks linked to the context

One PI took important administrative responsibilities (deputy director of the unit; director since 2023; deputy director for IBPS), which will have impacted on his leadership of the team. While succession planning is in place, the international visibility and scientific production of the co-PI is not as prominent and he has a heavy teaching load. This may be problematic once the PI (and another senior researcher) retires, but it could be mitigated by the recent recruitments (CR Inserm, arrival of an assistant professor and soon of 2 other senior researchers). Following the presentation, the committee expressed great confidence in co-PI.

While the publication list of the team is very strong, and while their national and international collaborations clearly currently represent a strength, developing a dependency of the team on such collaborative work could also represent a risk.

While the developed transcriptomics approaches represent a strength, the apparent current uncertainty about reliable bioinformatic support is of concern.

Considering the size of the team, there is still room for hosting more PhD students and postdocs.

The two PhD students who left the lab in early 2023 have not yet published an article as first author.

## Analysis of the team's trajectory

The team will continue to take advantage of its unique expertise in the study of the hemogenic endothelium to characterise hematopoietic progenitor/stem-cells emergence and the influence of their microenvironment. They have developed state-of-the-art techniques (scRNA-seq, 12 colors FACS sorting, ex vivo culture, targeted differentiation of hiPSC, transplantation assays..) and use a valuable combination of models (zebrafish, chicken, mouse, human) to tackle three main projects related to HSC production (hemogenic endothelium cell

functional diversity, interactions between nervous system and stromal cells) and leukemogenesis (interplay between pre-LSC and mesenchymal stromal cells in the context of DNMT3A/TET2-induced leukemia). This is an ambitious research program which is in line with the excellent levels of the team.

## RECOMMENDATIONS TO THE TEAM

In anticipation of the future retirement of one PI during the next mandate, the committee recommends for better implementation of the intended succession planning that co-PI applies for a reduction in his teaching duties via the CNRS or the IUF to allow him to embrace a stronger leadership position.

Several young or senior researchers have just or will arrive in the team; it will be important to ensure a good blend for their integration.

The translational aspect of the research could be further increased.

**Team 9:** Biology Of The Oocyte

Name of the supervisor: Ms Catherine Jessus

## THEMES OF THE TEAM

Using *Xenopus laevis* model the team studies the molecular mechanisms controlling meiotic division in oocytes.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- The team should focus on obtaining long-term funding and perhaps on rebuilding their national and international collaborations given their well-recognised expertise in oocyte meiosis."* The team still presented difficulties during this period to obtain important long-term funding. The activity of the team during the ongoing contract was ensured by a funding from the national funding ANR agency (160k€), a Tremplin grant from Sorbonne University (12k€) and a postdoc salary (ARC). However, they have successfully established a national collaboration from which the obtained data have been sent for publication and an international collaboration on the basis of the expertise of the team on Xenopus oocyte model.

*2- The team should recruit more non-permanent scientists (PhD students and post-docs) and ensure that the newly arrived team members are properly integrated into the interests of the existing team.*
The team has not significantly evolved in this area. The number of PhD in the previous evaluated period was of three. Two defended their PhD and one was in progress. In the current evaluated period, there have been the same number of PhDs, because of the presence of only one HDR holder. One defended and two are in progress. One postdoc was also recruited for two years and obtained a permanent position at CNRS to work in the team.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 3 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **6** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **2** |
| **Total personnels** | **8** |

# EVALUATION

## Overall assessment of the team

This is a well-recognised team in the field of meiosis that significantly contributed to the understanding of meiotic maturation during this period and that presented a very good to excellent scientific production. The team is also deeply engaged and performed an outstanding job in education of general public in science, in organising scientific life biologist community, in teaching and in university administrative tasks.

### Strengths and possibilities linked to the context

The team had a very good to excellent visibility. They published twelve reviews/book chapters.
During this period three PhD, two master 1, two master 2, one BTS student and one CNRS researcher were recruited. The team obtained three grants, one ANR-PRC funding where the team leader is the coordinator, a Sorbonne University "Tremplin" granted to one young researcher in the team and a postdoc salary funded by ARC.The level of funding

The scientific production of the team is very good to excellent. Team successfully finished up their main projects and provided significant insights into the mechanisms controlling meiosis in oocytes. Two of their projects focused in the role of Arpp19 in conferring meiotic maturation timing are already published in leading journals (Nature Communications and Cell Cycle). The other two, focused in the role of this protein in meiotic I arrest in other species, notably in jellyfish, have been sent for publication. The team also has collaborative studies, one of them already published in Journal of Cell Biol.

The team leader is highly engaged and performed an outstanding job in science communication to the general public participating in interviews, book chapters, public debates… The team leader is member of several governmental councils, funding committees and academies and, importantly, participated to the administration of the national community of life biologists. Finally, other team members are also deeply involved in teaching and in university administrative tasks.

### Weaknesses and risks linked to the context

The level of funding has been moderate during the ongoing contract.

The scientific production with a total of 3 original articles, two led by the team, is less prominent than expected considering the high team's international visibility and size. This could be linked to the lack of sufficient PhDs and postdocs that would provide the critical human resources to continue their attractive projects considering the heavy teaching and administrative tasks of the permanent members of the team.

### Analysis of the team's trajectory

The team will close at the end of 2024. A young researcher of the team applied for a LBD group leader position. He was offered to create his own team provided that funding is secured for the next years. His project will be to study mRNA translation during meiosis using the *Xenopus* oocyte model. Several permanent members of the team would join him. It would be important for the young researcher to ensure the funding and an appropriate balance of permanent/non-permanent positions before starting the team.

# RECOMMENDATIONS TO THE TEAM

No recommendation as the team will close.

**Team 10:** Mechanical Forces Behind Tissue Morphogenesis

Name of the supervisor: Mr Michel Labouesse

## THEMES OF THE TEAM

The team research focuses on mechanics of development, using elongation of the C. elegans embryo as model system.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- secure funding following the ERC grant*. This has been addressed by obtaining ANR funding as coordinator, and a second ANR as partner.

*2- carefully consider how to maintain the quality of the group and his involvement, in combination with the directorship of the IBPS*. The team has maintained high scientific quality and productivity.

*3- consider some mammalian (vertebrate?) models to validate the findings in C. elegans for a larger audience* The team has successfully extended its research on cell biology and mechanics of the mammalian gut, with publications in high standard journals.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 0 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **3** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 1 |
| **Sous-total personnels non permanents en activité** | **1** |
| **Total personnels** | **4** |

# EVALUATION

## Overall assessment of the team

The research of the team has been outstanding. It has exploited an original and powerful experimental model to study a particular aspect of morphogenesis, i.e. mechanisms based on cell shape changes that can produce tissue elongation in the absence of cell migration and division. These are fundamental questions that have potential implications for any metazoan organism, from lower marine invertebrates to arthropods and vertebrates. The team has ceased activity in 2023, with the retirement of the team leader.

### Strengths and possibilities linked to the context

The visibility of the team is outstanding. The team benefited from an ERC advanced till 2018, and since then secured funding from a coordinated ANR. Three reviews were written including one in Developmental Cell. The team leader is frequently invited to international meetings (>10), is Vice chair of the EMBO council and has been part of numerous scientific committees, ERC, ANR, Welcome trust and several Scientific Advisory Boards, and has directed the IBPS since 2013.

The team has continued producing outstanding research in the main topic on C. elegans development while also obtaining interesting new data on the mammalian intestine. Ten research articles, including eight as lead author, were published in highly visible journals (Nature, eLife, Physics Rev Lett, Development).

Since the team has closed, the projects are likely to stop relatively soon.

### Weaknesses and risks linked to the context

One potential slight weakness of the *C. elegans* project was the question of whether the results from this process could be generalised to other systems, but from the point of view of fundamental developmental biology and mechanobiology, this has been original and exciting research.

### Analysis of the team's trajectory

No analysis as the team will close.

# RECOMMENDATIONS TO THE TEAM

No recommendation as the team will close.

