

EVALUATION REPORT OF THE UNIT
UGBD - Génétique et biologie du
développement

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Institut Curie

Institut national de la santé et de la
recherche médicale - Inserm

Sorbonne Université

Centre national de la recherche scientifique -
CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 16/02/2024



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, CSIC-Spain

Experts:

Ms Claire Chazaud, Icred-Clermont-Ferrand, (representative of Inserm)

Ms Maria Dominguez, CSIC-UMH, Spain

Mr. Joel Drevet, Université Clermont Auvergne (representative of CNRS)

Ms Kinneret Keren, Technion, Israel

Ms Anne Magglot-Roth, IGBMC-Strasbourg (representative of research support personnel)

Ms Catherine Mura, université d'Orléans (representative of CNU)

Ms Cristina Pujades, Universitat Pompeu Fabra-Spain

Mr. Lucas Jacques Waltzer, Icred-Clermont-Ferrand

HCÉRES REPRESENTATIVE

Mr. Yacine Graba

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr. Patrick Blader, CNRS

Mr. Thierry Galli, Inserm

Ms Tatiana Malherbe, Institut Curie

Ms Frédérique Peronnet, Sorbonne University

CHARACTERISATION OF THE UNIT

- Name: Genetics and Developmental Biology
- Acronym: UGBD
- Label and number: UMR3215
- Number of teams : 9
- Composition of the executive team: Mr. Pierre Leopold, Director of the unit; Mr. Yohanns Bellaiche, Deputy Director of the unit; Mrs. Virginie Bourgeois, Administrative Director of the unit

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

UGBD is composed of nine teams and three platforms (Imaging, Metabolomics and the new Crispr'it platform) comprising around 100 researchers (technicians and engineers). The unit develops curiosity-driven research, providing a key component of a continuum spanning fundamental and more applied research. The main topic of their research is Developmental Biology using different models including zebrafish, Drosophila and mice. The unit also does research using mammalian cell culture, including human cell lines, and has more recently introduced organoids.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit was created in 2009 with the aim of becoming a centre of excellence in Developmental Biology within the Institut Curie. Located in the Developmental Biology and Cancer building built in 2009 at the Paris Campus of the Institut Curie, the unit is affiliated to the Institut Curie, CNRS, Inserm, Sorbonne University and the new Paris Sciences & Lettres (PSL University, created 10 years ago). The unit is housing teams led both by senior researchers, and others led by promising young team leaders. To maintain scientific excellence, the unit has a very strict recruiting policy aiming to reach high standards of research.

RESEARCH ENVIRONMENT OF THE UNIT

The unit is one of the thirteen research units integrated in the Institut Curie and as such it has interaction with the new Paris Science et Lettres University which integrates several prestigious institutions including, among others, the College de France and the ENS. The unit is also associated to the Sorbonne University, which organises a doctoral school on the Complexity of life. The main funding and positions are provided by CNRS and Inserm, while the Institut Curie provides support with technicians and administration. The unit shares an idex/Labex excellence funding with the *Nuclear Dynamics* Unit (also housed at the Institut Curie) that will last until 2024.

UNIT WORKFORCE: 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	8
Chargés de recherche et assimilés	8
Personnels d'appui à la recherche	40
Sous-total personnels permanents en activité	57
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	23
Doctorants	17
Sous-total personnels non permanents en activité	41
Total personnels	98

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
Institut Curie	0	0	29
CNRS	0	6	7
Inserm	0	8	4
Sorbonne Université	1	0	0
Total personnels	1	14	40

GLOBAL ASSESSMENT

UGBD is focused on producing high quality, curiosity-driven basic research in the broad field of developmental biology aiming at opening new avenues of knowledge, encouraged by the Institut Curie, which despite having a medical orientation, has a tradition to promote the exploration of novel directions that may result in unexpected breakthroughs in biology and biomedicine. UGBD is part of the basic research-biomedical continuum developed within the Institut Curie's thirteen research units. UGBD benefits from multiple affiliations (CNRS, Inserm, Sorbonne Université and PSL) and is part of an extremely rich local academic ecosystem, including Collège de France and Ibens, organised around structuring programs (shared international courses, Qlife school, Labex Deep). The unit, with staff approaching 100 people, is extremely well funded, with yearly income averaging 10 M€ including salaries. It is solidly structured into nine research teams and three up-to-date technology platforms (Imaging, Metabolomics and Crispr-based screening).

The unit's visibility, attractiveness and scientific influence are exceptional. This is evidenced by the many awards received (>17 including Schlumberger, Bettenconrt, CNRS Paoletti, Loundberry), participation in international academies and scientific councils (Embo, Academia Europaea and Académie des Sciences), scientific councils and international scientific committees. This high level of recognition is corroborated by an exceptional level of funding at both national level (LNCC, ARC and FRM team accreditation) and international level, with seven ERC contracts (either at the Starting, Consolidator or Advanced levels) and coordination/participation in four ITNs. Unit visibility is also provided through teaching at the Institut Curie, Sorbonne University and PSL University. UGBD visibility is translated in the unit's excellent attractiveness to international postdoctoral fellows and PHD students. The unit has also set a highly selective recruiting policy to attract both excellent senior

researchers with an internationally recognised scientific career, and junior group leaders with innovative ideas and potential to become the future leaders of the discipline. The policy of the unit allowing all the competitive funds obtained to be used entirely by each team, and the attractive start-up packages new teams are offered, promotes the attraction of talented team leaders. While the visibility is outstanding, its full potential for attractiveness is limited by the physical size of the unit.

The success of the recruitment policy is reflected in the unit's outstanding publication production and its high international reputation. Their research is performed using original and up-to-date approaches using a large set of models including zebrafish, *Drosophila*, mice, mammalian cell culture, and organoids. The unit's work has addressed a wide range of central questions in developmental biology, and has led to significant advances in the fields of epigenetics and gene regulation in particular the function of non-coding RNA, the maintenance of stem cell plasticity, the role of mechanical forces in shape formation, and the role of inter-organ communication in the physiological control of growth. Together, the research produced forms a corpus of 57 original articles, the vast majority published in the most prestigious international journals (*Science*, *Cell*, *Nature*, *Molecular Cell*, *Nature Cell biology*, *Nature Commun*, *Current Biology*, *PLoS Biology*, *Dev Cell*...).

Although deeply rooted in fundamental research, the unit fully explores technological and commercial prospects, notably through an established partnership with Zeiss to develop innovative imaging tools. The unit is also heavily involved in outreach activities (publication of articles for the general public, radio, TV) and is behind an original initiative of courses dedicated to young children.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the previous report, there was concern that three groups would be leaving, and the recommendation to recruit new and dynamic teams.

Two teams have been recruited since then: one directed by Dr. P. Leopold, a senior PI and current director of the unit, and another directed by P. Hernandez, a Junior PI. Both of these PI's were awarded during the evaluation period a prestigious ERC grant (Advanced and Starting grant respectively). Although this leaves one less team, the institute is aiming for a further recruitment.

The previous report suggested promoting self-ambition among the brightest students. The outcome of several students that started their groups outside the Institut Curie (one of which has been awarded with a starting ERC Grant), shows the the unit foments mobility and progress among postdoctoral researchers. However, there has not been much progress in the promotion of staff working at the unit's teams with a permanent position (Chargés de recherche or Maîtres de conférences) whose career progression and independence are thwarted unless they leave the unit.

The previous committee also recommended that those groups that were minimally involved in teaching increased their load. It is difficult to assess if this has been achieved. However, the current reported involvement of the unit members in lecturing seems satisfactory. Moreover, with the creation of the PSL Doctoral School in life science, more lecturing opportunities may arise in the near future.

The previous report suggested that the unit made efforts to be more competitive when recruiting new researchers by making better start-up offers that could help attract the brightest researchers. The unit has accomplished this by employing LabEx funds to top up the starting packages to the already attractive packages offered by Institut Curie to new group leaders.

B – EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The UGBD unit has clearly defined high standard scientific objectives and a coherent scientific strategy. The UGBD focuses on fundamental research. The main research topics include how the non-coding genome and the epigenetic landscape control gene expression; how stem and germ cells maintain their plasticity; how cell division and mechanical forces shape the animal; and how different organs communicate with each other to achieve homogeneous growth, offering a wide view of different aspects that cover most of the relevant areas of development. Their work is curiosity driven, analysing novel areas of gene regulation, physiology and cell biology without any need for obvious translational objective.

Assessment on the unit's resources

The UGBD unit has very strong financial resources, converging from institutions and prestigious national and international grants, including seven ERC grants during the reporting period, and Labex funds. The unit also benefits from high-level core facilities: besides the unit's three platforms on Imaging, Metabolomics and Crispr-Cas9-based screening, The CoreTech provides advanced core facilities to the unit allowing researchers to access in a cost-effective manner the latest expertise and developments in essential technological aspects ranging from Next Generation Sequencing, a large Bioinformatics platform, Proteomics, Recombinant antibodies and Custom single cell-omics. In this period three grants (over 900k euros) were obtained to acquire new state-of-the-art equipment for the proteomics and the imaging platforms. Maintaining sufficient human resources to sustain the functioning of the platforms is challenging.