**Team 11:** Epigenetic Control Of Developmental Homeostasis And Plasticity

Name of the supervisor: Mr Jean-Michel GIBERT / Ms Frédérique PERONNET

## THEMES OF THE TEAM

The team investigates the genetic and epigenetic mechanisms which control developmental plasticity or robustness in response to environmental changes, using *Drosophila* as a model organism. It focuses its research on two paradigms: the fluctuating asymmetry of the wing in chromatin mutant contexts, and variations in body pigmentation upon genetic and/or environmental changes.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended to increase the team international visibility notably in the field of developmental phenotypic plasticity and expressed its concerns about the level of funding of the team. These recommendations did not have particularly strong impact.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 1 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 2 |
| Personnels d'appui à la recherche | 2 |
| **Sous-total personnels permanents en activité** | **7** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **2** |
| **Total personnels** | **9** |

## EVALUATION

### Overall assessment of the team

The team tackles important fundamental questions in the field of developmental plasticity and evo-devo. Considering its size and composition, the team produced a very good number of excellent publications. The team is strongly involved in teaching and scientific diffusion at the local level. Its international recognition and attractiveness are very good.

### Strengths and possibilities linked to the context

The scientific visibility was assessed as very good to excellent. This is a well-established team, which benefits from a number of research staff (2 CR, 1DR, 1MdC & 1 Pr, 1IE). Two members of the team are involved in a national expertise board for universities (CNU 65). One person is strongly involved in Sorbonne University (e.g. Vice Dean for Research; Vice Dean for HR & social issues); she is associate editor for Frontiers in CDB and involved in the SFG (Société Française de Génétique). Two researchers edited a special issue of "Epigenetics in Insect". They

were invited to seven workshops or conferences. The team attracted five PhD students (two ongoing). The team published five review articles (three in French) on phenotypic plasticity. The team has established collaborations with renowned teams (MNHN, Curie Institute, Vienna) and is member of the DrosEU consortium. These collaborations increase the visibility of the team and the impact of their work.

The scientific production of the team has been very good to excellent. The team conduct research combining genetic and molecular biology to decipher how developmental stability is achieved at the chromatin level and how pigmentation patterns evolve in Drosophilids. Their lines of research are very original and tackle important fundamental questions. They obtained interesting results concerning the mechanisms underlying the control of inter-organ developmental noise by Cyclin G in relation with PRC1 and PR-DUB, linking developmental noise to H2AK118 ubiquitination levels. They also provided new insights into the gene regulatory network controlling body pigmentation variations in response to temperature or natural variations, showing that the transcription factors Bab1/Bab2 are involved in the regulation of pigmentation enzymes. They also found that muscle attachment sites constitute a developmental constraint on pigmentation. These findings were published in very well-recognised international journals (*PLoS Genetics* 2018, 2018; short article in *Genome Biology* 2017). In addition, team members were main authors on two *Scientific Reports* (2017, 2018) and one *PLoS One* (2022) and they contributed as collaborators to three more publications (*Mol Ecol, Scientific Reports, Dev Cell*).

The team is strongly involved in teaching, notably with two professor/ assistant-professors having important duties at SU, and both team leaders are also involved in teaching. The team is well engaged in outreach activities. In particular, it coached the SU team for the iGEM (international Genetic Engineered Machine) competition and contributes to science diffusion toward the general public. Within the institute, F Perronet is in charge of the LBD twitter/X account and one researcher is responsible for internal seminars.

### Weaknesses and risks linked to the context

The recent production of the team has been somehow limited as some lines of research did not flourish or give breakthrough results. While the impact of their work has not been so strong in the past, their recent findings seem to be more visible.

With only ~120k€ of competitive grants (one grant of each funding agency: ARC, GEFLUC, ANSES, MITI CNRS, IBPS) and one external PhD fellowships (MITI CNRS) acquired during this period, the funding level of the team is limited and not sufficient to embark into more ambitious projects

### Analysis of the team's trajectory

The team will close at the end of 2024, and a new team based on the fusion with members of another team will be proposed; two PIs will retire in mid-2026.

## RECOMMENDATIONS TO THE TEAM

No recommendation as the team will close.

**Team 12:** Cortical Actomyosin Dynamics In Development And Morphogenesis

Name of the supervisor: Mr François Robin

## THEMES OF THE TEAM

The team aims to investigate morphogenesis during early embryogenesis with a particular focus on the mechanics of cells and the actomyosin cortex. The team seeks to bridge length-scales between molecular processes assembling the cytoskeleton and shape change. A new additional objective is to explore the interplay between energy metabolism and mechanics.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was established in 2016. The previous evaluation recommended to find a niche within the competitive field of actomyosin dynamics and morphogenesis. They recommended to find a balance between safe and more risky projects.

Over the past period, the team has recruited staff, gained funding, and published key papers establishing its niche in the field. The team leader has organised several conferences and been invited to give a number of seminars, a testament to his gain in visibility. Overall, the recommendations of the previous evaluation have been addressed.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 0 |
| Directeurs de recherche et assimilés | 0 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 0 |
| **Sous-total personnels permanents en activité** | **1** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 1 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **5** |
| **Total personnels** | **6** |

# EVALUATION

## Overall assessment of the team

The team has recruited new staff members to support their scientific activity and long-term funding has been secured. The team has published several studies that leverage their core expertise (high end microscopy and multidisciplinary science). These have served to establish the team's reputation in the field. The proposed projects for the upcoming period are original and innovative. They represent a good balance between "safe" projects that are part of the core expertise of the lab and more risky projects that will serve to expand the lab's remit. Several multidisciplinary collaborations have been established with each bringing in expertise complementary to the team. Overall, the team is on the right trajectory to become world class.

## Strengths and possibilities linked to the context

The visibility and attractivity of the team have been excellent considering its recent start (2016). The team has recruited staff at all levels (3 PhDs in progress, 1 engineer, 3 permanent researchers joined in 2023). Following on from this influx, the team can now afford to be more ambitious. While funding has remained low till the end of 2022, the team has raised substantial funding (ANR coordinated running till 2027), ensuring the long term functioning of the team. In addition, it helped secure further funds (ANR coordinated) for a new collaborative making space dedicated to microfabrication and microfluidics at IBPS, which will be used by multiple teams in LBD. The team contributes to training researchers, as shown by the number of Master and Licence students that they host, as well as lecturing with two of its members contributing substantial teaching.

The scientific production of the team has been very good to excellent. The team has developed a core expertise in high-end single molecule microscopy and advanced image analysis that build on C elegans genetics. Combined with computational modelling, these quantitative approaches allow the team to probe simple models for how signalling controls cytoskeletal assembly and how this in turn controls mechanics and morphogenesis. Thanks to these approaches, the team has characterised the excitable dynamics of RhoA regulation as well as its kinetics. They have shown that pulsed signalling drives cortical contractility and examined how different actin networks within the cell compete for monomers. Building on these results, the team is now collaborating with mathematicians to explore how modulation of actin dynamics impacts the architecture of the network generated and with physicists and chemist to link modulation of cytoskeletal machinery at the molecular scale to cell scale shape changes. The team provides a good thematic fit with the other teams interested in mechanical signalling during development/mechanobiology at IBPS/LBD/Dev2A. Furthermore, a number of collaborations have been established with local universities and departments, making the team well integrated in its surroundings. The work produced 6 research articles, four as lead authors, often published in well regarded journals (Cell reports, Journal of Cell Biology). It is important to note that during this time the team leader started with very little staff.

The team interacts with society: several members contribute to outreach through lab demonstrations to the public, hosting of middle and high school students, and communications to media.

## Weaknesses and risks linked to the context

Funding for most of the reporting period (2017-2022) has been low.

The team leader and one of the staff members have significant teaching duties. This will slow progress.

While the team has been able to recruit permanent researchers, PhD students, and an engineer, it is still lacking a dedicated molecular biology technician, which is crucial for the ambitious experiments that the group wants to achieve.