Assessment on the functioning of the unit

The functioning of the unit is overall excellent, with an appreciated leadership from the unit directions. Meetings for the unit management are held regularly, and the unit fully complies with its institutional requirements regarding health and safety and scientific procedures. The small size of the unit favours communication between its members and the direction. Promotion of non-PI permanent research staff is a difficult issue that so far could not be resolved.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

UGBD is focused on producing high-quality, curiosity-driven basic research with the aim of opening new avenues of knowledge. This approach is encouraged by the Institut Curie that despite having a medical orientation, has a tradition to promote the exploration of novel directions that may result in unexpected breakthroughs in biology and biomedicine.

To achieve excellence, the unit has set a highly selective recruiting policy to attract both excellent senior researchers with an internationally recognised scientific career, and junior group leaders with innovative ideas and potential to become the future leaders of the discipline. The success of the recruitment policy is reflected in the unit's outstanding publication production and its high international reputation.

The unit research is performed using original, coherent and up-to-date approaches: Gene regulation is studied focusing on the function of the less well-understood non-coding RNA and epigenetic analysis; cell growth is analysed with *in vivo* and biophysical approaches; physiological control of development is analysed aiming to understand how inter organ communication is coordinated during normal development.

The proximity to other research groups in the Institut Curie, in the Pierre et Marie Curie Campus, Sorbonne University, PSL University (College de France and Ibens), together with incentive actions toward promoting interactions with them, offer an excellent and incredibly rich scientific environment.

Weaknesses and risks linked to the context

None identified

2/ The unit has resources that are suited to its activity profile and research environment and mobilises them.

Strengths and possibilities linked to the context

The location of the unit in a building finished in 2009 provides an excellent environment for the different laboratories within a relatively modern site.

The unit being part of the Institut Curie is extremely well equipped, being able to make use of nineteen different services and platforms including a metabolomics and lipidomics, a zebrafish facility, a *Drosophila* fly food and stock maintenance service and washing service, metabolomics, microscopy platform with four technical support engineers, Crispr-based screening platform, RNA-protein interaction screening and single cell technologies.

The unit is extremely well funded, Institut Curie offers an annual endowment of 280k euros that can be used to pay salaries, help groups by providing temporary contracts for students, or to attract new teams. Apart from this, the other supervising bodies pay salaries amounting more than 3 million euros. The unit's joint success at obtaining the LabEx (Deep) grant has additionally provided 1 million euros to share with the co-applicant unit.

UGBD teams are very successful at obtaining individual project grants. The unit's teams obtain frequent national and international highly competitive grants. During the evaluated period, seven out of nine teams that composed the unit had or received the prestigious ERC grant (either at the Starting, Consolidator or Advanced level).

There is a very equilibrated ratio of young to senior PIs leading the teams.

Weaknesses and risks linked to the context

Some of the platforms are technically demanding, and it is important to have a number of engineers and technicians that can run them. The number of engineers and technicians in some services is currently too close to the minimal requirements, which could result in the services underperforming during holiday periods or in cases of disease or retirement. In the current evaluated period, this has negatively affected the imaging platform due to its senior manager moving away. It is important that an adequate level of expert technicians and engineers is maintained through time to support these services.

A possible risk could be the decrease of funding after the LabEx grant runs out in 2024, as this would affect the extra funds that the unit has employed to attract new team leaders. However, it is likely that the unit will be successful at obtaining a new program with similar capabilities-the PSL Grands Programmes support-they have applied for.

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

Strengths and possibilities linked to the context

Meetings for the unit management are held regularly. A Laboratory Council composed of representatives of students, postdoctoral students, technicians and permanent researchers (excluding PIs) meet with the director and the administrative director at least twice a year with an open agenda provided ahead of the meeting to be able to propose topics of discussion. A monthly informal PI meeting is also held to discuss important issues about the budget and recruitment during the year. The Director takes final decisions after consultation with all team leaders and the Deputy director of the unit.

The unit favours scientific animation by promoting internal and external seminar programs, UMR meetings, annual retreats and Labex associated meetings. Social events are also regularly organised (Christmas party, tea time...)

Each group has a person involved in analysing ways in which the team can reduce their waste and energy consumption, with the aim of finding ideas to do their research more sustainable.

The unit has a very good proportion of male-to-female group leaders and has also a good rate of young and established senior teams.

The policy of the unit allowing all the competitive funds obtained to be used entirely by each team, and the attractive start-up packages new teams are offered, promotes the attraction of talented team leaders.

The postdoctoral students at the unit receive guidance to apply for their own funding and become independent. In this evaluated period, five young researchers have successfully started their own group after obtaining national or international competitive grants (three ATIP/Avenir grants and two ERC Starting grants).

Health and safety is covered by three unit assistants that interact with the main IC health and safety officers, implementing procedures and following up any accidents/incidents if they occur and analysing ways to prevent them. A system is provided to researchers working in isolation so that they can call for help if required. The unit also has one person in Charge of Radioprotection (PCR), two L2 lab managers, one Laser Security Manager, one Chemical Waste Disposal manager, five Rescue workers and two Evacuation managers. A compulsory safety course is required for all unit newcomers.

Institut Curie has created a dedicated board and a Scientific Integrity Officer to supervise research integrity. All personnel are encouraged to attend research integrity courses, and on arrival in the unit are asked to sign a charter of deontology.

The unit performs animal research and follows all ethical procedures including the three R principles (Replace, Reduce and Refine) to reduce numbers of animals employed in research and care for their well-being.

Weaknesses and risks linked to the context

The Green agenda is not put in common by the different teams and units at Institut Curie to learn from each other's progress. The different teams propose ways of becoming more sustainable, which is very positive, but they should also be advised by a professional team specialised in such issues to become more efficient.

Promotion of non-PI permanent research staff is curtailed by the restriction to recruit personnel under their supervision. This is due to a general policy imposed on the unit that cannot increase in size due to being integrated in the Institut Curie which itself is unable to expand.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness and visibility of the UGBD are outstanding. UGBD members are highly regarded as demonstrated by the prizes received and their membership to international academies and scientific boards (EMBO members and members of the Academia europaea and the Académie des Sciences). The team leaders are also participating in multiple international Scientific Advisory Boards and Scientific committees. This high level of recognition is corroborated by an exceptional level of funding, with most teams obtaining highly competitive national (Team labialisation by LNCC, ARC and FRM) and international grants, including from the ERC (seven for nine teams during the reporting period). New team leaders are attracted to join UGBD by very competitive start-up funds.

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

The team leaders of the unit have a high scientific reputation, receiving national and international prizes (>17, including Schlumberger, Bettencourt, Cancerology AdS, CNRS Paoletti, Loundberry AdS) as well as having been elected members of international academies. Of the nine-team leaders, three are Embo members and one of them is also a member of the Academia Europaea and the Académie des sciences. The team leaders are also participating in international Scientific Advisory Boards and scientific committees (five PIs are members of editorial advisory boards or board members of journals including eLife, Developmental Cell, Cell Reports, Development, Scientific Reports, J. Mammary Gland Biology and Neoplasia, Non-Coding RNA, Philos. Trans. R. Soc. B).

The PIs are frequently invited to present their research as invited speakers at conferences (Gordon Research Conferences, Embo meetings, Keystone Symposia, Cold Spring Harbor Laboratory meetings, ESMO, FASEB meetings) as well as frequently invited to give seminars in other research centers. In the evaluated period, five PIs were involved in the organisation of meetings and conferences in Germany (Embo), Greece, Spain and Switzerland.

The unit's teams are highly successful at obtaining competitive national and international grants and are exceptionally well funded (Team labialisation by LNCC, ARC, FRM and ERC): seven out of nine teams have benefited from ERC grants in the reporting period.

The unit has recruited an international Scientific Advisory Board that helps to maintain high recruitment standards. This has resulted in the unit being able to recruit outstanding national and international researchers. Nearly half of the unit's team leaders are foreigners [two European (Italy and Belarus) and two American researchers (Chile and the US)].

The unit has an active scientific life inviting prestigious scientists to deliver seminars as well as attracting international visitors for short stays (two from the US, one from Chile and the UK).

Unit members and PI have an outstanding level of international networking, illustrated by high-level collaborative publications and the participation to four European Innovative training programs (ITN).

The postdoctoral students at the unit receive guidance to apply for their own funding and become independent. In the reporting period, four young researchers have successfully started their own groups outside the unit after obtaining national and international competitive grants.

The unit, being part of the Institut Curie, is extremely well-equipped being able to make use of nineteen different services and platforms including a metabolomics and lipidomics, a zebrafish facility, a Drosophila fly food and stock maintenance service and washing service, metabolomics, microscopy platform with four technical support engineers, Crispr-based screening platform, RNA-protein interaction screening, single cell technologies. These platforms are continuously upgraded through competitive funds. In this period three ITMO Cancer initiatives were obtained to maintain a state-of the art microscopy and metabolomics equipment.

The unit has recruited very active research groups that are publishing excellent or outstanding work. The unit's recruiting policy is very successful, replacing retiring groups with experienced senior teams and younger group leaders with great research potential that will help to maintain the level of excellence.

The teams have recruited international PHD students through IC3i and EuReCa programs.

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

Due to its integration at Institut Curie, the unit cannot physically grow, curtailing the possibility to attract additional outstanding team leaders. This limits the unit size to only nine teams, and consequently the retirement of one group or its move to another research institute impacts the global strength of the unit.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The outstanding scientific production of the unit is one of its major strengths. The work explores highly original topics that open up new avenues in research. On average, the unit publishes two papers per year per team (53 primary research article in the reporting period), which appear frequently in the most prestigious journals (Science, Cell, Nature, Molecular Cell, Nature Cell biology, Nature Commun, Current Biology, PLoS Biology, Dev Cell...). Some of these publications are collaborations with external groups, but most are led by the unit's teams. All teams contribute high quality outstanding research, including junior groups.

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

The unit has recruited very active research groups that are publishing excellent or outstanding work. Breakthrough findings span the fields of genome and epigenome dynamics, mechanical forces and morphogenesis, tissue growth and homeostasis and stem cell biology.

The originality of the research and its scientific quality results in the frequent publication in the most prestigious journals including multidisciplinary and specialised journals (Nature, Nature Communications, Nature genetics, Nature Cell Biology, Nature Chemical Biology, Cell, Developmental Cell, Current Biology, Molecular Cell, Cell reports, Science, Science Advances, eLife, PLoS biology, PLoS genetics, Journal of Cell biology, Embo Journal, Embo reports, Oncogene, Development, etc.).

All teams are participating to a similar level in this publication level, although some newly recruited teams need some time to develop their full potential. The PIs have obtained competitive national and international grants that should allow them to maintain the same level of excellence in research.

The unit follows Open Science policy by depositing their publications in Open archives like the French HAL or the Cold Spring Harbor BioRxiv.

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

There are no major risks. The unit is very successful.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit is focused on fundamental research, positioning itself within a continuum from fundamental research to human health. Within this context, the unit fully explores technology and valorisation prospects, which led to two patents during the reporting period. The unit is also strongly involved in outreach activities with participation well above average, including publication of articles for the public, broadcast and scientific introductory courses for children.

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

The work of the unit is focused on fundamental research, positioning itself within a continuum from fundamental research to human health. Within this context the unit fully taking advantage of the Institut Curie technology transfer office to identify projects with valorisation potential, and is engaged in pre-maturation scheme supported by the Labex, and in partnering with companies for exploring economic perspectives. This is well illustrated by the partnership with an imaging company (Zeiss) that have led to the joint development of a spinning disc microscope, testing of microscope modules and the development of a membrane that allows intravital imaging, especially useful for the analysis of tumour growth. These approaches have led to two patents filled.

The unit is highly involved in sharing its knowledge with the general public. Members of the unit contribute to newspaper articles and magazines, ranging from heredity to the use of animal models in science. They also participated in the design and preparation of scientific introductory courses for children (Les Petit's curieux and En quête de Bio) that have been standardised and shared with other units. Members of the unit also participated in the translation of a book on Crispr and genome editing that is informative to both scientists and the public. The unit also participates in the organisation of specialised courses and workshops for specialists. Globally considered, this is a great contribution given the size of the unit.

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

Given the small size of the unit and its focus on fundamental research, the unit cannot make too many contributions to the economic world, as is common to all research centres with a focus on quality science.

ANALYSIS OF THE UNIT'S TRAJECTORY

The outstanding character of UGBD has relied on the clarity of its scientific objectives and direction, the efficacy of obtaining strong support at the team and unit levels and its attractiveness for outstanding scientists. Several of these aspects will have to be dealt with within the next contract.

The current director will retire during the next period. Therefore, a new director will be appointed starting January 2025. The transition in the direction of the unit has already been well anticipated by first nominating a deputy director during the current contract, which is one of the current team leaders with an outstanding scientific career, and promoting him as director for the next contract. The unit has developed a four-point plan of research to reinforce their position at the forefront of science. This plan includes the reinforcement of research on organoids and embryoids, synthetic models that will allow approaching novel questions with direct medical applications. There is also planned a reinforcement of the computational teams with the creation of a temporary space to favour collaborations with modelling experts. This offers a very pertinent track for the next contract.

The current Labex Deep will end in 2024. To replace the existing Labex, the unit has applied to a new initiative offered by the PSL University called 'Grands Programmes'. The new scientific project, focused on tissue development, homeostasis and disease, has been submitted jointly with teams of College de France and Ibens and has great chances to be awarded. At the team level, the recent publication track record will facilitate obtaining high-level support from the most competitive grants, although reaching the same level of funding at the European level (7 ERC and 4 ITNs) will be very challenging.

The recent departure of a junior team plus the future departure of the current director will offer novel recruiting possibilities, allowing the implementation of a clearly set scientific strategy. With a very strict recruitment procedure and an attractive starting package, UGBD has been in the past successful in attracting extraordinary scientists at various stages of their career. The continuation of existing practices and the impressive local academic environment should help to maintain the unit extremely high scientific standards.

Helping define the future of UGBD, the unit frequently consults external committees composed of national and international experts. These include the Institut Curie's Scientific Advisory Board and the UGBD Scientific Advisory Board. This consultation should be praised as they can provide precious advice on the recent trends at the forefront of science.

RECOMMENDATIONS TO THE UNIT

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

The imaging platform requires urgent support due to the head of the service recently moving away from the unit. Animal facilities are also in need of support, especially during weekends. A system to cover for essential work on these periods has to be established.

An excellent mentoring program for PHD students and staff is organised by the Institut Curie. However, the number of slots available to participate in these courses should be increased as there are not enough slots to cover for the existing demand.

The impossibility to expand the unit's size and its very strict policy of recruitment is impacting the career progression of non-PI permanent scientists in the teams, as they are not allowed to recruit personnel directly under their supervision on grants they apply for. This has come as a surprise to some of them that were unaware of such conditions when they took the position at UGBD. The unit should publish a public charter describing particular conditions that are specific to this unit, so that potential new staff are made aware before taking up the position at UGBD.

Recommendations Regarding the Evaluation Area 2: Attractiveness

The unit may want to consider having a more relaxed policy to allow permanent senior researchers in each team to hire personnel under their direction with project grants they apply for. This will make the unit more attractive for senior researchers interested in joining an existing team. Allowing senior researchers to direct their own projects should be allowed only if the scientific project is in line with that followed by the team leader, the team leader agrees, and the project proposed does not interfere with the team leader's research program.

Recommendations Regarding Evaluation Area 3: Scientific Production

No specific recommendation. Maintain the current outstanding scientific production.

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

No specific recommendation. The UGBD's contributions to society are very satisfactory.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Genetics and Physiology of Growth
 Name of the supervisor: Mr. Pierre Leopold

THEMES OF THE TEAM

The research team uses the *Drosophila* model to explore the molecular mechanisms and neural circuits of organ and organism size determination and developmental precision.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous UGBD Hcéres report highlighted the international recognition and uniqueness of the PI's research lines but also expressed some concerns about the short-term evolution of the team. The projects were tailored for the PI team in Nice, and most of his former researchers did not relocate to Paris, so there could be a certain hiatus in the research as a new team would have to be assembled and acquire new knowledge and experience. Added to this was the concern that the team leader's new and important administrative responsibilities, for which he was not experienced, could slow down such research and compromise his competitiveness in the field.

Concerning these concerns, the PI has put together an active and competent team consisting of five postdoctoral students, two PHDs, and two engineers (1 IE CDD) that has made important contributions to the field and largely maintained the PI's level of excellence and leadership.

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	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	14
Sous-total personnels permanents en activité	15
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	20

EVALUATION

Overall assessment of the team

The research team has consistently maintained outstanding performance despite the challenges of assembling and training a new team's members and the administrative responsibilities involved in running the unit. The team is attractive to PHD students and postdoctoral students, and its funding level is excellent. The PI enjoys exceptional recognition and participates in multiple scientific events and outreach activities.

Strengths and possibilities linked to the context

The team visibility and attractiveness are outstanding. The PI is regularly invited to prestigious international conferences (5 Embo, 2 Gordon,) and participates in multiple review and selection panels and editorial boards and engages in outreach activities. Additionally, he has been honoured as a member of two prestigious academies, the Academia Europaea and the Académie des Sciences in France. These awards underscore the exceptional visibility and excellence of the PI and the research team. The team's funding is exceptional, including an ERC Advanced Grant, an HFSP grant, and three ANR. The team was also very attractive to PHD (4) and postdoctoral student (8).

The scientific production of the team is outstanding. During this period, the team has made several significant discoveries, leading to eleven research publications (10, as corresponding author). Two 2019 papers in *Current Biology* and *Developmental Cell* reported a circuit and novel elements crucial for ensuring developmental precision. Furthermore, they recently published a study elucidating a mechanism through which the relaxin hormone Dilp8 assures developmental precision at a specific stage of development (*Nat Commun.*, 2022). In addition to their developmental research, the team delved into the processes and signalling involved in tumour-induced cachexia in flies involving the steroid hormone. Their work sheds light on the role of the OATP importer in this complex physiological phenomenon (*Dev Cell* 2019). Finally, a study in *PNAS* in 2022 reported on female preferences for symmetrical male flies, adding an interesting dimension to the understanding of mating preferences in females. Overall, the contribution of the team has been of very high standards.