The lack of large funding makes it difficult to attract postdocs for a sufficient time to fulfil ambitious projects that are crucial to their career progression.

These factors put the advances made by the team in the past period of activity at risk.

## Analysis of the team's trajectory

The team leader established his team in 2016. At the start of the current period of evaluation, the team leader was the only member in the team. Since then, the team leader has been very active in applying to and obtaining funding. This allowed the team to really establish itself as one of the leaders of quantitative cytoskeletal biology and fulfil an ambitious programme of high-quality research. The team leader has been able to substantially enlarge the team and recruit permanent members. He has made connections with multidisciplinary collaborators locally and internationally. Altogether, this is an impressive outcome for the past period.

Going forward, the team wishes to build on their established expertise in high specification single molecule imaging and advanced image analysis combined with computational modelling to bridge the gap between molecular and cellular scales. They will further examine how different molecular actors participate in specific aspects of morphogenesis. To add a further dimension to this research theme, they will develop optogenetic actuators to control signalling. This will allow them to bridge the gap between signalling, mechanics, and morphogenesis. A new theme examines the role of ATP metabolism during morphogenesis. This will build on the microscopy and image analysis expertise alongside newly established collaborations. A final theme will take advantage of the expertise brought in by a new team member and will examine how mechanical inputs control skin homeostasis and repair.

The project is timely and examines exciting aspects of physiology and developmental biology. It builds on the team's established expertise, combining "safer" projects that follow on from previous work alongside new "riskier" projects. The team's track record, the coordination of two recently starting ANR grants (2023) and the new recruitments, provides confidence that this new direction will result in promising outputs.

# RECOMMENDATIONS TO THE TEAM

The team needs to recruit a molecular biology technician.

The team needs to still secure larger funding to recruit postdocs. This will allow them to build on their very promising past activity.

The team should continue to focus on high quality multidisciplinary publications that they have built their reputation on.

**Team 13:** Morphogenesis of the Vertebrate Brain

Name of the supervisor: Ms Sylvie Schneider-Maunoury

## THEMES OF THE TEAM

The team studies how progenitor cells in the developing central nervous system respond to mechanical and biochemical signals from their environment in order to proliferate, maintain, and differentiate into different types of neurons and glia. The team focuses mainly on the role of cilia and ciliary proteins, using complementary in vivo and in vitro models.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- The committee is concerned about the fact that the team leader's time commitment to leading the institute is consuming. The reinforcement of the team should be assured with the arrival of two new researchers at the beginning of the next contract period.* Despite the heavy administrative duty of the team leader, the team has continued to publish regularly in leading journals. The size of the team has apparently shrunk during the last contract but it remains quite large with five permanent researchers/teachers.

*2- Care should be taken to secure funding on project 1 that will become the main project of the team.* The team has secured funding for its main projects. Altogether, it raised more than 1 M€ during the last contract.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 1 |
| Maîtres de conférences et assimilés | 2 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **6** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 1 |
| Post-doctorants | 1 |
| Doctorants | 1 |
| **Sous-total personnels non permanents en activité** | **3** |
| **Total personnels** | **9** |

## EVALUATION

### Overall assessment of the team

The team has an excellent to outstanding visibility in the field of primary cilia and brain development. The team's strategy to mainly focus on basic research in connection to clinical research on a specific human syndrome has high impact and led to an excellent scientific production. The team non-academic activities, including outreach activities, remain limited with regard to the potential of the team's size and projects.

## Strengths and possibilities linked to the context

The team has an excellent to outstanding visibility and recognition in the field of cilia and neurodevelopment. The team is attractive for students and postdocs, three PhD students were trained during the contract, three PhD students are currently in the team and two post-docs were hired. Most PhD students and postdocs published as first authors, which is excellent. The team has a strong capacity to lead research projects with two full-time tenured researchers (among which the head of the team), two university teacher/researchers and one medical professor. In addition, four of these permanent researchers hold an HDR which provide an excellent capacity to recruit and train PhD students within the team. The team has a very good capacity to obtain grants from national agencies (2 ANR grants as partner) and from charity associations (1 FRM and 1 ARC). The team also obtained 1 grant from ERA-Net, attesting its European visibility. The team's visibility is also attested by regular invitations of the team leader and other members of the team to scientific meetings and by organising 1 international scientific meeting ("Cilia, Flagella and Centrosome"). In addition, team members participated in ad-hoc university selection committees and in 2 CNRS institutional committees. The team leader has been directing the LBD and more recently the IBPS.

The scientific production is excellent. In the last five years, the team has focused its research on cilia, ciliary proteins and neurodevelopment and since 2019 it published almost exclusively on this topic. Collectively, these publications provide a comprehensive corpus of knowledge, from the scales of molecules and cells to tissues and organisms. Four studies from the team were published as first/last co-authors in leading journals (J. Neuroscience, Development, Nat Commun) and the team also contributed to a number of collaborative publications. Altogether, during the period of evaluation, the team published an impressive 32 publications (including primary articles, reviews, books and chapters).

The non-academic activities of the team are good, the team reports 3 large audience conferences given.

## Weaknesses and risks linked to the context

Although six PhD students were trained during the ongoing contract, three of them defended their PhD between 2017 and 2019, which means that for two years during this contract, only one PhD student at a time was hosted by the team. This is a somewhat low number considering the number of HDR.

Several members of the team do not seem to participate in non-academic or outreach activities.

## Analysis of the team's trajectory

For the next contract, the team will pursue three separate but interconnected axis of research related to cilia and neurodevelopment. The first one will investigate morphogenesis of the ventricular system in zebrafish and how this impact on progenitor behaviour; the second one is a direct follow up of previous studies, it will investigate the function of specific ciliary proteins in different species, taking advantage of in vitro culture models (mouse ESC and human iPSC); the third axis is part of a European grant investigating human variants detected in patients with Joubert Syndrome. The team will assess four variants in different integrated models, zebrafish, mESC and hiPSC. The team also proposes to start investigating the role of ciliary proteins in cerebellar structures.

All projects will presumably be achieved using state of the art methodology (laser ablation, live imaging, immunohistology, expansion microscopy). Most of the expertise for these projects is already present in the team. Overall, the future trajectory is clear and pertinent. It is a well-balanced combination of basic and more disease-oriented research, with a diversification of experimental models, including human 3D in vitro models.

# RECOMMENDATIONS TO THE TEAM

Interaction with the society and outreach activities could be strengthened.

**Team 14:** Induction and Differentiation During Vertebrate Embryonic Development

Name of the supervisor: Mr De-Li Shi

## THEMES OF THE TEAM

The team investigates developmental processes with focus on regulation of embryonic axis patterning and embryonic lineage differentiation. They are using Xenopus, zebrafish and mice as models.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- They should improve their funding for research, which should impact on the team productivity.*

*2- They should improve the capacity for training young scientists.*

*3- Strategy proposed for their scientific projects should be improved, as the tasks might turn out to be too ambitious considering the team size/human resources.*

These recommendations were essentially not followed.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **4** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **0** |
| **Total personnels** | **4** |

## EVALUATION

### Overall assessment of the team

The team is closing down. The scientific production of this team has been excellent considering the small team size, with publications in well-respected journals. Attractiveness and visibility were very good.

## Strengths and possibilities linked to the context

The visibility and attractivity of the team have been very good. The team leader has been member of the Inserm CSS2 committee and is associate editor at three journals (BMC Genomics, Biology and Front Cell Dev Biol). The team attracted five Master students and trained two PhD students, and published ten reviews in moderately visible journals.

The scientific production of the team has been excellent, with nineteen original articles, seventeen as lead authors, some published in highly visible journals (1 Nature Commun, 1 PNAS, 1 Development), demonstrating the team productivity and competitivity in spite of very limited funding (<100k€) and rather small team size. The use of several relevant models, and identifying as well as characterising new factors in development were both strengths and led to several possibilities.

No non-academic activities were reported. One team member is heavily involved in teaching and bear several responsibilities in training programs.

## Weaknesses and risks linked to the context

The scientific field is highly competitive and the team leader did not succeed in attracting sufficient funding and personnel.

The team is closing as the team leader retires. In spite of rather limited funding, the team has been successful and quite a force in the field. Recruitment challenges appear to have been an issue for the team, however, it was productive considering the limited size.

## Analysis of the team's trajectory

The team is closing as the team leader retires. In spite of rather limited funding, the team has been successful and quite a force in the field.

# RECOMMENDATIONS TO THE TEAM

NA

**Team 15:** Signalling and Morphogenesis

Name of the supervisor: Ms Muriel Umbhauer / Mr Jean-François Riou

## THEMES OF THE TEAM

The team focuses on studying vertebrate kidney development.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- recommended to increase the number of publications, grants and participation in international meetings.* The team has published relatively well considering the amount of external funding, there is, however, still no current external funding (though applications are under consideration) and there is still limited active participation at international meetings.

*2- to concentrate on the single-cell approach and the study of the role of ECM in morphogenesis and combine the GRN data with cell imaging of nephron tubule morphogenesis so as to propose a predictive model explaining how regulation of gene expression shapes form during renal development.* The team have only partially implemented this suggestion.

*3- There was also a more general comment about "the high ratio between researchers with teaching duties and those without, which is not compensated by hiring post-docs or PhDs."*. This appears still to be an issue, though this team has been able to attract PhD (and Masters) students in recent years, but not currently.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 2 |
| Maîtres de conférences et assimilés | 3 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **8** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 2 |
| **Sous-total personnels non permanents en activité** | **2** |
| **Total personnels** | **10** |

# EVALUATION

## Overall assessment of the team

This team focuses on vertebrate kidney development by deploying advantages of the Xenopus pronephros experimental system and by initiating mammalian models (mouse and human organoids) to establish a pax8 to hnf1b regulatory axis. The scientific production and visibility of the team is very good. The team had not secured external funding in the second part of the reporting period and has lost attractivity. The trajectory was not seen positively since the plans presented at the meeting were not considered convincing.

## Strengths and possibilities linked to the context

The team visibility and attractivity was very good. The team has established useful collaborations, nationally with clinical researchers (renal pathology) and internationally with experts in useful technology (Xenopus transcriptional analysis, in Japan), analysis methods in mammals (in California) and human organoid model (Manchester, UK). The team was part of the European Renal tract consortium and trained four PhD students and a large number of Master students (>10), though the committee was informed that this was no longer the case. The team members also contributed to six reviews and book chapters.

The team scientific production was assessed as very good, with thirteen original articles, six as lead authors, including in respected journals (Development, Developmental Biology, Scientific reports…). The experimentally accessible Xenopus model system remains a strength of this research team, as it is used by them in a comparative way in conjunction with mammalian models (mouse and human organoids).

The team with five Teachers is heavily involved in teaching at the university, as well as in university connected responsibilities (including the direction of Doctoral college). Team members also lead or contribute to a large number of outreach activities.

## Weaknesses and risks linked to the context

This is a teaching-intensive team with many Teachers-Researchers, who presumably only have limited time available for research (and research supervision of PhD/Masters students).

The team has only secured limited external research funding. Probably, related to this, the team has not hosted any postdoctoral researchers. Reliance on Teachers-Researchers and PhD (and Masters) students puts enormous intellectual responsibility on the team supervisor(s) to keep up with conceptional and technical developments in the research field, which if not addressed may in the future represent a risk for the team.

The team has currently mostly a prominent national reputation, though with the established national and international collaborations that have already been established a clear trajectory towards more international recognition has already been initiated.

Research Administration duties had been time-consuming; however, these administrative responsibilities seem to have decreased more recently and will hopefully remain low in the future (see below).

## Analysis of the team's trajectory

The team's self-assessment document proposes to strengthen the link to clinical renal pathology (particularly patients with HNF1B mutations) and comparative analysis of the vertebrate kidney Gene Regulatory Network from frogs to humans. The strengthened link to renal pathology is also a strategy to increase external funding (ANR application) to the team and possibly securing positions for postdocs to join the team.

The evolutionary history and developmental progression of the development of the mammalian metanephros (i.e., requiring pro- before meso- before metanephric development) clearly justifies the suggested comparative analysis from frogs to humans. The proposed identification of cis-regulatory elements (particularly for regulation of HNF1B expression) through phylogenetic footprinting is exciting, yet non-conservation of elements between frogs and humans may also be informative for studying evolution and normal and abnormal development of the metanephros (and abbreviated pronephros development) in human.

Proposing the frog as a model for understanding human disease is credible, as is being demonstrated successfully in the cardiovascular field (e.g. Yale), cancer (Belgium) and even specifically for renal pathologies (Switzerland) as suggested by the team; yet as suggested in the self-assessment document, the team has a unique niche in studying such renal pathologies in the context of their comparative analysis.

Although the above-discussed refocusing may improve the team scientific impact and provides means for better funding in the future, the committee was not convinced by the trajectory plans presented, which mostly rely on classical approaches, taking little advantage of the potentialities that modern biology offers.

The team suggests a rename from "Signaling and Morphogenesis: to "Renal Development and Disease". There is a concern that "renal" is not a sufficiently familiar term among non-experts leading to the suggestion to rename the team "Kidney Development and Renal Disease".

## RECOMMENDATIONS TO THE TEAM

The committee recommends

- to improve the scientific strategic plan for the next contract.

- to keep administrative duties to a manageable level in line with a successful international research career of the team supervisors.

- to Increase funding and postdocs.

- to secure support for advanced bioinformatics analysis, a recommendation, that possibly transcends many teams within the LBD (and the IBPS)

**Team 16:** Meiosis and its Mechanisms

Name of the supervisor: Ms Katja Wassmann

## THEMES OF THE TEAM

The team uses mouse oocyte model to dissect the signalling pathways regulating meiotic I and II divisions and to understand how errors in chromosome/chromatid partitioning take place.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) was to continue on their excellent upward trajectory. To continue the outstanding progress over the last five years strong support to improve the infrastructure of the laboratory, particularly microscopy and the mouse house – will be important.
The team performance during the last contract attests an upward trajectory. The team moved to the Jacques Monod Institute in 2022 that provides the team the required infrastructures.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **4** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **0** |
| **Total personnels** | **4** |

## EVALUATION

### Overall assessment of the team

The team addresses fundamental research questions in the meiosis field. The team had an outstanding scientific production and benefits from an excellent to outstanding visibility. The team also presents and strong network of collaborations and secured a significant number of grants. In 2022, the team moved to the Jacques Monod Institute.

### Strengths and possibilities linked to the context

The team has an excellent to outstanding visibility and attractivity. four postdocs and six PhDs were hired. The team leader also secured strong financial resources with the obtention of two ANRs, two "Team FRMs", one ARC and one Sorbone University funding. She also displays outstanding national and international visibility as attested

by the regular number of invitations to international renown conferences (Jacques Monod, Gordon Meiosis meeting, Embo Meisosis meeting…), by the organisation of some of these meetings and by her participation to administrative and funding committees.

The scientific production of the team is outstanding. The team continued its upward trajectory and produced 9 outstanding publications in leading journals such as J; Cell Biol, Nat Commun, Dev Cell, EMBO J or Current Biol, as well as five review articles. The seminal data on the role of cylin B3 in metaphase II arrest significantly participated to the understanding of meiotic maturation. The team also produced very interesting data on the role of separase activity in physical separation of sister kinetochore during meiosis I and in the subsequent centromeric cleavage during meiosis II.

### Weaknesses and risks linked to the context

None

### Analysis of the team's trajectory

Since 2022 the team moved to Jacques Monod Institute.