Weaknesses and risks linked to the context

The PI has maintained an excellent level of research and production despite facing considerable challenges, such as the costs associated with relocating the team and recruiting and training new staff and the unit's administrative burden. While some highly original proposed research lines highlighted in the previous UGDB Hcéres report have yet to be fully realised in published papers, it showcased the PI's continued willingness to explore uncharted domains. Nevertheless, with the impending retirement of the PI in just two years, it is evident that he has significantly reduced the breadth and depth of his research pursuits. As a result, some of the original research projects may not be sustained if they cannot ensure the permanence of an experienced researcher who could carry forward these research avenues.

Analysis of the team's trajectory

The research focuses on organ size determination and metabolic homeostasis and growth.

In the first research line, the team focuses on the comprehensive examination of hormonal signals and physical constraints' contributions to regulating growth arrest and size adjustment during the early pupal stage. The plan is that this or a large part of this research line is overseen by a senior postdoctoral researcher, forming the cornerstone of her application for an independent group leader.

The second line of research focuses on metabolic homeostasis and growth. They study the role of storage proteins in controlling organ size and scale. They will also investigate on tumour growth, a priority topic at the Institut Curie, focusing notably on the role of LSP/hexamerin protein storage. Also related to tumour growth, they developed a paradigm to investigate the influence of the microbiota on tumour development.

As the PI will retire in two years, this second research project will be taken over by a former postdoctoral student who has already obtained an independent PI position in Japan.

Both lines of research are interesting and promising, and the supervision and continuation by researchers trained in the team demonstrate good strategic plans and mentoring to ensure a smooth transition.

RECOMMENDATIONS TO THE TEAM

As the PI's retirement approaches, the recommendation is to ensure a smooth transition of these lines of research and to make the best use of his remaining time in the field.

The committee wishes to recognise the outstanding career of the PI and the important contributions he made to the field of systemic growth control.

Team 2: Polarity Division and Morphogenesis
 Name of the supervisor: Mr. Yohanns Bellaïche

THEMES OF THE TEAM

The team studies the regulation of cell polarity during division and morphogenesis, using cutting-edge live imaging and physics to explore the interplay of mechanical forces and cell size and physiology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No major recommendations were made

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	2
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	2
Sous-total personnels non permanents en activité	6
Total personnels	14

EVALUATION

Overall assessment of the team

The team has made influential contributions to the field with an outstanding scientific production both in quantity and quality. The team implements innovative methods to understand tissue dynamics using an interdisciplinary approach that includes physics and bioinformatics to complement the studies of cellular biology and complex live imaging data and modelling. The PI has outstanding international visibility and is invited to major conferences and co-organises prestigious courses and conferences. The team's funding is outstanding with two ERC grants.

Strengths and possibilities linked to the context

The team has outstanding visibility in the field and is continuously invited to major conferences and to participate in organising highly prestigious courses and conferences. The team has participated in 48 seminars and wrote seven review/book chapters. The level of funding is outstanding, including notably two ERC Advanced Grants awarded to the principal investigator. The attractiveness of the team is reflected by its composition, with three

senior researchers and eight postdoctoral students over the period under evaluation who have made one or more contributions to the team's publications. Also, showcasing the PI's excellent mentoring skills, he has supervised five PHD students, who contributed to several publications each, and a former postdoctoral student has obtained a permanent position as a lecturer. The team is strongly engaged in training, contributing to master courses, organising workshops and international courses, and teaching.

The scientific production of the team is outstanding, with 21 articles in top-ranked journals. The team is interdisciplinary, including physics and bioinformatics and modelling to complement cellular biology and the complex live imaging data. The team has made influential contributions. They discovered cytokinesis relies on interactions between the dividing cells and their neighbours, mechanical forces and specific RhoGTPases (Nature 2017, JCS, 2018; CB, 2023). Quantitative assessment of mechanical stress and morphogenetic forces revealed novel features of tissue morphogenesis involving actomyosin stress fibres (Science 2020). These studies also provided new evidence of the existence of a cell-size ruler and how such a ruler may tune proliferation and apoptosis and ultimately regulate cell numbers and tissue scaling. The team has also continued implementing innovative methods to understand tissue dynamics (Dev Cell 2021, Dev 2022,) that also opened collaborations with researchers using vertebrate systems (NCB 2017, and 2022, Science 2019).

The PI also engages in many outreach activities, training, and gender equality.

Weaknesses and risks linked to the context

The only potential risk of this outstanding research team is that their research may generate vast amount of data, and storage could become an issue. However, it is worth noting that in the previous report, this concern was also raised, but the principal investigator did not express any concerns in this regard.

Analysis of the team's trajectory

The four research lines have demonstrated high productivity, use innovative approaches, and have fostered collaborations with other members of the units, enabling the expansion of their research into vertebrate systems. One project delves into the investigation of cell division dynamics during morphogenesis, while the others concentrate on the problem of scaling. These are outstanding research lines that focus on understanding how developmental time influences and impacts morphogenetic events and cell properties during scaling, both at the organ and organism levels. These research directions build upon the team's previous work and propose intriguing hypotheses that can be tested to uncover the cellular dynamic properties, ensuring cell migration velocity scales with body size and occurs at the correct timing.

RECOMMENDATIONS TO THE TEAM

No specific recommendations. The team is performing outstandingly at all levels, with an outstanding level of production, funding and excellent mentoring.

Team 3: Epigenetic Decisions and Reproduction
 Name of the supervisor: Mr.s Déborah Bourc'his

THEMES OF THE TEAM

The team analyses the epigenetic information regulating processes of reproduction and early development in the mouse. Their work is mainly focused on DNA methylation and explores how several aspects of genome biology such as genomic imprinting and transposon regulation control cell fate.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No major recommendations were made in the previous report except to secure funding for animal housing. This has been largely addressed with the numerous grants obtained, including an ERC grant.

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	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	11

EVALUATION

Overall assessment of the team

The team has been extremely productive publishing outstanding research in top journals. It has an outstanding visibility and recognition.

Strengths and possibilities linked to the context

The visibility and attractiveness are outstanding. Five prizes were attributed to team members, including the prestigious Grand Prix FRM to the PI. The PI is regularly invited to international conferences (5/year), including prestigious ones such as FEBS, CSHL, Gordon conferences, and was the keynote speaker at an Embo workshop. She presents around three seminars/year at academic institutions. She is, or has been, part of seven advisory boards including two international ones (Embo council, Babraham institute) and has formed part of the Reviewing board of the journal eLife. The team has outstanding capacity to obtain major grants (ERC Consolidator grant; four ANRs with three in coordination; FRM team label and ARC team label; Bettencourt Schuller Foundation Prize); between 2017 and 2022. The team is attractive for students and postdoctoral students. Seven postdoctoral students and eight PHD students were hired during the last contract, which is

excellent for a team of this size. Nearly all PHD students published, with four of them as the first author (the others might have graduated too recently), which is excellent. Since the last evaluation, the team has strengthened with two CRCN (both of them left to build their own team) and four engineers at all times, including a bioinformatician.

The team has an outstanding scientific production with a long-lasting expertise in deciphering the DNA methylation impact. Their analyses encompass the role of DNMT3s during spermatogenesis, Transposable Element (TE) regulation during spermatogenesis as well as early embryo development during germ layers and germ cell differentiation. Using a powerful mutagenesis screen, they uncovered a novel pathway, m6a RNA to tame TE activity. Local and foreign collaborations also brought excellent production. Collectively the work led to ten publications as first/last co-authors, often published in leading journals (Nature, Nature Genetics, eLife, Genome Biology), nine articles in collaboration and six reviews/book chapters (Nature Reviews Mol Cell Biol, Embo J).

The non-academic activities are outstanding, with interviews for TV and radio, public debates and interactions with schools.

Weaknesses and risks linked to the context

The two CRCN have left the team to build their own teams in 2019 and 2022. While this indicates the high quality of the team, the structure of the team will probably be impacted.

Analysis of the team's trajectory

The team is changing its main focus, leaving aside DNA methylation and focusing their interest on transposable elements. Using state-of-the-art techniques, they are building on their recent publications to 1) decipher further the impact of m6A RNA methylation, 2) find other pathways of TE repression, and 3) TE expression regulation and its impact in male germ cells. These three lines of research are ambitious and have strong preliminary data. An ERC Advanced grant was obtained in 2023, securing the funding of the project.

RECOMMENDATIONS TO THE TEAM

The committee recommends continuing the outstanding work.

Team 4: Mechanism of repression by Polycomb proteins
 Name of the supervisor: Mr. Raphaël Margueron

THEMES OF THE TEAM

The team is interested in understanding the mechanisms underlying the epigenetic regulation of gene expression in mammals. It focuses most of its research on the Polycomb group proteins and uses a variety of state-of-the-art molecular approaches to reveal how they repress transcription and how their activity is regulated.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was praised for the excellent quality of its work and its efforts in setting up the Crispr-Cas9 platform in the institute, but it was recommended to increase international visibility and to prioritise its projects in view of limited funding. It is unclear whether the team took specific measures into those directions. Yet, the funding of the team was not a limitation to develop several projects to maturity and make important scientific contributions in different subfields of epigenetics, which strengthened the international standing of 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	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	12

EVALUATION

Overall assessment of the team

The team tackles important questions in the epigenetic field and made groundbreaking discoveries in this highly competitive field. Given the size of the team, its production has been outstanding both in terms of quality and quantity. The team's reputation is very strong too. It is well recognised at the international level and is extremely attractive to PHD and postdocs. Its level of funding acquisition was outstanding.