## RECOMMENDATIONS TO THE TEAM

None

**Team 17:** Compartmentation and Intracellular Traffic of Mrnps

Name of the supervisor: Ms Dominique Weil

## THEMES OF THE TEAM

The team is focused on the study of the role of cytoplasmic membrane-less organelles in post-transcriptional regulation, with a particular focus on P-bodies. They use human fibroblasts and human patient cells, as well as synthetic biology approaches to address different aspects of P-body biogenesis and function: how they assemble, what is their molecular composition, and what is their function in RNA metabolism and physiology.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (italics) were:

*1- to increase the publication rate and intensify its communication activities.* The team leader and team members have participated in numerous national and international meetings. The publication rate of projects led by the team remains relatively low (4), however, three of these publications are in highly regarded journals (Mol Cell, eLife, AJMG) and one of them (Mol Cell, 2017) represents a major breakthrough in the field.

*2- to increase its attractiveness towards young scientist and increase HDR number.* The team trained two PhD students during the period under evaluation, however there are no PhD students at the moment. The team trained two postdocs during the period under evaluation and has two postdocs at the moment. The number of team members with HDR has not changed.

*3- to assess the project tasks to prioritize the most advanced/promising to assure high impact publication.* The team managed to produce three publications of high impact.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 1 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 1 |
| **Sous-total personnels permanents en activité** | **4** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 3 |
| Post-doctorants | 0 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **3** |
| **Total personnels** | **7** |

# EVALUATION

## Overall assessment of the team

The team's research topic is of major interest, combining basic studies on P-body biology with more translational approaches that look at the role of these membrane-less organelles in neurodevelopmental disorders. The team shows excellent to outstanding national and international visibility and scientific production. However, the recruitment of young scientists is limited, with only a small number of PhD students being trained in the evaluation period. There is an active involvement of the team in outreach activities.

## Strengths and possibilities linked to the context

The visibility and attractiveness of the team is excellent to outstanding. The PI has participated as organizer or invited speaker in 16 international and ten national meetings/seminars (including RNA Society meeting, CSH Translational Control meeting and four EMBO meetings), and team members have been selected for oral presentations at eleven international and three national meetings and received awards for their publications or presentations. The team leader has held numerous positions of scientific responsibility beyond leading the team: elected member and scientific secretary of the section CoNRS 21; co-president of the SU Committee of HDR Biology; member of the UFR teaching Council, the LBD Unit Council and the LBD Staff Council; as well participating in the selection committee for different positions. The PI is also member of the editorial board of NAR and acts as reviewer for numerous high standard journals and for national and international funding agencies (ERC, MRC or Wellcome Trust among them). The team has developed an extensive network of collaborations leading to team members co-authoring high impact publications (Nat Commun, PNAS, Sci Adv, Cell Rep). Regarding attractiveness, two postdocs and two PhD students were supervised during the period under evaluation and the team hosted a visiting scientist from University of Mexico for six months. The team has secured funding from national (1 INCa (partner), three ANR: two as coordinator and 1 as partner), and local (1 IBPS (joint coordinator), one i-Bio (coordinator) funding bodies and charities (1 FRM (partner), 1 ARC). The recognition of the team as a leader in the field is also acknowledged by their participation in reviews for Mol Cell (2018) and Trends in Genet (2018).

The scientific production is also excellent to outstanding. In 2017 the team published a seminal work on P-body purification and content analysis that represented a major breakthrough in the field (Mol Cell 2017). Since then, they have made very insightful contributions to the understanding of the biology and function of RNP condensates. Whereas in 2019 they showed how mRNA GC content correlates with different aspects of mRNA storage and decay (eLife 2019), more recently they have demonstrated, in collaboration with the Gueroui group, that RNA is key for the size and composition of RNA-protein condensates (Biophysical J 2022). Additionally, they have further explored the physiological functions of P-bodies in human cells and identified miss-sense variants of the helicase DDX6, required for P-body formation, linked to a neurodevelopmental syndrome (AAJHC 2019). The team has also established multiple successful national and international collaborations leading to 7 additional publications (Cell Rep 2017, Sci Rep 2017, BBA 2018, Nat Commun 2019, Sci Adv 2020, PNAS 2021).

The team has been involved in multiple outreach activities aimed at engaging with the public and bringing science to society, like the participation in the LBD Open Day, the participation in a science fair and in courses, and hosting a high school teacher for building a research-applied project.

## Weaknesses and risks linked to the context

The number of PhD students trained (2) is low and only one of them has publications as first author.

The number of publications with team members as first/last author is moderate (4).

Although the team has followed up their 2017 breakthrough study with publications in leading journals and is involved in various successful collaborations, an increase in the team size would be useful for an improved scientific output.

## Analysis of the team's trajectory

For the upcoming period the team plans to follow up on their previous work and develop their research plan focusing on three main lines. The first one looks into the properties of PB content and how dynamic changes in

it contribute to cell adaptation to changing conditions in the context of cell cycle progression. This project was funded by an ANR grant finishing at the end of 2023 and has already produced significant results showing how mRNA storage in PBs changes according to cell cycle phase and the observation that mRNA isoforms are differentially recruited to PBs independently of their GC content. This is setting the grounds to further study dynamic changes in PB recruitment of specific transcripts according to cell needs and the determinants of differential storage of largely similar RNA isoforms. To complement these studies, they will perform functional assays to determine the effect of PB depletion on cell cycle progression and mRNA translation under optimal or stress conditions.

The second research line, based on their work on mutant DDX6 (AJHG 2019), aims to further characterise the alterations in mRNA translation and mRNA decay pathways in fibroblast from patients carrying DDX6 miss-sense mutations, as well as evaluating mutant DDX6 activity in terms of its interactors and ATPase and RNA binding properties, and its biophysical properties in the context of PB assembly. Interestingly, they will also expand their studies on DDX6 mutant alleles to analyse their function in the context of neural differentiation, using human iPSCs (either genetically engineered to carry patient-specific mutations or from new patients) and zebrafish as a model. These studies should offer a very interesting context to study PB function in development and differentiation and provide very insightful information into the role of mutant DDX6's association with neurodevelopmental disorders. The team has an ongoing ANR grant application in collaboration with three other groups dedicated to this research line.

The third research line continues their previous work in collaboration (Biophys J 2022) to elucidate the extent PBs biophysical properties affect mRNA translation and decay and has already produced another high impact publication (EMBO J 2023).

All research lines are well founded on the team's previous work and expertise and are likely to produce major contributions to the advance of knowledge in the RNA field, addressing how cells regulate gene expression through dynamic changes in mRNA localisation affecting mRNA stability and translation. In addition, the broadening of the team's model system to include human iPSCs and zebrafish should raise the impact of their investigation.

## RECOMMENDATIONS TO THE TEAM

Although they have the expertise and a well-established network of collaborators to carry out the main research lines, the small size of the team and its involvement in multiple collaborations besides the team main projects may represent a challenge for the progression of the latter. It would be good to try to increase the team size to take advantage of the high visibility and international recognition acquired during the past years and remain at the cutting edge of the field.

Given the high number of scientific responsibilities held by the team leader, increasing the number of team members having an HDR would allow to attract and train more PhD students. In addition, whereas the team has an ongoing application to fund one of the research lines, funding for the other may be a limiting factor and additional grants should be secured.

# TEAMS ASSESSED ON TRAJECTORY ONLY

**Team 18:** Heterochromatine, Cell Fate and Exposome

Name of the supervisor: Agnès Audibert/Jean-Michel Gibert

## THEMES OF THE TEAM

This new team will explore role of constitutive heterochromatin in development and in response to environmental changes using *Drosophila* as a model system.

## PROVISIONAL WORKFORCE OF THE TEAM: in physical persons at 01/01/2025

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 3 |
| Maîtres de conférences et assimilés | 2 |
| Directeurs de recherche et assimilés | 2 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 2,5 |
| **Sous-total personnels permanents en activité** | **10;5** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 0 |
| Post-doctorants | 0 |
| Doctorants | 0 |
| **Sous-total personnels non permanents en activité** | **0** |
| **Total personnels** | **10,5** |

### Analysis of the team's trajectory

The proposed team will arise from the merge of the former teams "Cell Cycle and Cell Determination" and "Epigenetic control of developmental homeostasis and plasticity" in January 2025. It will be co-headed and regroups all the current staff members of the two teams (10;5 people), with the exception of one person, who will retire in 2023. A Professor of the team will become deputy director of the Dev2A unit. Of note two PIs will retire in mid-2026.

The team will benefit from the respective expertise of each team to develop a new project aimed at characterising the role of constitutive heterochromatin in the regulation of cell identity and in the response to environmental changes. This project is a good fit between the interests in chromatin regulation, developmental robustness and response to environmental changes, and that on imaging and cell fate acquisition. The team members appear very eager to work together; they already elicited some technological developments and experiments to lay the basis for their common project.

The proposed project should provide very interesting insights into the function and regulation of this particular chromatin compartment which remains poorly explored. This thematic will be developed looking at fluctuating asymmetry in the wing or variation in abdominal pigmentation as well as during cell fate acquisition/differentiation during mechanosensory organs (bristles) development in the notum. Even though the new team presents valuable expertise to tackle these questions, this project will be a significant departure from the current experimental and conceptual framework of both teams. Beyond the valuable description of c-het

dynamics, one difficulty will be to perform functional assays demonstrating specifically the importance of changes in c-het organisation for cell fate acquisition/differentiation and/or in the response to environmental changes. The project relies on a good set of genetic tools which nonetheless needs to be carefully controlled. The possible impact of transposable element mobilisation or c-het-embedded gene expression need to be further taken into consideration. The usage of scRNA-seq to measure transcriptional noise may necessitate deep sequencing depth and further bioinformatic skills in the team.

While both PIs have a very good track record in their specific fields, their capacity to raise competitive funding for their project is not very well sustained and their international standing is still limited. In addition, most team members will have heavy teaching duties, which will hamper their implication in the project. In sum, while the project is of high interest, the team will need to build a stronger research core to become highly competitive at the international level.

## RECOMMENDATIONS TO THE TEAM

The committee recommends that the team engages some collaboration with leading labs in the field of epigenetic/ chromatin structure analyses to develop its projects and to gain a higher international standing.

The committee feels that there is a risk of dispersion, especially when starting such a new project. It will be important to focus rapidly on a particular environmental change to provide a deep molecular analysis of its impact on c-het. This may also help attract higher levels of funding by putting more emphasis on the general significance of the project beyond fundamental research.

The team is encouraged to apply for further competitive grants in order to secure sufficient funding and to invest in bioinformatic skills development for the analysis of NGS/scRNA-seq data.

Efforts for attracting PhD students and postdocs would be important for the stability of the new team and for its international visibility.

**Team 19:** Plant Nuclear Dynamics and Signaling

Name of the supervisor: Ms Clara Bourbousse / Mr Fredy Barneche

## THEMES OF THE TEAM

The team seeks to understand how plant chromatin-based mechanisms contribute to photomorphogenesis in Arabidopsis seedlings, a crucial step towards plant establishment after germination. It investigates how chromatin constituents and the machineries controlling its spatial organisation regulate the light-induced reshaping of the transcriptome and epigenome.

## WORKFORCE OF THE TEAM: in physical persons at 01/02/2024

| Catégories de personnel | Effectifs |
|---|---|
| Professeurs et assimilés | 0 |
| Maîtres de conférences et assimilés | 0 |
| Directeurs de recherche et assimilés | 1 |
| Chargés de recherche et assimilés | 1 |
| Personnels d'appui à la recherche | 0 |
| **Sous-total personnels permanents en activité** | **2** |
| Enseignants-chercheurs et chercheurs non permanents et assimilés | 0 |
| Personnels d'appui non permanents | 2 |
| Post-doctorants | 2 |
| Doctorants | 3 |
| **Sous-total personnels non permanents en activité** | **7** |
| **Total personnels** | **9** |

### Analysis of the team's trajectory

The proposed project is highly original and will maintain the team at the forefront of research deciphering the chromatin-based and epigenetically controlled mechanisms regulating photomorphogenesis. Indeed, the proposal moves the field into new grounds in several exciting and original ways as follows. Firstly, relying both on their ground-breaking findings on how light sensing impacts nuclear architecture and epigenome landscapes the team aims at identifying which genes form transcription "superclusters" upon light and decipher their regulatory roles. The team will also take advantage of the observation that a short prior exposure to light (priming effect) enhances photomorphogenesis to further establish functional links between photosensing, epigenome and 3D transcriptional landscapes. In seed and stress biology, understanding the mechanisms regulating priming effects have become a hot topic and this project could lead to innovation rupture. Secondly, capitalising on new findings showing that plastidial activity and metabolism influence nuclear organisation and transcriptional regimes, the team will investigate how plastid-to-nucleus retrograde signalling mediates chromatin rearrangements. Understanding retrograde signalling has attracted the attention of many plant biologists from the plastid side, leading to the identification of four major pathways. Here, the question is seen from the perspective of chromatin organisation and thus addresses a mostly unexplored side of retrograde signalling. Thirdly, the proposal will look into the safeguarding mechanisms that maintain epigenome homeostasis upon stress based on two types of stressors: UV light, ROS signalling/damage. The study of ITS polymorphic variants is very attractive because it will give new insights into mechanisms of plant adaptation and genetic instability during stress.

To achieve its research objectives, the team relies on a track-record expertise in epigenome and genome-profiling techniques and a network of world-renown laboratories developing cutting-edge techniques. Funding worth 641 k€ is secured for up to 2026 and several additional ANR applications were under evaluation for funding

at the time of writing. This project also consolidates newly established collaborations with LBD and IBPS teams, which is bound to generate an added value to the team expertise portfolio.

## RECOMMENDATIONS TO THE TEAM

For such a small team, the breath of the topics and ambitions of the project might be a challenge. The team is encouraged to seek national and international postdoctoral fellowships to alleviate PhD supervision charges and administrative burden.

Both team leaders are encouraged to increase visibility of this starting team.

**Team 20:** Stem Cells, Cardiovascular Pathophysiology and Biotherapies

Name of the supervisor: Mr Onnik Agbulut/ Mr Zhenlin Li

# THEMES OF THE TEAM

The team aims at developing studies in the cardiovascular field both in fundamental research and medical domains, using physiology, molecular biology, biochemistry and the physics of biomaterials.

## Analysis of the team's trajectory

The team addresses questions related to one of the major public health issues, cardiovascular diseases. They have established a large number of collaborations, allowing them to tackle problems and questions concerning cardiovascular diseases and allowing them to produce a large number of publications over the last years. For the next few years, they focus on the role of the cytoskeleton and its deregulation in cardiomyopathy, with special emphasis on the interaction of the cytoskeleton and mitochondria.

A major line of research will deal with the interaction between intermediate filaments and mitochondria. Disruption of intermediate filament organisation leads to mitochondrial disfunction, and more insight into these two components and their interactions might unravel strategies for novel therapies. Based on the observation that in pathological and aging conditions, mitochondria are released from cardiomyocytes towards macrophages, the hypothesis that surrounding cells read out the state of cardiomyocytes and respond to it will also be tested.

In addition, collaborations with industry and clinicians will be intensified in order to develop therapeutic approaches. These lines of research include the development and characterisation of biomaterials for screening and/or therapeutic purposes, the design and testing of cell therapy products, including adoptive T cell therapies, as well as the performance of high-throughput drug testing using patient-derived cardiomyocytes derived from hiPSC.

The team has shown in the past that it can be very productive in these large networks with biotech and clinical researchers, and they will know how to capitalise on this and contribute to a better understanding and treatment of cardiovascular diseases.

# RECOMMENDATIONS TO THE TEAM

None

**Team 21:** Quantum Biology

Name of the supervisor: Ms Margaret Ahmad / Ms Nathalie Jourdan

# THEMES OF THE TEAM

This new team is joining Dev2A (coming from B2A) and they will explore Quantum Signal (magnetic fields, radiofrequency fields or infrared light) induced ROS signalling pathways in plants and in mammalian cell culture models.