Strengths and possibilities linked to the context

The team visibility and attractiveness are excellent to outstanding. The PI is involved in science evaluation as VP of Inserm CSS1, and he is well recognised at the international level, as shown by several contributions to reviews or commentaries for well-established journals (Curr. Opin. Chem. Biol., Nat Chem. Bio., Oncogene, Trends Biochem. Sci...) and invitations to international conferences (Embl, Esmo, FASEB). He was awarded a prize in cancerology from the French Academy of Sciences in 2017 and obtained a 'Grand Prix Junior' from the Fondation de France in 2022. The team was extremely attractive and strongly involved in training through research, with six PHD students and five postdoctoral fellows hosted during this period. Of note, one of the postdoctoral students in the team recently obtained a permanent Inserm research position. This should compensate for the departure of a permanent researcher from Dr Heard's former team, who joined in fall 2019 and now wishes to develop more independent lines of research. With ~2.3M€ raised during this period, the team was very well funded. In particular, it obtained several major national grants as coordinator (INCa, FRM Team, ANR) or partner (2 INCa, 2ANR), as well as one Gilbert Foundation grant (as partner).

The scientific production of the team is outstanding. The team obtained several major results during the past period. Notably, their work provided deep insights into the mechanisms underlying PRC2-mediated gene repression, they identified and characterised new regulators of PRC1 and PRC2, and their work challenged the idea that the lncRNA Hotair bridges PRC2 to chromatin. The team also revealed the impact of the lncRNA Xist in the maintenance of X inactivation and its relationship with breast tumour development. Altogether, the production of the team is impressive: it published 21 research articles, including six major publications as PDC (Cell, Embo J, 2 Nature Comms., Nature Genetics, PNAS).

The team contributed to science valorisation: it obtained one patent and another one is in progress.

Weaknesses and risks linked to the context

The involvement of the team in the diffusion of science toward the general public or cancer associations is limited.

Analysis of the team's trajectory

The team projects are organised along four main axes of research which are very ambitious and rely on cutting-edge technologies. The first one, which aims at identifying the interplay between chromatin regulators by performing a large-scale screen coupled with scRNA-seq (Perturb-seq), might lead to a significant shift in the team's focus. The other three axes are more focused on Polycomb regulation and mode of action in line with the team's expertise. The fundamental interest of these lines of research is very strong, and they also hold good potential in terms of cancerology.

Several contracts and some human resources have been secured already to develop these projects.

RECOMMENDATIONS TO THE TEAM

The PI is encouraged to apply to major European grants and to increase the international exposure of the team.

The team could interact more with the society.

Team 5: Fate and plasticity of epithelial stem cells
 Name of the supervisor: Mrs. Silvia Fre

THEMES OF THE TEAM

The team's research focuses on tissue-specific stem cells, differentiation, and plasticity during embryogenesis and adult homeostasis. The team seeks to unravel the molecular circuits that control stem cell behaviour in context to understand better how organs are formed and also how breast tumours arise.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Below, we outline how the team has addressed each of the recommendations provided in the previous evaluation, including the suggestion to increase collaborative authorship and reviews and more public engagement.

—Several of the team's publications of this period included international collaborators, and notably, the team contributed to a high-impact international collaboration published in Nature Communications in 2022.

—Furthermore, the team has made substantial contributions to the field reviewing methods and the current state-of-the art of mammary gland field and cancer, including Current Opinions in Cell Biology (2019), Biomedicines (2018), Methods in Molecular Biology (2022), book chapters in Stem Cell Biology and Regenerative Medicine (2021), 'Intestinal Stem Cells' (1st Edition in 2014) and 'Mammary Stem Cells' (2nd Edition in 2021).

—The team leader has also played an active role in the academic community and public engagement, being an invited speaker at over 30 conferences, including as a keynote speaker in important international conferences, organising a top-tier international meeting (the Notch Meeting XI in Athens, Greece), and a national meeting at the Institut Curie (Paris, 2019).

Moreover, the team leader has expanded her involvement in committees and juries responsible for evaluating prestigious international and national grants and faculty positions.

It was also recommended to explore effective ways to further investigate newfound lineage events, developing in vitro systems and conducting molecular studies for insights. During this period, the team has shifted their research focus from intestinal stem cells to breast cancer, capitalising on their discoveries and innovative tools.

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	2
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	3
Total personnels	7

EVALUATION

Overall assessment of the team

The team focuses on the intricate field of stem cells and cancer using several systems, innovative tools and mouse genetics, producing excellent to outstanding publications. At present, the visibility of the team, excellent, is increasing. The funding remains national, and some are relatively modest grants.

Strengths and possibilities linked to the context

The team has achieved excellent visibility and recognition. The PI has participated in 30 communications/conferences, several as a keynote speaker. In addition, she has organised and co-chaired national and international conferences and courses in her field of expertise. The team has been an attractive choice for master students, graduates, and postdoctoral researchers. During this time frame, one CRHC researcher joined the group in 2019 and contributed to two publications. Notably, six out of seven postdoctoral researchers have actively contributed as authors in the team's publications: One postdoctoral researcher has notably co-authored four publications and served as a co-senior author alongside the PI in one of these publications. Three ex-lab members obtained independent PI positions. This exceptional level of engagement shows the PI's mentorship skills. The team is now more actively engaged in international collaborations in line with the recommendations from the previous Hcéres evaluation report. Beyond their research publications, the team has contributed to the field by producing reviews/book chapter on mammary glands, stem cells and cancer. The team leader is the coordinator of ARC 2022-25 and a partner in ANR 2022-26 and 2023-27.

The scientific production has been excellent to outstanding. The team has continued to excel in their scientific works in stem cell biology and mammary gland morphogenesis, and has consistently demonstrated its commitment to advance these areas of study by utilising and pioneering innovative tools in mouse models for the analysis and tracking of stem cells and their progeny. Additionally, their research scope has broadened to include breast cancer studies, and they have leveraged cutting-edge methodologies to trace cell lineage and explore tumour heterogeneity. These investigations have yielded significant outcomes, resulting in the publication of five original research papers where the PI either served as the last or co-senior author, with their work being featured in reputable journals, *Nature Cell Biology* (2018), *eLife* (2022), *Science Advances* (2021), *Cell Reports* (2022), *Scientific Reports* (2019). Additionally, two studies have been made available on BioRxiv.

The team leader and team engaged in public communications to promote awareness and understanding of their breast cancer project.

Weaknesses and risks linked to the context

The team leader has highlighted several challenges and concerns. She has raised concerns about the availability of permanent technical positions. She has expressed difficulties in recruiting and attracting postdoctoral researchers with the required expertise and the team's limited administrative support.

The team research generates a substantial amount of data, necessitating additional data storage space and utilities to manage and process this data effectively.

Analysis of the team's trajectory

The team has two main axes of research.

Project 1 relates to the coordination between cell fate specification and morphogenesis, focusing on branched organs like the mammary gland. The overarching goal is to scrutinise the molecular and cellular underpinnings of such coordination between stem cell behaviour and morphogenesis. The team leverages tools to label stem cell lineage to track cell and tissue dynamics, including barcode-based lineage tracing, single-cell RNA seq, spatial transcriptomics, multistage live imaging in organoids and functional assessment in mice. Using the same tools, the team will investigate the mechanisms behind acquiring multipotency during tumour initiation. Collaborations with a Czech researcher and another unit member will offer additional expertise in investigating fibroblasts in cellular and tissue dynamics and in implementing methods for recording gland cellular dynamics.

Project 2 aims to study the clonal history of breast cancer in mice using the barcode-based cell lineage tools. The team has already made significant breakthroughs in this problem and will continue using this paradigm and

tools to track tumour cell lineage precisely. The team aims to answer critical questions in the field, such as the hierarchical relationship of tumour cells and, what mechanisms contribute to intra-tumoral heterogeneity and the fitness of malignant clones.

In addition, the team is collaborating with Institute de la Vision, Paris to study redox signalling and its role in the maintenance and proliferation or differentiation of stem cells.

Overall, the scientific trajectory and the two lines of research are highly promising and demonstrate a commitment to advancing the field, investigating long-standing questions in cancer with new angles and tools that could have significant implications. The team's previous publications showcase their excellent ability to lead cutting-edge research, both basic and with significant translational potential.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to pursue high-quality science by consistently employing innovative techniques. To sustain the exceptional trajectory they have established, it is recommended that the team augment their workforce by hiring additional permanent engineers and attract researchers.

The utilisation of mouse models demands substantial resources, not only manpower but also funding. The ARC coordinated program is scheduled to end in 2025, and there are two ANR partnerships set to end in 2025 and 2026. Considering this, the recommendation is to secure adequate funding to maintain the current level of research activity by applying for international grants.

Although both axes of research are excellent and have high potential, the second addresses long-standing questions in cancer which are also highly competitive field. It is recommended that the team strive to find a unique niche that would help to secure and diversify their funding sources.