## Analysis of the team's trajectory

This is a new team based on a team founded in 1999. New co-PI joined in 2014 with expertise in how electromagnetic fields interact with mammalian cells and disease models. During the new period, one PI will retire and co-PI will become new team leader. The team is well recognised, publishes well, and is well funded. The team activity is based on cryptochrome light receptors structure & function, mainly in plants. The team has gradually expanded (also due to arrival of co-PI) to focus on quantum signals, and with receptor systems being in vitro, mammalian and plants. Thus, the team has three research lines and use different types of signal exposures. The signals (magnetic fields, radiofrequency fields or infrared light) are indeed related in the sense that they are low energy, in essence, being different from high energy signals like ionising radiation as used in the clinic.

More specifically, three continuing goals are outlined on: 1) How isolated plant Cry receptor mediates magnetic field effects; 2) Effect of quantum forces on ROS signalling in mammalian cell cultures; 3) Effect of quantum forces on plant ROS signalling pathways. In general, the goal description is kept short and at a very general level making it difficult to analyse trajectories, except for the fact that the goals all appear as logical extensions of ongoing research lines.

It is not clear if the retirement of PI will result in research strategic changes, though it appears that funding and competitiveness for grants will be reduced. It is also not clear where exactly the competitive edge for the team will be going forward (post-Ahmad).

# RECOMMENDATIONS TO THE TEAM

The team has three research lines and use different types of exposures. They are related at the conceptual level though with little to moderate experimental coherence (in vitro, mammalian cell culture models, plant models vs magnetic fields, radiofrequency fields or infrared light). There are scientific and historical arguments behind this based on current staff. However, the team historical PI will retire during/or at the end of the next contract. A clear and focused profile would be beneficial for the future of the team. The team argues that collaborations can lift part of this as essentially an extra major resource, however, it is a challenging path forward to rely extensively on collaborations (collaborators need to have the time, funding, interest, opportunities etc. throughout the collaboration).

The team could focus on research lines with breakthrough possibilities (prioritize ongoing and future projects), or put more emphasis on projects where the general significance (to the public) is clear and easy to explain with support from specific public health data.

**Team 22:** Rnamodbio

Name of the supervisor: Mr Damien Brégeon / Mr Djemel Hamdane

# THEMES OF THE TEAM

The main focus of the team will be the study of the functional role of two novel flavin-dependent RNA modifications, dihydrouridine (D) and 5-taurinoaminomethyluridine (tm5U) in the maintenance of cell homeostasis and in the context of pathology. For this they will use eukaryote (yeast and human) cells as a model and apply the expertise of both team leaders to combine molecular biology and biochemistry approaches.

## Analysis of the team's trajectory

The newly created team will follow up on the previous work from both team leaders, that have a strong background and high recognition in the field of epitranscriptomics, and that have already worked together though successful collaborations for many years.

The proposed research, focused on the regulation and functional impact of RNA epigenetic modifications, is at the cutting edge of the field and tackles questions of major interest as are how RNA modifications are established, their dynamics and how they impact cell homeostasis and disease. The team will focus on two modifications that, despite being highly abundant in different RNA species, have not been deeply studied: dihydrouridine (D) and 5-taurinoaminomethyluridine (tm5U). Previous results from the team members have made important advances to the understanding of the structural basis and evolution of the Dus enzyme, responsible for D modification in tRNA. Interestingly, preliminary results from the team point to this modification being reversible and possibly link to the redox status of the cell. They will use yeast and human cells to further evaluate to what extent the cells use D modifications as a novel mechanism to rapidly respond to changes in oxygen concentrations.

The second research project will focus on the involvement of toxic formaldehyde on mtRNA tm5U, a modification that is important for the translation of mitochondrial respiratory chain proteins and which defect is associated to cardiomyopathies in human. The team will combine molecular biology, genetics and structural biology to tackle different questions related to their projects, which will make them highly competitive in an emerging field.

In addition, the team has already established collaboration within LBD/Dev2A as well as external national and international collaborations that should contribute to the successful integration within the unit as well as its progression at a national and international level. The proven experience of the team leaders both scientifically and in terms of supervision and funding procurement should facilitate the establishment of the new team.

# RECOMMENDATIONS TO THE TEAM

The team will need to secure funding for the next period as it is only covered until 2024.

**Team 23:** Integrated Cellular Ageing and Inflamation

Name of the supervisor: Ms Chahrazade El Amri

# THEMES OF THE TEAM

The team's research is centred on cellular ageing in the context of normal ageing and age-related-diseases with a focus on cell proteostasis, pathological proteolysis, cellular senescence and inflammation.

## Analysis of the team's trajectory

The team has a long-standing expertise in the field of normal aging and age-related diseases. This large team is composed of nine researchers and teachers/researchers from different disciplines with one engineer and one technician. For the upcoming period, the proposed team leader is a replacement of current PI, who will be retiring.

The research project is in the continuity of the team interests in dissecting cellular ageing processes with two main research lines. The first aim is focused on cellular senescence and its role in age-related diseases with the identification of novel pathways and biomarkers. They propose to investigate the impact of senescence on accelerated ageing and its impact in the development of age-related diseases. They will study the impact of sleep apnea, a very important public health issue. Sleep apnea is associated with intermittent hypoxia, a driver of senescence. They propose to evaluate its impact on the brain aging and on the cognitive abilities in Alzheimer disease models. They will investigate the role of senescence in various neuronal populations. In addition, they will test whether the deleterious effects of intermittent hypoxia can be rescued by targeting the senescence-associated inflammation and by identifying the intracellular deregulated targets.

The second aim will focus on proteostasis and pathological proteolysis by investigating impacts on ageing at molecular and cellular levels and potential interests in the design of new therapeutic agents. For instance, previous results from the team showed that circulating level of Trx-80, a truncated form of thioredoxin 1, increases with aging, switching macrophages to pro-inflammatory phenotype. They propose to characterise the proteolytic machinery in thioredoxin 1 cleavage to identify potential therapeutical targets in inflammation during aging and related pathologies. A third axis is to develop therapies against senescence by improving their selectivity.

The projects are well supported by the team's previous research, they ask important questions of broad interest and in particular for the understanding of the impact of senescence in aging and age-related disease. However, considering the high number of permanent positions and the number of PhD students, the current proposal does not provide a good understanding about the strength and the future plan of the team under the novel direction. Although secured until 2025, funding could be a difficulty since securing new important grants will be organised with a new leader before the end of the upcoming period. Finally, the integration into DEV2A is an important step but this is only briefly mentioned in the current report with undetailed interactions.

# RECOMMENDATIONS TO THE TEAM

The team will be entering in a challenging phase in the upcoming period by joining the DEV2A institute and changing the team leader. The committee would like to stress that it might represent a complex transition that would need support from the unit direction.

The team is large and the future projects are presented with a compartmentalised view. The committee would recommend that interactions within the team to be strengthened to gain in efficiency and clarity. This alternative strategy will reinforce cohesion between team members. This will be beneficial in order to publish into interdisciplinary journals with a broader audience and gain in visibility. This step may be very helpful to reach higher scientific standards, secure competitive funding and attract talented post docs.

**Team 24:** Neuroplasticity of Reproductive Behaviour

Name of the supervisor: Ms Sakina Mhaouty-Kodja

# THEMES OF THE TEAM

The team studies the molecular mechanisms underlying the neural regulation by sex steroid hormones of neuroendocrine functions and behavior, and whether and how endocrine disrupting compounds (EDCs) can interfere with these processes.

## Analysis of the team's trajectory

For the next contract, the team will continue with its strategy to pursue basic and more applied projects in parallel.

The basic science project aims to identify molecular targets of sex steroids in sexual maturation, function and behaviour. The team will use mouse genetics, hiPSC-derived hypothalamic neurons and viral mediated loss of function in mice. The team has most of the tools and expertise to carry out this project with, may be, the exception of hiPSC cultures.