The team should aim to maintain and strengthen its communication and interaction toward society.

Team 6: Stem Cells and Tissue Homoeostasis

Name of the supervisor: Mrs. Allison Bardin

THEMES OF THE TEAM

The team is interested in the regulation of stem cell fate and function during a lifetime. Using the *Drosophila* intestine as a model system, it conducts genetic and molecular analyses to study the transcriptional and chromatin changes that orchestrate stem cell differentiation and to analyse stem cell genome stability.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Overall, the team was encouraged to sustain its excellent activity and to pursue its current projects. The analysis of the team's report shows that these recommendations were 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	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	5
Doctorants	1
Sous-total personnels non permanents en activité	6
Total personnels	10

EVALUATION

Overall assessment of the team

The scientific production of the team is original and of excellent to outstanding quality, with 6 important research publications in the field of stem cell differentiation and genome stability. The team is recognised at the international level and very attractive to students and postdocs. It obtained an excellent level of funding. The interactions with society are remarkable, with a strong dedication of the PI toward outreach activities.

Strengths and possibilities linked to the context

The visibility and attractiveness of the team are excellent to outstanding. The international recognition of the PI is very strong as demonstrated by many invitations (42) including as a speaker to major conferences (International Stem Cell Society, Embo workshop on Aging), or by invitations to write reviews and commentaries (6) in respected journals (Current Op. Cell Biol. Current Biol. Nature Cell Biol...). She obtained a prestigious Schlumberger Foundation award in 2017 and participated in various evaluation committees (Fondation ARC, grant agencies in Belgium, Denmark and Poland). The level of funding of the team is excellent (~1.4M€ since 2016), with two ANR, two FRM Team, one WWCR UK and one Fondation ARC grants. The team was particularly

attractive to postdoctoral student (7), including foreigners, and five of them obtained their own grant (3 Fondation ARC, 1 FRM, Korean NRF). The team also hosted a very good number of PHD students (4). Of note, one young researcher recruited in 2016 in the team obtained an ATIP as well as an ERC Starting Grant and established her own team in another Institute in 2023 to pursue her line of research on somatic transposition.

The scientific production of the team is excellent to outstanding. This well-established team continues to develop some very original lines of research. It made important contributions in the field of stem cell biology and genome stability thanks to its expertise in genetic, imaging and molecular analyses and to the development of advanced bioinformatic pipelines for whole genome sequence analysis. For instance, the team unravelled new players in the regulation of intestinal stem cell (ISC) self-renewal and characterised the genomic landscape of somatic mutations in ISC. Their findings led to six research publications of excellent level, including five as corresponding author in *EmboJ* (2), *Genome Research*, *Dev Cell* and *PLoS Genetics*. They also accumulated interesting results concerning chromatin state remodelling during ISC differentiation and the process of loss of heterozygosity in the fly intestine.

The PI is strongly involved in teaching, for instance with the organisation of an International Course in Dev Biol and Stem cells. She is very active in the animation of the French developmental biology community, for which she spearheaded the creation of a French Stem Cell Network (GDR). She also launched an interesting program 'En Quête de Bio' for primary school pupils and other members of the team are involved in outreach activities.

Weaknesses and risks linked to the context

At the time of the visit, two former PHD students have not yet obtained a first author publication.

Although the PI is well recognised, the international collaborative network of the team is not particularly strong.

Analysis of the team's trajectory

The project of the team is largely in continuation with its present activities and will encompass three main areas of research on ISC: (1) gain further insights into ISC differentiation at the chromatin level, with a challenging project on the impact of an early diet on ISC fate at later stages (an ANR grant has recently been secure to develop this line) of research; (2) explore the changes in stem cell genome during aging (mechanisms underlying natural loss of chromosome X or loss of heterozygosity); (3) explore the impact of tissue mechanics on ISC (in collaboration with one team in the unit). These three lines of research are interesting and very ambitious. However, the synergy between the three axes of research (themselves subdivided in 2 or 3 themes) is not fully apparent and there is a slight risk of dispersion. In addition, the project may need to be accommodated depending on the team workforce.

RECOMMENDATIONS TO THE TEAM

The other senior researcher in the team should seek to obtain an HDR in order to increase the capacity of the team to host PHD students.

The team should strengthen its network of international collaborations and consider integrating European networks.

Team 7: Long noncoding RNAs in vertebrate development
 Name of the supervisor: Mrs. Alena Shkumatava

THEMES OF THE TEAM

The team's research is based on the study of the cellular and molecular functions of regulatory non-coding RNAs and their biological function. Recently, they developed an interest in the identification, characterisation and targeting of regulatory RNA motifs within untranslated domains.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations from the previous report (*italics*) have been addressed as follows:

a) To finalise the ongoing projects as fast as possible. To exploit its expertise to establish contact with clinically oriented teams and with private biotech or pharmaceutical companies.

This has been partially addressed with the team publishing papers in high-ranking journals (Nature Strc Mol Biol, Nature Commun, Genome Biology), other papers such as iScience and RNA, plus two manuscripts in preparation. Moreover, the PI got closer to private biotech and got funding from Biogen (90k€).

b) To strengthen the composition of the team and to increase the number of technical staff (engineers) to help in the postdoctoral/student research activities.

This seems not to have been addressed, at least according to the information provided. The PI has been promoted to DR1 and got the HDR. However, no additional permanent researchers, technicians or engineers have been incorporated into the team.

c) To focus its research on one or few biological questions in view of limited funding and the size of the lab.

It is unclear whether the team took specific measures in this respect. However, the team's funding has not been a limitation as they obtained 904k€ since 2018 from different funding agencies (FRM, ANR and Biogen). On the other hand, the team recently expanded their scientific interests to the identification, characterisation and targeting of regulatory RNA motifs within untranslated regions of mRNA and viral RNAs.

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	3
Sous-total personnels permanents en activité	4
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	5

EVALUATION

Overall assessment of the team

The team studies important questions in the non-coding RNA field and made important discoveries. Its production has been excellent, although considering the size of the team and the available funding the publication record is a bit limited. The team is well recognised with high international visibility of the PI. Its level of funding was excellent. The team is very active in teaching activities.

Strengths and possibilities linked to the context

The visibility and attractiveness of the team are excellent. The PI is involved in science evaluation as a grant peer reviewer for several national and international funding agencies. She is well recognised at the international level, as shown by invitation to international conferences (Embo, Royal Society, Katzir Conference, etc.). The team was strongly involved in research training with six PHD students and three postdoctoral fellows hosted since 2013. According to the proposal, the group has been composed by three PHD students, one postdoctoral student and the PI during the last five years. The PI has been highly involved in organising teaching courses at Institut Curie, Cambridge (UK) and Embo. With ~900k€ raised during this period, the team was well funded. In particular, it obtained three national grants as coordinator (1FRM, 1ANR) or partner (1ANR), as well as funding from Biogen as coordinator.

The scientific production of the team is excellent. The team obtained several important results during the past period. Notably, they demonstrated the importance of an endogenous RNA-directed miRNA degradation required for normal animal behaviour, and therefore demonstrated the physiological relevance of post-transcription miRNA degraded directed by a genome-encoded transcript. They observed that functions of rapidly evolving lncRNA transcripts could be defined by conserved RNA-protein interactions, and that different subcellular localisations may result in different functions. The team also developed strategies for genetic inactivation of long non-coding RNAs in animals, and the iNCPrint (an in-cell method to identify RNA-protein interactions). Altogether, the production of the team is excellent: it published five research articles from the lab, including three major publications (Nature Commun., Nature Str Mol Biol., Genome Res.), three collaborative articles, and three invited reviews. They are preparing two more manuscripts.

Weaknesses and risks linked to the context

Although the team has been productive with the functional studies and the development of different tools/techniques, there is a risk of thematic dispersion focusing in the tool development since they face several technological challenges working with lncRNA. Now, they have the opportunity to demonstrate how structure lncRNA and biological function can be related.

Analysis of the team's trajectory

Not applicable.
The team left UGBD on 1 October 2023.

RECOMMENDATIONS TO THE TEAM

Not applicable.
The team left UGBD on 1 October 2023.

Team 8: Mechanics of mammalian development

Name of the supervisor: Mr. Jean-Léon Maître

THEMES OF THE TEAM

The team studies how early mammalian embryos shape themselves. They employ live imaging, biophysical tools and genetic perturbations to characterise the forces that form the embryo and reveal the underlying processes.

CONSIDERATION OF THE RECOMMENDATIONS OF 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	0
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	3
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	5
Total personnels	8

EVALUATION

Overall assessment of the team

The team currently formed by biologists, physicists and engineers, uses innovative interdisciplinary approaches to quantitatively measure and perturb the forces involved in shaping the early mammalian embryos. The team has made outstanding contributions to the field of mammalian preimplantation mechanobiology. The team has managed to secure an outstanding amount of funding.

Strengths and possibilities linked to the context

The visibility and attractiveness are outstanding. The PI visibility is attested by his multiple meetings and seminar invitations, being awarded the CNRS Bronze medal and the Embo Young investigator prize. The team has managed to secure outstanding funding, including two ERC Grants (Starting and Consolidator) awarded to the principal investigator. The PI has supervised five PHD students (three of which have already graduated), who contributed to several publications, as well as five postdocs and 6 master students. The team is engaged in training, contributing to multiple PHD and master courses, organising workshops and international courses and teaching. This interdisciplinary team has grown substantially from the last reporting period, and includes biologists, physicists, engineers working together to understand the preimplantation embryo in mice and more recently also in humans. Four review papers were published.

The scientific production of the team is outstanding. The team has made substantial contributions to the field of mammalian preimplantation mechanobiology. They discovered the mechanism by which the first mammalian lumen forms through hydraulic pressure that breaks cell-cell contacts (Science 2019). They found that intercellular fluid accumulation is cell autonomous (eLife 2021) with inverse blebs growing at cell-cell contact (bioRxiv, 2023). The group also studied the reorganisation of the cytoskeleton in the early mouse embryos that undergo periodic contraction (PLoS Biology 2022). More recently, the group diversified and initiated studies on human preimplantation development. They characterised the mechanics of human embryo compaction (bioRxiv), and studied the origin of failure in compaction which is known to negatively impact fertility in assisted reproductive technologies (bioRxiv).

The team is also engaged in various outreach activities with high school students and the public.

Weaknesses and risks linked to the context

No weaknesses observed

Analysis of the team's trajectory

The team has a well-defined research direction, focusing on morphogenesis in the early mammalian preimplantation embryos. The team uses innovative approaches to quantitatively measure and perturb the forces involved in shaping the early embryos. This includes microfluidic approaches to control the embryo's environment and micromanipulation using optical tweezers and micropipette aspiration to measure and perturb membrane and nuclear mechanics. These biophysical tools are combined with various genetic and chemical perturbations that modify the properties of the embryo. Using these tools combined with extensive live imaging, the team has made important discoveries and seems on track to make further impactful contributions to our understanding of the role of physical cues in shaping the early mammalian embryo. Their research addresses fundamental questions in animal morphogenesis, which also have important implications for human health and fertility.

The team has established fruitful interactions with several groups (both local and external) to promote the different aspects of their research agenda, including theoreticians (Sens, Turlier, Mukherjee), experimental biophysicists (Bassereau, Piel, Descroix), as well as physicians in fertility clinics (Patrat).

RECOMMENDATIONS TO THE TEAM

The committee recommends continuing the outstanding work.

Team 9: Development and Homoeostasis of Mucosal Tissues
 Name of the supervisor: Mr. Pedro Hernandez

THEMES OF THE TEAM

Team's project focuses on the crosstalk between gut microbiota and the resident immune system. The objective is to decipher the role of the microbiota on the immune system and tissue development using the zebrafish model. The role of cytokine signals, and interactions between host cells and the microbiota in gut development, are especially studied.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team leader was recruited as CRCN Inserm and was appointed junior group leader in September 2019, and thus was not previously evaluated.

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	3
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	5
Total personnels	9

EVALUATION

Overall assessment of the team

This team is a new group that joined Institut Curie in 09/2019 and was thus impacted by the Covid-19 pandemic. The team leader has not yet published as first/last/corresponding author from the new lab. The recent high funding raising and recruitment of PHDs and Post-doctoral fellows should be beneficial for the next years.

Strengths and possibilities linked to the context

This team is a new group that joined Institut Curie in 09/2019. The recent start of the team, together with the Covid pandemics, makes an evaluation of the scientific production at this time point difficult or premature.

The team leader obtained his HDR in 2020 allowing PHD supervision (3 recruited) and has attracted three postdoctoral students. The team has a suitable size with a good balance of scientists, students and research assistants.

The team leader has strong financial support as coordinator: the team leader obtained financial support from ANR-TERC 2020-21, FRM-amorçage (150k€) 2020-22, Ville de Paris Emergence (210k€) 2022-25, ATIP-Avenir (175k€) 2022-25, team leader is now the recipient of an ERC starting grant (2022/2027), and raised 1.5 M€. The team attracted two postdoctoral students (02/2020-01/2024; 01/2021-09/2023) and now mentor three PHD students (beginning 2019, 2020, 2021); technical staff (3) joined the team.

During the period of evaluation, the PI has published three papers as a co-author. Two publications are collaborations with foreign groups, one where the PI is second author is from his previous labs when working as Postdoctoral student in Freiburg.

The team leader has succeeded in obtaining grant funding and has established collaborations with Institut Pasteur, Karolinska Institute, Imagine Institute, Hong Kong and Chile.

Overall, the team has gathered what is needed to succeed in the future.

Weaknesses and risks linked to the context

A more in-depth presentation of the team preliminary results would have allowed a more realistic evaluation of this junior group.

The supervision of three PHDs and three postdoctoral students by a single junior group leader can raise problems of efficacy in resolving trouble shootings and training.

The turnover of non-permanent personnel during the next period could impact the team's scientific research output.

Since joining the Institut Curie, the team leader has published high quality papers from his previous laboratories but, at the time of the visit, had not yet published an article as last or corresponding author.

Analysis of the team's trajectory

The project has two aims. 1/ Study the role of cytokines in gut development and regeneration. The work will focus on the role of IL22 and IL26 cytokines using the zebrafish model. IL22 was shown by the team leader in previous labs to be involved in the development of the enteric nervous system. The team is now interested in the mechanisms of action of IL22 in neuronal and gut development. The possible involvement of IL26 in gut regeneration is also analysed. 2/ Study the role of developmental waves of immune cells: the team is developing new optogenetics tools for spatiotemporal tracing associated with specific ablation of immune cells (neutrophils, macrophages, ILCs). The project is ambitious. The team leader has set the human resources and funding required to implement the work planned. Post docs and PHD students are each assigned part of the project and relevant collaborations have been established.

RECOMMENDATIONS TO THE TEAM

Moving to Institut Curie represents a serious challenge for any junior team leader. The committee recommends the team to make sure that when publishing any future collaborative work, the team members appear in a strategic position that reflects the involvement of its postdoctoral and PHD students as well as the PI's leadership in the work.

The committee recommends that the team leader surrounds himself with experienced postdoctoral researchers and actively pursues collaborations to carry out their work.

CONDUCT OF THE INTERVIEWS

Dates

Start: 10 octobre 2023 à 8 h

End : 11 octobre 2023 à 13 h

Interview conducted online

INTERVIEW SCHEDULE

Day 1, October 10 2023

- 8:45 – 9:00** —Welcome Coffee – *BDD Hall*
 —Preliminary meeting of the expert committee (closed hearing)
Attending: expert committee, Scientific Officer (Yacine Graba, Scientific Officer – SO)
- 9:00 – 9:15** Presentation of the Hcéres evaluation to the unit (SO)–*BDD Amphitheater*
Attending: expert committee, SO, representatives of institutions and all unit members.
- 9:15–10:15** Presentation of the research unit by the current and future unit directors (including 15 min questions)–*BDD Amphitheater*
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 (4 teams)–Individual desks**
 (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.*
10:30–Leopold
11:05–Bellaïche
11:40–Bourc’his
12:15–Margueron
- 12:50–1:30 p.m.** **Lunch**
- 1:30 p.m.–2:15 p.m.** **Parallel meetings (3 sub-committees)**
 —Meeting with technical and administrative personnel – *BDD annexes 3.4*
Attending: Technicians, Engineers, Administrative staff, subcommittee 1 of expert committee, SO
 —Meeting with thesis students and postdocs–*BDD Amphitheater* *Attending: PHD students and postdocs, subcommittee 2 of expert committee, SO*
 —Meeting with researchers and professors (without PIs) – *3rd floor office*
Attending: Researchers except group leaders, subcommittee 3 of the expert committee, SO
- 2:15 p.m.–2:30 p.m.** **Committee debrief** (closed hearing)
- 2:30 p.m.–3:15 p.m.** **Meeting with the representatives of supervising bodies** (CNRS, Inserm, Curie, University).
Attending: expert committee, representatives of Institutions, SO
- 3:15 p.m.–3:30 p.m.** **Break**
- 3:30 p.m.–5:50 p.m.** **Team scientific presentation Session 2 (4 teams)**

3:30 p.m. —Fre
4:05 p.m. —Bardin
16 h 40—Maitre
5:15 p.m. —Hernandez

Day 2, October 11 2023

- 9:00–9:30 **Committee debrief** (closed hearing)
Attending: expert committee, SO
- 9:30–10:00 **Meeting of the Committee with the head of the unit.**
Attending: Unit Director, expert committee, SO
<https://hceres-fr.zoom.us/j/91733978264?pwd=TENaT0ErWE1oN1lUbw5GTVhNTU93QT09>
ID de réunion : 917 3397 8264
Code secret: 595,677
- 10:00–1 p.m. **Deliberation of the Committee** (closed hearing)
Attending: expert committee, SO

GENERAL OBSERVATIONS OF THE SUPERVISORS

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Objet

Comments to HCERES Evaluation report of the Unit
UGBD - Génétique et Biologie du Développement
DER- PUR250024485 - EV 0753172R
Evaluation campaign 2023-2024 / Group D

HCERES

For the attention of HCERES President,
Mr Stéphane Le Bouler
and the HCERES Expert Committee

Paris, 30th January 2024

Dear All,

We thank the Committee for the extensive assessment of our work and the very positive evaluation of our unit. We provide here answers to a few points raised in the written report.