The second, more applied project is to assess the effects of combined exposure to chemical and environmental factors on neuroendocrine neurodevelopment and reproductive function. Specifically, the team will study the consequences of exposure to milk contaminants on neurodevelopment and neuroendocrine functions. Further it will assess the effect of combined exposure to substandard diets and EDCs on reproductive functions.

The team's project is straightforward and the trajectory is clear. The team has no difficulty in funding its research and is visible at national and International levels. It is attractive for PhD students and strongly involved in non academic activities. The team mentioned collaborative projects with 2 Dev2A teams, which is an excellent way to provide cohesion to the new Dev2A unit. The team leader will become deputy director of the Dev2A unit.

# RECOMMENDATIONS TO THE TEAM

None

**Team 25:** Axon growth and regeneration

Name of the supervisor: Ms Silvia Soares/ Ms Fatiha Nothias

# THEMES OF THE TEAM

The team's research is centred on identifying the molecular and cellular mechanisms required for axonal plasticity after injury and developing innovative strategies for neural repair.

## Analysis of the team's trajectory

The team will be created for the upcoming period from the association of three researchers and four teachers/researchers coming from four different structures. Their previous research topics share a common interest focused on neuronal biology.

The new team propose to investigate the molecular and cellular mechanisms involved in axonal plasticity and neural cell remodelling in the nervous system, particularly in response to traumatic lesions. It will explore 3 main topics. First, unravelling the role of the intracellular transport and mitochondrial function in axon growth in normal condition or during regeneration after injury. Besides, they propose to explore the interactions between axons and myelinating cells after neuronal lesions. A second axis is centred on exploring the contribution of the stem cells in neural repair using different approaches. Finally, the third axis proposes to develop innovative therapeutic strategies for neural repair based on their expertise on degradable biomaterial to facilitate local tissue repair. In their proposal, this will be combined with low-intensity magnetic stimulation to promote neurogenesis and appropriated reinnervation in the damaged area.

The current proposal is a convincing effort to fuse expertise of each member into a new team. The project outlines are promising and should generate new and original knowledge in a topic of major interest. The new team leaders will have to build a good synergy among the members coming from different origins within a new research unit. Funding is only secured until 2025 and this may create a financial insecurity for the research projects for the upcoming period.

# RECOMMENDATIONS TO THE TEAM

Integration of researchers from different origins within one team is challenging. The committee would suggest that the team members unify their effort to consolidate the development and cohesion with the team.

## CONDUCT OF THE INTERVIEWS

### Dates

**Start:** 21 novembre 2023 à 08h00

**End:** 22 novembre 2023 à 18h00

**Interview conducted: on-site**

## INTERVIEW SCHEDULE

### Day 1, Nov 21, 2023

**8:45 - 9:00** **Preliminary meeting of the expert committee (closed hearing)**
*Attending: expert committee, (Y. Graba and M. J. Stasia, SO)*

**9:00** - 9:15 Presentation of the HCERES evaluation to the unit *(Y. Graba)*
*Attending: expert committee, SO, representatives of institutions and all unit members*

9:15 - 10:15 Presentation of the research unit by the unit director (including 15 min questions)
*Attending: expert committee, SO, representatives of institutions and all unit members*

10:15 - 10:30 Break

10:30 - 12:50 Team scientific presentation Session 1
(15 min presentation + 10 min questions + 5 min with PI + 5 min debriefing of the committee). *Attending: Team members, expert committee, SO, director of Unit, representatives of Institutions*

Sub-committee 1

| | |
|---|---|
| BREAU<br>HAUTEFEUILLE | 10:30-11:05<br>11:05-11:40 |
| ROBIN | 11:40-12:15 |
| SCHNEIDER-MAUNOURY | 12:15-12:50 |

Sub-committee 2

| | |
|---|---|
| JESSUS | 10:30-11:00 |
| WASSMANN | 11:00-11:30 |
| GALY | 11:30-12:05 |
| CARRE / TEYSSET | 12:05-12:40 |

12:50 - 14:00 Lunch

14:30 - 15:15 Parallel meetings (3 subcommittees)
- Meeting with technical and administrative personnel (in French 45 min). *Attending: Technicians, Engineers, Administrative staff, sub-committee 1 of expert committee, SO*
- Meeting with thesis students and post-docs (45 min). *Attending: PhD students and postdocs, sub-committee 2 of expert committee, SO*
- Meeting with researchers and professors (in English 30 min). *Attending: Researchers except group leaders, sub-committee 3 of expert committee, SO*

15:15 - 15:45 Committee debrief (closed hearing)

15:45 - 16:00 Break

16:00 -18:20 Team scientific presentation Session 2

Sub-committee

| | |
|---|---|
| DUPREZ | 16:00-16:35 |
| UMBHAUER//RIOU | 16:35-17:10 |
| GHO | 17:10-17:40 |

| | |
|---|---|
| GIBERT/PERRONET | 17:40-18:10 |
| AUDIBERT/GIBERT | 18:10-18:40 |

Sub-committee 2: Room B120

| | |
|---|---|
| WEIL | 16:00-16:35 |
| SHI * | 16 :35-17 :05 |
| BOURBOUSSE / BARNECHE ** | 17 :05-17 :35 |
| BAILLY | 17:35-18:10 |
| EL AMRI ** | 18:10-18 :40 |

20:00 Diner

## Day 2, Nov 22, 2023

**8:30** - 10:00 Team scientific presentation Session 3

Sub-committee 1

| | |
|---|---|
| AGBULUT / LI | 8:30-9:00 |
| MHAOUTY-KODJA | 9:00-9:30 # |
| JAFFREDO/DURAND | 9:30-10:05 |

Sub-committee 2

| | |
|---|---|
| SOARES / NOTHIAS | 8:30-9:00 |
| BRÉGEON /HAMDANE | 9:00-9:30 |
| AHMAD /JOURDAN | 9:30-10:00 |

10:00-10:30 Break

**10:30 – 11:30** Meeting with the representatives of supervising bodies (CNRS, Inserm, University).
*Attending: expert committee, representatives of Institutions, SO*

11:30- 12:30 Deliberation of the sub-committees (closed hearing).
*Attending: expert committee, SO*

12:30 – 13:30 Lunch

13:30- 14:00 Meeting of the Committee with the head of the unit.
*Attending: Unit Director, expert committee, SO*

14:00- 18:00 Final deliberation of the committees (closed hearing).
*Attending: expert committee, SO*

## PARTICULAR POINT TO BE MENTIONED

No particular point to be mentioned

# GENERAL OBSERVATIONS OF THE SUPERVISORS

SORBONNE UNIVERSITÉ

Marie-Aude Vitrani
Vice-Présidente Vie institutionnelle et démarche participative
Sorbonne Université

à

Monsieur Eric Saint-Aman
Directeur du Département d'évaluation de la recherche
HCERES – Haut conseil de l'évaluation de la recherche et de l'enseignement supérieur
2 rue Albert Einstein
75013 Paris

Paris, le 15 mars 2024

Objet : Rapport d'évaluation – LBD - Laboratoire de biologie du développement

Cher Collègue,

Sorbonne Université vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « LBD ».

Sorbonne Université n'a aucune observation de portée générale à formuler sur le rapport d'évaluation transmis.

Je vous prie d'agréer, Cher Collègue, l'expression de mes cordiales salutations

**Marie-Aude Vitrani**
Vice-Présidente Vie institutionnelle
et démarche participative

The Hcéres' evaluation reports are available online:
www.hceres.fr

**Evaluation of Universities and Schools**
**Evaluation of research units**
**Evaluation of the academic formations**
**Evaluation of the national research organisms**
**Evaluation and International accreditation**

Évaluation · Recherche · Enseignement supérieur
Hcéres

2 rue Albert Einstein
75013 Paris, France
T.33 (0)1 55 55 60 10

hceres.fr @Hceres_ Hcéres