- p.6 "While the visibility is outstanding, its full potential for attractiveness is limited by the physical size of the unit."

Indeed, the size of our unit is constrained by the physical limits of our building. However, we would like to make two remarks on this point.

- we have discussed with the Direction of the Research Center the possibility to gain some space on the 5th floor of the building (approx. 60m² of dry lab) after the move of the Department of Information Services (DIS) to another location. This will allow recruiting a new team of computational biology/physical modeling through an official call end of 2024/beginning of 2025. This initiative is jointly supported by the Department of Physics (CNRS UMR 168) with the aim of strengthening scientific interactions with modeling experts on site. In case the space is made available before, we propose to use it for a "Collaborarium" to host visiting experts in computational science involved in collaborative work with teams of the Research Center. Our scientific expertise in tissue growth, physiology and synthetic embryology will greatly benefit from the future implementation of mathematical/physical modeling.

- keeping the unit to its medium size (10 groups after the recruitment of the modeling team) can be an asset in terms of team interactions and management. In addition, as mentioned by the committee, our unit is embedded in a very rich and diverse local academic environment within and around the Institut Curie, which ensures strong synergies both at the scientific and organizational levels.

- p.7 "However there has not been much progress in the promotion of staff working at the unit's teams with a permanent position (...), whose career progression and independence are thwarted unless they leave the unit".

This is a major point made by the present HCERES committee, which is reiterated at different places in the report (see also recommendations). Of note, the evaluation made by the previous HCERES report (2017) on this same point was the following:

“One serious issue that appeared to the committee was a clear lack of ambition and self-confidence from postdocs. This means that the ambition for many of them was to remain as a CR in their current lab rather than go out and develop their own group. This is highly surprising from a group of international postdocs working in a top institution and publishing high profile papers! This was attributed to several factors: The ‘comfort’ of staying in a well-funded lab in a well-supported institution at the heart of Paris; the problem of twobody problems that makes it very difficult to move to a smaller town in France where opportunities for two jobs might be limited; perhaps also a lack of enough mentoring from PIs to promote their postdocs and encourage them to leave with their project. So far, only one group has produced independent PIs. The others have recruited CRs who are producing well but soon realized that it would be difficult for them to go on to the job market.

During the discussion with non-PI permanent researchers, it appeared that most expressed reservations about what was required to establish themselves as PIs in the French system. They indicated that they would have benefited from a better mentoring system within the Institut Curie to make them aware of all the options available at the different stages of their careers, about understanding how to apply to the French grant system and what the best options were for them to obtain ‘corresponding’ authorship on papers. However, a few recognized that they had been encouraged to become independent by their PI.”

We have since addressed this important issue through a series of active discussions between the unit direction and the permanent CRs, the non-permanent postdocs, as well as the unit PIs. From there, we put forward principles to be applied by all research teams and included in the following charter:

Principle 1: the career evolution of all non-PI PRs, including those who wish to remain within their team, should be promoted by supporting their access to research supervision and recognition.

Principle 2: the emergence of new independent teams led by senior postdocs or non-PI PRs outside the unit should be encouraged.

Principle 3: The rule established by the CdR is of a maximum of 6 people + PI for junior teams, 12 people + PI for senior teams. Teams can only evolve within this constrained framework, which does not support the emergence of sub-teams within teams.

In line with these principles, the unit proposes the following guidelines:

- 1- **Non-PI PRs who wish to stay within their teams** are encouraged to discuss with their PIs the possibility to apply for grants on their name. These include ARC, Ligue and ANR grants but exclude those considered to promote the emergence of a new independent team (for ex. ANR-JCJC, see point 2). Prior agreement should be discussed with the PI on the perimeter of the project, the proposed collaborations and the funding request. Funding requests should include running money and tech/engineer salary, but should exclude the recruitment of postdocs, since long term evolution of postdocs within the team remains the decision of the PI. However, postdocs already recruited by the team could be included in the project after discussion with the PI. Non-PI PRs are encouraged to obtain their HDR and a PhD student funded by the local ED under the supervision of the non-PI PR can be involved in the project. The project holder will benefit from independence in the scientific and financial management of the project. This independence should be highlighted by co-last positions in publications resulting from the project.
- 2- **Non-PI PRs and senior postdocs who wish to set up their own team** are encouraged to apply to all appropriate funding grants without restriction. If needed, the PI's team could serve as an incubator to foster the emergence of the future PI. This must be preceded by a signed agreement between the project holder, the PI and the unit direction concerning:
 - autonomy of recruitment, scientific and financial management by the project holder.
 - space within the team devoted to the project
 - last or co-last signature on publications deriving from the project.
 - departure of the project holder with the project, funding, equipment and possibly personnel during the funding period.

We think that this charter fulfills the two requests made by the two most recent HCRERES reports, in accordance with the local constraints of our unit, i.e.:

- (i)- support the careers of permanent CRs working within a team.
- (ii)- support the emergence of new independent PIs budding off from existing teams.

This charter has recently been approved and voted by the Unit Council, including the representatives of the non-PI permanent researchers, and will be included into the unit internal regulation after approval by the tutelles.

- p.9 “The number of engineers and technicians in some services is currently too close to the minimal requirements, which could result in the services underperforming during holiday periods or in cases of disease or retirement. In the current evaluated period, this has negatively affected the imaging platform due to its senior manager moving away. It is important that an adequate level of expert technicians and engineers is maintained through time to support these services.”

We thank the committee for pointing this. Indeed, the post-pandemic years have been marked by a drastic increase in professional mobility of the permanent staff, which put our unit in challenging situations on several fronts. We have benefited from a strong support both from CNRS and Institut Curie HRs, which allowed to compensate for some losses, in particular for the imaging platform (open mobility for an imaging engineer to replace the departure of O. Renaud). Despite this help, we are still missing 4 permanent staff positions after their departure from our unit. The replacement of these position is one of the priorities for the future of our unit.

Specific comments on team reports

Team 6: A. BARDIN

- “Some (2) former PhD students have not yet obtained a first author publication.”

2 papers of students were accepted just after the HCERES visit:

Al Zouabi et al, Cell Reports, 2023

Josserand et al, Dev Cell, 2023.

- “Although the PI is well recognized, the international collaborative network of the team is not particularly strong.”

The PI is part of 2 ongoing applications for international networks: 1 ITN and 1 Germany-based large collaborative network.

Team 9: P. HERNANDEZ

This junior team joined the unit in Sept. 2019, and is still under ATIP/Avenir contract.

The report on Team 9 mentions the absence of publication by the PI in corresponding author position during the period. Although formally true, one publication was under revision during the period, which has now been accepted and published (Nat. Commun. 2023).

The report mentions “good financial support” for the Team. Indeed, the team leader has gathered what we consider as an exceptional funding for the period, including ATIP/Avenir, Ville de Paris Emergence, FRM Amorçage and an ERC Starting.

In the Weaknesses and Risks paragraph, several items are mentioned, which are puzzling to us:

- ***“At this stage, preliminary team results should have been presented...”*** We do not understand this point, since the PI made a clear presentation of all his present results and projects both in the written document and during the oral presentation, including the discovery of the role of IL-22 in enteric nervous system development, the establishment of a new model to study gut regeneration and the role of cytokines after severe damage, the role of ontogenetically distinct myeloid populations in tissue homeostasis, and the implementation of new optogenetic tools for lineage tracing.

- ***“The supervision of three PhDs and three postdocs by a single junior group leader can raise problems of efficacy in resolving trouble shootings and training.”*** The team is currently composed of 3 PhD students and 2 postdocs, which is reasonable given its level of funding. The policy in our unit, and more generally at the IC, is to provide junior group leaders with important starting packages to allow developing their team in a fast and efficient manner. We consider that this is mandatory for junior PIs embarking on demanding and internationally competitive projects. Of note, junior PI are evaluated for tenure 6 to 9 years after establishing their group.

- ***“The team leader has published good quality papers from his previous laboratories but since joining the Institut Curie, the team leader has not yet published an article as last or corresponding author.”*** This is a rather toned-down description of the trajectory of this group leader, who previously published his work as first and co-corresponding author in Nature, Nature Immunol. and Science Immunol., all top journals, and whose project was awarded an outstanding recognition by an ERC starting grant award, as well as full approval by the institute Curie international iSAB, and our unit SAB. Concerning publications of the group, one publication was under revision during the period, which has now been accepted and published (Nat. Commun. 2023).

Concerning the recommendations for the team, indeed, ***“moving to Institut Curie represents a serious challenge for any young team leader”***. However, it should be noted that P. Hernandez successfully passed an international selection for our JPI call in 2019 in front of an international committee. He now benefits from a very supportive environment at the institute Curie and from an exceptional level of funding to develop his ambitious projects successfully.

Once again, we thank you for the very positive evaluation of our evaluation and hope our comments could help you reach a better understanding of some aspects.

Yours sincerely,

Pr Alain PUISIEUX
Directeur du Centre de Recherche de l'Institut Curie

Dr Pierre LEOPOLD
Directeur de l'Unité UMR3215-U934

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